3rd Congress of Asian Society of Sleep Medicine

Conference Proceeding

Organized by The Asian Society of Sleep Medicine(ASSM)

Hosted by Chinese Sleep Research Society(CSRS)

Beijing,China   May, 14-17, 2021

Dear Distinguished Guests, Colleagues, and Friends,

Welcome to the ASSM 2021 Congress, the 3rd Sleep Congress of the Asian Society of Sleep Medicine. It's a special period in public health field. Considering the ongoing COVID-19 pandemic, this year's program is an offline meeting combined with online meeting.

The Asian society of sleep medicine succeeded in conducting a yearly scientific congress that brings all the brilliant minds to one place. This year in Beijing, we offer a forum for open discussion to sleep professionals all around Asia, where sleep physicians, researchers, psychologists, dentists, technologists, educators, and trainees from over 16 participating Asian society members will meet to promote knowledge about sleep including the aspects below, medicine, public health, physiology , and the diagnosis and treatment of disorders. The congress also provides an encouraging environment for communication and collaboration in both clinical and basic research in Asia.

Your involvement in this congress is highly valued. You may learn and share knowledge and skills that will advance sleep medicine and sleep research, which is the mainly mission of our organization. We are looking forward to your joining to ASSM 2021. Thank you!

Sincerely,
the ASSM organizing committee

Seung Bong Hong, M.D.	**Fang Han, M.D.**	**Zhili Huang, M.D.**
President	Chair	Co-Chair
Asian Society of	Organizing Committee	Organizing Committee
Sleep Medicine	ASSM 2021	ASSM 2021

ASSM2021 Organizing Committee

Fang HAN (Chair)

Zhili HUANG (Co-Chair)

Heming ZUO (Secretary General)

Xiangshan YUAN (Vice Secretary General)

Xuemei GAO (Treasurer)

Xilong ZHANG (Chair, Scientific Committee)

Jihui ZHANG (Co-Chair, Scientific Committee)

Ying XU (Vice Chair, Scientific Committee)

Jie SHI (Chair, Publication Committee)

Guanhua LIN (Vice Chair, Publication Committee)

Hanqiao WANG (Chair, Intl. Relations Committee)

Xiangdong TANG (Chair, Public Relations Committee)

Donghong FU (Vice Chair, Public Relations Committee)

Jing YANG (Administrative Assistant)

MEMBERS, Local Organizing Committee (Names are in alphabetical order)

Changjun SU	Fujun JIA	Guihai CHEN	Hongqiang SUN	Jian XU	Jingying YE
Jiyou TANG	Ke HU	Tingli LI	Weidong WANG	Xi ZHANG	Yanzhong LI
Yuanming LUO	Yunfei CHEN	Yunhui LV	Yuping WANG		

MEMBERS, Local Scientific Committee (Names are in alphabetical order)

Bin ZHANG	Chia-Mo LIN	Fengfei DING	Hsueh-Yu LI	Hua ZHAO	Jiyang PAN
Kah Lin CHOO	Liyue XU	Ning-Hung CHEN	Qingyun LI	Shankai YIN	Shuqin ZHAN
Tao WANG	Yun-Kwok WING	Yushu HUANG	Zhian HU		

Advisory Board (Names are in alphabetical order)

Chen WANG	Demin HAN	Jinxing ZHANG	Lin LU	Xizhen HUANG	Yanfang CHEN

International Board of Organizing and Scientific Committee (Names are in alphabetical order)

Ahmed Bahammam	Aroonwan Preutthipan	Babak Amra	Iris Haimov
JC Suri	Keith Aguilera	Ki-young Jung	Manjari Tripathi
Michael Chee	Mohammed Al Abri	Rimawati Tedjasukmana	Rusdi Abd Rashid
Seockhoon Chung	Seung Bong Hong	Seung Chyul Hong	Sy Duong-Quy
Tayard Desudchit	Virginia s. Delos Reyes	Yuichi Inoue	

Keynote speakers

- A1 -

Combined cognitive behavioral therapy and medication for the management of insomnia disorder

Charles Morin, Sleep Research Centre, Université Laval

Professor Morin is a world leader on insomnia research. He has been at the forefront of new developments on behavioral approaches to treating insomnia and on studying the natural history of insomnia with its risk factors and long-term consequences. He has conducted pivotal clinical trials comparing behavioral and pharmacological therapies for insomnia, which have had significant impact on how insomnia is dealt with in clinical practice.

- A2 -

Sleep apnea in Asia, the pathogenesis, outcomes and treatment

Ning-Hung Chen, Department of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital

Dr. Chen is the Professor of Chang Gung University. He was the Chief of the Department of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital from 2012-2018. He was also the founder and the director of Sleep Center in Chang Gung Memorial Hospital since 1997. He was elected as the President of Asian Society of Sleep Medicine in 2014, also serve as the Secretary General of World Sleep Federation, Past Vice President of Asian Sleep Research Society and past President of Taiwan Society of Sleep Medicine in 2006. He was also the founder and the 1st President of Asian Society of Sleep Medicine. He is now the Head-elect and will be the head of the Assembly of Neurobiology and Sleep of Asia Pacific Society of Respirology (APSR).

Dr. Chen was trained sleep medicine at Stanford Sleep Disorders Clinic at 2000 and the Division of sleep medicine, Center for Sleep and Respiratory Neurobiology-CSRN, and The Children's Hospital of Philadelphia, USA during 2009. His major research is sleep medicine especially obstructive sleep apnea syndromes and the epidemiology of restless legs syndrome.

- A3 -

Neuroimaging studies in OSA, insomnia and narcolepsy

Seung Bong Hong, Department of Neurology, Sungkyunkwan University School of Medicine

Prof. Hong has served at a director of Epilepsy and Sleep center since 1995 at Samsung Medical Center, Sungkyunkwan University and established one of the best and largest Epilepsy and Sleep center in Korea. He is a direct of Epilepsy and Sleep Center since 1995 and trained many epileptologists and sleep specialists in Korea.

Currently Prof. Hong is a president of Korean Neurological Association and a president of Asian Society of Sleep Medicine. He is a director of National Epilepsy Care Center in Korea too.

Natural progression of childhood obstructive sleep apnea (OSA): Does baseline disease status predict adulthood cardiovascular outcomes?

Albert Li, Department of Pediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong

Prof. Li graduated from the University of Wales College of Medicine and received his pediatric training at King's College Hospital and Great Ormond Street Hospital, United Kingdom. He joined the Chinese University of Hong Kong as a lecturer in August 2001. His training took him back to the UK where he worked as a clinical research fellow at the Royal Bromton Hospital, London in 2002, under the guidance of Prof. Andy Bush. His clinical and research interest is in respiratory and sleep medicine.

Albert is the person-in-charge of the Respiratory and Sleep Medicine Service in the Department of Pediatrics, Prince of Wales Hospital.

Surgery of Sleep Disordered Breathing

Demin Han, Chinese Academician of the Academy of Engineering,

Academic appointment and management position

2014.5–present, Dean of Beijing Medical Center Capital Medical University

2012.10–present, Chairman of Unicare Health Group

2011.2–present, Director of Chinese Ministry of Education Otolaryngology Head and Neck Surgery key laboratory

2003.10–present, Dean of Capital Medical University Otolaryngology college

2002.6–present, Director of Beijing Otolaryngology Head and Neck Surgery Research center

2000.11–2012.3, Chairman of Beijing TongRen Hospital Capital Medical University

1995.8–present, Doctoral supervisor, Capital Medical University

1994.12–present, Professor, Capital Medical University

1994.8–2012.3, Director of Beijing Otolaryngology institute

1992.3–present, Graduate student mentor, Capital Medical University

1991.12–present, Chief Physician, Beijing TongRen Hospital Capital Medical University

1976.12–1991.3, Resident, Attending physician, Otolaryngology Department The first affiliated hospital China Medical University

Membership：

Chinese Academician of the Academy of Engineering

The President of China International Exchange and Promotive Association for Medical and Health Care

The Chairman of the Chinese Medical Doctor Association Otolaryngology

Chairman of the World Chinese Association of Otolaryngology Head and Neck Surgery

Director of the World Health Organization (WHO) Collaborating Centre for the Deaf

Editor–in–Chief of the Chinese Journal of Otorhinolaryngology Head and Neck Surgery

Editor–in–Chief of the Chinese Archives of Otolaryngology Head and Neck Surgery.

The Editorial Boards of the Journal of ORL and its Related Specialties.

The Journal of Acta Oto–Laryngologica.

Honors and Awards：

2013, Awarded the title of "Beijing Scholar"

2012, Humanitarian Award from the UN South–South Awards Committee

2009, Awarded 2nd class prize of National Science and Technology Progress in research and diagnosis for OSAHS

2007, Awarded "Scientific and Technological Progress Prize" by the Ho Leung Ho Lee Foundation

2006, Awarded 2nd class prize of National Science and Technology Progress in clinical application and research in Cochlear Implants

2001, Awarded 2nd class prize of National Science and Technology Progress in research and diagnosis of Rhinosinusitis & Nasal Polyposis

Circadian medicine: does timing matter in development and treatment of disease?

Phyllis C. Zee, Division of Sleep Medicine, Northwestern University's Feinberg School of Medicine

Phyllis C. Zee, MD, PhD is the Benjamin and Virginia T. Boshes Professor in Neurology and Professor of Neurobiology at Northwestern University. She is also the Director of the Center for Circadian and Sleep Medicine (CCSM) and Chief of the Division of Sleep Medicine at Northwestern University's Feinberg School of Medicine. As Director of CCSM, Dr. Zee oversees an interdisciplinary program in basic and translational sleep and circadian rhythm research, and findings from her team have paved the way for innovative approaches to improve sleep and circadian health. Dr. Zee is the founder of the first circadian medicine clinic in the US, where innovative treatments are available for patients with circadian rhythm disorders.

A central theme of her research program is understanding the role of circadian-sleep interactions on the expression and development of cardiometabolic and neurologic disorders. Dr. Zee's research has focused on the effects of age and neurodegeneration on sleep and circadian rhythms and pathophysiology of circadian sleep-wake disorders. In addition, her laboratory is studying the effects of circadian-sleep based interventions, such as exercise, bright light and feed-fast schedules on cognitive, cardiovascular and metabolic functions and their potential to delay cardiometabolic aging and neurodegeneration. Recently her research team has also been interested in the use of acoustic and electrical neurostimulation to enhance slow wave sleep and memory in older adults.

Long term follow up of MSLT variables in type 2 narcolepsy in Korea

Seung Chul Hong, Department of Neuropsychiatry, Catholic University of Korea

Diagnosis of Narcolepsy is divided into type 1 narcolepsy and type 2 narcolepsy by the presence of cataplexy. There are distinct differences in the aspect of clinical symptoms, genetic profile, autoimmune pathophysiology between them.

1) HLA and Hypocretin study: The Genetic study showed that the diagnostic category of type 1 narcolepsy (N=79) was easy to use and highly predictive of biologic and polysomnographic findings. Indeed, 92% of these cases were DQB1*0602 positive with low CSF hypocretin-1 levels. However, 40% of type 2 narcolepsy (n=22) was HLA positive and had low CSF hypocretin-1 levels.

2) Newly developed cases with narcolepsy after 2009 H1N1 vaccine are all type 1 narcolepsy: Several new cases with narcolepsy after 2009 H1N1 vaccine were reported in Korea. Their symptoms included severe EDS and cataplexy.

3) Diagnostic issue of type 2 narcolepsy: The longitudinal follow up of 8 year's MSLT study of narcolepsy type 1(39/41) had a good repeatability. More than 95.1% of them retained meeting MSLT criteria. However, type 2 narcolepsy (9/19) presented only 47.4% remained type 2 narcolepsy.

Type 2 narcolepsy is heterogeneous compare to Type 1 narcolepsy. Further study is needed to define the pathophysiology of type 2 narcolepsy.

Sleep Medicine in China

Lin Lu, Institute of Mental Health/Peking University Sixth Hospital, Peking University

Prof. Lin Lu is a member of the Chinese Academy of Sciences. He currently works as the director of Peking University Institute of Mental Health/Peking University Sixth Hospital, National Clinical Research Center for Mental Disorders, and National Center for Mental Health of Chinese Center for Disease Control and Prevention. His research focuses on the neurobiological mechanisms and clinical intervention measures of psychiatric disorders (e.g., sleep disorders, substance addiction and depression). He has published more than 200 peer-reviewed articles (with total citation over 10000) in leading journals in the fields of psychiatry and sleep, including Science, JAMA Psychiatry, Biological Psychiatry, and Sleep Medicine Reviews.

Physiological hybrid surgery, multi–disciplinary combined surgery and holistic care for obstructive sleep apnea

Hsueh-yu Li, Department of Otolaryngology, Chang Gung Memorial Hospital

Academic appointment:

1.Professor, Otolaryngology and Sleep Center, Chang Gung Memorial Hospital

2.Professor, School of Medicine, Chang Gung University

3.Chairperson, International Affairs, Chang Gung Memorial Hospital

4.President of Taiwan Voice Society (2017-2020)

5.President of Taiwan Society of Sleep Medicine (2018-2020)

Prof Li is world authority in the field of sleep medicine and sleep surgery. He has travelled worldwide to lecture and teach. In addition, he has developed new and novel surgical techniques, and published more than 100 SCI papers and book chapters. Recently, he is interested in sleep technology and working on novel device to improve snoring and sleep apnea. Prof Li is sitting on numerous leader positions of international academy of sleep breathing.

The Basal Ganglia Control Sleep–Wake Cycles and Modulate Sleep Disorders of Parkinson's Disease

Zhi-Li Huang

Department of Pharmacology, School of Basic Medical Sciences; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science, and Institutes of Brain Science, Fudan University, Shanghai, China

Email: huangzl@fudan.edu.cn

Abstract: The basal ganglia (BG) act as a cohesive functional unit that regulates motor function, habit formation, and reward/addictive behaviors. However, it remains unrevealed how the BG initialize and maintain wakefulness, regulate all above behaviors until the recent development of genetically modulation techniques. We focused on studying the functional roles of the adenosine A2A and dopamine D1 Receptors (R) in the BG and obtained following 4 major findings: (1) Nucleus accumbens (NAc) dopamine D1R-expressing neurons are essential in controlling wakefulness and are involved in physiological arousal via the lateral hypothalamus and midbrain circuits; (2) Opposite to the D1R in the NAc, A2AR made a prominent contribution to sleep control associated with motivation; (3) The ventral pallidal GABAergic neurons, which densely receive projections from D1R neurons in the NAc, control wakefulness associated with motivation through the ventral tegmental pathway; (4) Striatal adenosine A2AR neurons control active-period sleep via parvalbumin (PV) neurons in external globus pallidus. Taken together, we proposed a plausible model demonstrating that the caudate-putamen and NAc integrate behaviors with sleep/wakefulness via adenosine and dopamine receptors. In addition, we discussed the impacts of the BG in insomnia and Parkinson's disease, and reported that propagated alpha-synucleinopathy recapitulates mouse model of rapid eye movement sleep behavior disorder (RBD) with onset after the Parkinsonian phenotypes.

Key words: adeno-associated virus, basal ganglia, DREADD, optogenetics

Toward the molecular basis of "sleepiness"

Masashi Yanagisawa, International Institute for Integrative Sleep Medicine, University of Tsukuba

Although sleep is a ubiquitous behavior in animal species with well-developed central nervous systems, many aspects in the neurobiology of sleep remain mysterious. Our discovery of orexin, a hypothalamic neuropeptide involved in the maintenance of wakefulness, has triggered an intensive research examining the exact role of the orexinergic and other neural pathways in the regulation of sleep/wakefulness. The orexin receptor antagonist suvorexant, which specifically block the endogenous waking system, has been approved as a new drug to treat insomnia. Also, since the sleep disorder narcolepsy- cataplexy is caused by orexin deficiency, orexin receptor agonists are expected to provide mechanistic therapy for narcolepsy; they will likely be also useful for treating excessive sleepiness due to other etiologies.

Despite the fact that the executive neurocircuitry and neurochemistry for sleep/wake switching has been increasingly revealed in recent years, the mechanism for homeostatic regulation of sleep, as well as the neural substrate for "sleepiness" (sleep need), remains unknown. To crack open this black box, we have initiated a large-scale forward genetic screen of sleep/wake phenotype in mice based on true somnographic (EEG/EMG) measurements. We have so far screened >8,000 heterozygous ENU-mutagenized founders and established a number of pedigrees exhibiting heritable and specific sleep/wake abnormalities. By combining linkage analysis and the next-generation whole exome sequencing, we have molecularly identified and verified the causal mutation in several of these pedigrees. Biochemical and neurophysiological analyses of these mutations are underway. Since these dominant mutations cause strong phenotypic traits, we expect that the mutated genes will provide new insights into the elusive pathway regulating sleep/wakefulness. Indeed, through a systematic cross-comparison of the Sleepy mutants and sleep-deprived mice, we have recently found that the cumulative phosphorylation state of a specific set of mostly synaptic proteins may be the molecular substrate of sleep need.

Symposia

Symposium 1: Precision medicine in OSA

Summary

Current diagnosis and treatment strategy of OSA does not consider the heterogeneity of individuals with OSA, reflected by varying risk factors, clinical manifestations, consequences, especially the pathophysiological mechanism. Recently, cluster analysis studies described the potential role of phenotypic subtypes in precision medicine for OSA, and studies have linked the phenotype to clinically relevant outcomes. As for the management strategy, the lack of effective drugs has been a clinical challenge. Exploring the pathogenesis is the basis for the development of drug. The existing pathophysiological PALM model theory explains the idea that anatomic and non-anatomic factors participate in the pathogenesis of OSA. The four elements include abnormal critical closure pressure (P), low arousal threshold (A), and loop gain(L), which represents the instability of respiratory control, and dilator muscle dysfunction (M). All the elements may be the potential drug targets. About 70% of the patients have anatomic and non-anatomic abnormalities. Besides the CPAP, the above aspects may present an alternative treatment selection, including medicine. Identifying the weight of each element of PALM model individually will help to choose the ideal precise treatment for patients with OSA.

Learning Objectives

OSA is a heterogeneity disease,

Symptom subtypes of OSA will help to identify the different consequences, comorbidities, and especially for the treatment approach decision.

The treatment strategies based on the pathophysiological mechanism model (PALM)

Target Audience

Pulmonologists, General physicians, Sleep physicians, technicians, pharmacologist, college students, master and PHD candidates, etc

Chairs

Qingyun Li, Yuanming Luo (Co-chair)

Medication therapy of OSA based on PALM model: research and perspective

Qingyun Li (China)

Diagnosis and treatment of OSA guided by neural respiratory drive

Yuanming Luo (China)

Symptom subtypes of OSA and its clinical significance

Brendan T. Keenan (USA)

The role of the respiratory arousal threshold in OSA pathogenesis

Rui Chen (China)

OSA and upper airway dilator muscles

Wei Wang (China)

Medication therapy of OSA based on PALM model: research and perspective

Qing Yun Li, Department of Respiratory and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine

The lack of effective drugs has been a clinical challenge for OSA treatment. Exploring the pathogenesis is the basis for the development of drug. The existing pathophysiological PALM model theory explains the idea that anatomic and non-anatomic factors participate in the pathogenesis of OSA. The four elements include abnormal critical closure pressure (P), low arousal threshold (A), and loop gain(L), which represents the instability of respiratory control, and dilator muscle dysfunction (M). All the elements might be potential drug targets. Identifying the weight of each element of PALM model individually will help to choose the ideal precise treatment for patients with OSA.

Diagnosis and treatment of OSA guided by neural respiratory drive

Yuan-Ming Luo, Guangzhou Medical University

Neural respiratory drive which contributes to development of OSA could be assessed by measurement of diaphragm EMG and esophageal pressure. Neural respiratory drive during obstructive sleep apnea event usually decreases but it is absent during central sleep apnea. Neural drive changes little when CPAP is lower than 1O cmH2O. However, neural respiratory drive increases significantly when CPAP is higher than 12 cmH2O. Accurate titration of CPAP may not always be necessary in clinical practice.

Symptom subtypes of OSA and its clinical significance

Brendan T. Keenan, Division of Sleep Medicine, Department of Medicine, University of Pennsylvania Perelman School of Medicine

Obstructive sleep apnea is a heterogeneous disorder. Research has identified generalizable subtypes based on self-reported symptoms in patients with moderate-severe disease from clinical and population-based samples throughout the world. These subtypes are most commonly distinguished by symptoms of disturbed sleep, excessive sleepiness, or a lack of traditional symptoms (e.g., minimally symptomatic). Importantly, data show a difference in treatment responses and cardiovascular risk based on symptom subtype. Patients in the excessively sleepy subtype have increased risk for cardiovascular events compared to other subtypes and patients without OSA, and the exclusion of sleepy patients from recent trials may contribute to the lack of perceived benefit of OSA therapy for cardiovascular risk. Understanding the biological causes and other consequences of these subtypes is an area of opportunity. Ultimately, recognizing and accounting for symptom subtype in clinical care is an important step towards more personalized OSA medicine.

The role of the respiratory arousal threshold in OSA pathogenesis

Rui Chen, The Second Affiliated Hospital of Soochow University

It was thought that arousals were essential to restore airflow at the end of a respiratory event in

OSA, and most respiratory events are associated with brief cortical arousals. Recent studies indicate that a low respiratory arousal threshold phenotype may be an important non-anatomical factor to OSA pathogenesis, as low arousal threshold may lead to respiratory center instability. Non-benzodiazepines drugs have been reported to increase arousal thresholds in OSA patients with low arousal threshold. The clinical significance of low arousal threshold in the pathogenesis of OSA will be briefly described in this presentation.

OSA and upper airway dilator muscles

Wei Wang, The First Hospital of China Medical University

Upper airway dilator muscles play an important role in keeping upper airway patency. The dysfunction of these muscles contributes to the occurrence of OSA. However, the mechanism is still unknown. We have explored the central control of genioglossus during chronic intermittent hypoxia in rats and during wakefulness in OSA patients. The results showed that neuromuscular decompensation is responsible for OSA.

Symposium 2: Circadian Rhythms and Circadian Medicine

Summary

Circadian clocks are organisms' natural timing devices that regulates cycles of alertness, sleepiness, cardiovascular system, metabolism, endocrine system, immune etc. by responding to light changes in our environment. Disruption of circadian rhythms is broadly pathogenic, causing including from irregular sleep-wake patterns, poor sleep quality to cancer, myocardial infarctions. Nutritional interventions such as time-restricted feeding regulate expression of oscillating genes improve metabolic health. In this context, chrono-pharmacological methods for directly drugging circadian rhythms or chronotherapeutic strategies might be useful to ameliorate dysfunctions in the circadian dependent symptoms. Recently, Circadian clock is as one of hallmark of health, reflecting its key role for the maintenance of physiological homeostasis. In the present symposium, five speakers will talk their brand new findings related with the genetics of sleep, circadian medicine and chemical perturbation in circadian phase including unpublished results. Integration of these reports will reveal the dynamics of a circuit connecting the circadian clock and sleep/wakefulness in environmental impacts, and circadian medicine.

Learning Objectives

1. Circadian clock
2. Sleep genetics
3. Circadian medicine
4. Chronotherapeutic strategies

Target Audience

Basic science, clinic doctors, biological and medical students

Chairs

Ying Xu, Qinghua Liu (Co-chair)

Somatic genetics analysis of sleep in adult mice
Qinghua Liu (China)
The role of Imp in regulation of drosophila sleep
Yong Zhang (China)
The genetic basis of natural short sleep
Guangsen Shi (USA)
Circadian medicine: a new frontier of precision medicine
Gang Wu (USA)
Chemical perturbations reveal that RUVBL2 regulates the circadian phase in mammals
Dapeng Ju (China)

Somatic Genetics Analysis of Sleep in Adult Mice

Qinghua Liu, National Institute of Biological Sciences, Beijing

The molecular mechanisms of mammalian sleep regulation remain largely unknown. Classical forward and reverse mouse genetic approaches require germline mutations and, thus, are unwieldy to study the sleep functions of essential genes or redundant pathways. It is also costly and time-consuming to conduct large-scale electroencephalogram (EEG)/electromyogram (EMG)-based mouse sleep screening owning to lengthy genetic crosses and labor-intensive surgeries. Here, we develop a highly efficient adult brain chimeric (ABC) expression/knockout (KO) platform and a highly accurate AI-augmented SleepV (video) system for high-throughput somatic genetics analysis of sleep in adult mice. This ABC platform involves intravenous administration of adeno-associated viruses (AAV) that bypass the blood brain barrier and transduce the majority of adult brain neurons. Constitutive or inducible ABC-expression of CREB and CRTC1 reduces both quantity and quality of non-rapid-eye-movement sleep (NREMS), whereas ABC-KO of CREB by AAV-mediated Cre/loxP recombination increases daily NREMS amount. Moreover, ABC-KO of exon 13 of Sik3 by AAV-Cre injection of Sik3-E13flox/flox adult mice phenocopies Sleepy (Sik3Slp/Slp) mice, which carry a germline splicing mutation resulting in skipping of exon 13 of Sik3. While both long and short isoforms of SLP kinase contribute to, ABC-KO of Slp allele by CRISPR/Cas9 rescues the hypersomnia of Sik3Slp/+ mice. Double ABC-KO of orexin/hypocretin receptors by CRISPR/Cas9 results in chocolate-induced narcolepsy episodes. We envision that these somatic genetics approaches should facilitate efficient and sophisticated studies of many brain-related cellular, physiological and behavioral processes in adult mice without genetic crosses.

The role of Imp in regulation of Drosophila sleep

Yong Zhang, Soochow University, Cam-Su Genomic Resource Center

Sleep is an essential behavior found across animal species. However, the underlying mechanisms of sleep regulation remain largely unknown. The fruit fly, Drosophila melanogaster, has proven to be a valuable model for studying the regulation of sleep. RNA binding proteins are crucial post-transcriptional regulators, which control all aspects of RNA metabolism. Here we identified that an RNA binding protein-Imp (IGF-II mRNA-binding protein) regulates sleep in Drosophila melanogaster. Imp mutants induce daytime sleep while decrease nighttime sleep, exhibiting shorter day time sleep latency and longer night time sleep latency. IMP is expressed in a large population of neurons in the fly brain, including mushroom bodies and circadian neurons. We further tested in which neurons IMP is required to regulate sleep by using multiple GAL4 drivers expressed in known sleep circuitry. Downregulation of Imp in circadian neurons recapitulated the sleep phenotype observed in Imp mutants. Remarkably, re-expression of Imp in circadian neurons rescued Imp mutants sleep defects. Mechanical sleep deprivation in the Imp downregulation flies showed normal sleep rebound, which indicates that Imp is not involved in sleep homeostasis. Taken together our results demonstrate that Imp is required in circadian neurons for Drosophila sleep regulation.

The Genetic Basis of Natural Short Sleep

Guangsen Shi, University of California, San Francisco

Sleep is an important part of our lives. According to our daily experience and epidemiological survey results, the average time of adult's daily sleep is generally about 8 hours. But there is such a special group of people in the population, whose lifetime sleep time is only 4-6 hours a day, living a normal and energetic life. This type of person is defined as a natural short sleeper. At present, it has been confirmed that a considerable number of natural short sleep phenomenon can be caused by single gene mutation, which presents familial genetic phenomenon. These families are called short sleep families, and the corresponding genes are also defined as short sleep genes. Mutations in the short sleep gene result in shortened sleep time and / or increased sleep efficiency. The discovery of short sleep genes has a positive significance for us to understand our own sleep and the diversity of human genome. In this report, the reporter will introduce the history of the discovery of short sleep gene, the workflow of screening short sleep gene in the population, the discovery of new members of short sleep gene and some application prospects in the future.

Circadian medicine: a new frontier of precision medicine

Gang Wu, Cincinnati Children's Hospital

The circadian clock regulates ~50% of protein coding genes in the genome, and controls multiple biological processes related to human health, including angiogenesis, immunity, apoptosis, DNA repair and cell proliferation. Circadian disruption is associated with multiple human diseases, including sleep disorders, cancers, metabolic syndromes, and neurodegenerative diseases. In addition, thousands of circadian regulated genes are drug targets. Therefore, circadian medicine, which aims to incorporate knowledge of ~24-hour biological rhythms to enhance diagnosis and treatment of human diseases, is in rapid development these years. Until now, more than 100 clinical trials of improving therapeutic index by leveraging time in disease treatments are finished, covering cancers, hypertension, asthma, allergy, arthritis and hyperlipidemia. Over 75% of tested drugs show time effect. For example, Simvastatin, used to treat hyperlipidemia, has better clinical outcomes when dosing before sleep. For patients with symptoms of gastroesophageal reflux disease, the better time of taking esomeprazole is after wake up. Currently, drugging the clock and clocking the drugs are two major directions of circadian medicine. Drugging the clock aims to develop drugs directly targeting the core clock genes for adjusting the phase or enhancing the robustness of the circadian clock. Clocking the drugs aims to identify and test drugs targeting the down-regulated genes of circadian clock for maximizing the efficacy and minimizing the toxicity. Although circadian medicine shows the great opportunity of improving clinical outcomes, it meets major challenges: 1) lack a method that can accurately indicate the internal body time; 2) lack mechanism-driven design in the clinical trials of circadian medicine; 3) the pharma companies have not recognized the importance of the time effect in developing new drugs. With recent progress of answering these challenges, circadian medicine becomes a new frontier of precision medicine. In the future,

precision medicine will support the rapid development of circadian medicine, and circadian medicine will make the medicine more precise.

Chemical perturbations reveal that RUVBL2 regulates the circadian phase in mammals

Dapeng Ju, Department of Anesthesiology, The Second Affiliated Hospital, Chongqing Medical University

Circadian rhythms are manifest in most physiological processes in mammals. These rhythms are driven by endogenous circadian clocks, which is based on a transcriptional-translational feedback loop. There are three parameters to describe circadian rhythms: period, amplitude, and phase. Most of the previous investigations of circadian oscillation have focused on the clock period, because it has been a fundamental question in the field to understand how circadian rhythms are gated at around 24 hours. Substantially fewer studies have examined the phase and amplitude of the clock, which are very sensitive to environmental perturbations. However, the circadian phase turns out to be the most related to human health in modern society, as for example in circadian rhythm sleep disorders that result from jet leg and shift work, sleep phase advance disorder in aged people, and metabolic diseases resulting from circadian phase dysregulation. A better understanding of circadian phase regulation should therefore provide recommendations for future chronotherapies. Starting from a chemical screen, here we found that RuvB-like ATPase 2 (RUVBL2) interacts with other known clock proteins on chromatin to regulate the circadian phase both in human cells and in mice. Pharmacological perturbation of RUVBL2 with the adenosine analog compound cordycepin resulted in a rapid-onset 12-hour clock phase-shift phenotype at human cell, mouse tissue, and whole-animal live imaging levels. Using simple peripheral injection treatment, we found that cordycepin penetrated the blood-brain barrier and caused rapid entrainment of the circadian phase, facilitating reduced duration of recovery in a mouse jet-lag model. We solved a crystal structure for human RUVBL2 in complex with a physiological metabolite of cordycepin, and biochemical assays showed that cordycepin treatment caused disassembly of an interaction between RUVBL2 and the core clock component BMAL1. Moreover, we showed with spike-in ChIP-seq analysis and binding assays that cordycepin treatment caused disassembly of the circadian super-complex, which normally resides at E-box chromatin loci such as PER1, PER2, DBP, and NR1D1. Mathematical modeling supported that the observed type 0 phase shifts resulted from derepression of E-box clock gene transcription.

Symposium 3: Traditional and complementary medicine for insomnia

Summary

The symposium entitled traditional and complementary medicine for insomnia aims to share the knowledge on traditional and complementary medicine such as Chinese herbal medicine and acupuncture for insomnia with the community of sleep medicine. The 90-min symposium will comprise a mixture of inspirational talks from multi-disciplinary speakers such as clinical trial investigators, evidence-based medicine pioneers, sleep medicine practitioners, herbalist, and acupuncturist, and interactive discussions. Attendees will learn more about the latest clinical trials on traditional and complementary medicine for menopausal insomnia, anxiety associated insomnia and chronic insomnia, as well as gain an overview of their historical views and contemporary evidence on insomnia disorders.

Learning Objectives

1. Gain an overview of historical views and contemporary evidence on traditional and complementary medicine for insomnia
2. Update the knowledge on clinical trials and meta-analysis of herbal medicine and acupuncture for insomnia
3. Learn about specific role of traditional medicine for an integrative approach for insomnia and its sub-types

Target Audience

Sleep medicine practitioners or researchers who are interested in traditional and complementary medicine for insomnia

Chairs

Jian Xu, Yunfei Chen (Co-chair)

The potential benefits of Chinese herbal medicine to anxiety associated insomnia: a multi-center, randomized, double-blind, placebo-controlled trial

Jian Xu (China)

Acupuncture improves menopausal insomnia: a randomized controlled trial

Yunfei Chen (China)

Comparative effectiveness of multiple acupuncture therapies on insomnia: a network meta-analysis

Long Ge (China)

Clinical evidence on traditional and complementary medicine for insomnia and priorities settings for future clinical trials

Xiaojia Ni (China)

The add-on effect of Chinese herbal medicine on insomnia treated with CBT-i: a controlled clinical trial

Liyu Lin (China)

The potential benefits of Chinese herbal medicine to anxiety associated insomnia: a multi-center, randomized, double-blind, placebo-controlled trial

Jian Xu, Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine

This trial aimed to evaluate the clinical efficacy and safety of Antianxiety Granule, a granular Chinese medicine compound, for treatment of GAD. Methods/design: The current work is a multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical trial with a 6-week treatment schedule. The study consists of three periods: a 1-7-day screening period, a 6-week primary treatment period, and a 1-week follow-up period. Follow-up assessments will be conducted 1 week after the last visit with a face-to-face interview or by telephone. The clinical efficacy of Antianxiety Granule for the treatment of GAD will be evaluated by examining the change in the Hamilton anxiety scale (HAMA) score, state-trait anxiety inventory (STAI) score, and TCM symptom scale in patients with GAD who receive daily TCM treatment. Moreover, an intention-to-treat (ITT) analysis will also be used in this randomized controlled trial (RCT). In our preliminary studies, Antianxiety Granule, which is composed of Cyperi rhizoma, Amomum aurantiacum, Cinnamomi cortex, Curcumae radix, Radix salviae, Gardeniae fructus, licorice, Polygala tenuifolia, Albizia bark, Polygoni multiflori caulis and daylily, has been shown to effectively ameliorate symptoms of anxiety and insomnia in patients with GAD. The results of this trial will provide valuable clinical evidence for the treatment of GAD.

Acupuncture improves menopausal insomnia: a randomized controlled trial

Chen Yunfei, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine

Objectives: To evaluate the short-term efficacy of acupuncture for the treatment of peri-menopausal insomnia (PMI). Methods: Design: A randomized, participant-blind, placebo-controlled trial consisted of the acupuncture group (n = 38) and placebo-acupuncture group (n = 38). Setting: A tertiary teaching and general hospital. Participants: 76 peri-menopausal women with insomnia disorder based on the International Classification of Sleep Disorders, Third Edition. Interventions: A 10-session of acupuncture at bilateral Shenshu (BL 23) and Ganshu (BL 18) with unilateral Qimen (LR 14) and Jingmen (GB 25) or Streitberger needles at the same acupoints was performed for over 3 weeks. Measurements: Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) with over-night polysomnography (PSG) exam were completed at baseline and post-treatment. Results: After the treatments, the decrease from baseline in PSQI score was 8.03 points in acupuncture group and 1.29 points in placebo-acupuncture group. The change from baseline in ISI score was 11.35 points in acupuncture group and 2.87 points in placebo-acupuncture group. In PSG data, acupuncture significantly improved the sleep efficiency and total sleep time, associated with less wake after sleep onset and lower percent stage 1 after the treatment. No significant differences from baseline to post-treatment were found in placebo-acupuncture group. Conclusions: Acupuncture can contribute to a clinically relevant improvement in the short-term treatment of PMI, both subjectively and objectively.

Comparative effectiveness of multiple acupuncture therapies on insomnia: a network meta-analysis

Long Ge, Evidence-Based Social Science Research Center, School of Public Health, Lanzhou University

Background: Acupuncture has been widely practiced for primary insomnia. However, the relative benefit and harm among acupuncture therapies remain uncertain. Objectives: To compare and evaluate the effect differences of multiple acupuncture therapies on patients with primary insomnia using network meta-analysis method. Methods: We searched Embase, the Cochrane Library, PubMed, and Web of science from their inception to March 2021, with a rigorous eligibility criterion, to include randomized controlled trials evaluating acupuncture with or without additional treatments to an alternative treatment (e.g. placebo, sham acupuncture, no treatment, etc.) for primary insomnia. We also tracked the references of relevant reviews to identify any potential studies. We excluded trials that compared acupuncture against drugs treatments. Two reviewers independently conducted the literature screening, data extraction, and risk of bias assessment. We used the Grading of Recommendations Assessment, Development, and Evaluation system (GRADE) to assess the certainty of evidence and interpret the results. We used risk ratio (RR) and mean difference (MD) for binary and continuous outcomes, respectively. Bayesian network meta-analysis was conducted using gemtc package of R software. Results: We included 57 randomized trials involved 3870 patients, involving conventional acupuncture, electroacupuncture, fire needle, intradermal needle, hand penetration needle, plum blossom needle, acupoints catgut embedding, and a combination of different acupuncture therapies. The results of the network meta-analysis showed that except balanced needles and intradermal needles, all other acupuncture therapies were better than sham acupuncture in improving the PSQI score (44 trials, 2797 patients) and effective rate (33 trials, 2070 patients) for treating primary insomnia. We also found that there were no significant differences in the improvement of insomnia among different acupuncture therapies, and the combined therapies did not show the benefit than acupuncture alone. This study is still ongoing, more results on other outcomes, subgroup differences, and GRADE rating will be presented on the conference. Conclusions: An initial result showed that different acupuncture methods are effective in treating primary insomnia, and there were no significant differences among different acupuncture therapies. However, the lack of high-quality randomized controlled trials restricted the dissemination of acupuncture treatment.

Clinical evidence on traditional and complementary medicine for insomnia and priorities settings for future clinical trials

Xiaojia Ni, Guangdong Provincial Hospital of Chinese Medicine, Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou University of Chinese Medicine

This study is to evaluate the clinical evidence on traditional and complementary medicine for insomnia and assist with setting priorities for future clinical trials. We searched clinical practice guidelines, systematic reviews, randomized controlled trials (RCTs), cohort studies, case-controlled

studies, and other clinical studies on traditional and integrative Chinese medicine for insomnia disorders, and evaluated them with instruments for methodological quality. We find that though the number of clinical studies is large, the methodological quality of most studies is low, and few of them prospectively registered their protocols in the clinical trial registries. Overall, Chinese herbal medicine outperforms placebo and pharmacotherapies, for improving sleep quality, but none of high-quality randomized controlled trials on individual herbal formulae or herbal products have been published. Acupuncture reveals potential benefits to the people with insomnia; however, the effect size is small when compared with placebo/sham acupuncture. Systematic reviews are over produced while more clinical trials of quality are in the demand, particularly RCTs on Chinese herbal formulae or drugs with solid pharmacological actions and with a long history for clinical practice, as well as trials including placebo/sham acupuncture as the controls.

The add-on effect of Chinese herbal medicine on insomnia treated with CBT-i: a controlled clinical trial

Liyu Lin, Nanjing Municipal Hospital of Chinese Medicine, Nanjing University of Chinese Medicine

Extracted herbal paste is one of the oral dosage forms of Chinese medicine, with its main function of strengthening the body, reconciling deficiency and correcting the deviation. It is a convenient, efficient and easy-to-accept treatment for patients. The formula of Shuxin Anshen Paste is derived from the experience formula of Professor Zhimin YANG from Guangdong Provincial Hospital of Chinese Medicine, uses Sini Decoction and Guizhi Gancao Longgu Muli Decoction as the main ingredients, which aims to improve the fatigue at daytime and promote sleep at night and has a good long-term effect in treating chronic insomnia. This non-randomized concurrent controlled trial was designed to evaluate the clinical efficacy of Shuxin Anshen Paste in the treatment of chronic primary insomnia compared with Cognitive Behaviral Therapy for Insomnia (CBTI). 232 insomniacs were recruited in this study since 2016 and divided into 2 groups, with 116 cases in each group. 29 cases dropped the trial halfway, 13 of which was in the experimental group. The experimental group was treated with Shuxin Anshen Paste, and the control group was given group CBTI. The two groups were both treated for 2 months and followed up for 1 month. Sleep-related scales such as Pittsburgh Sleep Quality Index(PSQI), Patient Health Questionnaire 9(PHQ9), Severe Anxiety Disorder 7(GAD7), and Insomnia Traditional Chinese Medicine Quality of Life Scale (CMQLSI) and data based on polysomnography (PSG) such as sleep latency, sleep efficiency, sleep maintenance time, total sleep time, number of wakefulness, number of awakenings, blood oxygen concentration, heart rate, duration of sleep in each period were used to measure the subjective and objective sleep condition before and after treatment. Shuxin Anshen Paste obviously improved the subjective and objective sleep qualities of chronic insomnia and was particularly prominent in the improvement of daytime function. Besides, the anxiety or depression emotions and life quality index had significant improvements as well.

Symposium 4: Wearable devices and telemedicine in sleep

Summary

Wearable devices and telemedicine are developed rapidly during the last year, not only because of the technical progress, but also the worldwide pandemic of COVID-19. Commercial wearables were used lots by the consumers, however their clinical and research usage is the hot topic in the area of sleep medicine. How to evaluate a wearable device should be discussed. Most of sleep disorders are chronic diseases, which should be treated and followed up for a long time, eg. CPAP adherence for patients with OSA. Sleep telemedicine provided a new way for physicians to manage their patients and to promote better outcomes. The telemedicine was planted into sleep clinical practice in different area and the speakers will share their experience in this area.

Learning Objectives

1. To understand the definition of the wearable devices and their utility in sleep area.
2. To understand the evaluation steps of the wearables for clinical and research use.
3. To know the telemedicine advantage in the management of the patients with sleep disorders.

Target Audience

Sleep physician, Nurse practitioner, Sleep technician, Graduate students

Chairs

Xiaosong Dong, Naricha Chirakalwasan (Co-chair)

Wearable devices utility in OSA
Xiaosong Dong (China)
Efficacy of telemonitoring system in continuous positive airway pressure therapy in Asian OSA patients
Naricha Chirakalwasan (Thailand)
Telemedicine in OSA management: experience of the veterans health administration's TeleSleep program
Samuel T. Kuna (USA)
Personalized insomnia therapy: a proposition of implementation at scale
Pierrick Arnal (France)
Population data of snoring analysis based on smartphone app
Jianguo Sun (China)
Serving Deep Learning Models for Wearable Healthcare Devices
Shenda Hong（China）

Symposium 5: Surgical Intervention for Obstructive Sleep Apnea Based on Phenotype Classification

Summary

Surgical treatment is an important intervention for obstructive sleep apnea. However, a considerable proportion of patients can't benefit enough from surgery. OSA patients with different phenotypes showed very different response to the same treatment. So we believed that phenotype identification is critical for the success of surgery, and should be the standard procedure for OSA surgery.

Learning Objectives

1. To know the common phenotypes of OSA
2. To know the methods of phenotype identification
3. To know how to select the proper surgical intervention based on the phenotype

Target Audience

Sleep surgeons, Medical students, Sleep doctor

Chairs

Jingying Ye, Hsueh-Yu Li (Co-chair)

Hypoglossal nerve stimulation for treatment of obstructive sleep apnea
Stanley Yung-Chuan Liu
MMA treatment for obstructive sleep apnea: mechanisms and indications
Biao Yi
Pharyngeal surgery strategies for OSA
Hsin-Ching Lin

Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnea

Stanley Yung-Chuan Liu, Stanford University School of Medicine

Obstructive sleep apnea is a multilevel process consisting of physiologic and anatomic obstructive patterns leading to partial or complete collapse of the upper airway and resulting comorbidities. Studies have shown apnea-hypopnea index (AHI) response rate of 75% (AHI less than 20 events per hour and overall >50% reduction) and improvement in quality of life in patients treated with upper airway stimulation (UAS). UAS is indicated in patients with positive airway pressure failure, who are 22 years of age or older, with AHI 15 to 65, with body mass index less than or equal to 32 and anatomy amenable to implantation and likelihood of high success. Drug-induced sleep endoscopy is an essential evaluation step to exclude patients with retropalatal concentric collapse. Preparation of cranial nerve XII and determination of functional breakpoint to exclude the lateral XII branches and include the medial XII branches are critical to optimize surgical success.

Pharyngeal surgery strategies for OSA

Hsin-Ching Lin, Kaohsiung Chang Gung Memorial Hospital

Initially described in 1981, uvulopalatopharyngoplasty was the first surgical procedure specially designed at the palatal level for snoring and obstructive sleep apnea (OSA). To date, palatal surgery remains the most commonly used surgery for OSA. The advancement of this surgery over the past 30 years has been a process of evolution in concepts, examination, and technique to increase safety and effectiveness in the treatment of OSA. Concept changes have emerged in the disease etiology, purpose of surgery, treatment priorities, staging of operations, integration therapy, and surgical endpoints. Drug-induced sleep examination has become the mainstream for forming a surgical plan. The surgical technique has tended toward the functional expansion and stabilization of airway tissue instead of excision. Here, drug-induced sleep computed tomography is introduced. In addition, palatal surgery is further divided into palatoplasty and pharyngoplasty for individual clinical application.

Symposium 6: Various Sleep Disordered Breathing Derived from Various Diseases

Summary

Obstructive sleep apnea (OSA) is a spectrum of common, chronic diseases. With a great body of basic and clinical research, we manage OSA using various methods including CPAP, oral appliance, surgery, and newer therapy. The management of OSA in those with inherent or coexisting cardiopulmonary disease requires knowledge and skills in the general field of sleep disordered breathing (SDB) and in chronic respiratory care. In sleep disordered breathing, respiratory support and care must be tailored to night time as well as daytime needs. In this sense, physicians need to pay attention more to what is happening in breathing behavior during sleep in each patient. Additionally, an appreciation of respiratory physiology is definitely needed to understand the etiology of SDB in various diseases. The purpose of this symposium is to address basic science of respiratory physiology including inheritance of SDB and then to understand the management of various SDB in chronic opioid users and in patients with neuromuscular diseases and Down syndrome with the knowledge of respiratory physiology.

Learning Objectives

1. Apply principles of respiratory physiology to understand various presentations of SDB
2. Describe how respiratory care at night affects waketime behavior and physical activity.
3. Compare expert opinions for the treatment strategy of SDB derived from neuromuscular diseases, Down syndrome, and Opioids.
4. Identify polysomnographic features of syndrome presentations.

Target Audience

Sleep physicians and researchers, Sleep technicians, Respiratory therapists, Nurses

Chairs

Motoo Yamauchi, Kingman P. Strohl (Co-chair)

Polysomnographic features of sleep disordered breathing in neuromuscular diseases

Motoo Yamauchi

Inherited features and sleep disordered breathing

Kingman P. Strohl

Chronic opioid use and central sleep apnea, where are we now and where to go?

David Wang

Sleep disordered breathing in down syndrome

Pei Lin Lee

Polysomnographic features of Sleep Disordered Breathing in Neuromuscular Diseases

Motoo Yamauchi, Department of Respiratory Medicine, Nara Medical University

Although it is quite common that muscle activity decreases during sleep as compared with during wakefulness, nocturnal breathing is not adversely affected for healthy individuals. However, in patients with myopathy, muscles activity would be profoundly decreased once they fall asleep, and something in terms of nocturnal breathing might happen during sleep. Thus, my hypothesis is that careful looking at breathing pattern in the polysomnography is a novel tool for identifying the early-stage of myopathic diseases. I've just launched a prospective multicenter observational cohort study to clarify this hypothesis. Target disease is a late-onset Pompe disease (LOPD). Pompe disease is one of the few myopathies, for which an established therapy is available. Thus, earlier detection gives larger benefit to LOPD. I would like to introduce a rationale for this study (Sleep and Breathing 2020 in press, DOI 10.1007/s11325-020-02170-6) in this symposium. Also, I would like to share the idea regarding when and how NIV implementation should be made.

Inherited Features and Sleep Disordered Breathing

Kingman P. Strohl, Case Western Reserve University

A genetic architecture for breathing came to light with an identification of syndromes in early childhood. PHOX2b, identified originally through an unbiased association of genetic polymorphisms to disease traits in childhood, led to the identification of parental phenotypes of sleep apnea and hypoventilation. Other syndromes, like Pierre Robin Prader-Willi, Elers-Danlos Syndrome, and Downs Syndrome, while recognizable at in childhood, can present with symptomatic sleep-disordered breathing in young adulthood. Pompe disease can be noticed in childhood; however, there are those who present in early adulthood, and be part of the differential diagnosis of all adult hypoventilation syndromes. These causal genes form less than 1% of all adult presentations for sleep disordered breathing. Adult sleep disordered breathing is a complex disease, where no one gene polymorphisms or one physiologic pathway leads to the findings of obstructive and non-obstructive apneas during sleep. There is a current effort to collect thousands of international patients with common sleep apnea presentations in an attempt to find the range of polymorphisms present in adult disease. Due to gene orthologues for critical biologic functions among the mouse, rat and human, we use complementary rodent studies that dissect phenotypes for ventilatory stability. Our finding of post-hypoxic periodic breathing and sleep apnea in the C57Bl/6J (B6) linked to higher brainstem mRNA expression for apolipoprotein A2 (Apoa2); thus, the ApoA2 gene plays a novel, biologic role in breathing. This finding illustrates the complexity in respiratory control and the difficulty in the discovery of genes for adult sleep disordered breathing.

Chronic Opioid Use and Central Sleep Apnea, Where are We Now and Where to Go?

David Wang, University of Sydney

Opioids are commonly used for pain management, peri-operative procedures, and addiction treatment. There is a current opioid-epidemic in North America which is paralleled by a markedly

increase in related deaths. Since 2000, chronic opioid users were reported to have significant central sleep apnea (CSA). Besides heart failure-related Cheyne-Stokes Breathing (CSB), opioid-induced CSA has become one of the two most commonly seen CSA. It occurs in around 24% of chronic opioid users, typically after opioids were used for over two months, and usually corresponds to opioid dose/plasma concentration. Opioid-induced CSA events often mix with episodes of ataxic breathing. The pathophysiology of opioid-induced CSA can be mainly explained from respiratory rhythm generation and ventilatory chemoreflexes. Opioids have a paradoxical effect on different brain regions which can cause an irregular respiratory rhythm. In ventilatory chemoreflexes, chronic opioid use induces hypoxia which may stimulate an augmented hypoxic ventilatory response (high loop gain) and cause a narrow CO_2 reserve, this combination in mechanism make it prone to respiratory instability. To date, no direct evidence has shown any major clinical consequence from CSA in chronic opioid users. While a line of evidence suggested increased morbidity and mortality in overall chronic opioid users. CSA in chronic opioid users is likely to be a compensatory mechanism to avoid opioid injury and is potentially beneficial. The increased morbidity and mortality are more likely on those who did not develop the compensatory mechanism (CSA with high loop gain). The current treatments of CSA in chronic opioid users mainly focus on continuous positive airway pressure (CPAP) and adaptive servo-ventilation (ASV) or adding oxygen. ASV is more effective in reducing CSA events than CPAP. However, recent ASV trial suggested an increased all-cause and cardiovascular mortality with the removal of CSA/CSB in cardiac failure patients. A major reason could be counteracting of the compensatory mechanism. No similar trial has been conducted for chronic opioid-related CSA. Future studies should focus on 1) investigating the phenotypes and genotypes of opioid-induced CSA which may have different clinical outcomes. 2) validating if CSA in chronic opioid users is beneficial or detrimental? 3) assessing clinical consequences on different treatment options on opioid-induced CSA.

Sleep Disordered Breathing in Down Syndrome

Pei-Lin Lee, Center of Sleep Disorder, National Taiwan University Hospital

Obstructive sleep apnea (OSA) is prevalent in hospital- based cohorts of people with Down syndrome (DS), having an estimated prevalence between 22 and 79%, which is much higher than the rate in the general population (1.1-3.5%). The prevalence of OSA in the population- based DS patients varies among the limited studies. The OSA related neurobehavioral consequences in children include memory impairment, inattention, hyperactivity, and deficits in learning, executive, visuospatial and cognitive function. It has been proposed that the verbal deficit in DS emerges during school age and persists into adulthood while visuospatial ability and sensory processing continuously improve in school-aged DS children. The exact impact of concomitant OSA on DS children's behavior and cognitive function is still open for discussion. However, it has been demonstrated that total sleep time and slow wave sleep but not OSA were associated with the cognitive ability and comprehension. Moreover, the sleep efficiency has been associated with the language expressive development. These inconsistent results warrant further investigation.

Symposium 7: Pediatric Sleep Breathing disorder: growth, development and targeted treatment

Summary

Pediatric sleep breathing disorder is closely related to their growth and development. The normal growth and development of upper airway and jaws are characterized by age stage. Hypoxia, adenoid hypertrophy and craniofacial malformation will have different manifestations in different periods. The treatment for children and adolescents needs to consider the factors of growth and development in particular in order to have effective results. This section describes the effects of hypoxia on the growth and development of children, and the morphological manifestations of the upper airway at different ages, and different craniofacial malformations caused by adenoid and tonsil hypertrophy respectively. This section also describes the treatment of the upper airway in children with cleft lip and palate by means of growth improvement, and the progress of the means used to observe the growth and development of children.

Learning Objectives

1. To understand the consequences of intermittent hypoxia during growth period.
2. Introduce the growth and development of upper airway in different ages.
3. Describe Changes of upper airway in children with cleft lip and palate after maxillary protraction.

Target Audience

Clinicians, Physicians, dentists, researchers and health care professional

Chairs

Takashi Ono, Weiran Li (Co-chair)

Consequences of intermittent hypoxia during growth period
Takashi Ono (Japan)
Describe changes of upper airway in children with cleft lip and palate after maxillary protraction
Weiran Li (China)
3D imaging application in OSA
Bingshuang Zou (Canada)
Different craniofacial malformations associated with upper airway morphology
Jingjing Zhang (China)
Describe the characteristics of upper airway at different ages
Xuemei Gao (China)

Symposium 8: Genetics of Sleep: Insights to the Function and Evolution of Sleep

Summary

Many animal species spend a substantial fraction of their life sleeping. Sleep deprivation strongly impacts health in various species, suggesting some essential roles of sleep. Exactly why sleep is necessary, however, remains largely unknown. From an evolutionary point of view, almost all animal species that have been investigated exhibit sleep. Previously, it was not possible to estimate whether sleep in mammals and other animal species are of a common evolutionary origin or they emerged independently. However, recent advances about the molecular mechanisms of sleep have revealed that sleep in invertebrate and vertebrate animals are deeply conserved at the molecular level, supporting the possibility that sleep emerged from a common origin. The speakers of this symposium have played central roles in elucidating such deeply conserved sleep-regulating mechanisms using animals such as the nematode Caenorhabditis elegans (1,7,8), the fruit fly Drosophila melanogaster (2,5,6,7), the mouse Mus musculus (3,4,7), and the cnidarian Hydra vulgaris (9). Such molecular pathways include the transcription factor AP2 (1-4), the dopamine pathway (5,6), the salt-inducible kinase (SIK) pathway (7), the melatonin pathway (8,9) etc. These studies have revealed a surprising commonness between slow wave sleep in mammals and sleep in animals that do not have a central nervous system. Sleep might thus be of an extremely ancient origin, and sleep studies using diverse animal species may reveal the fundamental functions of this essential yet mysterious physiologic state. Reference: 1. Turek et al., Current Biology, 2013 2. Kucherenko et al., BMC Neuroscience, 2016 3. Hu et al., Genetics, 2020 4. Nakai et al., Genetics, 2020 5. Kume et al., J. Neurosci., 2005 6. Ueno et al., Nature Neuroscience, 2012 7. Funato et al., Nature, 2016 8. Niu et al., Proc. Natl. Acad. Sci. U. S. A., 2020 9. Kanaya et al., Science Advances, 2020

Learning Objectives

1. To learn the latest knowledge about genes, proteins, and signaling pathways that regulate sleep.
2. To learn the latest knowledge about how sleep is deeply conserved across various animal species at the molecular level.
3. To learn how simple model animals can be extremely effective in identifying novel factors that control sleep.

Target Audience

A broad audience, especially those interested in the molecular mechanism, evolution, genetics, and function of sleep.

Chairs

Yu Hayashi, Henrik Bringmann (Co-chair)

Sleep-regulating mechanisms revealed by genetics in mice and worms

Yu Hayashi (Japan)

Sleep: a worm's eye view

Henrik Bringmann (Germany)

A novel arousal-regulating pathway in the central complex of drosophila

Kazuhiko Kume (Japan)

Melatonin promotes sleep by activating SLO-1 potassium channel in C. Elegans

Zhao-Wen Wang (USA)

Origin of sleep regulation observed in brain-less hydra

Hiroyuki Kanaya (Japan)

Sleep-regulating mechanisms revealed by genetics in mice and worms

Yu Hayashi, Graduate School of Medicine, Kyoto University; International Institute for Integrative Sleep Medicine, University of Tsukuba

Sleep is a familiar phenomenon, but there are currently no clear answers to simple questions such as "What is sleepiness?" and "Why do we feel sick and tired if we don't sleep?". In addition, mammals have evolved to acquire a complex sleep architecture consisting of cycles of rapid eye movement (REM) sleep and non-REM sleep. Moreover, during sleep, humans generate a unique state of consciousness called dreaming. However, the roles and mechanisms of the sleep architecture and dreams are also a great mystery. To elucidate the functions of REM sleep, we have taken a genetic approach using mice. By genetically manipulating the function of various neurons in the brain stem pontine tegmental area, we have identified neurons that either negatively or positively regulate REM sleep in mice. Furthermore, by activating, inhibiting, or ablating these neurons using chemogenetics or genetically encoded toxins, we have succeeded in creating mice in which REM sleep can be temporally or chronically manipulated, or mice that exhibit aggressive behavior during REM sleep as if they were acting out their dreams. These mice are expected to be useful for understanding the functions and mechanism of REM sleep and dreaming. More recently, we have taken a genetic approach in the nematode Caenorhabditis elegans to elucidate the conserved functions and mechanism of sleep. Based on these studies, I would like to discuss the roles and mechanisms of sleep at the molecular, circuit, and behavioral levels.

Nakai et al., Sleep Architecture in Mice Is Shaped by the Transcription Factor AP-2β. Genetics 216, 753-764 (2020).

Miyazaki et al., Sleep in vertebrate and invertebrate animals, and insights into the function and evolution of sleep. Neuroscience Research 118, 3-12 (2017).

Funato et al., Forward-genetics analysis of sleep in randomly mutagenized mice. Nature 539, 378-383, 2016.

Hayashi et al., Cells of a common developmental origin regulate REM/non-REM sleep and wakefulness in mice. Science 350, 957-961 (2015).

Sleep: A worm's eye view

Henrik Bringmann, Technical University Dresden

Sleep is conserved from jellyfish to humans and can thus be studied in simple model systems. One of the simplest yet molecularly highly developed model system that sleeps is C. elegans. How and why does a simple animal such as "the worm" sleep? The answers to this question might shed light on the fundamental reasons for how and why we sleep. Our lab is applying a combination of genetics, functional imaging, optogenetics, and physiological analysis to find out how and why C. elegans sleeps. We showed that C. elegans requires a single sleep-active neuron called RIS to induce sleep. RIS activates during sleep bouts, its ablation strongly impairs sleep, and its optogenetic activation induces sleep. Thus, RIS is a bona-fide sleep-active neuron that is highly similar to sleep neurons in mammals. RIS is controlled by upstream circuits that measure and translate wakefulness into sleep. Cellular stress and antimicrobial peptides produced as part of a wounding response activate RIS through EGFR signaling and through the stress-sensing ALA neuron, thus increasing sleep following cellular stress or injury and infection. Without sleep, developmentally arrested larvae show an increased progression of aging phenotypes. Also, in the absence of sleep there is decreased survival of larvae during starvation and of adult worms following wounding. C. elegans facilitates genetic screening for sleep genes and led to the identification of aptf-1, an AP2 transcription factor gene that is crucial for RIS function. Translational work using mouse models indicates that AP2 transcription factors also are required for mammalian sleep, indicating conservation of a sleep gene. Thus, sleep in C. elegans is highly simplified: It requires a small number of sleep neurons that is controlled by upstream pathways and these sleep circuits respond to sleep need. Sleep appears to serve basic functions that include counteracting the progression of aging phenotypes. Genes and mechanisms controlling sleep function and regulation in C. elegans may be conserved across species.

A novel arousal-regulating pathway in the central complex of Drosophila

Kazuhiko Kume, Nagoya City University

Sleep and arousal are two distinct states occurring in various animals including mammals and insects, and many physiological functions operating during arousal require sleep for their sustainable maintenance. For its genetic and anatomical tractability, Drosophila melanogaster has been widely used for sleep research last two decades, and many sleep related genes have been reported. But specific neuronal function of many of them have not been well characterized yet. This is mainly due to the limited understanding about sleep-regulatory circuits. In Drosophila brain, central complex which consisting of protocerebral bridge (PB), ellipsoid body (EB), fan-shaped body (FB) and noduli (NO) is regarded as the center of their behavior regulation. Mushroom body

(MB), EB and FB of central complex are known to function in sleep and arousal regulation. We and other groups revealed that dopamine plays a major role in inducing arousal in Drosophila (Kume et al. J Neurosci 2006) and identified PPM3 dopamine neurons induce arousal through dorsal FB (dFB) which induce sleep when activated (Ueno et al. Nat Neurosci 2012). Recently we identified that PB of the central complex is another target of arousal regulation. T1 dopamine neurons which innervate PB induce arousal when activated and they are also important in the courtship regulation as recently shown by Koh's group (Duhart et al. eLife 2020). We confirmed T1 dopamine neurons indirectly connect with PFN neurons, which span from PB to FB and NO. These PFN neurons induce arousal when activated (Tomita et al, unpublished). We also discovered PFN neurons connect with FB interneurons called pontine neurons (PN) on their ventral side (ventral FB, vFB) which transmit the signal to dorsal side of FB (dFB). We showed the activation of PFN resulted in the activation of PN, which induce arousal. PN are cholinergic neurons, and they are regarded to inhibit dFB through inhibitory acetylcholine receptors (Kato et al, unpublished). Altogether, we identified another novel dopaminergic arousal inducing pathway in the central complex. The results demonstrated the multiple dopaminergic pathways regulate arousal, revealing a complex behavior regulation at central complex.

Melatonin promotes sleep by activating SLO-1 potassium channel in C. elegans

Zhao-Wen Wang, Department of Neuroscience, University of Connecticut School of Medicine

Melatonin is a sleep-promoting hormone that functions through two G protein-coupled receptors in mammals: MT1 and MT2. However, it is not fully understood how activation of melatonin receptors may produce the sleep-promoting effect. It is also unknown whether melatonin may play a similar role in lower species such as worms. In a genetic screen for mutants that suppressed a sluggish phenotype caused by a hyperactive SLO-1 in C. elegans, we isolated a loss-of-function (lf) mutant of pcdr-1, which encodes a putative melatonin receptor. SLO-1 is an ortholog of mammalian and fly Slo1. SLO-1 and Slo1 (also known as the BK channel) are high-conductance potassium channels with important roles in regulating neuronal excitability and neurotransmitter release. Through electrophysiological, pharmacological, genetic, and behavioral analyses of various mutant strains, we found that PCDR-1 is a functional melatonin receptor that allows melatonin to inhibit neurotransmitter release by activating SLO-1. We also found that lf mutations of either slo-1, pcdr-1, or a gene required for melatonin synthesis shorten the duration of a sleep state in worms, and that the sleep phenotypes are similar between slo-1(lf), pcdr-1(lf) single mutants, and slo-1(lf); pcdr-1(lf) double mutant. Furthermore, application of exogenous melatonin increases sleep duration in wild-type worms but not in slo-1(lf) and pcdr-1(lf) mutants. These results suggest that melatonin enhances sleep by activating SLO-1 through PCDR-1 in worms. In a heterologous expression system coexpressing mammalian MT1 and Slo1, melatonin may activate the channel by releasing free Gβγ subunits from G proteins, suggesting that the regulatory mechanism might be conserved in mammals. In summary, we have uncovered an evolutionarily conserved role of melatonin in C.

elegans sleep, and discovered that melatonin promotes sleep by activating the SLO-1 potassium channel.

Origin of sleep regulation observed in brain-less Hydra

Hiroyuki Kanaya, Department of Systems Pharmacology, Graduate School of Medicine, The University of Tokyo

Sleep is an evolutionarily conserved phenomenon that is observed even in flies and nematodes. Genetic studies with these tiny model organisms and comparisons with mammalian studies have revealed that even the mechanisms of sleep are shared among different animal species. However, it is still unclear how far the origin of sleep dates back and how regulatory mechanisms have been programmed during evolution. A cnidarian Hydra has a primitive nervous organization (diffuse nerve net) lacking a centralized nervous system (CNS). We used Hydra as a model of ancestral sleep and examined the commonality of molecular mechanisms. Behavioral analyses revealed that Hydra exhibits a sleep-like state with reduced responsiveness and homeostatic regulation, although the circadian regulation is not incorporated in Hydra sleep. Moreover, the necessity of Hydra sleep for cell proliferation suggests physiological relevance. Consistent with the previous report in cnidarian jellyfish, these findings in Hydra support the hypothesis that the phylogenetic origin of sleep has preceded the CNS evolution. Treatment with sleep-relevant chemicals (melatonin, GABA, and dopamine) changes the length of Hydra sleep, although unexpectedly arousing dopamine promotes sleep in Hydra. Transcriptome analysis in sleep-deprived Hydra identified sleep-relevant genes, including the orthologues of voltage-gated potassium channels (Shaker) and cGMP-dependent protein kinase 1 (PRKG1). Indeed, consistent with findings in flies and nematodes, PRKG1 has a sleep-promoting function in Hydra. RNAi screening for the corresponding orthologues of the sleep-relevant genes in Drosophila revealed that ornithine aminotransferase (OAT) is involved in sleep regulation. Interestingly, the effects of ornithine metabolism on sleep were opposing between Hydra and Drosophila. These commonalities of sleep-relevant chemicals and regulatory genes suggest that sleep mechanisms have already been acquired at the molecular level in the ancestral sleep of Hydra. Furthermore, several opposing functions of regulatory components may provide insight into how sleep-regulatory pathways have been reprogrammed during the evolutionary development of CNS.

Symposium 9: The interaction of upper–lower airways and OSA: the role of multidisciplinary healthcare actors in contemporary century

Summary

The concept of united airway interaction comprising upper airway disease such as AR (allergic rhinitis), lower airway disorders with asthma and COPD (chronic obstructive pulmonary disease) and OSA (obstructive sleep apnea) has been demonstrated in the last decades. It embodies a coherent pathophysiology and a comprehensive approach to diagnosing and treating each disease entity under an overlap condition with other co-morbidities for optimal disease control. AR, asthma and COPD, for example, may usually overlap with OSA and make OSA more severe and more difficult to treat. Conversely, OSA patients with other upper or lower airway diseases like AR, asthma or COPD may frequently experience symptomatic exacerbation and uncontrolled symptoms. However, treating each mentioned obstructive airway disease will make OSA easier to treat and manage. In fact, the optimal treatment of patients with AR, especially for those with nasal congestion, uncontrolled asthma or severe COPD may reduce OSA symptoms and severity, improve the quality of life, life expectancy and health care burden, and vice versa. Therefore, many objectives in the interaction concept between upper-lower airway disease and OSA and the efficacy of airway disease management should be achieved academically in the near future for reliable control of each disease and to assure a good quality of sleep. More awareness of upper and lower airway disease and its comorbidity with OSA should be emphasized in the patients' management programs. Progress in the diagnosis of OSA with the advanced polysomnography, relevant biomarkers and accurate imagery techniques, and international guidelines on the management of airway diseases such as AR, asthma and COPD might help physicians focus on the target treatment for achieving the optimal management. Finally, more research on the interaction between upper and lower airway diseases and OSA should be done for having a deep and clear overview on the disease overlap.

Learning Objectives

1. Understand the interaction between upper and lower airways and OSA
2. Describe the current evidence on allergic rhinitis in OSA Management
3. Describe the overlap of COPD and OSA
4. Describe the interaction between OSA and asthma
5. Describe the current evidence on physical therapy for OSA

Target Audience

ENT, respirology physician, physical therapist, sleep specialist, and other medical staff who are interested in this topic.

Chairs

Sy Duong-Quy, Naricha Chirakalwasan (Co-chair)

The interaction between upper and lower airways and OSA: facts and challenges
Sy Duong Quy (Vietnam)
Current evidence on allergic rhinitis in OSA management
Naricha Chirakalwasan (Thailand)
Overlap of chronic obstructive pulmonary disease and obstructive sleep apnea
Vinh Nguyen (Vietnam)
Interaction between OSA and asthma
Quan Vu-Tran-Thien (Vietnam)
Physical therapy for obstructive sleep apnea patients
Khue Bui Diem (Vietnam)

The interaction between upper and lower airways and OSA: Facts and Challenges

Sy Duong-Quy, Lam Dong Medical College; Penn State Medical College Hershey Medical Center; Paris Descartes University

The concept of united airway interaction comprising upper airway disease such as allergic rhinitis, lower airway disorders with asthma and COPD (chronic obstructive pulmonary disease) and OSA (obstructive sleep apnea) has been demonstrated in the last decades. It embodies a coherent pathophysiology and a comprehensive approach to the diagnosis and treatment of each disease entity under overlap condition with other co-morbidities for having optimal disease control. Allergic rhinitis, asthma and COPD, for example, may usually overlap with OSA and make the last one more severe and more difficult to treat. Conversely, patients with OSA who have other upper or lower airway diseases such as allergic rhinitis, asthma or COPD might experience frequently symptomatic exacerbation and uncontrolled symptoms. However, the treatment of each mentioned obstructive airway disease will make OSA easier to treat and manage. In fact, the optimal treatment of patients with allergic rhinitis, especially for those with nasal congestion, uncontrolled asthma or severe COPD may reduce OSA symptoms and severity and also improve the quality of life, life expectancy and health care burden, and vice versa. Therefore, many objectives in the interaction concept between upper - lower airway disease and OSA and the efficacy of airway disease management should be achieved academically in the near future for reliable control of each disease and to assure a good quality of sleep. More awareness of upper and lower airway disease and its comorbidity with OSA should be emphasized in the patients' management programs. Progress in diagnosis of OSA with the support of the advanced polysomnography devices, relevant biomarkers and accurate imagery techniques, associated with international guidelines on the management of airway diseases

such as allergic rhinitis, asthma and COPD might help physicians to focus on the target treatment for achieving the optimal management. Finally, more research on the interaction between upper and lower airway diseases and OSA should be done by physicians and researchers for having an deep and clear overview on the disease overlap.

Current Evidence on Allergic Rhinitis in OSA Management

Naricha Chirakalwasan, Division of Pulmonary and Critical Care medicine, Department of Medicine, Faculty of Medicine, Chulalongkorn University Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital, Thai Red Cross Society

Physiological and epidemiological studies support that AR contributes to snoring and is likely to impact AHI in OSA. 1 Intranasal steroid is the most effective treatment for AR and recommended as the first line treatment particularly in moderate to severe persistent symptoms. There is emerging evidence on the use of intranasal steroid as the potential/adjunctive treatment in selective OSA population with AR. Current publication demonstrated that the use of intranasal steroid effectively reduced RDI in non-supine position. Evidence of intranasal steroid in improving CPAP compliance is still controversial. Recent meta-analysis did not demonstrate overall improvement in CPAP compliance. However, intranasal steroid may improve CPAP compliance particularly in the group with symptoms of allergic rhinitis.

Overlap of chronic obstructive pulmonary disease and obstructive sleep apnea

Vinh Nguyen, University of Medicine and Pharmacy at Ho Chi Minh City

Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) affect at least 10% of the adult population in each group so that patients have both disorders, commonly referred to as overlap syndrome, also relatively common. There is an interaction between COPD and OSA in that certain features of COPD may promote OSA (such as cigarette smoke, rostral fluid shift, skeletal muscle weakness and corticosteroid using) but some other features of COPD to be protective against the emergence of OSA in COPD patients (such as low BMI, lung hyperinflation, diminished REM sleep, older ages and theophylline using). COPD and OSA are associated with a number of overlapping physiological and biological disorders, which can contribute to many comorbid conditions. Therefore, there is a higher probability that the overlap patients may have a higher risk of comorbidities than patients with either disease alone. The diagnosis of OSA in COPD patients may require PSG, but in many cases, respiratory polygraph or nocturnal oxygen saturation monitoring is particularly helpful. Noninvasive pressure support is the most appropriate treatment option for overlap patients, however, the types of device may target to the prominent condition in this overlap syndrome. In patients with predominant OSA, continuous positive airway pressure therapy (CPAP) is the preferred option, but where COPD is the main one, non-invasive ventilation (NIV) as bi-level positive airway pressure (BiPAP) may be preferable.

Interaction between OSA and Asthma

Quan Vu-Tran-Thien, University of Medicine and Pharmacy at Ho Chi Minh City

Obstructive sleep apnea (OSA) and asthma are two of the most common chronic respiratory diseases. These disorders exhibit a reciprocal interaction in which each disease influences the severity of the other. Obesity, rhinitis, and gastroesophageal reflux (GERD) are shared risk factors for these diseases. Clinicians must be cautious and manage weight-control, nasal congestion, and GERD in that population. Evidence suggests that airway and systemic inflammation, neuroimmune interactions, and the effects of asthma maintenance medications are factors that predispose asthma patients to OSA. When asthma patients show symptoms of ventilatory disruptions during sleep, OSA may be suspected. Undiagnosed or inadequately adherence OSA will affect asthma, and vice versa. Continuous positive airway pressure (CPAP) administered by a nasal or full-face mask is the treatment option of choice for patients with OSA syndrome, which results in the absence of obstructive sleep apneas and hypopneas during sleep.

Physical Therapy for Obstructive Sleep Apnea Patients

Khue Bui-Diem, University of Medicine and Pharmacy at Ho Chi Minh City

Sleep apnea is defined as a condition in which there are repeated apnea or hypopnea in sleep that cause arousals, fragmented sleep, and decreased oxygen saturation in the blood. Obstructive sleep apnea (OSA) is the most common in 3 types of sleep apnea, accounting for 7-24% of the population. As recommended by the American Academy of Sleep Medicine and the American College of Physicians, all OSA patients should be initially treated with positive airway pressure (PAP), which is the standard treatment for moderate to severe OSA patients. The other treatment options, but less effective than PAP, or not enough evidence, are mandibular advancement device (MAD), upper airway surgery, physical therapy, and lifestyle counseling. Although PAP is the optimal treatment option, not all patients can afford or tolerate it. The collapse of the upper airway during sleep is the hallmark of OSA, and some methods of physical therapy had proven effective in improving the severity of OSA through apnea-hypopnea index (AHI), arousal index, mean SpO2, and oxygen desaturation index.

Symposium 10: Sleep in Professionals

Summary

Sleep is important to people for their productivity and mental health at work. Emerging evidence has shown sleep problems occur in different professionals, including healthcare workers, esports athletes, shift workers, and so on. This symposium will highlight the impacts of sleep loss and sleep disorders among college students and different ways to address them. Sleep problems and related risk factors in esports athletes will also be discussed. In addition, based on the latest data, the insomnia symptom network structure in Chinese psychiatric clinicians during the COVID-19 pandemic, and the associations between shift workers and COVID-19 infection will be also discussed. This symposium aims to provide new insight into sleep in different professionals.

Learning Objectives

1. to understand the insomnia symptom network structure in Chinese psychiatric clinicians during the COVID-19 pandemic.
2. to learn about the impacts of sleep loss and sleep disorders on attention, memory, cognitive control and mood disorders, and different ways to address sleep and psychological issues among college students.
3. to learn about sleep aspects and related risk factors in esports athletes
4. To learn about the associations between shift workers and COVID-19 infection, and discuss the potential mechanisms.

Target Audience

Psychiatrists, psychologists, and health care professionals

Chairs

Bin Zhang, Yu-Tao Xiang (Co-chair)

Network analysis of insomnia symptoms in Chinese psychiatric clinicians during the COVID-19 pandemic
Yu-Tao Xiang (Macau, China)
Sleep problems and practical intervention among college students in southern China
Ning Ma (China)
Sleep characteristics and risk factors of Korean esports athletes
Sangha Lee (Korea)
Associations of shift work with symptomatic COVID-19 infection: findings from the UK biobank cohort
Lulu Yang (China)

Network analysis of insomnia symptoms in Chinese psychiatric clinicians during the COVID-19 pandemic

Yu-Tao Xiang, University of Macau

Background: The coronavirus-19 (COVID-19) pandemic has led to common mental health problems in different populations. For instance, insomnia symptoms are an important mental health issue among healthcare workers during the COVID-19 pandemic. In the theory of network, central symptoms in a network can be identified and have the greatest influence on other symptoms. The aim of this study was to characterize the insomnia symptom network structure in Chinese psychiatric clinicians during the COVID-19 pandemic. Method: A total of 10,516 psychiatric clinicians were included. The Insomnia Severity Index (ISI) was used to evaluate the severity of insomnia symptoms with a cut-off value of 7. Item informativeness and redundancy were examined. The Extended Bayesian Information Criterion (EBIC) graphical least absolute shrinkage and selection operator (LASSO) network model were used to estimate the network structure. Central indices of insomnia symptom network (e.g., "strength", "closeness", and "closeness") were calculated to identify the central insomnia symptoms. Network stability was assessed by a case dropping procedure. All analyses were conducted by R program.Results: The prevalence of insomnia symptoms in psychiatric clinicians during the COVID-19 pandemic was 28.6% (95% CI: 27.7% - 29.5%). No ISI item was redundant or poor informativeness (MSD=0.80 ± 0.10). The current network was stable. The ISI symptoms "Severity of sleep onset" and "Sleep maintenance" had the strongest connection, followed by the edge "Early morning wakening problems" and "Sleep maintenance", and the edge "Distress caused by the sleep difficulties" and "Interference with daytime functioning". The symptoms of "Sleep maintenance" and "Interference with daily functioning" had the highest centrality values, while symptoms "Early morning wakening problems" had the lowest centrality value. Conclusions: The identified central symptoms (e.g., "Sleep maintenance" and "Interference with daily functioning") may be targets for pharmacotherapy and psychosocial interventions to improve insomnia among psychiatric clinicians during the pandemic. Keywords: Insomnia, network analysis, COVID-19, psychiatric clinicians

Sleep Problems and Practical Intervention among College Students in Southern China

Ning Ma, South China Normal University

Sleep problems are a common occurrence in college students. Sleep loss, Insomnia, and impaired sleep quality not only impair individuals' cognition and behavior but also lead to several mental health issues. To explore the impact of sleep loss and sleep disorders on attention, memory, cognitive control and mood disorders, several behavioral and neuroimaging tests were applied to examine the differences from behavioral and neural aspects. I will mainly present three studies on this topic. (1) Altered frontal connectivity after sleep deprivation predicts sustained attentional impairment： By applying resting-state functional magnetic resonance imaging with 42 participants under both

normal sleep and 24-hour sleep deprivation conditions, the amplitude of low-frequency fluctuations (ALFF) and functional connectivity were used to investigate the neurobiological change caused by sleep deprivation, and the psychomotor vigilance task (PVT) was used to measure sustained attention in each state. Correlation analysis was used to investigate the relationship between the change of ALFF/functional connectivity and vigilance performance. (2) The relations of chronotype, sleep quality and depressive symptoms: By using the questionnaires of MEQ, PSQI, and DASS21, we investigated the mediating role of sleep quality and the moderating role of resilience between chronotype and depressive symptoms. The results revealed that the association between chronotype and depressive symptoms was partially mediated by sleep quality, and the direct and indirect effects were moderated by resilience. (3) Changes of Sleep Patterns, Lifestyles, and Emotion during the COVID-19 Pandemic: To assess changes in sleep pattern and its influence on people's daily life and emotion in individuals during the COVID-19 pandemic. Self-developed questionnaires were used to measure the changes in the nocturnal sleep, daytime napping, lifestyles and negative emotions in individuals before and after the COVID-19 pandemic. The results demonstrated that under the influence of stress caused by the pandemic, maintaining regular daytime napping was an effective way to stabilize sleep pattern and biological rhythm, keep good lifestyles and alleviate the effect of acute psychological stress. Moreover, this talk will also highlight different ways to address sleep and psychological issues, such as mindfulness and resilience trainings. Most importantly, promotion of university and college policies and class schedules that encourage healthy and adequate sleep could have a significant impact on the sleep, learning, and health of college students.

Sleep Characteristics and Risk Factors of Korean Esports Athletes

Sangha Lee, Ajou University Medical Center

Objectives: Esports is becoming popular and professionalized, but research on esports athletes is lacking. Although sleep is a potentially important determinant of performance in esports, there have been no published data on the sleep behavior of professional esports athletes. The aim of this exploratory study is to investigate sleep aspects and sleep risk factors in esports athletes. Methods: Thirty-four esports athletes were compared with 21 nonathletes from the general population to assess their sleep patterns and mood. Study 1 is a quantitative study with a 2-week observation period of sleep that was performed after evaluating insomnia severity, daytime sleepiness, sleep knowledge, and mood state. During the sleep observation period, participants recorded sleep diaries. In Study 2, qualitative research was conducted with in-depth interviews of 6 participants including esports players and coaches. Results: The esports athlete group reported significantly delayed sleep phase compared to the nonathlete group (d=2:06, p<0.001). Quality of sleep and scores for feeling refreshed upon awakening were significantly lower (d=0.59, p<0.001; d=0.47, p<0.01, respectively). The esports athlete group showed significantly higher depression scores (d=11.53, p<0.001) and significantly higher proportion of individuals with clinical symptoms of depression compared to the non-athlete group (d=50.4%, p, p<0.001). In Study 2, in-depth interviews of six

participants were conducted using phenomenological research methods. Six themes emerged from the interviews with the participants: sleep risk factors, sleep protective factors, lifestyle, stress factors, organizational management, and demands for sleep/psychological intervention. Conclusion: The professional esports athletes showed more depressed mood and more delayed sleep phase compared to the non-athletes. A wide range of interventions including sleep education tailored to the level of esports athletes, Cognitive Behavioral Therapy for insomnia (CBT-I), social skills training, emotional management, and stress reduction programs should be developed and implemented on both individual and organizational levels. Keywords: Esports athletes, sleep problems, depressive symptoms, risk factors

Associations of shift work with symptomatic COVID-19 infection: findings from the UK Biobank cohort

Lulu Yang, Guangdong Provincial People's Hospital

Objectives: During the COVID-19 epidemic, some studies have identified some risk factors associated with COVID-19, such as older age, male sex, black ethnicity, higher body mass index, socioeconomic deprivation, smoking, and longstanding illness. On the other hand, evidence has shown shift work is associated with respiratory infections. However, whether the associations of shift work with COVID-19 infection is unclear. We aimed to investigate the associations of shift work with symptomatic COVID-19 infection in a large population-based cohort. Methods: This was a prospective cohort study based on the UK biobank, and 421373 participants resident in England and recruited between 2006 and 2010 were included. Shift work as the exposure was obtained. The main outcome was testing results of COVID-19 based on PCR (March 16, 2020 to May 31, 2020). Sensitivity analyses restricting to those who were tested for only once or were tested for more times but with the same results for COVID-19 infection were conducted. Results: A total of 421373 participants were included into analyses, of whom 18179 were healthcare workers. Of these, laboratory testing results of 6100 (1.45%) participants were available, and 5781 (0.35%) were with consistent testing results by May 31, 2020. Besides, 415273 participants without testing results were defaulted as negative. Among paid employers or self-employers, the frequency of shift work and type of shift work were associated with the risk of COVID-19 infection after adjustment for demographics, behavioral factors, obesity, chronic diseases and mental disorders [type: day-shift, OR (95% CI), 2.29 (1.86, 2.82), night-shift, OR (95% CI), 3.09 (2.57, 3.71); frequency: sometimes, OR (95% CI), 2.32 (1.87, 2.88), usually or always, OR (95% CI), 2.99 (2.50, 3.57)]. Sensitivity analyses confirmed the strong association between shift work and COVID-19 infection. Furthermore, shift work was consistently associated with COVID-19 infection when stratifying participants into healthcare workers and remaining participants after excluding healthcare workers. Conclusions: Shift work may enhance susceptibility towards symptomatic COVID-19 infection. Therefore, preventive strategies targeting at COVID-19 infection may set priority to those shift workers.

Symposium 11: Treatment of sleep disordered breathing in different comorbidities

Summary

Sleep-disordered breathing (SDB) is a highly prevalent condition, and is associated with many debilitating chronic diseases. The role of treatment in obstructive sleep apnea (OSA) in different chronic comorbidities has been recognized in international guidelines. Treatment with continuous positive airway pressure (CPAP) is associated with clinically-relevant benefits in chronic obstructive pulmonary disease, obesity hypoventilation syndrome, cardiovascular disease, kyphoscoliosis, neuromuscular disease and diabetes. Severe OSA increases the risk of arrhythmias, including atrial fibrillation, influences risk management in stroke, and is highly prevalent in patients with type 2 diabetes. The role of CPAP for secondary cardiovascular prevention remains to be determined. Data from large, well-conducted clinical trials have shown that noninvasive ventilation, targeted to markedly reduce hypercapnia, significantly improves survival and reduces readmission in stable hypercapnic chronic obstructive pulmonary disease. The association of SDB with chronic diseases contributes to the high healthcare costs incurred by SDB patients. SDB also has an important negative impact on quality of life, which is reversed by CPAP treatment. The diagnosis and treatment of SDB is vital for the common comorbid disease.

Learning Objectives

1. Treatment of sleep apnea in obesity hypoventilation syndrome
2. Treatment of sleep apnea in COPD
3. Treatment of sleep apnea in cardiovascular disease
4. Treatment of sleep apnea in diabetes
5. Treatment of sleep apnea in neuromuscular disease

Target Audience

Cardiologist in sleep medicine, Pulmonologist in sleep medicine, Sleep specialist, Physiologists interested in treatment of sleep apnea

Chairs

Thomas Penzel, Babak Amra (Co-chair)

Obesity hypoventilation syndrome
Babak Amera (Iran)
Chronic obstructive pulmonary disease
Ingo Fietze (Germany)
Cardiovascular disorder
Christoph Schöebel (Germany)

Neuromuscular disorder
Parisa Admi (Iran)
Diabetes melitus
Forogh Soltaninejd (Iran)

Obesity Hypoventilation Syndrome

Babak Amra, Bamdad Respiratory Research Center, Isfahan University of Medical Sciences
CPAP consists of a continuous pre-set pressure during the respiratory cycle to prevent obstructive apneas and hypopneas but unlike NIV, it does not provide additional ventilatory support. Nevertheless, CPAP can permit the unloading of carbon dioxide accumulated during long-lasting complete or partial obstructive events during sleep. There is no clear demonstration of superiority of either mode of PAP therapy and, therefore in practice, it usually depends on several factors including, but not limited to, the predominance of respiratory disturbances during sleep (obstructive events or hypoventilation), adjustment complexity and cost. Both PAP modalities seek to correct sleep hypoxemia, obstructive events and hypercapnia. Regardless of the chosen modality, PAP titration during sleep is strongly recommended. It is evident that patients' characteristics or "phenotype of OHS" is important for clinicians when trying to the select the most appropriate mode of PAP therapy. Accordingly, for patients with more pure forms of hypoventilation and with fewer obstructive events during sleep (i.e., mild to no OSA), the treatment of choice would be NIV. In contrast, for patients with a greater number of obstructive events during sleep, the first-choice would be CPAP. However, we encourage clinicians to monitor these patients closely for the first 2–3 months after initiating PAP therapy. In case of CPAP therapeutic failure, arbitrarily defined as inadequate clinical response or insufficient improvement in gas exchange during wakefulness or sleep, or continued hospital admissions for acute-on-chronic hypercapnic respiratory failure, it would be clinically prudent to consider switching the patient to NIV therapy. The underpinning base of the pathophysiology of OHS is obesity. Therefore, it is pertinent to incorporate weight management strategies into the care of patients with OHS. Bariatric surgery is a cost-effective strategy for managing severe obesity with comorbidity such as OSA with long-term efficacy data. The risk of surgery in patients with untreated OHS is high but once successfully established on PAP therapy, these risks appear to be mitigated. Untreated OHS is associated with significant morbidity including hospital admission and need for respiratory or critical care support.

Chronic Obstructive Pulmonary Disease

Ingo Fietze, Interdisciplinary Center of Sleep Medicine, CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN
Obstructive sleep apnea (OSA) and COPD are among the most common pulmonary diseases. COPD and OSA have common pathophysiology, for example, smoking. The two diseases are known to coexist, which was termed by Flenley as the "overlap syndrome". Flenley found that patients who had COPD with OSA had greater amount of nocturnal hypoxemia and hypercapnia than patients with COPD or OSA alone. Other studies have demonstrated that OSA/COPD overlap syndrome is associated with daytime oxygen desaturation, hypercapnia, and lower quality of life. Overlap syndrome is considered as a common disease, which may be different than the simple sum of OSA and COPD. A European-based study found that ~1% of the total population and 9.2% of those with

OSA had COPD as determined by spirometery. In particular, a synergistic relationship between OSA and COPD has been described and is often referred to as overlap syndrome. The mainstay of treatment for patients with OSA and overlap syndrome is positive airway pressure using either CPAP or bilevel positive airway pressure (PAP). Management of OSA-COPD overlap patients differs from COPD alone and the survival of overlap patients treated with nocturnal positive airway pressure is superior to those untreated during acute exacerbations with ventilatory failure, NIV is frequently used because it has been shown to improve survival interest in the use of NIV in chronic hypercapnic COPD has been renewed with studies of so-called "high-intensity" NIV, which refers to inspiratory pressures higher than those used in most previous randomized controlled trials (RCTs) as well as controlled ventilation with higher-than-baseline respiratory rates to maximally reduce the PaCO2. In stable patients with COPD and chronic hypercapnia (defined as FEV1/FVC<0.70; resting PaCO2>45 mm Hg; not during exacerbation), long-term NIV has the potential to improve physiological parameters (e.g., lung function or gas exchange), clinical symptoms (e.g., functional capacity, dyspnea, quality of life [QOL], and sleep quality) and patient-centered outcomes (e.g., hospital readmission and survival).

Cardiovascular Disorder

Christoph Schöbel, University Medicine Essen

Obstructive sleep apnea (OSA) has been associated with many different forms of CVD including hypertension, stroke, HF, coronary artery disease, and atrial fibrillation (AF). Adults with OSA not only have an increased risk of developing comorbid CVD but also have worse outcomes related to CVD. Despite the clear association between CVD and OSA, randomized trials have failed to demonstrate that treatment of sleep apnea improves hard cardiovascular outcomes in patients with established CVD. 25%-40% of patients with HF also experience CSA, with an equal or higher incidence than OSA. CSA seems to be triggered by the hypocapnia associated with pulmonary congestion, by the enhanced chemosensitivity and by the delayed circulation associated with HF itself. Other mechanisms, including overnight fluid shift from the legs to the upper body, may also play a role in the pathogenesis of CSA. Repetitive arousals and episodes of intermittent hypoxia and their associated sympathetic overactivation may lead to further deterioration of the cardiac function, leading to fatal arrhythmia, therefore to poor prognosis. In addition, hemodynamic alterations, especially when occurring during hyperpnea following CSA, may also contribute to the deterioration of the cardiac function. In contrast, considering that alterations in respiration associated with CSA (i.e., repetitive episodes of central apnea and subsequent hyperpnea) were hypothesized to help impaired cardiac pumps and to work as a compensatory mechanism for severe HF, and considering that CSA suppression by either continuous positive airway pressure (CPAP) or adaptive servo-ventilation (ASV) failed to show long-term beneficial effects in clinical trials with patients with both HF and CSA, whether CSA is just an epiphenomenon of HF or a causality of HF is still under debate. HF treatment (and its optimization) including beta blockers, angiotensin converting enzyme

inhibitors, cardiac resynchronization therapy, left ventricular assist device, cardiac rehabilitation, and heart transplantation are able to alleviate CSA. When CSA remained even under guideline-directed medication towards HF, positive airway pressure (PAP) therapy such as CPAP and ASV will be considered. Numerous observational and short-term randomized controlled trials reported these modalities to have positive effects, showing both an evident alleviation of CSA and a mild improvement of the cardiac function.

Neuromuscular Disorder

Parisa Admi, Shahid Bheshti University of Medical Sciences

Hypoventilation in neuromuscular disorders. Hypoventilation is actually said to exist when arterial pCO_2 ($PaCO_2$) exceeds the upper limit of normal. Data for the normal range of this parameter began to appear in the article since1942, with most sources estimating a mean value of about 38 mm Hg and the upper 95% confidence limit to be about 45 mm Hg. Therefore, a value of $PaCO_2$ greater than 45 mm Hg (presumably only applicable at or near sea level) is usually used to define the presence of hypoventilation. A vast variety of mechanism can cause to the hypoventilation. Hypoventilation in neurologic and neuromuscular disorders is basically can explain by weakness of respiratory muscles. It can lead to chest wall deformity and abnormal function of diaphragm as well. Hypoventilation in obstructive airways disease is readily explained; it is intuitively obvious that airflow limitation will necessarily constrain maximal minute ventilation and thus maximal alveolar ventilation, and this has been repeatedly demonstrated in such patients. Mechanical impairment of chest wall may aggravate by obesity, obstructive apnea and COPD, etc. One of the important points in the management of pulmonary disorders of the pulmonary muscles is the early attention to respiratory problems in sleep before the rise of muscle weakness. Attention to restless sleep, witnessed apnea and nocturia during sleep are important points. A polysomnography should be performed before clear signs of muscle weakness appear. In nocturnal monitoring, observation of hypoxia and respiratory events during sleep is treated step by step using the hypoxia correction protocol medical management. Oxygen remains the mainstay of treatment for the hypoxemia of stable COPD patients protocol, and at this stage, the patient uses the device only during the night. In this lecture treatment in all of these disorders involve coordinated management of primary disorder and the use of noninvasive ventilation.

Diabetes Mellitus

Forogh Soltaninejd, Bamdad Respiratory Research Center, Isfahan University of Medical Sciences

Treatment of sleep-disordered breathing in diabetes mellitus. Sleep-disordered breathing (SDB) is independently associated with insulin resistance, glucose intolerance, and type 2 diabetes mellitus (DM2). Patients with both of these disorders are frequently obese. Thus, it is not surprising that a significant number of patients suffer from both conditions. The most common form of SDB is obstructive sleep apnea (OSA). The reported prevalence of OSA in patients with DM2 or prediabetes

varies from 58% to 86%. Approximately 50% of patients with OSA have DM2 or impaired glucose tolerance. Multiple studies have suggested a link between OSA and DM2 independent of body mass index (BMI), age, gender, smoking status, waist circumference, and self-reported sleep duration. Increased oxidative stress and increased lipid peroxidation are the likely mechanisms through which hypoxia affects insulin resistance. Also, sympathetic nervous system activation due to recurrent hypoxia increases the release of catabolic hormones, which have diabetogenic effects. Some of the same clinical features of OSA including obesity, lethargy, hypertension, and cardiac abnormalities are as common in DM2 patients. Thus, the consideration of OSA and detailed screening and diagnosis in diabetic patients is very important. The treatment of choice for OSA is continuous positive airway pressure (CPAP), and studies utilizing the hyperinsulinemic- euglycemic clamp test (gold standard test) have shown improvement in insulin resistance after treatment of OSA with CPAP. In patients with OSA and DM2, CPAP therapy can lead to improvements in postprandial glucose levels and in glycosylated hemoglobin (HbA1c). In this manner, CPAP therapy might confer a significant improvement in long-term health, such as prevention of the macro-and micro vascular complications of DM2. The effects of OSA on increasing of insulin resistance are exerted in several ways including intermittent hypoxia, release of catabolic hormones due to intermittent awakening, and leptin resistance related to sleep disruption. CPAP therapy with the effect on these derangements improves insulin sensitivity or decrease insulin resistance. In summary, treatment of OSA in DM2 is an important component of patient management for glycemic control and prevention of complications.

Symposium 12: Impact of eveningness and efficacy of bright light therapy

Summary

Eveningness represents a circadian preference of a late wake time and late rise time. There is emerging evidence linking eveningness with adverse impact in health and performance outcomes. This symposium will highlight the association of eveningness to sleep parameters, mood and academic performance in university students, as well as the impact of eveningness in patients with insomnia and depression. The application of bright light therapy and its efficacy in treating adolescent delayed sleep wake phase disorders, youth insomnia and adult unipolar depression will also be discussed.

Learning O bjectives

1. To understand the factors associated with, and impact of eveningness in sleep and academic performance in university students
2. To become familiar with the potential mechanisms linking sleep and depression in youth.
3. To learn about the importance of addressing both sleep and circadian disturbance in adolescents and the latest research on the treatment approach for managing insomnia and eveningness in youths
4. To learn about the impact of eveningness in patients with depression and the treatment implications.

Target Audience

Psychologists, psychiatrists, pediatricians and health care professionals

Chairs

Joey Wing-Yan Chan, Shirley Xin Li (Co-chair)

The efficacy of adjunctive bright light therapy in patients with non-seasonal unipolar depression and evening chronotype
Joey Wing-yan Chan (Hong Kong, China)
The efficacy of cognitive behavioural therapy and bright light therapy for insomnia in adolescents with evening chronotype
Shirley Xin Li (Hong Kong, China)
University-wide chronotyping shows that late types have lower grades, shorter sleep, poorer well-being, and lower class attendance
Joshua J. Gooley (Singapore)
Effects on depression from bright light therapy for adolescents with delayed sleep-wake phase disorder
Michael Gradisar (Australia)

The efficacy of adjunctive bright light therapy in patients with non-seasonal unipolar depression and evening chronotype

Joey Wing-Yan Chan, The Chinese University of Hong Kong

Background: Eveningness was associated with more severe insomnia, depression and higher suicidality and non-remission rate in patients with unipolar depression. This study aims to examine the efficacy of adjunctive bright light therapy with gradual timing advance in a randomized, assessor and prescriber-blinded controlled trial. Method. Participants were randomly allocated to receive 5 weeks of either bright white light therapy (BLT) or dim red light (DRL) with the same advancement protocol. Participants were followed up till 5 months after treatment. Primary outcomes included (i) remission rate and (ii) the severity of depression. The analysis was conducted using Kaplan–Meier survival analysis, Cox proportional hazard analysis and linear mixed models. Results. A total of 93 participants (46.4 $\pm$ 11.7 years old, 80% female) were randomized. The cumulative remission rate for the BLT and the DRL groups was 67.4% and 46.7%, respectively. Time to remission was shorter for the BLT group relative to the DRL group and patients in the BLT group had a higher probability of achieving remission relative to patients in the DRL group. Conclusions. The use of bright light therapy with gradual advance protocol is an effective adjunctive treatment resulting in quicker and a higher rate of remission of depression in patients with non-seasonal unipolar depression and evening-chronotype.

The efficacy of cognitive behavioral therapy and bright light therapy for insomnia in adolescents with evening chronotype

Shirley Xin Li, The University of Hong Kong

Eveningness and insomnia symptoms are both common and may be linked to an increased risk for psychopathology in adolescents. However, the optimal treatment approach to address the concurrent sleep and circadian issues in this population remained unclear. This talk will present on the preliminary data on the effects of cognitive behavioural therapy for insomnia (CBT-I) and CBT-I plus bright light therapy on sleep and mood symptoms in adolescents with insomnia and eveningness.

University-wide chronotyping shows that late types have lower grades, shorter sleep, poorer well-being, and lower class attendance

Joshua Gooley, Duke-NUS Medical School

Background. Late chronotype is associated with negative health and performance outcomes. However, most findings in university students are based on small convenience samples. Recently, it was shown that chronotype can be derived from students' Learning Management System (LMS) login behavior (Smarr and Schirmer, Sci Rep, 2018;8(1):4793). We used this chronotyping method at a large university to test the hypothesis that late-type students show poorer academic performance, shorter sleep, poorer well-being, and lower class attendance. Methods. De-identified data were analysed for 33,645 undergraduates over 5 semesters at the National University of Singapore (52.5%

Female; Mean age $\pm$ SD = 21.1 $\pm$ 2.4 years). Students were assigned to different chronotype categories based on their median login phase of LMS activity on non-school days determined by circular statistics (early, n = 3,965; intermediate, n = 23,787; late, n = 5,893). Grades were examined for 5,797 course modules with class start times ranging from 0800 to 1800 in hourly intervals. Sleep behavior was measured in a subset of 181 students who wore an actigraphy watch over a 6-week period during the school term. Well-being and psychological attributes were assessed by surveys. Class attendance was evaluated by student's Wi-Fi connection data during lectures. ANOVA was used to compare cumulative grade point average (GPA), sleep duration, self-reported well-being, and class attendance between chronotype categories. Results. There was a significant association between chronotype and grades, in which GPA was lower in late-type students compared with early- and intermediate-type students. When grades were sorted by class start times, late-type students performed more poorly for all class start times. Relative to their peers, late-type students had shorter actigraphy-estimated sleep on school days, poorer self-rated health and greater fatigue, and were less likely to go to classes based on their Wi-Fi connection data. Conclusions. The LMS chronotype method can be used to derive chronotype for large samples of university students without requiring their active participation. Consistent with prior work (Smarr and Schirmer, 2018), late-type students showed poorer academic performance irrespective of class start time. Our findings suggest that poorer academic performance in late-type students is driven by multiple factors including cumulative sleep loss, decreased mood, and skipping classes. Acknowledgements. The authors have no conflicts of interest to declare. The work was supported by funding provided by the NUS Office of the Senior Deputy President & Provost and the NUS Institute for Applied Learning Sciences and Educational Technology.

Effects on depression from bright light therapy for adolescents with Delayed Sleep-Wake Phase Disorder

Michael Gradisar, Flinders University

Our previous meta-analysis demonstrated that sleep disturbance during adolescence may lead to the development of depression, and furthermore there is a reliable link between a late chronotype and depression. Our clinical trial of 60 adolescents and young adults diagnosed with Delayed Sleep-Wake Phase Disorder explored the links between sleep and depression. Improvements in sleep timing (e.g., earlier sleep onset) and sleep quality (e.g., faster sleep latency, greater sleep duration, etc.) coincided with decreased depression symptoms. Various mechanisms for this changes will be discussed.

Symposium 13: New Techniques of Sleep Research

Summary

Wake-sleep cycle is a universal phenomenon observed throughout mammals, but the neural circuits generating wake-sleep remain poorly understood. Recent technical advances in the study of animal behaviors provide an invaluable opportunity to address this question at multiple levels, including in genetically encoded fluorescent sensor, vivo multiple-channel recording, EEG-fMRI technique, or calcium imaging of the natural activity patterns of different neuronal types, optogenetic or pharmacogenetic manipulations of the activity of each cell type, and mapping the synaptic connectivity using slice recording or virus-mediated tracing. This symposium will show how these up-to-date technologies can be applied to wakefulness sleep research.

Learning Objectives

1. The application of new Genetically Encoded Fluorescent Sensor
2. Advanced imaging and labeling methods to decipher neuron organization and function
3. Resting-state EEG and its applications
4. The application of miniscope

Target Audience

sleep scientists

Chairs

Min Xu, Yulong Li (Co-chair)

The application of miniscope
Min Xu (China)
The application of new genetically encoded fluorescent sensor
Yulong Li (China)
Advanced imaging and labeling methods to decipher neuron organization and function
Chao He (China)
Resting-state EEG and its applications
Xu Lei (China)

Advanced imaging and labeling methods to decipher neuron organization and function

Chao He, Third Military Medical University

Wake-sleep cycle is a universal phenomenon observed throughout mammals, but the neural circuits generating wake-sleep remain poorly understood. Our lab is interested in the dissecting neural circuits underlying the wake-sleep behavior. Recent technical advances in the study of animal behaviors provide an invaluable opportunity to address this question at multiple levels, including in vivo multiple-channel recording or calcium imaging of the natural activity patterns of different neuronal types, optogenetic or pharmacogenetic manipulations of the activity of each cell type, and mapping the synaptic connectivity using slice recording or virus-mediated tracing. I'm going to show how these up-to-date technologies can be applied to wakefulness sleep research.

Resting-state EEG and its applications

Lei Xu, Faculty of Psychology, Southwest University

Resting state electroencephalography (rsEEG) is a useful technique to investigate the whole brain temporal dynamics of the large-scale neural circuits. With the utilization of high density EEG recordings and machine learning, rsEEG has greatly increased its spatial resolution and reproducibility. In this talk, some state-of-the-art phenomena in the field of rsEEG will be discussed: the large-scale brain network, the reproducible neuroimaging and the individual differences. Then a toolbox, resting-state cortex rhythms (RECOR), is proposed to estimate the power of EEG rhythms in the large-scale brain networks. Our recent progress in the global signal and the reproducibility of rsEEG will be introduced. We conclude that combining resting state EEG with the phenotypes of resting state cognition is a promising approach towards the study of brain networks in cognitive and clinical neurosciences.

Symposium 14: Smart Sensing for Sleep Health

Summary

Sleep, which accounts for almost one-third of the human lifespan, is a complex physiological process, and the quality of sleep directly affects the physical and mental human health. Currently, polysomnography (PSG) is regarded as the gold standard for evaluating sleep staging and sleep-related disorders. However, during the PSG-based sleep scoring, numerous contact sensors are attached to the subjects to acquire multiple physiological signals such as electroencephalography (EEG), electrooculography (EOG), electromyography (EMG), electrocardiography (ECG) as well as respiration. Moreover, the sleep scoring is a very tedious and time-consuming process, in which results are inevitably affected by personal subjective factors. The above limitations have become a key issue that restricts the long-term monitoring and further development of sleep health assessment of PSG-based methods. Smart sensing for sleep health is proposed to achieve large-scale, low-cost and decentralized sleep health monitoring. To date, extensive efforts have been devoted to seeking cost-effective alternatives for objective sleep assessment. Existing technologies estimate sleep health from physiological signals such as EEG signals, body movements, cardiorespiratory signals, and respiratory signals. This symposium will review new sensors and novel non-perceived or wearable technologies that have been emerged in the past years for sleep health sensing, e. g., capacitive coupling ECG, computer audition-based sensors. We will discuss the benefits of these technologies and their major challenges. Furthermore, perspectives will be provided in multi-modal sensor fusion, artificial intelligence technology for future sleep health.

Learning Objectives

1. The latest solutions for non-perceived and wearable sleep health monitoring
2. Design and development of sleep health sensing sensors
3. Technical challenges and approaches for sleep health information processing

Target Audience

Researchers, Company technicians and doctors in fields such as the development of sleep health monitoring sensors, Sleep health information processing technology, Medical research related to sleep health

Chairs

Hong Hong, Bei Wang (Co-chair)

Wearable sensing for sleep health: recent advancements and future prospects
Yuan Zhang (China)
Non-perceived sleep monitoring based on capacitive coupling ECG and respiration collection method

Chengyu Liu (China)

Computer audition for sleep health: perspectives on physical and psychological conditions

Kun Qian (Japan)

Emerging sensor and wearable technology for monitoring sleep quality

Ou Bai (USA)

Monitoring of non-invasive vital signs for detection of sleep apnea: opportunities and challenges

Han Zhang (China)

Wearable Sensing for Sleep Health: Recent Advancements and Future Prospects

Yuan Zhang, Southwest University

From the perspective of daily sleep monitoring, wearable devices can be divided into general-purpose and special-purpose types. General-purpose equipment serves for general sleep quality monitoring, featuring in long-range (perturbation/non-disturbance, integration, convenience, low cost) and prompt response (communication function, slightly lower accuracy, early warning). Dedicated equipment is usually designed for monitoring a certain type of sleep disorder tendency (short-range). The wearing positions include head-mounted, watch-style, vest, patch and mattress. Usually, one type of sensor can only detect a kind of physiological parameter (EEG, ECG, heart rate variability, EOG, EMG, Blood oxygen saturation, breathing airflow, body position, breathing exercise, snoring, etc.). If a general-purpose device can combine sleep quality analysis with several physiological parameters commonly used, and has the typical characteristics of long-range monitoring, it is expected to become a popular product for the general public. In this regard, wristwatch-style devices can use PPG chip, ECG chip, and acceleration sensor to bring breakthroughs through signal collection, analysis and application. However, the relationship between ECG, body position, blood oxygen saturation and other signals on sleep staging needs to be studied. Sleep quality assessment based on rough sleep staging lacks analysis and calculation standards, and it needs to be verified by a cohort and a large amount of samples.

Non-perceived sleep monitoring based on capacitive coupling ECG and respiration collection method

Chengyu Liu, Southwest University

Sleep is a complex physiological process, and the quality of sleep directly affects the health of the human body. There are many types of physiological signals for monitoring sleep, and ECG and respiration have been proved to be effective in sleep detection. Capacitive coupling ECG measurement method, can realize the collection of ECG and respiration in a non-contact way, which is of great significance for sleep monitoring. However, some problems need to be solved, including: electrode design, high input impedance design, static electricity, power line interference, and AI-based signal processing. In terms of electrode design, comfort, the influence of electromagnetic

interference and static electricity needs to be fully considered. Large electrostatic interference can cause loss of ECG signal. In terms of high-impedance circuits, input impedance type above G Ω is necessary, which can ensure the system has a good low-frequency response. Meanwhile, the larger linear input range of the circuit can reduce the influence of motion artifacts. AI analysis includes the signal quality assessment, robust feature extraction and its clinical applications.

Computer audition for sleep health: perspectives on physical and psychological conditions

Kun Qian, The University of Tokyo

Computer audition has been underestimated even though it has already shown promising potentials in sleep health. In this talk, Dr. Qian will introduce his studies on snore sound recognition and heart sound abnormality detection. He will introduce the most recent work on CA-enabled methods for diagnosing the COVID-19.

Emerging sensor and wearable technology for monitoring sleep quality

Ou Bai, Florida International University

This talk will review new sensor and wearable technologies that have been emerged in the past years for sleep monitoring. We will discuss the benefits of these emerging technologies and the major challenges in these technologies including the relevance to the gold standard, e.g., polysomnography (PSG). We will provide future perspectives in multiple sensor integration, artificial intelligence including deep learning technology, and cloud/edge computing for future sleep health and medical care.

Monitoring of non-invasive vital signs for detection of sleep apnea: opportunities and challenges

Han Zhang, South China Normal University

Noninvasive solution of monitoring vital signs during night sleep has the potential of detecting sleep apnea events. In this talk, Dr. Zhang will discuss the opportunities and challenges for non-invasive monitoring for vital signs, and will introduce his studies on sleep apnea detection by using noninvasive vital signs monitoring systems.

Symposium 15: Sleep problems in youth – What's new?

Summary

Sleep problems are prevalent in adolescents and young adults and may be associated with various psychosocial and behavioral factors. This symposium will explore the factors associated with sleep problems in youths and present the latest research on the intervention and prevention for sleep-related issues in this population. Specifically, the symposium will present the research findings investigating the possibility that teenagers with sleep difficulty use technology as a form of cognitive distraction from worry in the evening, and discuss the management of a common sleep-related phenomenon - bedtime procrastination, which is referred to the behavior of delaying bedtime, despite having no external reasons for doing so. In addition, the evidence on using cognitive behavioral approach to manage comorbid insomnia and depression and to prevent insomnia in adolescents will be presented.

Learning Objectives

1. To raise awareness of the opposing hypothesis that technology may not cause sleep problems
2. To be able to understand the concept of bedtime procrastination, which is often overlooked in clinical settings but is associated with multiple clinical indices
3. To learn how to provide interventions for bedtime procrastination in order to improve sleep
4. To learn about the treatment approaches for managing comorbid depression and insomnia in youth
5. To recognize the potential for insomnia prevention and develop ideas for future research on the strategies to promote sleep health in youth

Target Audience

Researchers, clinicians, and trainees (physicians, psychologists, nurses, nurse practitioners)

Chairs

Shirley Xin Li, Chun-Ting Au (Co-chair)

CBT-i for youths with comorbid insomnia and depression
Shirley Xin Li (Hong Kong, China)
Technological distraction when trying to fall asleep
Michael Gradisar (Australia)
Treatment development for decreasing bedtime procrastination: the bed-pro study
Sooyeon Aly Suh (Korea)
Prevention of insomnia in at-risk adolescents
Rachel Ngan Yin Chan

CBT-I for youths with comorbid insomnia and depression

Shirley Xin Li, The University of Hong Kong

Insomnia is one of the most common sleep problems and is often comorbid with depression in youths. The comorbidity of insomnia and depression may lead to adverse outcomes and pose significant treatment challenges. Despite the high comorbidity of insomnia and depression, currently there is no clear guideline on the clinical management of this comorbid condition. Increasing evidence showed that insomnia at baseline predicts depressive symptoms over time in young people, and this observation suggested a unique possibility of altering depression trajectory by addressing insomnia in youth. The present talk will present the preliminary analysis of a randomized controlled trial on the efficacy of cognitive behavioral therapy (CBT) for insomnia and CBT for depression (CBT-D) in youths with comorbid insomnia and depression. This clinical trial involved a total of 112 patients aged 12-24 years (67.9% female) with a diagnosis of insomnia and depression according to DSM-5 diagnostic criteria, who were randomized to one of the following conditions: 8-week group CBT-I (n=33), 8-week group CBT-D (n=39) or waiting-list control (n=40). The preliminary evidence supported the efficacy of CBT-I for improving both sleep and mood in youths with comorbid insomnia and depression.

Technological distraction when trying to fall asleep

Michael Gradisar, College of Education, Psychology and Social Work, Flinders University

Background: Findings from various studies have raised questions as to whether evening technology use causes sleep problems in adolescents. Longitudinal studies show sleep problems emerge prior to increases in evening technology use, and a large survey suggests some teenagers use technology as a sleep aid. The present study explored the possibility that teenagers may use evening technology to distract themselves from pre-sleep worries. Methods: 631 adolescents (Age range 12-18 years, mean age = 15.1, SD = 1.2 years, 46%f) completed an online survey of their technology use, sleep, and purpose of using technology. Adolescents were asked "Do you use any form of technology to help distract yourself from negative or distressing thoughts in the hour before bed?", with response options of "Yes", "Sometimes", or "No". Questions were developed to measure teenagers' evening technology use (i.e., devices, apps), as well as selected questions from the School Sleep Habits Survey to measure their sleep patterns and habits. This study received ethics approval to use opt-out consent for participation. Results: 62% of adolescents reported using technology to distract themselves from negative or distressing thoughts in the hour before bed (24%="Yes"; 38%="Sometimes"). Adolescents who self-reported having a sleep problem were more likely to use technology to distract (p<.001). Sleep latency, sleep onset time, and daytime sleepiness were significantly worse in teenagers who used technology as a distraction (all p<.001). Adolescents who used evening technology use to distract themselves preferred to use portable devices (phones=65%; laptop=14%; tablet=8%), and preferred to watch Youtube (24%), use Snapchat (17%), listen to music (e.g., Spotify; 15%), or Instagram (14%). Conclusion: These cross-sectional findings cast

doubt in the causal role of evening technology use on teenagers' sleep. Instead, this study raises the possibility that teenagers use technology in the evening to distract themselves from unwanted thoughts. However, this coping strategy may not resolve their sleep problem.

Treatment development for decreasing bedtime procrastination: The BED-PRO study

Aly Sooyeon Suh, Sungshin Women's University

Bedtime procrastination is defined as the behavior of an individual going to bed later than intended, despite a lack of external factors. People who report high levels of bedtime procrastination experience insufficient sleep and daytime fatigue, depression, anxiety, and insomnia. Previous studies have attributed longer bedtime procrastination to longer use of media devices prior to bedtime, especially smartphones. The current talk will focus on two studies, a Stage I feasibility study and Stage 2 RCT that investigates the effectiveness of a psychological intervention for reducing bedtime procrastination. The intervention, namely BED-PRO, was developed based on motivational interviewing techniques and behavior modification principles. The talk will present evidence of BED-PRO in reducing bedtime procrastination, and also the effect on other secondary outcomes, such as sleep and clinical indices.

Prevention of insomnia in at-risk adolescents

Rachel Ngan Yin Chan, Department of Psychiatry, The Chinese University of Hong Kong

Adolescence is a vulnerable period predisposing to the onset of insomnia, affecting more than 10% of adolescents. Insomnia tends to run a chronic course with considerable personal distress and health care burden. However, this common and distress sleep problem is often ignored and under-diagnosed. Although the evidence for effective treatments for insomnia in adolescents is increasing, the delay and low prevalence rate of help-seeking behavior, together with the limited accessibility of the effective treatment of established insomnia argue for the need of early intervention and preventive measures, particularly among at-risk adolescents. This talk presents the study findings of an insomnia prevention programme among at-risk adolescents and discusses the future direction in this area.

Symposium 16: Update on Comorbidities of Narcolepsy

Summary

There are many comorbidities of narcolepsy that should warrant special attention More research on this arena will help enhance quality of narcolepsy patients. The prevalence of narcolepsy in Korea is unknown. The associations between narcolepsy and other autoimmune disorders have rarely been reported. We sought to determine the prevalence of narcolepsy and diseases associated with narcolepsy using the National Health Insurance (NHI) database. Obstructive sleep apnea (OSA) is a common comorbid condition in narcolepsy patients. Since OSA and narcolepsy share the most common symptom of excessive daytime sleepiness, OSA can mask the treatment effect of narcolepsy and influence the quality of life in narcolepsy patients. Here we will review narcolepsy patients who have comorbid OSA pathology. Moreover, we will review recent literatures on OSA in narcolepsy patients. Psychiatric disorders in narcolepsy patients can detrimentally influence quality of life in narcolepsy patients. Especially, in the time of COVID-19, management of narcolepsy patients with psychiatric disorders can be challenging. Here we review narcolepsy patients with psychiatric disorders (depression, anxiety and psychoses) in the time of COVID-19, along with pertaining recent literatures.

Chairs

Seung Chul Hong

Overview
Seung Chul Hong (Korea)
Narcolepsy and autoimmune disorders
Ji-Hye Oh (Korea)
Narcolepsy and obstructive sleep apnea
Sung Min Kim (Korea)
Narcolepsy and psychiatric sisorders, with consideration for COVID-19
Yoo Hyun Um (Korea)

Symposium 17: Pediatric Sleep Hypoventilation Syndrome

Summary

Hypoventilation is a kind of disease that causes hypercapnia and hypoxemia due to insufficient alveolar ventilation, which is the main cause of death. This disease often appears first during sleep periods, and even when further advanced, has the most serious pathophysiological consequences during night sleep. Several common hypoventilation syndromes in children include: Congenital Central Hypoventilation Syndrome (CCHS), Obesity Hypoventilation Syndrome (OHS), Hypopnea syndromes associated with chest wall deformities, Neuromuscular Disease (NMD) and some others caused by and abnormality of, or affecting the respiratory center. If a patient has a primary disease that leads to insufficient ventilation, the doctor should be alert to the occurrence of nocturnal hypoventilation. Timely diagnosis and treatment can improve the gas exchange of the patient. In particular, Phox2b gene is a diagnostic gene of CCHS, which can make the structure and function of central respiratory chemoreceptors abnormal, cause the central respiratory driving force weakened, and eventually lead to central hypoventilation. Treatment can often be implemented using Noninvasive Ventilation, which is a relatively simple device, is easily tolerated by patients and has recognized benefits for the quality and duration of life when used for treatment of sleep hypoventilation syndrome(s). In this symposium, the speakers are going to discuss the following topics, aiming to provide an up-to-date review of the pathophysiology, diagnosis and treatment of hypoventilation syndrome and to share their experience of managing the disorders Internationally. 1. Sleep related Hypoventilation Syndrome in Children. 2. Phox2b and Breathing. 3. Experience of CCHS from Australia. 4. Noninvasive Ventilation for Pediatric Hypoventilation Syndrome

Learning Objectives

1. Gain a better understanding of the Pediatric Sleep Hypoventilation Syndrome.
2. Discuss the pathogenic mechanism of CCHS.
3. Share the experience of CCHS from Australia.
4. Up-to-date literature review on Noninvasive Ventilation for pediatric hypoventilation syndrome.

Target Audience

Pediatricians, physicians, psychologists, psychiatrists, nursing colleagues and allied health care workers interested in childhood sleep apnea

Chairs

Zhifei Xu, Aroonwan Preutthipan (Co-chair)

Sleep related hypoventilation syndrome in children
Zhifei Xu (China)
Noninvasive ventilation for pediatric hypoventilation syndrome
Aroonwan Preutthipan (Thailand)

Phox2b and breathing
Sheng Wang (China)
Experience of CCHS from Australia
Karen Waters (Australia)

Sleep related Hypoventilation Syndrome in Children

Zhifei Xu, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health

Hypoventilation is a kind of disease that causes hypercapnia and hypoxemia due to insufficient alveolar ventilation, which is the main cause of death. Several common hypoventilation syndromes in children include: Congenital Central Hypoventilation Syndrome (CCHS), Obesity Hypoventilation Syndrome (OHS), Hypopnea syndromes associated with chest wall deformities, Neuromuscular Disease (NMD) and some others caused by and abnormality of, or affecting the respiratory center. If a patient has a primary disease that leads to insufficient ventilation, the doctor should be alert to the occurrence of nocturnal hypoventilation. Timely diagnosis and treatment can improve the gas exchange of the patient.

Noninvasive Ventilation for Pediatric Hypoventilation Syndrome

Aroonwan Preutthipan, Division of Pediatric Pulmonology, Department of Pediatrics Ramathibodi Hospital, Mahidol University

1.Our experience in noninvasive ventilation (NIV) in children since 1995 2. Advantages and benefits of NIV, comparing to invasive mechanical ventilation via tracheostomy 3. How to initiate, select mode, mask fitting, set up the ventilators at bedside and under polysomnography 4. Complications and how to minimize 5. Techniques to improve adherence

Phox2b and Breathing

Sheng Wang, Department of Physiology, Hebei Medical University

The role of Phox2b-expressing brainstem neurons and deficiency of these neurons associated with hypoventilation as observed in CCHS.

Experience of CCHS from Australia

Karen Waters, Discipline of Child and Adolescent Health, University of Sydney David Read Sleep Laboratory, The Children's Hospital at Westmead

As a participant in a recent review of the home ventilation programs for Children in Australia, I will review the characteristics of children who are ventilated in their homes, and the recommendations made in a position paper from the Respiratory and Sleep Physicians in Australia.

Symposium 18: Sleep deprivation in Asian children and Adolescents – any evidence? What should we do?

Summary

Sleep deprivation is prevalent among children and adolescents, especially in Asia. Numerous sleep interventions have been initiated to tackle this alarming situation, albeit the evidence has been contradictory, particularly across different cultures. This symposium will bring together a diverse international group of researchers to address the current situation of sleep deprivation in Asian children and adolescents. In particular, the application of technologic advances in measuring sleep and its impact, existing and novel strategies in improving sleep health across -countries and cultural background will be explored. Prof. Chee's talk will describe how the information derived from sleep trackers compares to that as obtained from sleep dairies / self-report and PSG. In turn, the implications this has for the measurement of sleep and the creation of sleep duration recommendations for Asian people will be discussed. Dr. Massar's talk will examine how vigilance and willingness to deploy effort can be affected by rewarding performance, fatigue and sleep deprivation. Dr. Wang's talk will compare the secular trends of sleep/wake patterns in school-aged children in Hong Kong and Shanghai, two major metropolitan cities in China with two different policies that school start time was delayed in Shanghai, but advanced in Hong Kong in 10 years' time. Subcultural differences in sleep/wake patterns, and the benefits and barriers of delaying school start time for optimizing sleep health in school-aged children will be discussed. Dr. Kim will talk about delay school start project in Korea. He will discuss the prevalent problem of sleep deprivation and the impact of delay school start in Korea. Dr. Chan's talk will address the issue of late bedtime in adolescents, a common phenomenon in Hong Kong. She will discuss alternative approaches such as advancing adolescent bedtime by using motivational interviewing strategy, to improve adolescent sleep health. Preliminary data of this approach will also be presented.

Learning Objectives

Describe the application of advance technology in monitoring sleep and its impact. Understand the impact of sleep deprivation on neurocognitive impact especially on vigilance and willingness to deploy effort. Recognize and discuss the cross-cultural differences in sleep/wake patterns in Asian regions. Describe the efficacy of sleep intervention, notably delay school start in Asian populations and also the barriers in implementing such program in school setting. Discuss alternative approaches in addressing the issue of late bedtime in Asian adolescents.

Target Audience

Health care professional interested in promoting sleep health in children and adolescents, educators, policy makers, pediatric sleep researchers, psychologists.

Chairs

Yun Kwok Wing, Michael Chee (Co-chair)

Measuring sleep in the 21st century – how do we harness wearable data
Michael Chee (Singapore)
Modulation of willingness to deploy effort and framing effects by reward, fatigue and sleep
deprivation
Stijn Massar (Singapore)
A tale of two cities—ten-year secular trends in sleep/wake patterns in shanghai and Hong Kong
school-aged children
Guanghai Wang (China)
A benefit of delay school start time in Korea
Tae Won Kim (Korea)
Late owl city and sleep deprivation in adolescents – is it effective to advance bedtime
Rachel Ngan Yin Chan (Hong Kong, China)

Measuring sleep in the 21st Century – how do we harness wearable data

Michael Chee, Centre for Sleep and Cognition, Yong Loo Lin School of Medicine, Duke-NUS, National University of Singapore

Because East Asian students consistently top scholastic rankings, policy makers find it difficult to accept that poor sleep has significant negative effects. Empirical studies conducted using different combinations of sleep opportunities over multiple nights in adolescents show that this belief is incorrect. Cognitive testing suggests significant negative effects on vigilance, long-term memory and mood. Survey data show a strong dose dependent effect on sleep duration and mental wellbeing. Afternoon naps are helpful, but more research is needed to fine tune them. At this point in time, it appears that the US NSF sleep recommendations for adolescents likely apply to East Asians as well. Large-scale tracking of sleep using consumer wearables is an opportunity to collect advisory data, but challenges need to be overcome before this becomes a reality.

Modulation of willingness to deploy effort and framing effects by reward, fatigue and sleep deprivation

Stijn Massar, Centre for Sleep and Cognition, Yong Loo Lin School of Medicine, Duke-NUS, National University of Singapore

Sleep deprivation (SD) and fatigue interfere with our ability to perform cognitively demanding tasks. Besides the effects on the primary processes involved in cognitive performance, of SD and fatigue may particularly impact performance through a reduced motivation to exert effort. Studies

on effort-based decision making have revealed a specific neural circuitry related to the motivation to perform. In this presentation, I will discuss a series of studies in which we show that SD and fatigue lead participants to make more effort-avoidant choices. In addition, providing individuals with performance-contingent rewards, can partly alleviate performance decrements that are normally observed during SD, and can restore physiological measures of effort (i.e. pupil diameter). Lastly, I will discuss the neural mechanisms underlying motivation and its reduction under SD and fatigue. I will discuss how these findings have relevance to a wide range of cognitive tasks (e.g., vigilance, working memory, word typing).

A Tale of Two Cities—Ten-Year Secular Trends in Sleep/Wake Patterns in Shanghai and Hong Kong School-Aged Children

Guanghai Wang, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine

Study Objectives: To compare the secular trends of sleep/wake patterns in school-aged children in Hong Kong and Shanghai, two major metropolitan cities in China with two different policies that school start time was delayed in Shanghai, but advanced in Hong Kong in 10 years' time. Methods: Participants were from two waves of cross-sectional school-based surveys of children aged 6 to 11 years. In Shanghai, 4,339 and 13,795 children participated in the 2005 and 2014 surveys, respectively. In Hong Kong, 6,231 and 4,585 children participated in the 2003 and 2012 surveys, respectively. Parents reported their children's bedtime and wakeup time, and thus sleep duration, short sleep ($\leq$ 9 hours) and weekend oversleep (difference in sleep duration between weekday and weekend > 2 hours) were determined. Results: Hong Kong children had later bedtime and wakeup time and slept consistently less than their Shanghai counterparts at both survey time points. The shorter sleep duration was particularly marked during weekdays. Over the interval period, weekday sleep duration significantly decreased from 9.2 to 8.9 hours as wakeup time became earlier for Hong Kong children, but increased from 9.4 to 9.6 hours as wakeup time became later for children in Shanghai. Children from both cities slept longer on the weekends. Prevalence of weekend oversleep significantly increased in Hong Kong children, but no interval change was found in Shanghai children. Conclusions: The findings indicate subcultural differences in sleep/wake patterns in Shanghai and Hong Kong school-aged children. In particular, sleep duration had increased for Shanghai children, but decreased for Hong Kong children over 10 years. The benefits and barriers of delaying school start time for optimizing sleep health in school-aged children should be further explored.

A benefit of delay school start time in Korea

Tae Won Kim, Department of Psychiatry, The Catholic University of Korea

Background and Objective: The purpose of this study was to investigate the effect of delaying school start time on sleep quality, emotion and performance in Korean adolescents. Methods: Data were collected in 2 months and 12 months each using self-administering questionnaires by

238 students at a middle school located in Gyeonggi province. Questionnaires were composed of demographic data and various sleep and emotion related scales including Pittsburgh Sleep Quality Index (PSQI). Students were divided into two groups of increased or decreased total sleep time (TST). Wilcoxon signed rank test was used to identify significant differences in 2 months vs. 12 months in sleep parameters, emotions and school performance in both groups. Results: In both groups, PSQI total score and sleep efficiency significantly improved from 2 month to 12 month data. There were significant improvements in depression, stress, behavioral aggression, and verbal aggression in increased TST group. Increased TST group showed advancements in subjective feeling of happiness and number of being late for school per week between baseline and 12 months. Decreased TST group showed significant differences in subjective feeling of happiness, number of being late for school per week, sleepiness during class, concentration on class, relationship with friends, energy in daily life, general feeling in school, willingness to go to school, and anger in school life.

Late Owl city and sleep deprivation in adolescents – is it effective to advance bedtime

Rachel Chan, Department of Psychiatry, The Chinese University of Hong Kong

Lack of sleep in adolescents is becoming a concerning health issue and associated with an array of negative impacts on academic, mood, cognitive, cardiovascular, metabolic and general well-being. Early school start combined with natural circadian delay during puberty have contributed to significant sleep loss in adolescents, especially during school days. Although delaying school start time is found to be an effective measure to improve adolescent sleep, the implementation of later school start time has met many practical obstacles and difficulties. Thus, we have to try another feasible, practical and alternative implementation to ameliorate the sleep deprivation in adolescents, especially for those adolescents with late bedtime. Thus, advancement of adolescent bedtime becomes another potential approach for interventional proposal. A group-based sleep intervention using motivational interviewing and text message reminders were developed with the aim to advance adolescent bedtime. The preliminary findings and the obstacles in delivering group-based motivational enhancement therapy for sleep deprivation, and the future research direction will be discussed in this talk.

Symposium 19: Fatigue – State of Art, Epidemiology and Therapeutical Interventions

Summary

Sleep disorders, but also neurological and psychiatric disorders are often linked to fatigue, tiredness and / or excessive daytime sleepiness. It is usually difficult to make a distinction - our symposium will try to give an overview about this topic and the limitations of the terminology and the various associated symptomatic. Even we will present fatigue and its problems in elderly, epidemiological data for tumor-associated fatigue, and therapeutic options for tumor-associated fatigue. For example, 30-40% of all cancer patients suffer from cancer-related fatigue (CrF) due to a tumor disease and / or tumor therapy. CrF is defined as a stressful, persistent, subjective feeling of physical, emotional and / or cognitive exhaustion in the context of cancer and / or cancer treatment, whereby the symptoms are not proportional to the physical and / or mental activity, but they disturbed the physical and mental activity. This chronic fatigue of cancer patients is accompanied by sleep disorders (30-50%), pain (45-59%), anxiety / anxiety disorders (20%) and depression (10-25%) as well as cognitive impairment, medicinal side effects, nutritional disorders and lack of exercise. The occurrence and chronification of CrF are associated with inflammatory processes. The increased levels of pro-inflammatory cytokines in CrF disrupt the tryptophan-serotonin, dopamine and noradrenalin metabolism of CNS, which contributes to the promotion of depression. In addition, the increased metabolism of lipids due to the pro-inflammatory cytokines leads to the long-term maintenance of the inflammatory reaction, which is particularly pronounced in Western nutrition with a high proportion of pro-inflammatory omega-6 fatty acids (n-6-FS). Omega-3 fatty acids (n-3-FA) can compensate the pro-inflammatory effects of n-6-FS and thus effectively control inflammatory processes. The CrF represents a serious comorbidity of the underlying disease and of the tumor-specific treatment and has enormous physical, psychological, social and economic effects.

Learning Objectives

1.Definition of Fatigue and it's distinction of related terms

2.Sleep Disorder-Related Fatigue - State of Art

3.Epidemiology of Sleep Disorder-Related Fatigue

4.Therapeutical Interventions of Fatigue

5.Cancer-Related Fatigue (CrF)

Target Audience

Sleep Specialists & Scientists; Doctors of Psychiatry, Neurology and Internists; Doctoral Students; Technicians Nurses

Chairs

Büttner-Teleagă Antje, Richter Kneginja (Co-chair)

Cancer related fatigue (CRF) – epidemiological data. Results of a multicenter study
Antje Büttner-Teleaga (Germany, Korea)
Effects of cognitive behavior therapy in patients with CRF
Kneginja Richter (Germany, Macedonia)
Distinction between fatigue, sleepiness and tiredness. State of art
Peter Geisler (Germany)
Fatigue in elderly - geriatric patients
Nikolaus Netzer (Germany, Austria)

Cancer Related Fatigue (CRF) – Epidemiological Data. Results of a Multicenter Study

Büttner-Teleagă Antje, Department of Psychiatry, University Witten-Herdecke; Institute of Cognitive Science, Woosuk University

Introduction: Despite many advances in psycho-oncological research and care, structured psycho-oncological care through psycho-oncological services (POD) is currently not sufficiently established in the German Comprehensive Cancer Centers (CCC). The research project should carry out it and should research the psycho-oncological counseling and care in the various cancer centers from an individual as well as structural point of view. The project was cooperation with all 13 CCCs. In this multicentre study, the psychosocial stress in the patients was systematically determined, the need and the concerns of the patients for psycho-oncological help was researched for the users as well as the non-users of psycho-oncological support. The various criteria were recorded over four measurement times. Furthermore, special cancer-specific comobidities - such as insomnia, fatigue and pain - were also recorded. The fatigue results are to be presented in my lecture. Methods: All patients with malignant tumor diseases, who were older than 18 years and were being treated in one of the CCCs. Patient access was coordinated by the local cooperation partners Berlin, Dresden, Erlangen, Essen, Frankfurt / a. M., Freiburg, Hamburg, Heidelberg, Cologne-Bonn, Nuremberg, Tübingen, Ulm and Würzburg. All cancer patients should gradually receive psycho-oncological counseling and care. All endpoints of the study protocol should be evaluated for T0 to T3 - including Cancer-related Fatigue (CrF). The longitudinal multicenter study included 1,511 T1-patients with cancer (58.2% females – 41.8 males, mean age: 55.8 years; T3: N = 836). CrF was measured by the EORTC-Fatigue. Socio-demographic and clinical data, as well as psychological parameters (Distress Thermometer, PHQ-9, GAD-7, SF-12, SSUK-9, Pain Scale and Insomnia Severity Index (ISI)), were assessed at baseline (T1), even 6 months later (T2) and 12 months later (T3). Results: In our sample, a high prevalence of relevant fatigue symptoms (38.7 %, moderate and severe) was found. When fatigue was present at T1, this problem was persistent after one year in 28.4 %. However, significantly more women suffered from fatigue symptoms. Fatigue was associated with many clinical and psychological parameters, especially with insomnia ($r = 0.5$). In all participants,

levels of distress, depression, and anxiety decreased from T1 to T2 (p's < 0.016). Discussion: Cancer-related Fatigue (CrF) is a common in cancer patients. Although medical and psychological parameters improved during the 12-month course of cancer treatment. The results show that fatigue is highly persistent, especially in women. This indicates that adequate support for those affected is needed.

Effects of Cognitive Behaviour Therapy in Patients with CRF

Richter Kneginja, University Hospital for Psychiatry and Psychotherapy Nuremberg; Medical Faculty, Goce Delčev University of Štip

Introduction: Insomnia is a very common and frequent comorbidity in cancer patients. The cancer-related insomnia rate is nearly three times higher than that in generally. Different analyses have shown that 30-50% (up to 95%) of cancer patients have severe sleep difficulties like insomnia symptoms or like insomnia syndromes. Cancer-related insomnia are characterised by delayed sleep onset, sleep maintenance disorders, reduced total sleep time and / or early-morning awakenings, and are associated with excessive daytime sleepiness, fatigue, impaired performance and daytime wellbeing. Results: We conducted systematic literature review including 87 studies analysed for the topic sleep and sleep disorders in cancer, 26 studies for the topic sleep and fatigue in cancer, and 52 studies for the topic sleep disorders in cancer. The prevalence of sleep disturbences and / or sleep disorders in cancer is up to 95%. Discussion: Sleep disturbances in cancer can be caused by different pathophysiological mechanisms. Side effects of the anti-cancer treatment and the psychological status of the patients associated with cancer can trigger some sleep disorders and worsen the chronical fatigue. Early detection of sleep disorders especially Insomnia in Patients with Cancer is important, because CBT –I as evidence based Therapy for Insomnia can improve both the insomnia and fatigue symptoms.

Distinction between Fatigue, Sleepiness and Tiredness. State of Art

Geisler Peter, University Centre for Sleeping Disorders, Regensburg-Donaustauf

When the consequences of insufficient sleep are discussed, often the expressions fatigue, sleepiness and tiredness are used almost interchangeably without adherence to a precise terminology. However, to describe and understand these phenomena, it is important to differentiate these terms. All of them connotate complex, multidimensional concepts. To quantify the dimensions, a multitude of objective measurements and subjective scales are used. The dimensions frequently overlap, but correlations among them are generally low to moderate. A common feature is that they are a physiological consequence of prolonged wakefulness, insufficient sleep and / or high effort, but can also emerge in pathological conditions. The term fatigue refers to a sensation of reduced capacity not proportional to prior load in a clinical context, while in ergonomics, it is used to describe reduced function proportional to prior load. Sleepiness is defined as inability to stay awake and alert and can be objectively measured in defined conditions by assessing the time to fall asleep. Tiredness, on the other hand, is a sensation like hunger, which cannot be measured objectively. For assessment,

frequent correlates of tiredness are used, like reduced attention, slowing or impaired cognitive performance. In this talk, the differentiation of these concepts will be discussed and methods of assessment will be introduced.

Fatigue in Elderly - Geriatric Patients

Netzer Nikolaus, Hermann Buhl Institute; Faculty of Psychology and Sport Science, University of Innsbruck

Fatigue in the elderly is a common problem. However, not all complaints about fatigue by persons older than 65 years, the still defined definition for "elderly ", has an organic or psycho-organic correlation. Often fatigue in elderly results from a phase shift in sleep, most often advanced sleep phase syndrome. This means they try to shift the sleep onset towards an earlier time in order to receive the ideal 7 hrs or more, when they wake up. Fatigue in elderly often results from failing this aim and not accepting a natural polyphasic sleep with ageing. Aside from this sociocultural cause of elderly' fatigue, there exist of course an extensive variety of organic reasons for fatigue. Beside pain syndromes causing fragmented and disrupted sleep, cardiovascular, kidney and metabolic diseases are to be named here. Neurological disorders like Parkinson's disease and Alzheimer's dementia are most often causing fatigue in the elderly. The later in a final stage increasing sleep times linear from 7-8 hrs up to 20-22 hrs sleep versus wake time. The cause of fatigue in the elderly has to be diagnosed and treated to guarantee a sufficient quality of life in the last third of the lifespan.

Symposium 20: Work and intervention accomplished in hospitals during the COVID−19

Summary

COVID-19, a global pandemic, is also a public health emergency of global concern. It arouses severe psychological effects on humans and poses a huge challenge to the society's medical system. This symposium will highlight the remarkable work and share some successful experiences in dealing with the patients psychological distress during the COVID-19 epidemic in hospitals. The work which was accomplished in hospitals during the epidemic will be introduced. Based on the findings from the work, some risk factors of psychological distress among hospitalized patients will be discussed. In addition, the more specific details about the intervention method will be talked about, aiming to provide new insight into the prevention and treatment for COVID-19 related psychological problems among hospitalized patients.

Learning Objectives

1.To understand the importance of psychological intervention concerning hospitalized patients
2.To learn about the present evidence about psychological distress among hospitalized patients
3.To learn about the previous successful work and achievement in dealing with hospitalized patients' psychological problems
4.To learn about the effective future intervention methods from the remarkable and enlightening experiences

Target Audience

Psychiatrists, psychologists, and health care professionals

Chairs

Bin Zhang, Cailan Hou (Co-chair)

From the perspective of public health and psychiatry, we can see the crisis, challenge and response after the pandemic
Cailan Hou (China)
The work of the psychiatric department of the Second Xiangya Hospital of Central South University during the COVID-19 outbreak
Yan Zhang (China)
The psychological intervention at FANGCANG Hospital in Wuhan city: implementation and thoughts
Chuan Shi (China)
Working with COVID-19 patients with anxiety and insomnia - experiences from Shanghai
Jun Chen (China)

From the perspective of public health and psychiatry, we can see the crisis, challenge and response after the pandemic

Cailan Hou, Guangdong Mental Health Center

Covid-19, a global pandemic, is also a public health emergency of global concern. This crisis have bring great pressure to the whole world. When the epidemic subsides and we begin to return to normal or relatively normal life, epidemic related sequelae will appear and last for months and years. We have experienced natural and man-made disasters before, but in our lifetime, nothing can match the scope of the covid-19 crisis. In the past, although we know that these psychological effects are penetrating into people, we still don's t know enough their degree or impact of COVID-19. The rising incidence rate of various mental disorders and cumulative psychological pressure that our population will bear will further increase the mental health and primary health care system and expose the limitations of its infrastructure, labor and accessibility. It is also possible that the ratio of depression and Dutch act behavior will increase in the future. To stop this trend, we should start with those who are at greater risk of adverse mental health consequences, including those with previous mental disorders who are vulnerable to such stress. These people may need to adjust their treatment and increase the frequency of contact with mental health providers in order to meet the challenge of mental health. In addition, through routine screening for depression, anxiety and drug use, strengthening mental health monitoring in primary health care, and providing more mental health services in primary health care, more affected individuals will be able to receive mental health treatment in familiar primary health care environment. Mental health and emergency management communities should work together to identify, develop and disseminate evidence-based resources related to disaster mental health, mental health classification and referral, special population needs, death notification and bereavement care, and included in the general epidemiological services.

The work of the psychiatric department of the Second Xiangya Hospital of Central South University during the COVID-19 outbreak

Yan Zhang, Second Xiangya Hospital of Central South University

COVID-19 is not only posing serious public health threat to humans, but also causing severe psychological effects. Psychological Assistance team of the Second Xiangya Hospital provided mental health services for people in Wuhan during COVID-19 epidemic period. Our team accomplished the following three works: first, providing emergency psychological interventions for patients infected with the novel coronavirus. In addition, we offered mental health services to medical staff in Wuhan. Finally, we cooperated with government to compose the recommendation of mental health service on post-epidemic. We also have performed some works of scientific research. We have found that patients with COVID-19 suffered moderate to severe psychological distress including depression, anxiety, sleep and eating disorders, and even a third of patients who had recovered from COVID-19 still had obvious psychological distress 1 month after discharge. Depression and anxiety among the community workers are significantly higher than that of

community controls, in particular those who had contact history with patients with confirmed infection. Base on above findings, we conducted a further investigation. We found that being isolated and the severity of COVID-19 could explain depression and anxiety levels in patients. The psychological distress among patients also was associated with their poor resilience and negative appraisals. Furthermore, the change of negative appraisals in the COVID-19 social impact (i.e., financial stress, stigma, and concerns about family) might play a major role in reducing their depression and anxiety.

The psychological intervention at FANGCANG hospital in Wuhan city: Implementation and thoughts

Chuan Shi, The Peking University Sixth Hospital

Background: along with the pandemic of covid-19 in Wuhan city in the beginning of 2020, the mental health problem was gradually to be an important thing which should be pay attention to, psychological intervention among patients and medical staff were seriously needed, especially in FANGCANG hospital. Method: Government appoint 430 mental health professionals to the site to conduct psychological assessment and intervention. Our team distribute related self-help books, teaching the nurses about consultation skills, broadcasting and online support system application, interview patients bedside. Results: We found anxiety, insomnia, depression, PTSD were the common issues in FANGCANG city, patients' symptom were relieved after psychological intervention. Conclusion: Psychological service is an important part in the process of medical rescue, what is the optimal methods should be discussed in the future.

Working with COVID-19 patients with anxiety and insomnia - experiences from Shanghai

Jun Chen, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine

Anxiety and insomnia are common symptoms with COVID-19 patients, especially in the isolation ward setting. Induced by the stress of getting COVID-19, anxiety and insomnia impact patients' conditions significantly. In order to support liaison and cousiltion psychiatry in the COVID-19 isolation ward, psychiatrists are involved into the emergency medical team during the pandemic. In this topic, we will share the experience from Shanghai Mental Health Center to provide mental health service in the isolation ward. Especially how to identify, diagnose, and intervene for anxiety and insomnia.

Symposium 21: Artificial Intelligence (AI) for Sleep Analysis

Summary

Nowadays, sleep disorders like insomnia, restless legs syndrome, narcolepsy, sleep apnea, etc. are affecting more and more people. It can deteriorate the quality of life, affect the overall health, and even contribute to mental health problems like depression, anxiety, or cognitive disorders, etc. and exacerbate chronic health issues, such as heart disease, diabetes, hypertension, etc. Polysomnography, as the gold standard, remains the cornerstone of objective testing for sleep analysis and results in large amounts of electrophysiological data. Analysis of electrophysiological data requires visual inspection by trained scoring technicians. While, the visual inspection of data is an effort-intensive and time-consuming process, and may also involve subjective interpretation. With the emergence of technology on artificial intelligence like machine learning, deep learning, transfer learning, expert systems, etc., AI is expected to pave the way for dealing with the tremendous electrophysiological data, offer an objective and streamline interpretation of sleep disorders, provide new insights on sleep alterations and sleep disorders using heterogeneous data like fMRI, fNIRS. This symposium aims at offering a brief presentation and discussion on the latest developments and emergent technologies in AI for sleep data analysis, like accurate classification of sleep stages, characterization of sleep disorders subtypes, etc., and the potential applications of AI in sleep diagnosis and treatment.

Learning Objectives

1.AI in sleep staging

2.AI in sleep apnea detection

3.AI in micro-sleep event detection

4.AI in fMRI images for sleep analysis

Target Audience

Researchers with biomedical engineering, artificial intelligence, signal processing, image processing, etc. background, clinical technicians on sleep analysis, clinical physicians on sleep, engineers.

Chairs

Chen Chen, Qihong Zou (Co-chair)

Multi-modality neuroimaging in sleep: recent advances and role of AI

Qihong Zou (China)

Artificial intelligence and feature engineering for sleep monitoring

Wei Chen (China)

A gearing toward an intelligent ecosystem for sleep monitoring

Theerawit Wilaiprasitporn (Thailand)
Sleep staging technology based on machine learning
Lijuan Duan (China)
Title of presentation automatic sleep scoring based on multimodality polysomnography data
Fengyu Cong (China)

Multi-modality Neuroimaging in Sleep: Recent Advances and Role of AI

Qihong Zou, Peking University

Multi-modality neuroimaging techniques including EEG, fMRI, MEG and PET provided both high temporal and spatial resolutions in investigations of large-scale brain networks and activities. Fusion of multi-modality neuroimaging techniques have been extensively used related to neurophysiological and brain networks related to circadian rhythms, sleep pressure, sleep stages and progression from sleep health to sleep disease status. Advances in AI has been shown its tremendous role in sleep-stage classification and sleep-event detection based on physiological parameters such as EEG, ECG, and EOG. Pilot study of AI on neuroimaging data has demonstrated that automatic sleep staging could be performed using only fMRI functional connectivity data. Moreover, whether not have a dream during sleep could be predicted by both fMRI and high-density EEG data. Future AI study on multi-center, large-sample and multi-modality neuroimaging dataset in both sleep-healthy populations and sleep disorder patients are warranted.

Artificial Intelligence and Feature Engineering for Sleep Monitoring

Wei Chen, School of Information Science and Technology, Fudan University

Sleep, as an indispensable part of daily life, contributes to self-repairing and self-recovering. Nowadays more and more people are suffering from sleep disorders. It not only deteriorates the quality of life and raises health risks, but also becomes a significant cause of morbidity and mortality and imposes a significant economic and social burden. Seeking innovative solutions and new technologies for sleep monitoring is very important. The emerging development on artificial intelligence and feature engineering has inspired innovation in sleep research. Artificial intelligence including traditional machine learning methods, deep learning methods, and expert systems paves the way for accurate processing of vast amounts of multi-modal sleep data, for sleep staging, efficient detection of sleep alterations and sleep disorders, etc. In this talk, artificial intelligence and feature engineering methods will be presented for sleep monitoring, especially for sleep staging and sleep disease analysis. With multidisciplinary information fusion of clinical sleep science, biomedical engineering, artificial intelligence and feature engineering, new techniques have the potential to achieve accurate and efficient sleep monitoring for people ranging from babies to the aging population.

A Gearing Toward an Intelligent Ecosystem for Sleep Monitoring

Theerawit Wilaiprasitporn, Bio-inspired Robotics and Neural Engineering Lab, School of Information Science and Technology, Vidyasirimedhi Institute of Science & Technology

The recent journal published in the Institute of Electrical and Electronics Engineers (IEEE) database, with "sleep monitoring" as a keyword, presents the rising trend in using artificial neural networks and deep learning (AI) for sleep analysis and prediction around 2018. Apart from standard polysomnography (multi-modal sensing), the researchers have proposed alternative sensors with fewer modalities for a more user-friendly system such as biopotential measurement (EEG, EMG, and EOG), wrist-worn photoplethysmogram (PPG), neck PPG, consumer pulse oximeter, innovative mattress, and radar system. The lower numbers of sensors come with the higher demands of AI-based algorithms. In this talk, we present our two recently published works in the direction of AI in sleep medicine. They are MetaSleepLearner and SleepPoseNet. MetaSleepLearner is an algorithm in dealing with the training strategy on the biopotential datasets across multiple sleep centers. We also prove the concept of implementing MetaSleepLearner for man-machine collaboration (industry 5.0 scheme), which can help sleep experts reduce the labeling loads during the diagnosis. We interpret whether MetaSleepLearner works as similar to the sleep expert by using an explainable AI technique at the end of the study. Source code is available at https://github.com/IoBTVISTEC/ MetaSleepLearner. SleepPoseNet is an algorithm in dealing with sleep postural transition recognition using ultra-wideband (UWB) radar. UWB radar sensing has advantages in many terms, such as contact-free sensors, small and easy to set up, low power consumption, and non-intrusive privacy. SleepPoseNet exhibits the potential to support the current sleep monitoring systems' usage to measure vital signs and sleep stages. Raw datasets, code examples, and other supporting materials are available on https://github.com/IoBT-VISTEC/SleepPoseNet.

Sleep Staging Technology Based on Machine Learning

Lijuan Duan, Beijing University of Technology

Sleep is a physiological activity vital to human health. In clinical medicine, sleep staging is one of the key steps for effective diagnosis and treatment of sleep-related diseases. Manual sleep staging is undoubtedly a huge and arduous task, and it is also challenging work in the diagnosis. With the continuous development of computer science and technology, more and more algorithms are used in this tedious work to reduce the workload of doctors. In the research based on traditional machine learning methods, the effectiveness of feature extraction relies too much on the knowledge and experience of experts on sleep signal analysis. Sleep stage classification tasks based on deep learning algorithms and other technologies are a trend in the current sleep staging research. Its advantages are reflected in the realization of efficient and objective data recognition through sleep data-driven methods. Since deep learning requires a large amount of data, this poses a challenge to the privacy protection of users. Besides, most deep learning models are black-box models driven by data, and the interpretability of the models is relatively poor. We will demonstrate the two proposed

algorithms for automatic sleep staging, which can achieve efficient and accurate results. In these methods, time-frequency features are extracted to simulate doctors' cognition of sleep physiological signals. Furthermore, a deep learning network is used to extract multi granularity features or spatiotemporal relationship features of time-frequency information, which is used to expand the distinguishability of features. Our models are carried out from two aspects: the granularity of features and the multimodality of data, and the final experimental results show the effectiveness and stability of our works.

Automatic Sleep Scoring Based on Multimodality Polysomnography Data

Fengyu Cong, School of Biomedical Engineering Dalian University of Technology

Over the past decades, probably due to our hectic lifestyle in modern society, complaints about sleep problems have increased dramatically, affecting a large part of the world's population. The polysomnography (PSG) test is a common tool for diagnosing sleep problems, but the scoring of PSG recordings is an essential but time-consuming process. Therefore, automatic sleep scoring becomes crucial and urgent to settle the growing unmet needs in sleep research. In this presentation, we introduce popular scoring methods and analyze their advantage and drawback. Then, we further describe our research motivation and introduce our achievement. Specifically, our work extends the previous research on automatic sleep scoring from two aspects. One is to extensively explore signal modalities and feature types related to automatic sleep scoring. Our results demonstrate that diverse features and signal modalities are coordinative and complementary, which benefits the improvement of classification accuracy. The other one is to develop automatic sleep scoring tools that can accommodate different datasets and sample populations without adjusting model structure and parameters across tasks. In summary, this research finding will advance the understanding of underlying mechanism during automatic sleep scoring and clarify the association between manual scoring criteria and automatic scoring methods. The joint analysis of multiple signals enhances model versatility, which inspires the construction of cross-model in the field of automatic sleep scoring. Moreover, the proposed automatic sleep scoring methods can be integrated with diverse PSG systems, thereby facilitating sleep monitoring in clinical or routine care.

Symposium 22: Cross talk between Ramadan intermittent fasting, mealtime, sleep, and circadian rhythm

Summary

Over the past decade, the popularity of Intermittent fasting (IF) has increased among the public, and there has been a wide interest in the health effects of IF among the scientific community. IF, mealtime, sleep, and circadian rhythm interact. Fasting and mealtime have been shown to affect sleep and the biological clock. IF can be practiced in different forms, such as abstinence from food every other day, significant reduction in caloric consumption every other day, restricting of food to specific times of a 24-r period, which is called time-restricted feeding, as well as the diurnal IF performed by more than 1.5 billion Muslims during the month of Ramadan where fasting performers abstain from food as well as drinks from dawn to sunset for the whole month (29-30 days). The effect of diurnal IF during Ramadan on sleep patterns, sleep duration, daytime sleepiness, cognitive function, sleep architecture, and circadian rhythm is an interesting topic that provides a highly complex context for future research. Conflicting data have been reported about the effects of diurnal IF on sleep architecture, daytime sleepiness, and circadian rhythm in the context of Ramadan due to significant interactions between diurnal fasting and lifestyle changes. Several studies have consistently reported that the main change in sleep architecture during fasting is a reduction in the proportion of REM sleep, an area that needs further research. Increasing evidence indicates that time-restricted feeding closely interacts with the circadian clock and has a significant role in metabolic regulation. Eating during the wrong time of the day results in a misalignment between the peripheral circadian clocks and the central biologic clock. This symposium will present recent data that examined the relationship between intermittent fasting and mealtime on one side and sleep and circadian rhythm on the other.

Learning Objectives

1. To understand the recent evidence linking time-restricted feeding and mealtime with circadian rhythm.
2. To understand the changes in sleep pattern, sleep duration, sleep architecture, and daytime sleepiness during the month of Ramadan diurnal intermittent fasting

Target Audience

1.Sleep Medicine Physicians

2.Behavioral Sleep Medicine Specialists & Psychologists

3.Chronobiologists

4.Nutritionist & Dietitians

5.Metabolic Disorders Specialists/ Endocrinologists

Chairs

Ahmed BaHammam、Moezalislam Ezzat Faris (Co-chair)

The interactions between mealtime and the biological clock

Ahmed BaHammam (Saudi Arabia)

The effects of Ramadan intermittent fasting on circadian rhythm

Ahmed BaHammam (Saudi Arabia)

Ramadan diurnal intermittent fasting and other types of experimental fasting: an overview

Moezalislam Ezzat Faris (UAE)

Effect of Ramadan diurnal intermittent fasting on sleep duration

Haitham Jahrami (Bahrain)

Sleep pattern, sleep architecture, and daytime sleepiness during Ramada

Shaden O. Qasrawi (Saudi Arabia)

Symposium 23: Pathophysiological Mechanism and Non–Pharmacological Treatment of Restless Leg Syndrome

Summary

In recent years, more and more attention has been paid to sleep disorders. Restless legs syndrome (RLS) is one of the most common sleep disorders and is increasingly diagnosed in the clinical practice. There are many progresses on pathophysiology and non-pharmacological treatment of RLS in these years, especially electrophysiological and neuroimaging researches in sensory-motor disorder of RLS. Neuroimaging studies have shown that cortical and subcortical structures may play an important role in abnormal sensorimotor integration in patients with RLS. Furthermore, patients with RLS also show decreased intracortical inhibition and increased spinal cord excitability. Low frequency repetitive transcranial magnetic stimulation（rTMS）and transcutaneous spinal direct current stimulation (tsDCS) can alleviate sensorimotor complaints of RLS patients by modulating cortical dysfunction and spinal cord excitability. We would like to organize a symposium about restless legs syndrome to lecture on progress of pathophysiological mechanism and non-pharmacological treatment of RLS, to provide the electrophysiological and imaging evidence for the abnormality of sensory-motor processing, and based on this, effective non-pharmacological neuromodulation therapy is given.

Learning Objectives

1.The iron metabolism and pathogenesis of restless leg syndrome

2.The abnormal sensorimotor integration of RLS

3.The intracortical dysfunction and alteration of spinal excitability

4.The neuromodulation on cortical and spinal dysfunction in RLS

Target Audience

Audience who has an interest in sleep medicine and research, restless legs syndrome, movement disorder, electrophysiology, neuroimaging and neuromodulation

Chairs

Yuping Wang、Weidong Le (Co-chair)

Study on iron deficiency in the pathogenesis of restless legs syndrome
Yuncheng Wu (China)
Non-invasive brain stimulation in RLS: from diagnostic hints to experimental treatments
Francesco Fisicaro (Italy)
Functional magnetic resonance imaging study of restless leg syndrome
Jiaojian Wang (China)
Transcutaneous spinal cord direct-current stimulation for restless leg syndrome

Yuping Wang (China)

Pathogenetic mechanisms of restless leg syndrome

Weidong Le (China)

Symposium 24: Sleep Disorders and Psychiatric Disorders

Summary

There is a close relationship between sleep disorders and psychiatric disorders, but people have not paid enough attention to these problems. This symposium will describe clearly of the relationships between various sleep disorders, such as obstructive sleep apnea and narcolepsy, and mental disorders, such as depression, anxiety and psychotic problems. This symposium will also present how to accurately treat sleep apnea disorder and how to prevent occurring of depression in sleep apnea patients. Knowledge on suitable treatments for those sleep disorders accompanied with psychiatric disorders will be provided, as well.

Learning Objectives

1.Providing information on current condition and newly developments on sleep disorders and mental disorders

2.Providing knowledge on how to deal with and treat these problems

3.Finding problems and questions and facilitate further research on these fields

Target Audience

1.Sleep medicine workers, including physicians, nurses and students

2.Psychiatrists, nurses and related workers

3.Respiratory physicians and neurologists

Chairs

Jianhua Shen、Yun Li (Co-chair)

Narcolepsy and psychiatric disorders

Jianhua Shen (China)

Obstructive sleep apnea and depression

Yun Li (China)

Mental disorders and sleep and circadian rhythm dysregulation in the offspring of parents with bipolar disorder

Hongliang Feng (China)

Sleep in posttraumatic stress disorder

Xiangdong Tang (China)

Accurate treatment of sleep apnea

Qingyun Li (China)

Symposium 25: Current Evidence and Trend in CPAP Therapy in Sleep–Disordered Breathing

Summary

Positive airway pressure (PAP) is the main treatment for sleep-disordered breathing (SDB). Obstructive sleep apnea (OSA) and obesity hypoventilation syndrome (OHS) are among the most common SDB observed in clinical practice. Continuous positive airway pressure (CPAP) was invented in 1980 for OSA management and has remained to be the gold standard treatment for the past 4 decades. Previous study demonstrated that the impact of CPAP on cardiovascular outcomes and improvement in quality of life relying on its adherence. However, CPAP adherence is observed to be less than optimal ranging from 40 to 78%. Thus, interventions designed to improve CPAP adherence might be of benefit to improve the care for OSA patients. Advancement in technological aspects of CPAP and certain surgical interventions have been proven to enhance the effectiveness of CPAP therapy. Due to rising in obesity epidemic globally, OHS incidence is expected to be on the rise. Besides intensive weight loss, the use of PAP in OHS is recommended preferably with initiation of CPAP in stable ambulatory patients particularly with coexisting severe OSA. In hospitalized OHS patients admitted with respiratory failure, the use of non-invasive ventilation (NIV) is recommended during hospitalization and ideally for patients to be discharged with.

Learning Objectives

1. Upon completion of this CME activity, participants should be able to identify the factors associated with poor CPAP adherence.
2. Upon completion of this CME activity, participants should be able to choose the appropriate interventions to enhance CPAP adherence.
3. Upon completion of this CME activity, participants should be able to apply the knowledge to determine the appropriate PAP management in OHS.

Target Audience

Sleep Medicine Specialist, Pulmonologist, Otolaryngologist, Neurologist, Internist

Chairs

Seung Bong Hong, Naricha Chirakalwasan (Co-chair)

Non-surgical modality in CPAP non-adherence
Naricha Chirakalwasan
Individualized treatment of OSA in Asians
Ning-Hung Chen
Surgical modality in CPAP non-adherence
Yoke Yeow Yap

Factors affecting CPAP acceptance and adherence in elderly
Theerakorn Theerakittikul (Thailand)
Phenotypic approach towards management of obesity hypoventilation syndrome
Kah Lin Choo (Hong Kong, China)

Non-Surgical Modality in CPAP Non-Adherence

Naricha Chirakalwasan, Chulalongkorn University

Poor CPAP adherence has been a major challenge for OSA treatment. Many non-surgical modalities have promising benefit in terms of improvement in CPAP adherence. Previous study has shown that different type of mask may affect CPAP adherence. Meta-analysis demonstrated that nasal mask may be associated with better compliance compared to oronasal mask.1 Previous study in Asians demonstrated that the use of heated humidification in OSA patients with nasopharyngeal symptoms improved adherence.2 However, meta-analysis demonstrated no significant improvement in CPAP adherence. Nevertheless, there were limited number of studies enrolled in this analysis. Early use of hypnotics such as eszopiclone may improve CPAP adherence when utilized within the first 14 days.3 For intranasal steroid, the recent meta-analysis did now demonstrate overall improvement in CPAP adherence. However, only two studies were included in this analysis 4 However, recent publication indicated that the use of intranasal steroid decreased rhinorrhea and congestion symptom and improved 30-day and 90-day CPAP adherence.5 Auto-titrating PAP may marginally improve PAP compliance by 0.18 hrs.6   Psycho-support and troubleshooting interventions were shown to improve adherence.1 Lastly, recent data in Asians demonstrated that telemonitoring system improved median leakage per night, sleep quality, and CPAP adherence.7 Reference 1. Patil SP, Ayappa IA, Caples SM, et al. Treatment of Adult Obstructive Sleep Apnea Witwithsitive Airway Pressure: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. Journal of Clinical Sleep Medicine. 2019;15(02):301–34. 2. Soudorn C, Muntham D, Reutrakul S, Chirakalwasan N. Effect of Heated Humidification on CPAP Therapy Adherence in Subjects With Obstructive Sleep Apnea With Nasopharyngeal Symptoms. Respir Care. 2016;61(9):1151–9. 3.Lettieri CJ. Effects of a Short Course of Eszopiclone on Continuous Positive Airway Pressure Adherence. Ann Intern Med. 2009;151(10):696. 4. Charakorn N, Hirunwiwatkul P, Chirakalwasan N, et al. The effects of topical nasal steroids on continuous positive airway pressure compliance in patients with obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2016;21(1):3–8. 5. Segsarnviriya C, Chumthong R, Mahakit P. Effects of intranasal steroids on continuous positive airway pressure compliance among patients with obstructive sleep apnea. Sleep Breath. 2020 Oct 26. doi: 10.1007/s11325-020-02236-5. 6. Ip S, Dambrosio C, Patel K, et al. Auto-titrating versus fixed continuous positive airway pressure for the treatment of obstructive sleep apnea: a systematic review with meta-analyses. Syst Rev. 2012; 1:20. 7. Chumpangern W, Muntham

D, Chirakalwasan N. Efficacy of a telemonitoring system in continuous positive airway pressure therapy in Asian obstructive sleep apnea. J Clin Sleep Med. 2021;17(1):23-9.

Individualized treatment of OSA in Asians

Ning-Hung Chen, Chang Gung Hospital

Prevalence of Obstructive sleep apnea syndrome was 2-4 % of general population 20 years ago and getting higher and higher in recent years. Cardiovascular and neurocognitive dysfunction is the major complication on patients of OSA. Obesity, craniofacial profile and neuromuscular compensation are major factors contribute to the pathogenesis of OSA. However, the obesity prevalence is not as high as Caucasians in the report from the WHO but the prevalence of OSA reported from Korea and Hong Kong show the same level as United States. The importance of craniofacial structure of sleep apnea syndrome had been discussed widely, however, the different facial structure between races was recognized but not well studied. Some evidence suggested craniofacial profile play different role on the development of sleep apnea syndrome in Asian population. Rather than the anatomical factor, there are more and more evidence show more factors contribute to the pathogenesis of OSA. Is the PAP the only choice for the treatment of OSA in Asians? In this lecture, the presenter will introduce the importance of craniofacial structure on sleep apnea syndrome. Comparing the racial difference on the patient of sleep apnea syndrome, also discuss the different on the treatment modality on Asia than Western country.

Surgical Modality in CPAP Non-Adherence

Yoke-Yeow Yap, KPJ Johor Specialist Hospital

CPAP continues to be a highly effective method of treating OSA but non-adherence remains a major limitation to long-term compliance and successful therapy. Non-adherence can be attributed to psychological and physical factors. Physical factors include poor mask fit, skin sensitivity, lip seal, muscle tone and airway resistance. The nose is the main contributor to airway resistance and high CPAP pressures resulting in poor compliance. Nasal obstruction arises from a constricted maxilla, deviated septum, concha bullnose, and hypertrophic turbinates. Surgical methods directed at enlarging the box (maxillary expansions) or reducing the contents (septoplasty, concha bullosa surgery, turbinate reduction) can significantly reduce CPAP pressures, comfort in usage and hence compliance. Surgical approach should be minimally invasive while creating an adequate airway - respecting flow dynamics, preserving mucociliary function, and ensuring nitrous oxide extraction for immunity.

Factors Affecting CPAP Acceptance and Adherence in Elderly

Theerakorn Theerakittikul, Chiang Mai University

Sleep is one of the major health problems in the elderly. Sleep breathing disorder especially obstructive sleep apnea (OSA) also has been reported to be a higher prevalence when getting older. Continuous Positive Airway Pressure (CPAP) remains the most effective treatment for improving of the general medical conditions, quality of life and public safety. However, this device use could

cause cumbersome task in aging and its acceptance-adherence will warrant the authentic efficacy in each individual. The question for dealing with this difficulty is the elderly itself or the conditions associate with aging are the contributing factors effect of CPAP acceptance and adherence.

Phenotypic approach towards management of Obesity Hypoventilation Syndrome

Kah Lin Choo, North District Hospital

With the global epidemic of obesity, interest in obesity-related sleep-disordered breathing has heightened. It is also increasingly appreciated that daytime hypoventilation likely starts with sleep hypoventilation (stage I) according to European Respiratory Society's obesity hypoventilation staging system.1 Severity of hypoventilation would have reached advanced stages (III or IV) by the time hypercapnia becomes sustained during wakefulness with current definition of obesity hypoventilation syndrome (OHS). Majority of OHS patients have concomitant obstructive sleep apnea (OSA) with the remainder exhibiting the sleep hypoventilation (OHS-SH) phenotype. OHS-OSA patients tend to be younger, sleepier and more obese than OHS-SH patients.2 OHS-OSA patients are often ambulatory and present to the sleep laboratory with chronic respiratory failure. On the other hand, OHS-SH patients tend to decompensate and present with acute-on-chronic respiratory failure, cardiac failure and pulmonary hypertension.3 Apart from having lower hospitalization need than OHS-SH patients, the severity of OSA appeared to protect OHS-OSA patients from having cardiovascular morbidities such as chronic heart failure, stroke, pulmonary hypertension, cardiac arrhythmia, and leg arteriopathy.2 To address sleep disordered breathing (whether upper airway obstruction or hypoventilation), positive airway pressure (PAP) therapy would be the mainstay of treatment.4 OHS-SH patients tend to require bilevel PAP particularly during decompensated states while OHS-SA patients could be managed with continuous PAP. Since there is not a clear cut-off apnoea-hypopnoea index to guide treatment, phenotypic assessment for the individual patient is needed. Intensive PAP support strategies may also be warranted for OHS-SH patients who often report less daytime sleepiness than OHS-OSA patients.5 To reduce cardiovascular and metabolic complications, interventions beyond PAP therapy, such as increase in physical activity level, long term weight loss including bariatric surgery, should be considered. References 1. Randerath W, Verbraecken J, Andreas S, et al. Definition, discrimination, diagnosis and treatment of central breathing disturbances during sleep. Eur. Respir. J. 2017; 49: pii: 1600959. 2. Masa JF, Corral J, Romero A, et al. Protective cardiovascular effect of sleep apnea severity in obesity hypoventilation syndrome. Chest 2016; 150:68–79. 3. Murphy PB, Suh ES, Hart N. Non-invasive ventilation for obese patients with chronic respiratory failure: Are two pressures always better than one? Respir 2019; 24: 952-961. 4. Piper AJ, BaHammam A, Javaheri S. Obesity Hypoventilation Syndrome. Choosing the Appropriate Treatment of a Heterogeneous Disorder. Sleep Med Clin 2017; 12:587–596 5. Masa JF, Benítez I, Sánchez-Quiroga MA. Long-term Noninvasive Ventilation in Obesity Hypoventilation Syndrome Without Severe OSA The Pickwick Randomized Controlled Trial CHEST 2020; 158(3):1176-1186

Symposium 26: Sleepiness & Narcolepsy: Wake–Promoting Therapies, with a focus on H3–Receptor Inverse Agonist Pitolisant

Summary

Driven by life and various motivations, human beings are used to restricting their own sleep, considered as time wasted, and staying awake late at night. Thus, every civilization has its own culture to enhance wake, e.g. by consuming tea and coffee. Psychostimulants like caffeine and amphetamine constitute the first generation of wake-promoting compounds. Their use and abuse cause well-known medico-social problems e.g., behavioral excitation, addiction and cognitive declines. Sleep medicine had long been looking for an awakening pill with preserved cognitive abilities. In the 1980's, the discovery of modafinil (2nd generation) and its property of enhancing quiet waking in cats through multiple brain targets allows for the first time a successful therapy of hypersomniac symptoms and excessive sleepiness of diverse origins. Yet, it has a limited effect on cataplexy of narcolepsy with 15-25% of patients unresponsive. Ligands acting on specific brain targets are still in high demand. The wake-promoting histaminergic neurons control their own release, synthesis and activity through a negative feedback on H3-receptors whose inverse agonists have long been known for their wake enhancement in animals. Yet, a clinically-suitable ligand, pitolisant, has only recently become available, representing a third generation of wake-promoting compounds. This symposium reviews the three generations of wake-promoting therapies with focus on the discovery, pharmacological properties, mechanisms of action and medical perspectives of H3-receptor inverse agonist Pitolisant. References: Lin et al., Brain Res., 1990; Neurobiol Dis., 2008; J Pharmacol Exp Ther., 2011; Sleep Med., 2018; Parmentier et al., Biochem Pharmacol., 2007.

Learning Objectives

1.History of wake-promoting therapies;

2.Basic and clinical characteristics of three generations of wake-promoting compounds;

3.Therapies of excessive daytime sleepiness and narcolepsy;

4.Basic and preclinical properties of Pitolisant, H3-receptor inverse agonist;

5.Pitolisant in sleep medicine.

Target Audience

Sleep researchers and sleep medicine clinicians, MD and PhD students.

Chairs

Jian-Sheng Lin, Isabelle Arnulf (Co-chair)

Introduction to three generations of wake-promoting therapies

Jian-Sheng Lin (France)

Adult narcolepsy: overview & treatments

Isabelle Arnulf (France)

Overview of preclinical studies with Pitolisant, histamine H3-receptor inverse agonist

Xavier Ligneau (France)

H3-receptor inverse agonist Pitolisant, an overview of clinical studies

Christian Caussé (France)

Childhood narcolepsy, clinical characteristics & treatments

Patricia Franco (France)

Introduction to Three Generations of Wake-Promoting Therapies

Jian-Sheng Lin, French National Institute of Health & Medical Research; Claude Bernard University Driven by life and various motivations, human beings are used to restricting their own sleep, considered as time wasted, and staying awake late at night. Thus, every civilization has its own culture to enhance wake, e.g., by consuming tea and coffee. Psychostimulants like caffeine and amphetamine constitute the first generation of wake-promoting compounds. Their use and abuse cause well-known medico-social problems e.g., behavioral excitation, addiction and cognitive declines. Sleep medicine had long been looking for an awakening pill with preserved cognitive abilities. In the 1980's, the discovery of modafinil (2nd generation) and its property of enhancing quiet waking in cats through multiple brain targets allows for the first time a successful therapy of hypersomniac symptoms and excessive sleepiness of diverse origins. Yet, it has a limited effect on cataplexy of narcolepsy with 15-25% of patients unresponsive. Ligands acting on specific brain targets are still in high demand. The wake-promoting histaminergic neurons control their own release, synthesis and activity through a negative feedback on H3-receptors whose inverse agonists have long been known for their wake enhancement in animals. Yet, a clinically-suitable ligand, pitolisant, has only recently become available, representing a third generation of wake-promoting compounds. This presentation reviews the three generations of wake-promoting therapies with a focus on the discovery, pharmacological properties, mechanisms of action and medical perspectives of H3-receptor inverse agonist Pitolisant. References: Lin et al., Brain Res., 1990; Neurobiol Dis., 2008; J Pharmacol Exp Ther., 2011; Sleep Med., 2018; Parmentier et al., Biochem Pharmacol., 2007.

Adult Narcolepsy: Overview & Treatments

Isabelle Arnulf, Hôpital de la Pitié-Salpêtrière, Sorbonne University
Adult narcolepsy is characterized by the highest daytime sleepiness known in human, including

sleep attacks, recurrent need to nap (mostly brief and refreshing naps), automatic behaviors and attentional deficits. In addition, two thirds of narcolepsy patients suffer from cataplexies (complete or partial loss of postural muscle tone), nightmares, mild REM sleep behavior disorder, hypnagogic hallucinations and sleep paralysis; one third has a severe dyssomnia (2 or 3 sleep bouts per night, resembling an ultradian sleep rhythm) and a weight gain. Narcolepsy patients have frequent lucid dreams and are more creative, on average, than the general population. Despite narcolepsy with cataplexy is an autoimmune disorder, immune therapies have yet failed to block the loss of hypocretin cells. Narcolepsy is a lifelong disorder, requiring to adjust work schedules, obtain daily naps, restrict driving, and often use stimulants and anticataleptic drugs. In absence of marketed therapies substituting the hypocretin deficiency, most stimulants target the dopaminergic/ noradrenergic arousal system, including modafinil (well tolerated, but interacts with many drugs and has no anticataplectic effect), methylphenidate and amphetamines (alerting and having precognitive effects, their benefit is to be balanced with potential cardiovascular side effects). Sodium oxidate is used on a nightly basis and improves dyssomnia, sleep inertia, cataplexy as well as, on high (7.5-9 g) dosages, daytime sleepiness, to the price of a few side effects (confusion, enuresis). More recently, drugs targeting the histamine arousal system (the head of the class being marketed in narcolepsy as pitolisant) have been developed, and have shown awakening effects as well as some mild anti-catapeltic effects, and an excellent tolerance profile. The reduction of cataplexy often requires to add antidepressants (which decrease REM sleep associated muscle atonia) or tropatepine (anticholinergic drug) to the stimulant regimen. The narcolepsy is still in need of an all-in-one drug, which could compensate all the various symptoms of this devastating disorder.

Overview of preclinical studies with Pitolisant, histamine H3-receptor inverse agonist

Xavier Ligneau, Bioprojet- Biotech

Pitolisant (formerly named BF2.649 and tiprolisant) is a selective potent histamine H3 receptor (H3R) inverse agonist with an EC50 value of 1.5 nM at the human H3R and a competitive antagonist behaviour characterized by a Ki value of 0.16 nM. Its potency is ~6 times lower at rodent H3R. Its pharmacokinetics in mice evidenced a bioavailability of 84% and a high brain penetration with a brain/plasma level ratio of ~25. Consequently, pitolisant stimulates the histaminergic neurotransmission as shown by its ability to enhance tele-methylhistamine levels in mouse brain, an index of histaminergic neuron activity, with an ED50 value of 1.6 mg/kg, p.o. Modulations of other neurotransmitters by pitolisant were also evidenced by microdialysis in rats with increases in dopamine and acetylcholine in prefrontal cortex, whereas it was without any effect on dopamine in the nucleus accumbens, a brain region critical for the rewarding effect of drug of abuse, but also in the whole striatum. In line with this lack of effect on striatal dopamine, pitolisant was devoid of any effect on the spontaneous locomotion after single and repeated administration, contrary to psychostimulant. Pitolisant was shown to promote wakefulness at the expense of sleep

states in mice and cats leading to an enhanced vigilance and attention as shown by promnesic effects recorded in two-trial object recognition tests in mice. Finally, pitolisant was tested in the orexin-/- mouse, a unique model of narcolepsy presenting the features of this pathology. In these mice, pitolisant enhanced also wakefulness and more interestingly decreased abnormal direct onsets of REM sleep from wake (DREMs), one key feature of narcolepsy bringing the first evidences of the interest as therapeutic drugs of H3R inverse agonists/antagonists.

H3-receptor inverse agonist Pitolisant, an Overview of Clinical Studies

Christian Caussé, Bioprojet-Pharma

Pitolisant is a waking agent which has been developed by bioprojet in narcolepsy. Pitolisant is a potent, orally active histamine H3 receptor antagonist/inverse agonist which enhances the activity of brain histaminergic neurons, a major arousal system. Three phase 3 pivotal clinical studies demonstrated the efficacy and the safety of Pitolisant up to 36 mg/day to treat the major symptoms of narcolepsy allowing EMA and by FDA to approve Pitolisant to treat Excessive Daytime Sleepiness (EDS) and cataplexy in adult narcolepsy patients. Pitolisant reduces significantly Excessive Daytime Sleepiness (EDS) by 5.8 on the Epworth Sleepiness Score, reduces significantly cataplexy crisis by 75%, hallucinations, sleep paralysis and sleep attacks. Pitolisant can be prescribed alone or combined and its efficacy is maintained during long term. Because of its mode of action via histaminergic pathway, its safety profile is very good, in particular there is no electrocardiogram to request before prescription and no change in blood pressure and in heart rate were observed in the clinical development of Pitolisant reducing EDS in Obstructive Sleep Apnea patients. Most frequent side effects are minor insomnia (8.4%), headaches (7.7%), nausea (4.8%), anxiety (2.1%) and most of them disappeared after sometimes. Pitolisant demonstrated its very low abuse potential showing it is the only drug to treat narcolepsy which is not scheduled in the USA. Because of its efficacy and its safety profile, Pitolisant has a good benefit-risk balance confirmed by a network-meta-analysis. A pharmacokinetic study showed that narcolepsy children less than 40 kg (body weight) should receive half dosage compared to adults. This should be confirmed by the study evaluating Pitolisant in children with narcolepsy whose results will be available Q3 2021. The very next European Narcolepsy Guidelines will confirm that Pitolisant is a first line treatment for the narcolepsy management.

Childhood Narcolepsy, Clinical Characteristics & Treatments

Franco Patricia, Hôpital femme-mère-enfant; Claude Bernard University

Narcolepsy type 1 (also called hypocretin or orexin deficiency syndrome or narcolepsy with cataplexy) is a neurological disorder characterized by excessive daytime sleepiness (EDS), cataplexy (sudden loss of muscle tone triggered by emotions), hallucinations, sleep paralysis, impaired night-time sleep and short latency to rapid eye movement (REM) sleep after sleep onset. Narcolepsy Type 1 is caused by a deficiency of hypocretin neurons located in the dorso-lateral hypothalamus probably secondary to autoimmune destruction of hypocretin cells. More than half of narcoleptic patients

have an onset of symptoms prior to the age of 18. At diagnostic time, the clinical picture is quite different in children compared to adults. Children present more frequently obesity, night eating, parasomnia, sleep talking, drunkenness and Attention Deficit Hyperactivity Disorders' symptoms than adults. However, if depressive feelings affected not differently children and adults, they have a major impact on their quality of life. Compared to healthy children, those with narcolepsy have also more school difficulties, grade repetition and absenteeism. In this context, investigating narcoleptic children appears to constitute an interesting avenue and would allow detection of possible neurochemical changes. Indeed, the disease is more pronounced and better characterized at the onset and earlier stage of childhood than in the later and stable stage of adulthood. During this presentation, the clinical, electrophysiological and neurochemical characteristics of narcolepsy during childhood and its therapeutic management using psychostimulants, modafinil and H3-receptor inverse agonist pitolisant will be reviewed.

Symposium 27: Treatment Approaches for Childhood Obstructive Sleep Apnea

Summary

Childhood obstructive sleep apnea (OSA) is a common condition with significant complications namely cardiovascular, neurocognitive and metabolic disturbances. Timely and effective treatment is important. As adenotonsillar hypertrophy is one of the commonest causes of childhood OSA, adenotonsillectomy (AT) is widely recommended as the first line therapy. However, residual OSA is common. Aberrant anatomy, obesity and excessive airway collapsibility are the potential factors contributing to persistent OSA. Moreover, OSA is a heterogeneous disease with various etiologies therefore AT may not be the most suitable treatment option for all children with OSA. Positive airway pressure (PAP), anti-inflammatory therapy and orthodontic treatment are other currently available treatment options for childhood OSA. In this symposium, the speakers are going to discuss about the following topics that aim to provide an up-to-date review of therapeutic approaches for childhood OSA. 1. A cohort of pediatric OSA – what happens after surgery? 2. Adenotonsillectomy – can it reverse OSA-related complications? 3. Orthodontic treatment for childhood OSA 4.Anti-inflammatory therapy for childhood OSA 5.High flow nasal cannula therapy as an alternative treatment for childhood OSA – any evidence?

Learning Objectives

1.Gain a better understanding of the outcomes after adenotonsillectomy in childhood OSA.

2.Discuss the benefits and limitations of various treatment options for childhood OSA.

3.Up-to-date literature review on different treatment options.

4.Predictors of treatment outcomes and patient selection in different therapeutic options.

Target Audience

Pediatricians, physicians, psychologists, psychiatrists, nursing colleagues and allied health care workers interested in childhood sleep apnea

Chairs

Kate Ching-ching Chan, Chun Ting Au (Co-chair)

High flow nasal cannula therapy as an alternative treatment for childhood OSA – any evidence?

Kate Ching Ching Chan

Adenotonsillectomy – can it reverse OSA-related complications?

Chun Ting Au

A cohort of pediatric OSA – what happens after surgery?

Yu-Shu Huang

Orthodontic treatment for childhood OSA

Myung-Rip Kim
Anti-inflammatory therapy for childhood OSA
Zhifei Xu

High flow nasal cannula therapy as an alternative treatment for childhood OSA – any evidence?

Kate Ching-Ching Chan, The Chinese University of Hong Kong
Continuous positive airway pressure (CPAP) is often regarded as the second line therapy for childhood obstructive sleep apnea (OSA). However, poor tolerance and adherence remains a major obstacle in instituting CPAP in pediatric population. Furthermore, midface hypoplasia secondary to mask pressure is of the greatest concern particularly in children whose facial structures are still growing. As a result, CPAP treatment of many children with OSA has been suboptimal, and alternative therapeutic strategy is needed to manage this group of children with OSA. Heated humidified high-flow nasal cannula (HFNC) therapy has become an increasingly popular mode of non-invasive respiratory support for both acute and chronic respiratory failure in both adults and children. It is based upon a fixed high flow rate via nasal cannulae. It reduces work of breathing and improves efficiency of ventilation through several proposed mechanisms: washout of nasopharyngeal dead space leading to improved alveolar ventilation, reduction in the inspiratory resistance within the nasopharynx, improvement in conductance and pulmonary compliance by supplying adequately warmed and humidified gas, reduction in the metabolic work associated with gas conditioning and provision of positive distending pressure for lung recruitment. HFNC therapy is generally more tolerable than PAP as the former's interface and tubing are less cumbersome when compared with those of PAP therapy. The need to maintain an adequate seal in children receiving PAP therapy often makes the delivery and acceptance challenging, but this is not required with HFNC therapy. Successful use of HFNC therapy in children to manage OSA has been reported in some case series. Some predictors for treatment success were identified in adult studies, which include disease with predominantly obstructive hypopneas or rapid eye movement (REM)-related events. However, whether the use of HFNC can enhance compliance has not yet been evaluated. More studies are needed to evaluate the efficacy of HFNC therapy as an intervention for children with OSA and the compliance to home HFNC treatment in this population.

Adenotonsillectomy – can it reverse OSA-related complications?

Chun Ting Au, The Chinese University of Hong Kong
Adenotonsillectomy (AT) is the current recommended first-line treatment for childhood OSA. Although AT can effectively reduce OSA-related polysomnographic indexes and symptoms, its effects on reversing OSA-related complications have not yet been confirmed. Observational studies revelated that AT improved some but not all aspects of neurocognitive and neurobehavioral

performance in children with OSA. Moreover, AT was found to improve cardiovascular outcomes including blood pressure, cardiac function and remodeling, and endothelial function. However, most of these studies were limited by the lack of an untreated group for comparison. More recently, randomized controlled trials demonstrated AT improved neurocognitive outcomes with only small effect size. Long-term effect of AT on OSA-related complication has not been investigated

Orthodontic treatment for childhood OSA

Myung-Rip Kim, Department of Orthodontics, University of Illinois at Chicago; Korean Society of Sleep Medicine

Treatment options for pediatric OSA are adenotonsillectomy, anti-inflammatory medications, CPAP, weight control, and etc. Orthodontists can manage remaining symptoms of pediatric OSA even after these treatments in the multidisciplinary team. Proper engagement of managing pediatric OSA as an orthodontist will be discussed.

Anti-inflammatory therapy for childhood OSA

Zhifei Xu, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health

Anti-inflammatory medications are widely recognized and used in clinical practice, particularly in children with mild to moderate OSA. Studies have shown that repeated hypoxia and fragmentation of sleep in children with OSA can lead to local and systemic inflammation, which can in turn contribute to airway lymphoid tissue hyperplasia and endothelial cell dysfunction, imbalance of blood pressure regulation, and impaired cognitive function. Anti-inflammatory medications are, therefore, an option for treating OSA and preventing complications. Many studies have provided strong evidence for the efficacy of the treatment of pediatric OSA with anti-inflammatory medications. However, no studies with long-term follow-up have been focused on OSA recurrence after medication withdrawal. Additionally, the benefits of combining intranasal corticosteroids and montelukast versus the administration of a single medication are still not established, because no randomized controlled trials comparing these two treatments have been conducted so far. This talk focuses on current evidence of anti-inflammatory medications and discusses questions that remained unanswered.

Symposium 28: Sleep and Metabolism

Summary

Sleep is important in regulating metabolism. Mammalian sleep can be sub-divided into two distinct phases - REM (rapid eye movement) and non-REM (NREM) sleep. NREM is considered deep sleep, when metabolism is least active. Metabolism involves two biochemical processes. The first is anabolism, which refers to the build up of molecules. The other is catabolism, the breakdown of molecules. These two processes work to regulate the amount of energy the body uses to maintain itself. During non-REM sleep, metabolic rate and brain temperature are lowered to deal with damages that may have occurred during time of wakefulness. Sleep is intricately connected to various hormonal and metabolic processes and is important in keeping metabolic homeostasis. It is reported that sleep deprivation and sleep disorders may have profound metabolic and cardiovascular implications. Sleep deprivation, sleep disordered breathing, and circadian misalignment are believed to cause metabolic dysregulation through myriad pathways involving sympathetic overstimulation, hormonal imbalance, and subclinical inflammation. This symposium will talk about sleep and metabolism, and how sleep may be altering metabolism.

Chairs

Clifford B. Saper, Hailong Dong (Co-chair)

Preoptic control of sleep and body temperature

Clifford B. Saper (USA)

The regulative role of VTA neurons in the homeostasis of arousal states

Hailong Dong (China)

Living in the cold - what we can learn from a hibernator

Wei Li (USA)

Exploring the role of H2B propionylation in regulating circadian rhythm and physiology

Luoying Zhang (China)

Brain circadian clock in dawn phenomenon

Zheng Sun (USA)

Preoptic control of sleep and body temperature

Clifford B. Saper, Harvard Medical School, Beth Israel Deaconess Medical Center

The preoptic area is known to play a key role in regulation of both sleep and body temperature, but the circuitry controlling these functions and how they are related remains largely unexplored. We previously found that galanin neurons in the ventrolateral preoptic nucleus (VLPO) drive sleep behavior. However, we recently found that activation of these neurons also causes hypothermia. We also found that activation of GABAergic neurons in the median preoptic nucleus (MnPO) promotes sleep, but activation of glutamatergic MnPO neurons mainly causes hypothermia. Activation of glutamatergic cells, but not GABAergic cells, in the VLPO also caused hypothermia, suggesting that the VLPO galanin population contains two types of neurons, GABAergic sleep-promoting and glutamatergic hypothermia-promoting cells. Further exploration of the preoptic glutamatergic neurons that drive hypothermia demonstrated that many of them express either PACAP or QRFP peptides, and some express the EP3R prostaglandin receptor, which inhibit the hypothermia neurons and promote fever responses. Driving these preoptic hypothermic neurons with the hM3Dq receptor for 2-4 hrs causes a prolonged state of behavioral hyporesponsiveness and deep hypothermia lasting up to several days, with complete recovery. This state of torpor or hibernation cannot be reversed by warming the animal once it has reached deep hypothermia, and probably represents a distinct self-perpetuating physiological state of extremely low metabolic rate.

The regulative role of VTA neurons in the homeostasis of arousal states

Hailong Dong, Department of Anesthesiology and Perioperative Medicine, Xijing Hospital

Midbrain ventral tegmental area (VTA) is an essential brain region in the regulation of sleep and wakefulness. However, the network of multiple types of VTA neurons were not identified in the transitions of arousal states. Our research group found that VTA glutamatergic neurons promoted wakefulness through projections to the nucleus accumbens and lateral hypothalamus (LH), whereas activation of VTA GABAergic neurons and their projections to the LH produced a non-rapid eye movement (NREM) sleep state and facilitated the general anesthesia. Inhibiting VTA glutamatergic and dopaminergic neurons, these NREM-promoting VTA GABAergic neurons were selectively active during wakefulness and rapid eye movement (REM) sleep, indicating their role as limiting wakefulness to maintain a hemostasis of vigilance states. Following this speculation, the collabration study demonstrated that lesioning VTA GABAergic neurons could elicit a mania-like behavior partially due to the hyperactivation of excitatory neurons in the VTA. Together, these results revealed a role of VTA circuits in the homeostatic modulation of arousal states.

Living in the cold - what we can learn from a hibernator

Wei Li, National Eye Institute, National Institutes of Health

Hibernation is a fascinating biological phenomenon, featuring drastic body temperature regulation and substantial metabolic suppression. In addition to rebalancing the energy demand in the face of

nutrients and oxygen and glucose deficiency, metabolic suppression also shapes a myriad of cellular processes and in so doing alters their responses to stresses. Mammalian hibernators have evolved sophisticated survival mechanisms designed to cope with extremely stressful conditions that would be life-threatening to non-hibernators. However, the mechanisms of such promising protective mechanisms remain elusive, hindering potential clinical applications. We use thirteen-lined ground squirrel as an animal model to study adaptive strategies during hibernation focusing on the central nervous system. In this seminar, I will report adaptations that we observed in synapse, cytoskeleton, and local immune response from hibernating ground squirrels. Exploiting the knowledge of such adaptations in hibernation can facilitate the development of new therapeutic strategies for neuroprotection against neural injury and neurodegeneration.

Exploring the Role of H2B Propionylation in Regulating Circadian Rhythm and Physiology

Luoying Zhang, Huazhong University of Science and Technology

Most of our behavior and physiological processes exhibit 24h rhythms, or circadian rhythms. These rhythms are driven by endogenous clocks, which consist of a series of transcriptional/translational feedback loops at the molecular level. Although the regulatory mechanism of this molecular clock is well characterized, it remains largely unclear how this clock modulates the rhythms in various biological processes. Here we found that 23% of the propionylome in Drosophila heads show circadian variation that appears to be regulated by the molecular clock. We further investigated rhythmic propionylation at lysine 17 of H2B (H2BK17pr), as this is one of the sites with most robust propionylation rhythm. We found that timed feeding regulates the rhythm of H2BK17pr. At the molecular level, histone acetyltransferase CBP/NEJIRO enhances while histone deacetylase HDAC1/3 reduces propionylation of H2BK17. We further characterized the physiological role of this modification and found that H2BK17pr modulates proteinstasis by promoting ubiquitin-mediated protein degradation. Taken together, we identify a mechanism for how circadian system influences proteinstasis via H2B propionylation.

Brain circadian clock in dawn phenomenon

Zheng Sun, Baylor College of Medicine

Systemic insulin sensitivity shows a diurnal rhythm with a peak upon waking1,2. The molecular mechanism that underlies this temporal pattern is unclear. Here we show that the nuclear receptors REV-ERB-α and REV-ERB-β (referred to here as 'REV-ERB') in the GABAergic (γ-aminobutyric acid-producing) neurons in the suprachiasmatic nucleus (SCN) (SCNGABA neurons) control the diurnal rhythm of insulin-mediated suppression of hepatic glucose production in mice, without affecting diurnal eating or locomotor behaviors during regular light–dark cycles. REV-ERB regulates the rhythmic expression of genes that are involved in neurotransmission in the SCN, and modulates the oscillatory firing activity of SCNGABA neurons. Chemogenetic stimulation of SCNGABA neurons at waking leads to glucose intolerance, whereas restoration

of the temporal pattern of either SCNGABA neuron firing or REV-ERB expression rescues the time-dependent glucose metabolic phenotype caused by REV-ERB depletion. In individuals with diabetes, an increased level of blood glucose after waking is a defining feature of the 'extended dawn phenomenon' 3,4. Patients with type 2 diabetes with the extended dawn phenomenon exhibit a differential temporal pattern of expression of REV-ERB genes compared to patients with type 2 diabetes who do not have the extended dawn phenomenon. These findings provide mechanistic insights into how the central circadian clock regulates the diurnal rhythm of hepatic insulin sensitivity, with implications for our understanding of the extended dawn phenomenon in type 2 diabetes.

Symposium 29: Sleep Patterns and Metabolic Effect

Summary

Sleep is an imperative physiological need. There are many sleep patterns are recognized worldwide but more commonly is the monophasic pattern. nevertheless, in hot climate societies, sleep might be fragmented into different patterns such as bi-phasic (two times per 24 hours) or polyphasic (multiple times per 24 hours). many people practiced also afternoon napping which varies in duration from few minutes to multiple hours. sleeping less or more at night may cause metabolic effect especially with glucose metabolism and that may also predispose to cardiovascular damage. Moreover, long after napping may also add a negative impact to the metabolism by shifting the circadian towards late phase. in this symposium we will try to describe the sleep patterns in our local population and compare it with other patterns in other parts of the word. we also try to explore the metabolic effect of these sleep patterns, particularly, afternoon napping on glucose metabolism. And finally, we will shed lights on cardio-metabolic markers that may indicate any damage occurs because of sleeping in such manner.

Learning Objectives

1- to understand sleep patterns in our local population

2- to explore the effect of afternoon napping on glucose metabolism

3-the link between sleep and cardio-metabolic markers that may indicate any cardiovascular damage

Target Audience

general physicians, sleep scientists and sleep physicians

Chairs

Mohammed Al-Abri, Fahad Al-Zedjali (Co-chair)

Sleep patterns

Mohammed Al-Abri (Oman)

Sleep and cardiovascular markers

Fahad Al-Zedjali (Oman)

Afternoon napping and diabetes mellitus

Ibtisam Mustafa Juma Al Lawati (Oman)

Agreement analysis of sleep patterns between self-reported questionnaires and actigraphy in adults

Ibtisam Mustafa Juma Al Lawati (Oman)

Sleep patterns

Mohammed Al-Abri, Sultan Qaboos University

Sleep is an imperative physiological phenomenon. Because of climates, cultural and social demands, sleep patterns change according to this external factors. We found that people in Oman adapt four sleep patterns which include monophasic sleep, bi-phasic sleep (sleep after dawn pray), bi-phaisc siesta (sleeping one episode at night and one in afternoon) and polyphasic patterns (sleeping three or more episodes per 24 hours)

Sleep and cardiovascular markers

Fahad Al-Zedjali, Sultan Qaboos University

Sleeping with different patterns may cause some metabolic and vascular damage and that can manifest with certain biomarkers such as fractilkine, gultathione, peroxides. We found that some of these markers are associated with certain sleep patterns.

Afternoon Napping and Diabetes Mellitus

Ibtesam Al-Lawati, Oman College of health science

Sleeping in afternoon might be a good refreshing habit. However, adapting long afternoon napping may predispose people to deranged glucose metabolism and that consequently lead to increase in glycated hemoglobin and then T2DM. We will try to explore the link between afternoon napping and T2DM by comparing our finding with similar studies done around the world

Agreement Analysis of Sleep Patterns between Self-reported Questionnaires and Actigraphy in Adults

Ibtesam Al-Lawati, Oman College of health science

Purpose: To investigate the agreement in sleep pattern recording by self-reported sleep questionnaires and actigraphy in adults. Methods: This is a cross-sectional study. Men and women who met inclusion criteria were recruited for this study. The inclusion criteria were apparently healthy Omani national's ages 19 to 50 years. Sleep questionnaires were randomly distributed in Muscat either directly or via electronic and paper announcements. Data were collected from the participants using the self-reported questionnaires with four piloted questions for sleep pattern identification and through the actigraphy wristband given to subjects to wear for a week. Cohen's kappa test was performed for agreement analysis. Results: A total of 964 Omani subjects between ages 18 and 59 years of both genders were recruited and completed the questionnaires successfully. Out of these, only 321 subjects wore the actigraphy wristband for 1 week (response rate = 33%). Agreement analysis reported a mild level of agreement for the monophasic (41%), moderate level for biphasic (59%), and good level for polyphasic (70%) sleep patterns. The overall agreement level of sleep patterns between the two methods was 57%. There is a low specificity of self-reported assessment in reporting sleep pattern. Conclusion: The average agreement level of subjective versus objective assessments of sleep patterns was moderate at 57% and self-reported sleep pattern is not specific. The study recommends the use of actigraphy along with sleep questionnaires for accurate assessment of sleep patterns in cohort studies.

Symposium 30: Glymphatic System and Sleep

Summary

The Glymphatic system is an active fluid clearance pathway recently discovered in the rodent brain. The Glymphatic system is mainly functional during sleep and facilitates harmful metabolites peptides such as amyloid β. Astrocytic endfeet aquaporin-4 (AQP4) water channels play an important role for this system. Reduction in AQP4 expression links with dampened Glymphatic function, as well as Alzheimer's disease pathogenesis. It was revealed by MRI imaging that human CSF dynamics couple with neural and hemodynamic rhythms in sleep. Investigations of the Glymphatic system have revealed interesting findings in a variety of neurological diseases, such as neurodegenerative disease, stroke, traumatic brain injury (TBI), and emotional diseases. The field of Glymphatic research is a rapidly growing field owing to its potential as a target to prevent neurodegenerative diseases such as Alzheimer's disease. Speakers of this symposium include 5 neuroscientists in total. It is our honor to invite Dr. Maiken Nedergaard, the original discoverer of Glymphatic system to give a talk. The additional speakers are also at the forefront of the Glymphatic field and actively contributing to the research field of Glymphatic system and Sleep/neurological diseases. We believe the upcoming symposium would be fruitful and stimulate active scientific discussions and collision of smart ideas.

Learning Objectives

1. Introduction of recent progress in the field of"Glymphatic system".
2. Reporting frontier research findings of human Glymphatic system and future trends.
3. Discussing the connections between Glymphatic system and sleep disorders / neurodegenerative diseases with sleep disturbance.
4. Reporting the updated mechanisms of regulating Glymphatic system in sleep and wake cycles.

Target Audience

1.Clinicians
2.Medical and Bioscience graduate students
3.Neuroscientists
4.Neuroscience Researchers

Chairs

Fengfei Ding, Ming Xiao (Co-chair)

Chronic sleep fragmentation alters brain glymphatic function
Fengfei Ding (China)
An involvement of aquaporin 4 in chronic sleep disruption
Ming Xiao (China)

The glymphatic system
Maiken Nedergaard (USA, Denmark)
The glymphatic system, from mice and pigs to humans
Iben Lundgaard (Sweden)
Adrenergic blockers induce neuroprotection and facilitate recovery from K+-induced cortical
spreading depression and acute ischemic stroke
Hajime Hirase (Denmark)

Chronic sleep fragmentation alters brain glymphatic function

Fengfei Ding, Fudan University

Sleep disturbance could result in cognitive decline, emotional issues, as well as systemic immune abnormality. Sleep was reported probably responsible for cleaning metabolic wastes in brain by increasing extracellular bulk flow via a recently discovered cerebrospinal fluid circulation system, called glymphatic system. In previous studies, we found that chronic sleep insufficiency in young adult wild-type mice is linked with dysfunction of intracellular protein degradation pathways and microglia-mediated neuroinflammation, which are potentially important mechanisms in the initiation of neurodegeneration. In the current study, we characterized and compared the glymphatic function alterations induced by acute and chronic sleep fragmentation treatment in young wild type mice. Our study would provide evidence of explaining the mechanisms of sleep insufficiency-induced cognitive function decline.

An involvement of aquaporin 4 in chronic sleep disruption

Ming Xiao, Nanjing Medical University; The Affiliated Nanjing Brain Hospital of Nanjing Medical University

Sleep is a vital physiological state in human life, facilitating strength restoration, synaptic plasticity, and memory consolidation. Sleep insufficiency or disruption is associated with increased risks of various disorders, such as cardiovascular diseases, Alzheimer's disease, Parkinson's disease, depression, and anxiety. Recently, sleep has been shown to facilitate clearance of metabolic wastes from the brain. Subsequent studies indicate that the glymphatic system enhances brain macromolecular removal during the sleep period. The glymphatic system is a brain-wide paravascular pathway that is responsible for clearing interstitial solutes, including amyloid-β (Aβ) and Tau proteins, from the brain parenchyma. Several groups have independently shown that fast glymphatic transport depends upon the expression and perivascular localization of the astroglial water channel aquaporin-4 (AQP4). Perivascular AQP4 supports rapid water movement between perivascular space and glial syncytium, thus forming a convective bulk flow of interstitial fluid. In turn, this promotes clearance of interstitial solutes into the cerebrospinal fluid. Disrupted perivascular AQP4 polarization caused by reactive astrogliosis impairs glymphatic clearance,

subsequently increasing accumulation of metabolic wastes in aged, Alzheimer's disease and injured brains. However, the exact role of AQP4 in brain impairments following chronic sleep insufficiency remains elusive. To address this issue, we investigated glymphatic transport and accumulation of Aβ and Tau proteins following 7 days of sleep disruption (SD) using the improved rotating rod method, and assessed pathophysiological consequences of AQP4 deletion or overexpression in this process. Our results demonstrated that AQP4 deletion exacerbated glymphatic transport impairment, accumulation of brain Aβ and Tau proteins, activation of microglia, neuroinflammation, and synaptic protein loss in the hippocampus, as well as spatial memory malfunction. By contrast, transgenic overexpression of AQP4 ameliorated β-amyloid and Tau accumulation and cognitive dysfunction following SD. These results demonstrate that AQP4-mediated glymphatic clearance plays a critical neuroprotective role following chronic SD, serving as a potential target for sleep-related disorders.

The Glymphatic System

Maiken Nedergaard, University of Rochester; University of Copenhagen

The glymphatic concept along with the discovery of meningeal lymphatic vessels have, in recent years, highlighted that fluid is directionally transported within the central nervous system (CNS). Imaging studies, as well as manipulations of fluid transport, point to a key role of the glymphatic-lymphatic system in clearance of amyloid-β and other proteins. As such, the glymphatic-lymphatic system represents a new target in combating neurodegenerative diseases. Not unexpectedly, introduction of a new plumbing system in the brain has stirred controversies. This opinion article will highlight what we know about the brain's fluid transport systems, where experimental data are lacking, and what is still debated.

The glymphatic system, from mice and pigs to humans

Iben Lundgaard, Lund University

The recently discovered glymphatic system, which supports brain-wide clearance of metabolic waste, has become the subject of intense research within the past few years. Its nomenclature arose due to its functionally analogous nature to the lymphatic system in combination with glial cells that are part of its anatomical boundaries. The influx of cerebrospinal fluid (CSF) from perivascular spaces into the brain interstitium acts to clear intraparenchymal solutes. CSF is produced by the choroid plexus and flows from the ventricles to the subarachnoid space via the cisterna magna, and as such the injection of tracer molecules into any one of these spaces could be used for studying CSF movement through the glymphatic system. In the current study, we are interested in exploring the glymphatic system in rodents, pigs, and human beings.

Adrenergic blockers induce neuroprotection and facilitate recovery from K+-induced cortical spreading depression and acute ischemic stroke

Hajime Hirase, Center for Translations Neuromedicine, University of Copenhagen

Cortical spreading depolarization (CSD) is a propagating wave of tissue depolarization characterized

by a large increase of extracellular K+ concentration and prolonged subsequent electrical silencing of neurons. Waves of CSD arise spontaneously in various acute neurological settings, including migraine aura and ischemic stroke. In acutely induced stroke models, CSD induces secondary irreversible damage in the ischemic brain, suggesting that K+ homeostasis might constitute a novel therapeutic strategy in ischemic stroke. We here demonstrate a potent mitigation of stroke-induced brain damage by blocking adrenergic receptors (AdRs). We performed in vivo Ca2+ imaging of cortical neurons and astrocytes to investigate the neural activity recovery after CSD induced by high-K+ (KCl) application or photothrombotic stroke. Using the G-CaMP7 expressing transgenic mouse (BAC-GLT1-G-CAMP7#817, also known as G7NG817), we have observed that asynchronous astrocytic Ca2+ activity is initiated rodent cerebral cortex in the aftermath of high-K+-induced CSD. AdR blockade suppressed this aberrant astrocytic Ca2+ activity and accelerated normalization of extracellular K+, resulting in faster recovery of neural activity. Notably, similar aberrant astrocytic Ca2+ activity was observed in the mouse cortex after the passage of CSD induced by photothrombotic stroke. Moreover, systemic administration of AdR blockers before or within two hours of stroke occurrence facilitated functional locomotor recovery and reduced infarct volume. The AdR blocker-treatment also induced the preservation of the water channel aquaporin-4 in astrocytes. In high-K+-induced CSD, AdR blockade decreased the recurrence of CSD waves and accelerated the post-CSD recovery of both spontaneous and sensory-evoked neural activity, which paralleled with the facilitated normalization of the extracellular K+ level. Our results are in line with the notion that AdR blockade promotes cerebrospinal fluid exchange, a property put forward in the glymphatic system, and suggest that this may be the underlying mechanism for the neuroprotective effects of AdR pan-antagonism. From a translational standpoint, AdR blockade may offer a novel and affordable approach to current treatments for acute brain injury including thrombotic stroke.

Symposium 31: Insights into the Diagnosis and Management of OSA with Upper Airway Imaging

Summary

Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder. Obesity is the most important risk factor for OSA. Enlarged upper airway soft tissues, craniofacial abnormalities and their interactions play key roles in anatomical risk for OSA. Why obesity is associated with OSA, why weight loss improves OSA, and why weight gain exacerbates OSA remain fundamental questions. Are there unique anatomy characteristics in different population of patients with OSA (e.g., children, different ethnicities)? We need to understand how oral appliances effect the upper airway. Addressing these questions is relevant to improved clinical management and personalized treatments for OSA. In addition, different image techniques have been applied to evaluate the upper airway anatomy including ultrasound. Understanding advantages and disadvantages are important. The purpose of this symposium is to address basic science of upper airway anatomy then to understand the physiopathology and treatment of OSA.

Learning Objectives

1.Learn the upper airway anatomy risk factors of OSA.

2.Understand the effect of obesity on upper airway anatomy.

3.Describe the target of oral appliance treatment on upper airway anatomy.

4.Examine the utility of ultrasound in evaluating upper airway anatomy.

Target Audience

Sleep physicians and researchers, Sleep technicians, Respiratory therapists, Nurses

Chairs

Richard Schwab、Liyue Xu (Co-chair)

Mechanistic insights on oral appliance therapy and multilevel surgery from imaging studies

Peter Cistulli (Australia)

Tongue fat/obesity and its relationship to OSA

Richard Schwab (USA)

Ultrasonographic evaluation of upper airway structures in children and adults with obstructive sleep apnea

Pei Lin Lee (Taiwan, China)

Insights into the pathogenesis of OSA with dynamic imaging

Yuan Feng (China)

Ethnic differences in upper airway anatomy

Liyue Xu (China)

Symposium 32: Sleep, Circadian Rhythms and Neurodegeneration– a multidisciplinary perspective

Summary

Disruptions of sleep and circadian rhythms are very common in patients with neurodegenerative diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD). Importantly, growing evidence suggests that sleep and circadian disruptions could be early manifestations of neurodegeneration, and might even be risk factors for the development of neurodegenerative diseases in healthy older adults. A greater understanding of the relationship between sleep, circadian rhythms and neurodegeneration could be key to enabling the early identification and management of neurodegenerative diseases. In this symposium, an international and multidisciplinary panel of experts will discuss the latest in the research of sleep, circadian rhythms and neurodegeneration. Dr. Jihui Zhang from Guangdong Provincial People's Hospital will kick off the session by talking about the circadian rhythm disruptions in REM sleep behavior disorders and its roles in the conversion of-synucleinopathies and its potential molecular mechanisms. Next, Dr. Kun Hu from Harvard Medical School will review recent studies and share their cutting-edge work on the use of physiological measures derived from motor activity recordings for detection of AD and prediction of Alzheimer's dementia. Dr. Yue Leng from the University of California, San Francisco will present a series of epidemiological findings on the link between daytime napping, an important but understudied sleep behavior, and neurodegeneration, and will highlight potential implications. Dr Angela D'Rozario from the University of Sydney will summarize the objectively measured changes to sleep macro- and micro structure that occur in older adults at-risk of dementia. She will provide insights about how alterations to sleep neurophysiology relate to cognitive functioning. Finally, Dr. Christian Benedict from Uppsala University will present their recent findings on diurnal pattern of blood pressure, which might have implications for sleep apnea, and risk of AD over 24 years of follow-up.

Learning Objectives

1. Highlight the use of actigraphy/motor activity recordings in predicting neurodegeneration and related pathology.
2. Describe the evidence base linking objective measures of sleep architecture with cognitive impairment and brain changes in aging and mild cognitive impairment.
3. Discuss how sleep, napping and circadian parameters might be longitudinally linked to risk of developing neurodegenerative diseases.

Target Audience

Researchers and clinicians with an interest in the impact of sleep and circadian disturbance on neurodegeneration

Chairs

Yue Leng, Jihui Zhang (Co-chair)

Objective daytime napping and neurodegeneration- a bi-directional relationship
Yue Leng (USA)
Circadian rhythm disruptions in REM sleep behavior disorders
Jihui Zhang (China)
'Noise' and rhythms in daily motor activity: linking sleep/circadian disturbances to Alzheimer's disease
Kun Hu (USA)
Sleep neurophysiology in older adults at risk for dementia: insights from high-density EEG
Angela Rozario (Australia)
Diurnal pattern of blood pressure and risk of Alzheimer's disease – a longitudinal study over 24 years
Christian Benedict (Sweden)

Objective daytime napping and neurodegeneration- a bi-directional relationship

Yue Leng, University of California, San Francisco

Napping, both intentional and not, is very common in the elderly. Growing evidence suggests a close link between napping and adverse health outcomes in older adults. However, few studies have examined napping objectively, and little is known about the effects of napping on neurodegeneration. In this presentation, Dr. Leng will present a series of epidemiological studies, both cross-sectional and longitudinal, where daytime napping was measured objectively by actigraphy and was associated with both Alzheimer's disease (AD) and Parkinson's disease (PD). Specifically, in community-dwelling older women, those with a history of AD or PD were at least three times more likely to be long day nappers; In older men, those who had long daily napping duration were more likely to develop AD or PD over 12 years of follow-up. Furthermore, Leng will highlight their recent findings that suggested a potentially bidirectional relationship between daytime napping and AD: Longer/more frequent daytime napping and Alzheimer's dementia may share common pathophysiological mechanisms.

Circadian rhythm disruptions in REM sleep behavior disorders

Jihui Zhang, Guangdong Mental Health Center, Guangdong Provincial People's Hospital

Circadian rhythm disruptions are commonly found in late stage of neurodegeneration. Recent studies have suggested that circadian rhythm disruptions may predict the onset of neurodegeneration and serve as prodromal markers. By employing an ultra-high-risk cohort (idiopathic REM sleep

behavior disorder cohort, iRBD), we have previously found that circadian rhythm disturbance, as measured by 7-day actigraphic data, accelerates the conversion of α -synucleinopathies. These findings may also suggest that circadian rhythm disruption may be a reversible environmental risk factor for the prevention and intervention of α -synucleinopathies. In this presentation, Dr. Zhang will discuss the circadian rhythm disruptions in REM sleep behavior disorders and its roles in the conversion of α -synucleinopathies and its potential molecular mechanisms.

"Noise" and rhythms in daily motor activity: linking sleep/circadian disturbances to Alzheimer's disease

Kun Wu, Brigham & Women's Hospital, Harvard Medical School

Human motor activity display complex temporal fluctuations, including rhythms and seemingly irregular 'noise' at multiple time scales. Using analytical tools derived from both traditional sleep/ circadian physiology and modern concepts of nonlinear dynamics, studies have demonstrated the existence of rich information 'hidden' in such temporal fluctuations of motor activity that reflects the regulation of sleep and circadian rhythms and beyond. Taking advantages of these unobtrusive measures based on daily motor activity fluctuations, recent studies have provided cumulative evidence for the mechanistic links between sleep/circadian disturbances and Alzheimer's disease. This presentation will consider certain these activity-based measures including sleep fragmentation, the amplitude and stability of daily/circadian activity rhythms, and fractal activity patterns, discussing their physiological meanings and their relevance to Alzheimer's disease (AD). It has been accepted that AD may progress silently for a decade or even longer before the cognitive symptom can be diagnosed clinically. Previous treatments of AD have been exclusively focused on the stage after the clinical manifestation of the disease, but all failed. The preclinical phase may provide a better window for potentially effective interventions such that identifying individuals with a higher risk of Alzheimer's dementia or the early sign of AD at preclinical stage is important. Thus, one of the main questions in this presentation is: are those physiological measures derived from motor activity recordings useful for detection of AD and prediction of Alzheimer's dementia? To address this question, the presentation will review some recent studies, showing how those activity measures change with aging, and whether and how Alzheimer's disease impacts these age processes at different stages of AD, especially preclinical stages with normal cognition. In addition, one puzzling phenomenon in AD is that some patients maintain normal cognition despite well pronounced AD pathology in the brain. Understanding of such cognitive resilience to AD is clearly of great importance for future design of treatments/therapies in order to slow down or prevent AD effects on cognition. To this end, some published or newly obtained results in on-going studies will be presented to illustrate the potential role of sleep/circadian regulation in cognitive resilience to AD pathology.

Sleep neurophysiology in older adults at risk for dementia: Insights from high-density EEG

Angela D'Rozario, The University of Sydney, Woolcock Institute of Medical Research

Sleep disturbance and sleep disorders are increasingly recognized as risk factors for dementia. Almost two thirds of clinical patients with mild cognitive impairment, the prodromal stage of dementia, report disturbed sleep. Objectively measured changes to sleep macro-structure in MCI include less sleep time and more time spent awake, with more light sleep and less REM sleep. Analysis of sleep micro-structure using limited channel EEG suggests deficits in key neural oscillations crucial for learning and memory processes. Loss of sleep spindles and slow wave activity during NREM sleep, and abnormal EEG slowing during REM sleep have been reported in MCI. However, no prior studies have used high-density EEG to investigate regional changes in local sleep and relationships with sleep-dependent memory consolidation in older adults with MCI, an important gap addressed by this study. Older adults with multi-domain MCI (n=19, mean age 68.5 years) and age-matched controls (n=22, 69 years) had 256-channel high-density EEG recordings during overnight polysomnography. Declarative (word paired associates) and procedural (finger tapping) memory tasks were administered before and after sleep. Participants also underwent neuropsychological testing and a brain MRI scan. After artefact processing, spectral analysis was performed for high-density EEG recordings. Topographical power maps were calculated for standard frequency ranges for sleep stages. Maps were compared between groups using both absolute and normalized power (z-scores computed for each subject). Compared to cognitively-intact controls, sleep-dependent memory consolidation was impaired in the MCI group. Preliminary topographic analysis of high-density EEG data revealed regional abnormalities during sleep in MCI. Exploring sleep EEG abnormalities and changes to underlying brain structures may provide mechanistic insights into the impact of regional sleep deficits on cognitive outcomes and identify therapeutic targets for future sleep interventions in older adults at risk for dementia.

Diurnal pattern of blood pressure and risk of Alzheimer's disease – A longitudinal study over 24 years

Christian Benedict, Uppsala University

Background: A lower day-to-night systolic blood pressure (BP) dip has previously been associated with poor brain health and cognitive functions. Here, we sought to examine whether reduced (nighttime/daytime ratio of systolic BP >0.9 and ≤1) and reverse (nighttime/daytime ratio of systolic BP >1) dipping of systolic BP is associated with future risk of dementia in Swedish older men. Methods: Twenty-four-hour ambulatory BP monitoring was used to estimate the nocturnal systolic BP dipping status of men at age 70 (n = 997) and 77 (n = 611). Dementia incidence during the observational period up to 24 years was determined by reviewing participants' medical history and independently confirmed by at least two experienced geriatricians. The association between systolic BP dipping status and incidences of all-cause dementia, Alzheimer's disease (AD), and vascular dementia was analyzed using time-updated Cox regression. These analyses were adjusted for age, body mass index, educational status, daytime systolic BP, treatment of hypertension,

3rd

diabetes, hyperlipidemia, physical activity, smoking, and cohabitation status. Results: Reverse systolic BP dipping was associated with a higher risk of all-cause dementia (HR [95%CI]: 1.64 [1.14, 2.34], P=0.007) and AD (1.67 [1.01, 2.76], P=0.047) but not vascular dementia (1.29 [0.55, 3.06], P=0.559). No associations between reduced dipping of nocturnal systolic BP and the outcome variables were found in the fully-adjusted analyses (P≥0.315). Conclusions: Reverse systolic BP dipping may represent an independent risk factor for dementia and AD in older men. Future studies should decipher whether therapies lowering nocturnal systolic BP below daytime levels can meaningfully curb the development of dementia.

Symposium 33: Translational studies for orexin and receptors

Chairs

Zhili Huang

Levels of wakefulness and sensory input

Zhian Hu (China)

On-demand control of arousal by hypocretin/orexin

Xiao-Bing Gao (USA)

Hypocretin/orexin receptor pharmacology and drug development: past, present and future

Thomas Kilduff (USA)

From gene transfer to neuron regeneration: history of orexin function restoration

Meng Liu (USA)

Increased numbers of histamine neurons containing histidine decarboxylase in narcolepsy type 1

Ling Shan (Netherland)

On-demand control of arousal by hypocretin/orexin

Xiao-Bing Gao, Dept of Comparative Medicine, Yale University School of Medicine

Sleep is a natural process that exists across species in the animal kingdom. It has been proposed and widely accepted that the sleep/wake cycle is regulated by two distinctive process, i.e., a circadian process C and homeostatic process S. The circadian process determines the timing of sleep and wakefulness while the homeostatic process depends on the "sleep debt" (prior wake time or loss of sleep). Although this two-process theory has been supported by intensive investigations, there is evidence suggesting that to certain extent wakefulness and arousal may be maintained either independent on the circadian clock within animal bodies or against the accumulating homeostatic regulators (such as adenosine) in animals. In this presentation, we would like to argue that wakefulness and arousal could be regulated in an on-demand way to meet environmental challenges that impact the survival of animals. The hypocretin/orexin (Hcrt) system in the perifornical/lateral hypothalamus (Pf/LH), is a central hub for the integration of a wide range of inputs from brain areas encoding metabolic, behavioral and environmental cues. Hcrt cells regulate both physiological homeostasis and complex behaviors in animals and humans. Our previous results indicate that changes in metabolic status, sleep/wake cycle, and reward-seeking behaviors, which always accompany with altered arousal levels, led to re-organization of the functionality of the Hcrt system. Most recently, our results suggest that an impaired Hcrt system is likely responsible for hypo-arousal in obese animals, which result in altered behaviors in obese animals. Therefore, we propose that the Hcrt system may be a mediator of the on-demand regulation of wakefulness and arousal in animals.

Hypocretin/orexin receptor pharmacology and drug development: past, present and future

Thomas S. Kilduff, SRI International

The two hypocretin/orexin excitatory neuropeptides, alternately called HCRT1 or orexin-A and HCRT2 or orexin-B, are the endogenous ligands for two G protein-coupled receptors, HCRTR1/OX1R and HCRTR2/OX2R. Shortly after the discovery of the hypocretin/orexin system, degeneration of hypocretin/orexin-producing neurons was implicated in the etiology of the sleep disorder narcolepsy. The involvement of this system in a disorder characterized by the loss of control over arousal state boundaries also suggested its role as a critical component of endogenous sleep/wake regulatory circuitry. The broad projections of the hypocretin/orexin-producing neurons, along with differential expression of the two receptors in the projection fields of these neurons, suggest distinct roles for these receptors. While HCRTR1/OX1R is associated with regulation of motivation, reward, and autonomic functions, HCRTR2/OX2R is strongly linked to sleep/wake control. The association of hypocretin/orexin with these physiological processes has led to intense interest in the therapeutic potential of compounds targeting these receptors. Agonists and antagonists for the hypocretin/orexin receptors have shown potential for the treatment of disorders of excessive

daytime somnolence and nocturnal hyperarousal, respectively, with two antagonists approved by the U.S. Food and Drug Administration (FDA) to date for the treatment of insomnia. These and related compounds have also been useful tools to advance hypocretin/orexin neurobiology. In this presentation, I will provide an overview of compounds directed toward hypocretin/orexin receptors that are currently marketed and under development for insomnia, narcolepsy and other potential indications.

From gene transfer to neuron regeneration: History of orexin function restoration

Meng Liu, Medical University of South Carolina

The loss of orexin neurons causes human narcolepsy. Restoring orexin function, the ultimate cure for narcolepsy, is still absent. The history of research efforts to restore orexin functions in animal models, along with the promising orexin neuron regeneration strategy, will be discussed in this presentation.

Increased numbers of histamine neurons containing histidine decarboxylase in narcolepsy type 1

Ling Shan, Department of Neuropsychiatric Disorders, Netherlands Institute for Neuroscience; Department of Neurology, Leiden University Medical Centre

The most recent neuropathological finding, that a greatly increased number of histamine neurons in narcolepsy with cataplexy (type 1) patients, is not seen in animal models in which only the hypocretin/orexin deficiency were mimicked by genetic modifications. In order to further investigate this human-only finding, we used 4 narcolepsy type 1 cases and 6 matched controls. Both the histaminergic neurons immunohistochemically marked by histidine decarboxylase (HDC) and the typical human tuberomamillary nucleus (TMN) neurons profile under the Nissl staining were blindly stereologically counted. The narcolepsy type 1 showed an increase of HDC neurons but not typical histamine neurons. These data support the hypothesis of an increase of HDC expression by existing histaminergic neurons rather than the generation of new histaminergic neurons in narcolepsy type 1 which could result from the autoimmune processes that cause the hypocretin/orexin deficiency.

Symposium 34: New Trends for the Relationship of Sleep with Human Cognition and Emotion

Summary

Plenty of researches have suggested that sleep plays an important role in human cognition and behavior. This symposium will review the updated study on sleep and cognition, and integrate with different methods, including behavioral measurements, EEG and fMRI, to investigate the effect of sleep/sleep loss on human cognition and emotion. Moreover, based on the current state of the studies, this symposium will also discuss the implication of the recent studies and the future direction of sleep and human attention, memory, emotion, and social function. The symposium is also aimed to provide an insight to connect the in-laboratory sleep research with the clinical intervention of sleep disorders, such as insomnia.

Learning Objectives

1. Summarize relevant information on the recent sleep research on cognition
2. Integrate different methods to investigate sleep on cognition, such as behavioral testing, EEG, and fMRI
3. Discuss the present issues on sleep and cognition and future direction

Target Audience

Doctor and Psychologists in both clinical and basic sleep-related domains

Chairs

Ning Ma, Xu Lei (Co-chair)

Effect of sleep and sleep loss on cognition
Ning Ma (China)
Simultaneous EEG-fMRI and its application in sleep study
Xu Lei (China)
The impact of sleep vs. sleep deprivation on emotional memories
Xiaoqing Hu (Hong Kong, China)
Effect of dawn simulation on morning sleep inertia under mild sleep restriction
Yingying Zhu (China)

Effect of sleep and sleep loss on cognition

Ning Ma, South China Normal University

Sleep is crucial for human survival and daily performance, but sleep loss commonly occurs in modern society. Individuals experience acute or chronic sleep deprivation due to work pressure, shift work or sleep disorders, and insufficient sleep leads to various dysfunctions of health and cognitive performance. Sleep loss can strongly impair various human cognitive functions, including attention, working memory, executive function and decision making. In this talk, I will first review the impact of sleep deprivation on human attention. A meta-analysis revealed significantly reduced brain activation in multiple regions following sleep deprivation compared to rested wakefulness, including bilateral intraparietal sulcus, bilateral insula, right prefrontal cortex, medial frontal cortex, and right parahippocampal gyrus. Increased activation was found only in bilateral thalamus after sleep deprivation compared to rested wakefulness, which may reflect a complex interaction between the de-arousing effects of sleep loss and the arousing effects of task performance on thalamic activity. Based on the findings in the meta-analysis, as the ascending arousal input hub, the thalamus may play a crucial role in modulating the interaction between the DMN and FPN. To examine the interaction mechanism between thalamus and other brain areas after sleep loss, a resting-state functional magnetic resonance imaging study was conducted with 42 participants under both normal sleep and 24-hour sleep deprivation conditions. The results revealed that sleep deprivation induced a robust alteration in the resting brain, and sustained attentional impairment after sleep deprivation could be predicted by altered frontal connectivity with crucial neural nodes of stimulus input, such as the thalamus and visual cortex. Furthermore, to verify the correlation between activity of neural network and different attentional states, a study by using dynamic functional connectivity was conducted with forty-two college students after sleep deprivation. The findings suggested that the functional connectivity of thalamus with other brain networks, such as DMN and FPN, was correlated with high/low arousal state after sleep loss.

Simultaneous EEG-fMRI and its application in sleep study

Xu Lei, Southwest University

Simultaneous Electroencephalogram-functional Magnetic Resonance Imaging (EEG-fMRI) technology is used to evaluate the correlation between electrical brain activity and hemodynamic mutation and integrates the complementary advantages of the high temporal resolution of EEG and the high spatial resolution of fMRI. The data from these two modalities can be combined in a number of ways, but all of the methods rely on the acquisition of high-quality EEG and fMRI data. In addition, it is a non-invasive technique for the study of human cognitive, emotional, social behavior, as well as brain function. However, it remains many challenges such as the low signal-to-noise ratio, poor human comfort and difficulty in the data analysis. In this talk, I will firstly introduce the hardware of simultaneous EEG-fMRI system, which the use of specialized EEG hardware should be safe and compatible with the MR environment and comfortable to the

participant. Since the data obtained from the simultaneous acquisition of EEG-fMRI are strongly influenced by artifacts and data analysis is a fundamental step for EEG-fMRI research studies and for simultaneous multimodal acquisitions generally, a review will be given about the advance of this technique, including the EEG artifacts correction, the EEG-fMRI data fusion method. Importantly, the application of EEG-fMRI in sleep research will be discussed. Specifically, I will provide a systematic classification of sleep research paradigms from simple to complex levels. This classification separated EEG-informed fMRI methods into 4 subtypes: separate brain stages, identify Sleep EEG events; dynamic of EEG rhythm and single-trial ERP-fMRI. With increased number of channels and features, the realization of these four subtypes have increased complexity. Finally, I will discuss the prospects for future sleep research based on simultaneous EEG-fMRI, since the demand of studies in the domain of sleep research and sleep medicine requires both the electrical brain activity and hemodynamic function.

The impact of Sleep vs. sleep deprivation on emotional memories

Xiaoqing Hu, The University of Hong Kong

Sleep plays a pivotal role in the off-line processing of emotional memory. However, large remains unknown for sleep's immediate vs. long-term influences on emotional memories and their affective tones. Here, we employed behavioral and electrophysiological measures to investigate the short- and long-term impacts of sleep vs. sleep deprivation on emotional memory. Fifty-nine participants incidentally learnt 60 negative and 60 neutral pictures in the evening and were randomly assigned to either sleep or sleep deprivation conditions. We measured memory recognition and subjective affective ratings in 12- and 60-hour post-encoding tests. We additionally recorded EEGs during the 60-hour delayed test. We found that, in the12-hour post-encoding test, compared to sleep deprivation, sleep equally preserved both negative and neutral memory, as well as their affective tones. In 60-hour post-encoding test, negative and neutral memories declined significantly in the sleep group, which are accompanied by attenuated emotional ratings to negative memories. In contrast, only neutral memories declined significantly in Sleep Deprivation group. Furthermore, in the 60-hour post-encoding EEG tests, two groups showed spatial-temporally distinguishable event-related brain potentials (ERPs): while both groups showed the old/new frontal negativity (300-500 ms, FN400) that may indicate familiarity, sleep-deprived participants additionally showed an old-new parietal, Late Positive Component effect (600-1000 ms, LPC) that may indicate recollection. Multivariate whole brain ERPs decoding analyses further suggested that sleep prioritized neural representation of valence over memory processing; while they were less distinguishable in sleep deprivation group. These data suggested that sleep's impact on emotional memory and affective responses are time-dependent: sleep preserved memories and affective tones in the short term, while ameliorating affective tones in the long term. In terms of brain responses, univariate ERP results suggest that sleep and sleep deprivation participants engaged different neurocognitive processes in recognition of remote, emotional memories. Moreover, multivariate ERP decoding results suggest

that sleep and sleep deprivation had different impact on processing of emotional information and memory.

Effect of dawn simulation on morning sleep inertia under mild sleep restriction

Yingying Zhu, Tianjin Normal University

Sleep inertia is a process from sleep to fully wakeup. The transition entails a temporary period of confusion, disorientation, reduced alertness, bad affect and poor task performance. Previous studies have focused more on the pharmacological ways (e.g., caffeine, excitant) of counteracting sleep inertia. However, there is little study investigating the non-pharmacological ways such as light exposure on the impact of sleep inertia post awakening up to now. The aim of the current study was to use behavior and PSG technique to explore the effect of morning sleep inertia on subjective alertness and mood as well as cognitive performance in healthy adults. We also examined whether exposure to dynamic dawn-simulated light could be a valid countermeasure against the detrimental effects of sleep inertia after waking up in the morning. A single factor within-subject design with lighting condition (at eye level) as independent variable was used in the present study. Three different light settings (separated by 1wk) were administered each morning after one 6-h sleep restriction night: A dawn-simulating light (starting 30min before scheduled wake-up time, polychromatic light gradually increasing from 0 to 210lux), a constant light (40lux for 30min before scheduled wake-up time) and a control condition (no light exposure prior to wake up). 21 college students (9 males) participated in the study based on strict selection criteria. Sleep inertia was measured by a 2-h test protocol since wakeup, including subjective ratings of alertness, mood, and performance on a psychomotor vigilance task (PVT), a 2-back and a go/no-go task. Results were as follows: A paired t-test between baseline and the first post-sleep assessment revealed a significant difference in both KSS and PANAS scores such that subjective alertness and positive mood immediately after awakening were much lower than at baseline, thereafter declined over a 2-h period as indicated by a significant effect of time. Performance on PVT, 2-back and go/no-go tasks were found to be significantly worse at the first test after wakeup than at baseline, and the effect of sleep inertia on these tasks dissipated over the course of two hours as indicated by a significant effect of time in the analysis of variance. Moreover, performance speed was more impaired than accuracy. Compared with control and constant light condition, the dawn simulation light resulted in a significant improvement of subjective alertness and positive mood after wakeup. Similarly, response time on PVT and accuracy on Go/no-go task were much faster and higher respectively in the artificial dawn condition relative to the control and constant light. However, the light conditions had no differential effects on negative mood and the 2-back task. Our findings suggest that morning sleep inertia has a significant negative effect on subjective alertness and positive affect as well as some cognitive functions like sustained attention, working memory and inhibitory capacity. The simulated dawn light could help counteract sleep inertia after awakening in the morning, whose effect was highly related to the light pattern with a dynamic exponential change.

Symposium 35: Oral therapy and sleep disordered breathing

Summary

During this symposium, we will discuss the application of oral-specific therapies to sleep disordered breathing. Congenital malformations, such as Down syndrome, present elevated prevalence of OSA, the treatment of Down syndrome who have elevated OSA symptoms will be described and the supporting literature will be discussed. For the Mandibular Advancement Device commonly used in OSA and habitual snoring, we will discuss the titration effects of MAD application, and the related meta-analysis. Similarly, there are many points worth discussing about the surgical treatment of OSA with severe skeletal deformities.

Learning Objectives

1.Application of Oral appliance for Down Syndrome

2.Titration effects of adjustable appliance

3.Other therapy instead of mandibular advancement device

4.Orthognathic surgery on OSA

Target Audience

Clinicians, Physicians, dentists, researchers and health care professional

Chairs

Xuemei Gao, Fernanda Almeida (Co-chair)

Titration effects of adjustable appliance

Xuemei Gao (China)

Oral appliance for Downs syndrome

Fernanda Almeida (Canada)

Alternative therapy to mandibular advancement devices

Satoru Tsuiki (Japan)

Effect of orthognathic surgery on OSA with severe skeletal deformity

Yang Li (China)

Treatment of OSA with Le Fort III osteotomy in children with syndromic craniosynostosis

Yue Liu (China)

Symposium 36: The epidemiology and heterogeneity of REM Sleep Behavioral Disorder (RBD)

Summary

The discovery of REM Sleep Behavioral Disorder is a significant milestone development in the history of sleep medicine and research. Various approaches have been applied to estimate the epidemiology of RBD regarding to the prevalence, phenotypes, and its association with α -synucleinopathy. Albeit that substantial knowledge of RBD stemmed from clinic-based studies, population-based studies could provide more valid estimation on the prevalence and risk factors of RBD. Dr. Taeko Sasai-Sakuma will talk about the population-based studies in RBD. Heterogeneity of RBD is related to demographics (e.g. age, gender, ethnic and individual difference), comorbidities (e.g. psychiatric disorders), and clinical outcomes of RBD (e.g. difference in rate of phenoconversion and duration from RBD to phenoconversion). Understanding of the heterogeneity in RBD would pave the way for the management of RBD and neuroprotective intervention. Dr. Xiao Li will talk about gender difference in RBD to explore the evidence and controversy of male predominance in RBD from both population and clinical perspectives. Dr. Jing Wang will talk about the intricate relationship between psychiatric disorders and RBD – is there a link? As a prodromal stage of α -synucleinopathy neurodegeneration, RBD provides a critical time window for neuroprotective intervention. Moreover, efforts were made to advance the time window even earlier, to the prodromal stage of RBD, such as isolated REM sleep without atonia, and REM sleep behavior events. Dr. Yaping Liu will talk about the increasing evidences on the conception of a continuum or spectrum of RBD, which covers a range from the status of prodromal stage of isolated RBD features to full blown clinical RBD. This symposium would discuss about the population-based strategy in exploring the epidemiology of RBD, the heterogeneity of RBD, gender difference in RBD, the link between psychiatric disorder and RBD, and the concept of prodromal RBD.

Learning Objectives

1. Updated with the current understanding in the epidemiology of RBD and its heterogeneity in etiology, phenotype, and prognosis.
2. Understand the implication of studying the prodromal RBD in epidemiology, prediction, disease modification related to RBD and α -synucleinopathy.
3. Accommodate a conceptual shift towards a spectrum concept of RBD in clinical care, research and education.

Target Audience

Professionals in sleep medicine, general physicians, neurology, psychiatry, geriatricians, students

Chairs

Yun Kwok Wing, Yuichi Inoue (Co-chair)

Epidemiology of RBD in population-based studies
Taeko Sasai-Sakuma (Japan)
Gender differences in RBD
Xiao Li (Hong Kong, China)
RBD and psychiatric disorders – is there a link?
Jing Wang (Hong Kong, China)
Prodromal RBD – does it exist?
Yaping Liu (Hong Kong, China)

Epidemiology of RBD in population-based studies

Taeko Sasai-Sakuma, Department of Clinical Laboratory Science, Faculty of Medical Technology, Teikyo University

Various epidemiological studies estimated prevalence of RBD as 0.74–2.01% in Asian and European countries, although study protocols vary among them. Knowledge about RBD, especially markers indicating development of α -synucleinopathy, has been accumulated from clinic-based RBD population. Nevertheless, neurodegenerative findings have not been well assessed for population-based RBD patients. We conducted an epidemiological study on general Japanese elderly population. In this talk, physiological and neuropsychological findings indicating α -synucleinopathy as well as epidemiological information of RBD based on the population-based study will be shown.

Gender differences in RBD

Xiao Li, Department of Psychology, The University of Hong Kong

RBD has been considered as a male-predominant parasomnia in some epidemiological and clinical studies, however, gender differences in RBD have not been well studied in the current literature. The presentation explores the gender differences in prevalence, comorbidities, clinical characteristics, and outcomes of RBD by systematically review the literature using both meta-analysis and qualitative analysis techniques. A systematic search of records in four major databases from inception to February 2020 identified 135 eligible observational studies that reported gender differences of RBD. Only English written articles reporting the key outcome measures were included in this review. In the general population, RBD including possible RBD (pRBD, diagnosed using questionnaires) and confirmed RBD (diagnosed using PSG) appeared to be significantly more common in males than females (pooled RR 1.39 (1.04-1.85)). However, when pooled pRBD and PSG confirmed RBD separately, males somewhat had a relatively higher risk for pRBD (pooled RR 1.34 (0.99-1.82)), but without a higher risk for PSG confirmed RBD (pooled RR 1.62 (0.78-3.95)). In the general population aged 60 years or over, the consistent results showed that males had significantly higher risks for RBD, pRBD and PSG confirmed RBD than females. Females

exhibited a marginally increased risk for secondary RBD than males (pooled RR 0.88 (0.77-1.017)). Male patients with Parkinson's disease (PD) showed a higher risk of comorbidity with RBD than female PD patients (pooled RR 1.24 (1.147-1.34)). Among idiopathic RBD (iRBD) patients, the pooled standardized mean difference in age of onset was -0.5 (95% CI -0.8 to -0.1), which would mean that male iRBD patients had an earlier onset age of 0.5 year compared with females. No significant gender differences were found in age at RBD diagnosis, the symptom of sleep-related injury, and EMG activities (phasic and tonic EMG activities, separately or together). No significant gender differences were found in the risk of developing neurodegenerative diseases in the patients with RBD (pooled RR 1.13 (0.93; 1.37)) or iRBD (pooled RR 1.10 (0.88; 1.37)). Overall, gender differences of RBD were found in the prevalence, comorbidities and age of RBD onset. However, the male predominance of RBD in the general population depended on the diagnostic methods of RBD and the population's age. In addition, the risk of developing neurodegenerative diseases was similar between male and female RBD patients. Future studies that utilizing strict diagnostic criteria for RBD and with longitudinal designs are warranted to better investigate the gender differences in RBD.

RBD and Psychiatric disorders – is there a link?

Jing Wang, Department of Psychiatry, The Chinese University of Hong Kong

Idiopathic REM sleep behavior disorder (iRBD) and psychiatric disorders (e.g., depression and anxiety disorders) are regarded as prodromal markers as well as risk factors of synucleinopathy neurodegeneration. Referring to existing literature including data from our group, in RBD patients, the proportion of comorbid psychiatric disorders was around 10-33%; while in psychiatric patients (mostly depression), we found that the prevalence RBD was nearly 10% (which is several times higher than that of RBD in the general population). The etiological mechanisms for the increased risk of RBD in the context of psychiatric disorders (psy-RBD) were not clear, but the antidepressant-induced effect cannot be the ultimate explanation, despite that there were cases reports on the temporal association between the initiation of antidepressant therapy (especially SSRIs) and the occurrence of RBD symptoms. Our previous case-control study found that psy-RBD had comparable severity of symptoms as typical iRBD, albeit were younger, more female, and taking more antidepressants. To date, the most clinical-relevant question is that whether psy-RBD would have a similar ending compared to iRBD (i.e., would most patients with psy-RBD also convert to neurodegeneration in a given time?). Our group had done a series of work to approach this unknown in the past decade. For example, in a case-control study using PET-imaging, we found that patients with comorbid depression and RBD had significantly lower striatal dopamine transmission than the depression control and healthy control, in addition to the finding that the comorbid depression and RBD patients had significant olfactory dysfunction (another prodromal marker for synucleinopathy). This study suggested that the development of RBD in patients with depression may signal the prodromal stage of neurodegeneration. Our recent case-control-family study in psy-RBD found that

the family of psy-RBD had clustered features of RBD, also had a higher risk for neurodegeneration diagnoses and a higher proportion of positive prodromal markers, compared to that the family of psychiatric control only presented familial aggregation of depression but no increased risk for neurodegeneration. These findings further consolidated the potential association between psy-RBD and neurodegeneration, and also suggested heterogeneity of depression on the association with neurodegeneration (i.e., depression comorbid with RBD is neurodegeneration-related, while depression without RBD is less likely so). In this talk, Dr. Wang will take about the intricate relationship between RBD and psychiatric disorders, with a stress on the potential association with the risk of neurodegeneration.

Prodromal RBD – does it exist?

Yaping Liu, Department of Psychiatry, The Chinese University of Hong Kong

Idiopathic REM sleep behavior disorder (iRBD) is a distinct parasomnia characterized by dream enactment behaviors and excessive electromyographic (EMG) activity during REM sleep (REM sleep without atonia, RSWA). Accumulating evidence suggested that this sleep disorder is a reliable prodromal stage of α -synucleinopathies, such as PD and dementia with Lewy bodies (DLB) and multiple system atrophy. In other words, identifying iRBD and its associated neurodegenerative biomarkers will facilitate recognition of the prodromal stage of neurodegeneration such that proper interventions can be applied to prevent the progression. The features of iRBD are complex ranging from mild RSWA to sustained muscle atonia (severe tonic EMG activity during REM sleep), and from mild REM sleep events (RBEs) to violent and rigorous nighttime behaviors. Emerging evidence suggests that even though some mild features of iRBD may fail to meet the diagnostic criteria for a clinical diagnosis, they may also still predict future full-blown iRBD and neurodegenertation. Thus, it suggests a prodromal concept of iRBD that neurodegeneration starts even before full-blown iRBD. This talk will summarize the up-to-date evidence suggesting a prodromal concept of iRBD and contemplate a future research direction in this very early prodromal stage of alpha-synucleinopathy.

Symposium 37: Child and Adolescent Sleep: Conceptualization, Assessment, and Neurobehavioral and Emotional Outcomes

Summary

Sleep is vitally important to children's health and well-being. Poor sleep and daytime sleepiness in children and adolescents have short- and long-term consequences on various aspects of health, especially their neurobehavioral and emotional development. Conversely, optimal childhood sleep trajectories promote positive developmental outcomes. Therefore, it is important to identify reliable assessment instruments for child and adolescent sleep behaviors, examine the role of multiple dimensions of sleep (duration, quality, chronotype) in neurobehavioral and emotional outcomes using both cross-sectional and longitudinal designs, and understand mediating and interactive factors underlying sleep-related outcomes in children and adolescents. This panel gathers five interdisciplinary sleep researchers to present new findings on sleep assessment and positive and negative emotional and cognitive outcomes of multidimensional sleep factors, conceptualizations of prevention and intervention of childhood sleep problems, and their overall implications for practice, education, and research. Yanyun Yang reports the reliability and validity of three adolescent sleep scales for assessing insomnia, daytime sleepiness, and nightmare distress in a large cohort of Chinese adolescents; Naixue Cui presents the delaying effect of bedtime smartphone use on sleep phase in Chinese adolescents and its possible linking mechanism to internalizing behavior; Xiaopeng Ji illustrates the interactive effects between social risk factors and sleep and chronotype on with executive function in a group of American adolescents; Ying Dai demonstrates childhood sleep quality trajectories has a bidirectional relationship with child happiness across childhood through a longitudinal cohort study, and maternal psychosocial support is moderating this relationship; and Jianghong Liu presents a conceptual framework on childhood sleep problems, including their risk and protective factors, consequences, and prevention and intervention strategies.

Learning Objectives

1. The audience will understand the reliability and validity of properties of three scales for assessing adolescent sleep problems: insomnia, daytime sleepiness, and nightmare
2. The audience will examine the role of circadian phase in the relationship between screen exposure and internalizing behavior.

Target Audience

This symposium is for audiences who are interested in sleep assessments and impacts of sleep on neurobehavior and emotional outcomes in children and adolescents and their implications for child development, education, and healthcare.

Chairs

Jianghong Liu、Fan Jiang (Co-chair)

Childhood sleep: factors associated with, consequences, and implications

Jianghong Liu (USA)

Adolescent sleep assessment: insomnia, daytime sleepiness, and nightmare distress

Yanyun Yang (USA)

Bedtime smart phone use and adolescent internalizing behavior: mediating role of circadian phase delay

Naixue Cui (China)

Sleep, chronotype and executive function among adolescents in the united states: social risk as a moderator

Xiaopeng Ji (USA)

Childhood sleep quality trajectory and childhood happiness: the moderating role of maternal psychosocial support

Ying Dai (USA)

Adolescent Sleep Assessment: Insomnia, Daytime Sleepiness, and Nightmare Distress

Yanyun Yang, Florida State University

Insomnia, daytime sleepiness, and nightmares are common in adolescents. Scales and questionnaires are available to assess these sleep problems, but they were either developed for Western adolescents or for adult population and may not be appropriate assessment tools for Chinese adolescents. Using data collected from a large sample of Chinese adolescents (n=11,831), this presentation reports psychometric properties of scales for assessing Chinese adolescents' insomnia, daytime sleepiness, and nightmare distress, respectively. Insomnia. The Youth Self-Rating Insomnia Scale (YSIS) was developed to assess insomnia. The scale consists of eight items assessing insomnia symptoms, perceived sleep quality and insufficiency, and impaired daytime functioning. Each item is rated on a 5-point scale. Factor analyses yielded two dominant factors defined as insomnia symptoms (3 items) and daytime distress or impairment (5 items). The factor structure was consistent between male and female adolescents. Internal consistency reliability coefficient was 0.80 and a 2-week test–retest reliability coefficient based on a subsample was 0.82. A receiver operating characteristic (ROC) curve analysis revealed that the suggested cutoffs are useful for predicting reported general sleep disturbance. Daytime Sleepiness. The Chinese adolescent daytime sleepiness scale (CADSS) consists of seven items assessing adolescents' general feeling of drowsiness and dozing off at different situations during daytime within the past month. Each item is rated on a 5-point scale. Factor analyses revealed one dominant factor. Internal consistency reliability coefficient was 0.89 and a 2-week test-retest reliability coefficient based on a subsample was acceptable. Correlational analyses supported concurrent validity of the scale. Cutoffs for excessive daytime sleepiness of

CADSS were suggested. Nightmare Distress. Based on the Nightmare Distress Questionnaire (NDQ; Belicki, 1992), a Chinese version of NDQ was developed to assess waking distress associated with nightmares in Chinese adolescents. The NDQ-CV consists of 14 items, rated on a 5-point scale. Factor analyses revealed a 2-factor structure. One factor is interpreted as nightmare general distress (10 items) and the other is defined as nightmare daytime reality perception (4 items). Internal consistency reliability was 0.88. The NDQ-CV scale scores were moderately and positively correlated with nightmare frequency, insomnia, daytime sleepiness, anxiety/depression and were weakly and negatively correlated with nocturnal sleep duration and academic performance, evidencing satisfactory concurrent and convergent validity. A ROC curve analysis showed that the suggested cutoffs are adequate for predicting depressive symptoms a year later. The YSIS, CADSS, and NDQ-CV appear to be simple, reliable, and valid scales for assessing insomnia, daytime sleepiness, and nightmare distress in Chinese adolescents. Further research is warranted to test psychometric properties of the three scales with different populations

Bedtime smart phone use and adolescent internalizing behavior: Mediating role of circadian phase delay

Naixue Cui, Shandong University

Background: Smart phone use before sleep is prevalent in and related to internalizing behavior problems among adolescents. Circadian phase may play an important role in this relationship. This paper presents the delaying effect of bedtime smartphone use on sleep phase in Chinese adolescents and its possible linking mechanism to internalizing behavior. Objective: To analyze the mediating effect of two circadian phase indicators, namely, sleep midpoint time and chronotype, in the relationship between bedtime smart phone use and internalizing behavior among Chinese adolescents. Methods: All adolescents at a vocational high school were invited to participate a questionnaire survey and 2,655 (36.8% females, 16.69 ± 0.96 years old) responded. A general information questionnaire, Pittsburg Sleep Quality Index (PSQI), Horne and Östberg Morningness and Eveningness Questionnaire (rMEQ), and Youth Self Report (YSR) were used to assess sociodemographic variables and bedtime smart phone use, sleep onset and wake time, chronotype and internalizing behavior, respectively. The medeff package in Stata 15 was used for the mediation analysis. The bootstrapping with 1000 resampling strategy was used to generate the indirect effect, 95% confidence interval (CI), its percentage of the total effect. Results: Among the participants, 82.4% reported smart phone use before sleep for 39.36 ± 19.59 minutes. A total of 446 (16.9%) adolescents were classified as eveningness chronotype. The mean of sleep midpoint time was 01:51am. Adolescents with smart phone use before bedtime reported more internalizing behavior (b=1.43, se=0.47, p=0.003). Smart phone use before sleep significantly delayed the sleep midpoint time by 26.08 ± 4.33min, and increased the likelihood of being eveningness chronotype (OR=1.89, 95% CI: 1.34, 2.60). The relationship between smart phone use before sleep and internalizing behavior was significantly mediated by sleep midpoint time (0.07, 95% CI: 0.01, 0.16) and

eveningness chronotype (0.25, 95% CI 0.14, 0.40), respectively. The indirect effects account for 1.9% and 6.6% of the total effects. Conclusions: Bedtime smart phone use significantly delay sleep phase, which can be a mechanism linking to internalizing behavior. However, this cross- sectional designed study cannot make any causal inference.

Sleep, chronotype and executive function among adolescents in the United States: social risk as a moderator

Xiaopeng Ji, University of Delaware

Background: Executive function (EF) is essential to goal-directed behaviors, emotional responses and social interaction. While habitual sleep duration and quality have been associated with EF, less clear are 1) the role of circadian preference among adolescents; and 2) whether social determinates perpetuate sleep-related disparities in EF. Purpose: To examine 1) the associations of multiple sleep metrics, chronotype with EF and 2) the interaction between sleep and social risk factors on EF among adolescents. Methods: Using a convenience sample from high schools and a public university, 94 adolescents (13-21 y.o.) completed the Pittsburgh Sleep Quality Index (PSQI), the Morningness/Eveningness Questionnaire and the Epworth Sleepiness Scale (ESS). EF was measured using gender- and age-adjusted T-scores from the Behavior Rating Inventory of Executive Function-Adult (BRIEF-A, age>18) and the BRIEF2-SR (13-18 y.o.). Higher BRIEF scores indicating a greater degree of executive dysfunction. Social cumulative risk (SCR) was calculated as the total number of risk factors (non-White, parent education ≤high school, family income below poverty threshold, and single-parent household). Multilevel random-effects models (by-school random-intercepts) estimated the associations after adjusting for age and gender. Results: Participants slept 6.61 ± 1.13 hours, with 68% below recommended sleep duration by age. More than half of adolescents (n=53) reported poor sleep (PSQI<5), 33% had excessive daytime sleepiness and 19% had evening chronotype. There was no main effect of sleep duration on EF, but interaction between sleep duration and SCR (β =1.38, p=0.03). Increasing SCR attenuated or even reversed the association between increasing sleep duration and better EF. Adolescents with morningness chronotype tended to have the best EF compared with those with eveningness (β =9.10, p=0.002) and intermediate chronotype (β =17.41, p<0.001). However, increasing SCR attenuated the protective impact of morningness on EF (p<0.05). Poor sleep (β =4.82, p=0.02) and increasing ESS scores (β =0.88, p<0.001) were associated with worse EF scores independent of SCR. Conclusion: Poor sleep quality, excessive daytime sleepiness and eveningness chronotype increase the risk of executive dysfunction in adolescents. Increasing social risk attenuates potential protective impact of sleep duration and morningness chronotype on EF. Our findings warrant the need of investigating sleep-related disparities in EF through an accumulative social risk perspective.

Childhood Sleep Quality Trajectory and Childhood Happiness: the Moderating Role of Maternal Psychosocial Support

Ying Dai, University of Pennsylvania

Background: Child sleep quality is associated with child academic performance and daily functioning. Less is known about how child sleep quality changes across child and early adolescence developmental stage and its relationship with child happiness across developmental age. Purpose: To investigate the relationship between childhood sleep quality trajectory and happiness trajectory, and the potential moderating role of maternal psychosocial support in this relationship. Method: A subsample of 452 children aged 10-12 years in the China Jintan Cohort Study with complete sleep quality across 0-10 years were included in analysis. Maternal psychosocial support was recalled by mothers through a validated questionnaire. Childhood sleep quality and child happiness across 1, 3, 5, 11, and 12 years of age were reported by mothers. All analysis was conducted in R (version 4.0.2). Two-level linear mixed-effects modeling of maternal psychosocial support, child sleep quality trajectory, and child happiness trajectory was conducted with the lme4 package, and cross-lagged modeling of child sleep quality and child happiness was conducted with the Lavaan package. Results: Children's average sleep quality gradually increased, while child happiness decreased, respectively across age 1, 3, 5, 11, and 12 (all $p < 0.001$). Maternal psychosocial support ($\beta = 0.741$ SE $= 0.027$, $p < 0.001$), and better child sleep quality ($\beta = 0.203$, SE $= 0.027$, $p < 0.001$) were associated with higher happiness across childhood. The interaction between maternal psychosocial support and child sleep quality trajectory was statistically significant ($\beta = -0.128$, SE $= 0.038$, $p < 0.001$). There was a cross-lagged relationship between child happiness and sleep quality. Specifically, happiness during the previous developmental age was associated with later better sleep quality ($\beta = 0.064$, SE $= 0.032$, p=0.047). Sleep quality during the previous developmental age was also associated with later happiness ($\beta = 0.058$, SE $= 0.028$, p =0.039). Conclusion: Maternal psychosocial support was a protective factor of child happiness across 1-12 years of age. Maternal psychosocial support was moderating the relationship between child sleep quality trajectory and child happiness trajectory across childhood. There was a bidirectional relationship between child sleep quality and child happiness across childhood. Promoting maternal psychosocial support and child sleep has implications for children's happiness and wellbeing.

Symposium 38: Multi–omics approaches for sleep research

Summary

Omics is a rapidly evolving, multi-disciplinary, field that encompasses genomics, epigenomics, transcriptomics, proteomics, and metabolomics. Each of these omics sub-specialties offers a unique opportunity to understand the biological mechanisms underlying human diseases and health problems. Prior work in the sleep field discovered and mapped the neural circuitry of sleep-wake regulation as well as biological pathways shared with cardio-metabolic, cognitive, neurodegenerative, and psychiatric conditions, setting the stage for research aimed at translating these findings into improvements in human health. However, there is large inter-individual variability of sleep/sleep disorders, as well as their impact on health issues, which is not well understood. As sequencing and mass-spectrometry technologies improve and costs decline, omics technologies represent an opportunity for researchers to advance our understanding of such inter-individual variability and help translate basic research findings into improved human health in the era of precision medicine. It is imperative for sleep researchers to build a foundational understanding of managing large omics datasets to help answer such questions. This symposium showcases the latest approaches and findings from applying multi-omics analyses to sleep research including: 1) high-resolution genetic markers of DNA polymorphism at single base pair to map risk genes and pathways and inform genetic overlap and causality between traits; 2) transcriptome markers quantifying mRNA expression levels present in specific tissues; 3) epigenetic markers (e.g., DNA methylation) influencing gene expression as a result of interplay between DNA and environment; 4) small molecule metabolites (e.g., peptides and lipids) that are the products of regulation by the genome, transcriptome, and proteome, consisting of signaling and structural molecules.

Learning Objectives

Understand the principles and scope of omics research in: genomics, epigenomics, transcriptomics, and metabolomics. Understand the methods and challenges of analyzing multi-omics data in sleep research. Understand the bi-directional associations (mechanisms) between sleep and multi-omics outcomes. Learn the latest multi-omics findings for sleep and sleep disorders research.

Target Audience

sleep clinicians and researchers who are interested in learning new -omics approaches

Chairs

Heming Wang, Xiaoyu Li (Co-chair)

Upregulation in the heme biosynthesis pathway increases obstructive sleep apnea severity: a mendelian randomization study
Heming Wang (USA)

Association between obstructive sleep apnea and epigenetic age acceleration: evidence from the multi-ethnic study of atherosclerosis

Xiaoyu Li (China)

Genetic analysis of obstructive sleep apnea discovers a strong association with cardiometabolic health

Satu Strausz (Finland)

Associations between actigraphy-measured sleep irregularity and plasma metabolomics in the multi-ethnic study of atherosclerosis

Tianyi Huang (USA)

Human metabolomics-based biomarkers of insufficient sleep and their association with cognitive performance

Christopher M. Depner (USA)

Causal associations of short and long sleep durations with 12 cardiovascular diseases: linear and nonlinear mendelian randomization analyses in UK biobank

Sizhi Ai (USA)

Upregulation in the heme biosynthesis pathway increases obstructive sleep apnea severity: a mendelian randomization study

Heming Wang, Harvard Medical School; Brigham and Women's Hospital

Introduction: Obstructive sleep apnea (OSA) is a common disorder associated with increased risk of cardiovascular diseases and mortality. Recent observational admixture mapping analysis and gene enrichment analysis linked genes and pathways associated with heme metabolism to OSA traits, but the causal contribution is unclear. Iron and heme metabolism is associated with OSA comorbidities and carotid body ventilatory control mechanisms. In this study, we use gene expression data to examine whether iron and heme related pathways have a causal effect on OSA. Methods: We performed Mendelian randomization (MR) analyses considering the expression level of 15 candidate Gene Ontology pathways as exposures and four OSA traits as outcomes, including the apnea hypopnea index (AHI), and three nocturnal oxygen saturation measurements. In discovery analysis, we performed two-sample MR using local expression trait loci (cis-eQTLs) from the Genotype-Tissue Expression (GTEx) portal and published genome-wide association summary statistics for OSA traits. Significant pathways were then followed-up by one-sample MR using high coverage DNA and RNA sequencing data from the Multi-Ethnic Study of Atherosclerosis generated by the NHLBI Trans-Omics for Precision Medicine (TOPMed) project. Results: Discovery analysis identified putative causal associations between up-regulated heme biosynthetic process pathway on increased AHI and overnight hypoxemia (minimum P-value=0.018 across OSA traits). These associations were supported in European and Hispanic/Latino Americans but not in African

Americans in replication analysis, consistent with prior ancestry-specific associations between a heme-related gene and OSA traits. Conclusion: This study suggested a causal association between heme biosynthetic processes and OSA severity, suggesting novel biomarkers and possibly treatment targets. Future work is needed to identify the mechanisms for this association and to exclude reverse causality.

Association between obstructive sleep apnea and epigenetic age acceleration: evidence from the Multi-Ethnic Study of Atherosclerosis

Xiaoyu Li, Tsinghua University

Introduction: Obstructive sleep apnea (OSA) is a common disorder that results in oxidative stress and inflammation and is associated with multiple age-related health outcomes. Epigenetic age acceleration is a DNA methylation (DNAm)-based marker of fast biological aging. We examined the associations of OSA traits with epigenetic age acceleration. Methods: A sample of 622 participants from the Multi-Ethnic Study of Atherosclerosis (MESA) had blood DNAm measured and underwent Type 2 in-home polysomnography that assessed apnea-hypopnea index (AHI), percentage of sleep time with oxygen saturation lower than 90% (Per90), and arousal index. DNAm data provided measures of DNAm-Age acceleration and DNAm-PhenoAge acceleration. The association of each SDB trait with age acceleration was estimated using linear regression, controlling for covariates. In secondary analyses, we studied the associations of SDB traits with epigenetic age acceleration 2-10 years after sleep study in 530 individuals from the Framingham Heart Study (FHS). Results: In MESA, AHI was associated with greater DNAm-PhenoAge acceleration ($\beta = 0.03$; 95% CI [0.001, 0.06]). Arousal index was associated with greater DNAm-Age acceleration ($\beta = 0.04$; 95% CI [0.01, 0.07]). Both associations were stronger in women than men. In the secondary FHS analyses, Per90 was associated with greater DNAm-Age acceleration and this association was stronger in men. Conclusion: More severe OSA was associated with epigenetic age acceleration in both cohorts. Future work should prospectively study short- and long-term effects of OSA, and whether treatment reduces epigenetic age acceleration among those individuals with SBD.

Genetic analysis of obstructive sleep apnea discovers a strong association with cardiometabolic health

Satu Strausz, University of Helsinki; Helsinki University Hospital

Introduction: There is currently limited understanding of the genetic etiology of obstructive sleep apnea (OSA). We aimed at identifying genetic loci associated with OSA risk and to test if OSA and its comorbidities share a common genetic background. Methods: We conducted the first large-scale genome-wide association study of OSA using FinnGen Study (217,955 individuals) with 16,761 OSA patients identified using nationwide health registries. Results: We estimated 8.3% SNP-based heritability and identified five loci associated with OSA (P < $5.0 \times 10{-}8$): rs4837016 near GTPase activating protein and VPS9 domains 1 (GAPVD1), rs10928560 near C-X-C motif chemokine receptor 4 (CXCR4), rs185932673 near Calcium/calmodulin-dependent protein kinase

ID (CAMK1D) and rs9937053 near Fat mass and obesity-associated protein (FTO) - a variant previously associated with body mass index (BMI). In a BMI-adjusted analysis, an association was observed for rs10507084 near Rhabdomyosarcoma 2 associated transcript (RMST)/NEDD1 gamma-tubulin ring complex targeting factor (NEDD1). We found high genetic correlations between OSA and BMI (rg=0.72) and with comorbidities including hypertension, type 2 diabetes (T2D), coronary heart disease (CHD), stroke, depression, hypothyroidism, asthma and inflammatory rheumatic diseases (IRD) (rg > 0.30). Polygenic risk score (PRS) for BMI showed 1.98-fold increased OSA risk between the highest and the lowest quintile and Mendelian randomization supported a causal relationship between BMI and OSA. Conclusion: Our findings support the causal link between obesity and OSA and joint genetic basis between OSA and comorbidities.

Associations between actigraphy-measured sleep irregularity and plasma metabolomics in the Multi-Ethnic Study of Atherosclerosis

Tianyi Huang, Harvard Medical School/Brigham and Women's Hospital

Introduction: Night-to-night irregularity in sleep duration and timing may lead to chronic circadian disruption and sleep disturbances. Emerging research suggests increased risk of metabolic syndrome and cardiovascular disease among individuals following irregular sleep schedules. Metabolomic profiling provides an opportunity to understand the metabolic mechanisms linking sleep irregularity and adverse cardiometabolic outcomes. Methods: We analyzed the cross-sectional data from 496 participants in the Multi-Ethnic Study of Atherosclerosis who provided fasting blood samples and wore wrist actigraphs for 7 consecutive nights at Exam 5 (2010-2013). Sleep irregularity was quantified by 7-day standard deviations (SD) in actigraphy-measured sleep duration and sleep onset timing. Plasma metabolites were measured by a semi-targeted approach using liquid chromatography-tandem mass spectrometry, with 363 known metabolites identified. Metabolite-by-metabolite associations with sleep irregularity were examined using multivariable linear regression, and false discovery rate (FDR) was used to correct for multiple testing. Results: After adjusting for age, sex, race/ethnicity, study sites, education and smoking status, 62 metabolites were associated with sleep duration SD and 85 metabolites were associated with sleep onset timing SD (FDR<0.2), with 34 metabolites consistently associated with both measures. Higher sleep irregularity was associated with lower levels of serotonin, cholesterol esters and sphingomyelins and higher levels of deoxygcholylglycine, phenylacetylglutamine, carnitines, triglycerides, diglycerides, phosphatidylcholine plasmalogens and metformin. The strongest inverse association was observed for serotonin, whereas the strongest positive association was observed for deoxygcholylglycine, a secondary bile acid. A weighted metabolomic score derived from these metabolites was found to be associated with markers of atherosclerosis, including the coronary artery calcification score and the ankle-branchial index (P<0.01 for both). Conclusion: Higher sleep irregularity was associated with multiple lipid and amino acid metabolites in plasma, which may contribute to future development of cardiometabolic disease.

Human metabolomics-based biomarkers of insufficient sleep and their association with cognitive performance

Christopher M. Depner, University of Utah

Introduction: There are many potential benefits of developing objective biomarkers of insufficient sleep such as creating new screening and diagnostic tools, increasing our understanding of sleep disruption and associated adverse health outcomes, and supporting new sleep-based countermeasures. Our aims are to assess the performance of our published candidate metabolomics-based biomarkers of insufficient sleep in an independent "validation" cohort and to determine if these biomarkers are associated with adverse cognitive consequences of insufficient sleep. Methods: For our validation cohort 12 healthy adults (6M/6F), age 24 ± 5 (mean$\pm$SD), completed two 18-day protocols separated by 10 days. For each 18-day protocol, participants maintained 9h sleep schedules for two weeks at home and then completed 4-day laboratory visits with sleep opportunities of: 9h on night 1, 5h on nights 2 and 3, and recovery sleep on night 4. Blood was collected every 2h during scheduled wakefulness on days 1-2 (baseline) and days 3-4 (insufficient sleep) and was analyzed by untargeted liquid chromatography/mass-spectrometry. Sustained attention was assessed every 2 h during scheduled wakefulness with the Psychomotor Vigilance Test (PVT). Results: After filtering, we detected 6,822 metabolites. Out of our previous candidate biomarkers, elastic-net regression identified 21 metabolites consistently altered by insufficient sleep. This 21 metabolite biomarker fingerprint has 74.4% accuracy and 0.822 (0.782-0.858; 95%CI) area under the receiver operator curve to detect insufficient sleep. Median reaction time was slower (P<0.05) during insufficient sleep versus baseline. Mediation analyses show our biomarker fingerprint accounts for <1% of the slower reaction time during insufficient sleep. Conclusion: We identified a plasma metabolomics-based biomarker of insufficient sleep with "good" performance. However, this biomarker accounts for <1% of reduced PVT performance during insufficient sleep. Our findings suggest specific biomarkers for insufficient sleep versus cognitive deficits associated with insufficient sleep may be required.

Symposium 39: Neurological Disease and Sleep

Chairs

Shuqin Zhan, Tao Wang

Autoimmune encephalitis related sleep disorders

Tao Wang (China)

Validation and update of the clinical diagnostic criteria. For fatal familial insomnia

Liyong Wu (China)

The study of dynamic cerebral autoregulation in patients with central disorder of hypersomnia

Zan Wang (China)

Diagnosis of narcolepsy and the type of genes in HLA

Jiyou Tang (China)

The features of obstructive sleep apnea syndrome and restless legs syndrome in Parkinson's disease

Kangping Xiong (China)

Symposium 40: The latest progress in the field of REM sleep: from basic research to clinics

Summary

As one of the fundamental sleep states, rapid eye movement (REM) sleep is believed to be associated with dreaming and is characterized by low voltage, fast electroencephalography activity and complete loss of muscle tone. The mechanism of REM sleep generation and maintenance remains unclear and has drawn researchers' attention for many decades. REM sleep behavior disorder is one of the sleep muscle tone related disorders and can be caused by some medications such as noradrenergic antidepressants. Narcolepsy, with core symptoms of excessive daytime sleepiness and cataplexy, is strongly connected with orexin in early adulthood. In addition, there are many common clinical REM sleep disorders related diseases. This symposium will discuss the neurobiological mechanism of Paradoxical (REM) sleep muscle atonia as well as clinical research and discussion on this, with the hope of laying a foundation for clinical application by combining basic research with clinical practice.

Learning Objectives

1. The progress in the field of the mechanism of REM sleep
2. Research updates of REM sleep disorders related diseases
3. Research updates of neuroprotective trials in RBD patients

Target Audience

Sleep Science Researcher, Clinical sleep medicine practitioner, Researchers of senile disorders related diseases

Chairs

Yi-Qun Wang, Huan-Yu (Co-chair)

Neural circuitry underlying REM sleep
Yiqun Wang (China)
Research update of neuroprotective trials in RBD patients
Huan Yu (China)
Paradoxical (REM) sleep muscle atonia: how and why?
Luppi Pierre Hervé (France)
The characteristic and function of the hypothalamus-to-sublaterodorsal orexin pathway
Jun Zhang (China)
REM sleep related spectrum disorders
Shuqin Zhan (China)

Neural circuitry underlying REM sleep

Yi-Qun Wang, Fudan University

As one of the fundamental sleep states, rapid eye movement (REM) sleep is believed to be associated with dreaming and is characterized by low-voltage, fast electroencephalographic activity and loss of muscle tone. However, the mechanisms of REM sleep generation have remained unclear despite decades of research. Several models of REM sleep have been established, including a reciprocal interaction model, limit-cycle model, flip-flop model, and a model involving γ -amino butyric acid, glutamate, and aminergic/orexin/melanin-concentrating hormone neurons. In the present review, we discuss these models and summarize two typical disorders related to REM sleep, namely REM sleep behavior disorder and narcolepsy. REM sleep behavior disorder is a sleep muscle-tone-related disorder and can be induced by some medications, such as noradrenergic antidepressants. Narcolepsy, with core symptoms of excessive daytime sleepiness and cataplexy, is strongly connected with orexin in early adulthood.

Research update of neuroprotective trials in RBD patients

Huan-Yu, Huashan Hospital, Fudan University

The summary of the researches of the neuroprotective trials in RBD patients.

Paradoxical (REM) sleep muscle atonia: how and why?

Luppi Pierre-Hervé, Lyon Neuroscience Research Center; Claude Bernard University

The latest progress in the paradoxical (REM) sleep muscle atonia.

The characteristic and function of the hypothalamus-to-sublaterodorsal orexin pathway

Jun Zhang, Department of Physiology, Third Military Medical University

The hypothalamic neuropeptide orexin (also named hypocretin) is a critical regulator for many vital brain functions. Interestingly, loss of orexin signaling has been directly linked to several clinical symptoms characterizing by motor impairments. More specifically, in addition to the sudden loss of muscle tone (cataplexy) in wakefulness after orexin deficiency, impaired quality of muscle atonia in rapid eye movement (REM) sleep has been recently reported by many clinical reports. However, roles of orexin signaling in REM sleep regulation still remain elusive. Here, we first tried to distinguish the orexin neurons from an output allocation perspective. The orexin neurons were retrogradely labeled from the sublaterodorsal tegmental nucleus (SLD) (REM-promoting) and locus coeruleus (wake-promoting), respectively. Intriguingly, this strategy labeled two divided group of orexin neurons with minimal overlap. In addition, the labeled SLD-projecting orexin (OXSLD) neurons (~7%) also exhibited increased c-Fos expression after the REM sleep rebound, in the silent background of the orexin neuronal entirety. Therefore, a potential sub-division of the hypothalamic orexin neurons regulating REM sleep may exist, through projections to the SLD. Using series of electrophysiological assays, we further found that orexin directly excited ~3/4 SLD neurons and

increased gap junction conductance among the SLD. Their interactions spread the orexin-elicited partial-excitation to activate SLD network globally, and the activated SLD network exhibited increased probability of synchronized firings. Consequently. the SLD output to its downstream target was found to be enhanced in vivo. In free-moving mice, a brain state activation with muscle tone decrease can be immediately induced upon optogenetic activation of SLD orexin signaling during NREM sleep, although complete REM sleep transitions were not achieved. Importantly, these observed abilities were found to be integrated during REM sleep and contributes to its stabilization, as specific activation of SLD orexin signaling within a REM sleep episode prolonged its duration with consolidated EEG theta oscillations and a decreasing trend in the EMGREM/NREM ratio. Consistently, elevated activities of SLD orexin terminals during REM sleep were directly observed by fiber photometry, and optogenetic inhibition of SLD orexin signaling within REM sleep shortened its episodes. Chemogenetics or genetic ablation methods were further employed to silence the orexin-SLD pathway, for hours or permanently, respectively. After chemogenetic inhibition, a 17.0% reduction in the total REM sleep amount was detected. In this condition, the physiological muscle tone decrease from NREM to REM sleep was abolished, which resulted in a significant failure of muscle atonia during REM sleep. Moreover, the theta oscillation power in REM sleep was also decreased. Surprisingly, a total deletion of orexin-SLD pathway by transfection of Caspase-3 in OXSLD neurons for a month did not change daily REM sleep amount, although the failure of muscle atonia was still observed. This appeared discrepancy led us to consider potential impacts of compensatory effects after permanent loss of SLD orexin signaling. We thus further examined the homeostatic regulation of REM sleep in the OXSLD-taCasp3 mice after 24-hour REM sleep deprivation. In this condition, the normal REM sleep rebound was blunted in the OXSLD-taCasp3 mice, and was frequently disrupted by abnormally increased muscle activities. Taken together, long-term loss of SLD orexin signaling disrupts core EEG/EMG features of REM sleep, and may eventually impairs the homeostasis of REM sleep. Considering the above findings, we are now examining the monosynaptic input/output patterns of these specific REM sleep-related OXSLD neurons, aiming at revealing the neural circuit basis for their REM sleep-related actions. With a combination of virus tracing strategies, we have preliminary data showing that the OXSLD neurons most specifically innervated SLD, although relatively low density of OXSLD fibers were detected in the nearby locus coeruleus. Besides, the OXSLD fibers largely avoid several brain regions, such as the ventral pallidum and the paraventricular thalamus, which are known to be innervated by the orexin entirety in previous studies. The analysis of monosynaptic upstream regions from SLD-projecting orexin neurons demonstrated a similar pattern of that from the orexin entirety, suggesting that the modulation of this pathway on SLD and its related REM sleep regulation may come from a subtle discrepancy of input, and more details on their activities/specific actions should be considered.

REM sleep related spectrum disorders

Shuqin Zhan, Xuanwu Hospital of Capital Medical University

Based on the physiological characteristics of REM sleep, we have collected and analyzed the special characteristics of REM related sleep disorder in a group of patients. We propose the new concept, REM sleep related spectrum disorders, in order to analyze the difference and similarities of its clinical phenotypic characteristics and the pathophysiological mechanism, and to discuss the diagnosis and intervention strategies.

Symposium 41: Hypoventilation Derived from Rare Respiratory Genetic Disorders

Summary

This symposium summarizes current basic and clinical knowledge on two rare genetic disorders of respiratory control, congenital central hypoventilation syndrome (CCHS) and Prader-Willi syndrome (PWS). CCHS is characterized by lack of ventilatory chemosensitivity caused by PHOX2B gene abnormalities consisting mainly of alanine expansions. PWS manifests as sleep-disordered breathing with apneas and episodes of hypoventilation and is caused by the loss of a group of paternally inherited genes on chromosome 15. Studies of CCHS and PWS extend our knowledge of the molecular and cellular aspects of respiratory rhythm generation and suggest possible pharmacological approaches to respiratory control disorders. This knowledge is relevant for the clinical management of many respiratory disorders that are far more prevalent than the rare diseases discussed here.

Learning Objectives

1.To understand the underlying mechanism of CCHS
2.To understand diagnosis and management of Prader-Will syndrome
3.To learn basic knowledge of respiratory chemoreceptors
4.To help understand shared pathogenic mechanism underlying sleep-disordered breathing

Target Audience

Sleep physicians and researchers, Sleep technicians, Respiratory therapists, Physiologist

Chairs

Sheng Wang, Sergey Kasparov (Co-chair)

Neurobiology of CCHS
Sheng Wang (China)
Astrocyte-to-neuronal communication in control of cardio-respiratory homeostasis
Sergey Kasparov (UK)
The physiology of congenital central hypoventilation syndrome
Martin Samuels (UK)
Diagnosis and management of Prader-Willi syndrome
Yalei Pi (China)

Neurobiology of CCHS

Sheng Wang, Hebei Medical University

This talk will cover the findings showing characteristic of Phox2b-expressing neurons as central respiratory chemoreceptors in the brainstem, ionic mechanism of pH sensitivity of these neurons, circuit mechanism of controlling breathing.

Astrocyte-to-neuronal communication in control of cardio-respiratory homeostasis

Sergey Kasparov, University of Bristol

In this presentation I will discuss how non-neuronal components of the brain, called astrocytes modulate and control cardio-respiratory functions which we study in rodents. Molecular mechanisms of astrocytic homeostatic function and glia-neuronal communication will be discussed.

The Physiology of Congenital Central Hypoventilation Syndrome

Martin Samuels, Great Ormond Street Hospital

The talk will cover the findings of research studies examining the pathophysiology of CCHS, especially the disorder of respiratory control, its relationship to the more generalized dysautonomia, and what this teaches us about our understanding of respiratory control in humans.

Diagnosis and Management of Prader-Willi syndrome

Yalei Pi, The Second Hospital of Hebei Medical University

This talk will cover clinical manifestations, diagnosis and management of Prader-Willi syndrome.

Symposium 42: The gating and maintenance of sleep and wake: New circuits and insights

Summary

This symposium summarizes current basic and clinical knowledge on two rare There is increasing urgency to gain knowledge of the neural mechanisms and molecular substrates that regulate sleep and to reveal the causal links between sleep and health. New opto-/chemo-genetic-based tools and tracing methods for neural circuits have enabled unprecedented investigation of discrete circuit elements (e.g., transmitters, pathways, cell populations) and identification of genes and signaling pathways that regulate sleep/wake behavior. As a result, new cellular and molecular targets for treating sleep disorders have been identified. The objective of this symposium is to highlight some of this recent work and promote a more integrated approach to the understanding of sleep-wake regulation by bringing together efforts to identify sleep/wake controlling circuits by optogenetic and chemogenetic methods and genetic and biochemical work seeking to understand sleep/wake regulating mechanisms at a molecular and cellular level. The invited speakers will discuss their recent work in which they have identified new cellular and molecular circuits controlling the behavioral states, namely wake, NREM, and REM sleep. For example, Dr. Yadong Li will discuss his work on the gating of sleep and wakefulness in response to emotional behaviors. Dr. Arisa Hirano will discuss her lab's latest findings on the neural network regulating circadian sleep-wake rhythms, whereas Dr. Shoi Shi will discuss his findings that components of Ca2+-dependent hyperpolarization pathways play a role in sleep duration regulation. Finally, Dr. Mathias Treier will discuss his group's new finding on the links between metabolic demand, water/food availability and sleep amount. The speaker panel hails from 3 different countries, spanning from Germany to Japan to China, including Dr. Treier, an internationally renowned scientist on metabolic disorders, "up and coming" younger investigators (Drs. Li and Shi) as well as a female investigator (Dr. Hirano).

Learning Objectives

1. Differentiate and describe the neural circuits by which the brain executes behavioral state control, including maintenance of wake, non-rapid-eye-movement (NREM) sleep and rapid-eye-movement (REM; or paradoxical) sleep.
2. Evaluate and contrast old and new concepts and models describing the regulation of sleep and wakefulness by homeostatic, metabolic, circadian and motivational processes.
3. Give examples of, and critically evaluate, the appropriate application of cutting-edge molecular neuroscience tools, including optogenetics, chemogenetics, in-vivo photometry, and computational neuroscience.

Target Audience

Sleep neuroscientists/researchers, Sleep neurologists working with patients suffering from insomnia, excessive sleepiness or circadian sleep disorders

Level: graduate students, postdoctoral fellows and faculty

Chairs

Michael Lazarus、Yoan Cherasse (Co-chair)

Ventral basal ganglia control of arousal and related emotions

Yadong Li (USA)

Functional analysis of neural network regulating circadian sleep-wake rhythms

Arisa Hirano (Japan)

Ca2+-dependent/independent hyperpolarization pathways in sleep regulation

Shoi Shi (Japan)

No need to sleep if you should drink and eat

Mathias Treier (Germany)

Ventral basal ganglia control of arousal and related emotions

Yadong Li, Department of Pharmacology, University of North Carolina at Chapel Hill

The basal ganglia, a group of interconnected nuclei in the vertebrate fore- and mid-brain, has been broadly studied in numerous behaviors, including locomotion, learning, navigation, and sleep/wake behaviors. These studies, whether explicitly stated or not, mainly focus almost exclusively on the dorsal basal ganglia, which is formed by the well-known direct and indirect pathways. However, the same level of systematically grouped nuclei, compared to dorsal basal ganglia, are ventral basal ganglia, which are normally thought to specifically regulate behaviors, including motivation, reward, emotion, and addiction. However, our understanding of whether and how the ventral basal ganglia regulate sleep/wake behaviors is much less, compared to a large number of published papers on dorsal basal ganglia. Traditionally, the ventral basal ganglia have equal "direct" and "indirect" pathways: dopamine D1R neurons in the nucleus accumbens (NAc) send direct GABAergic projections to the ventral tegmental area (VTA), while NAc D2R neurons send GABAergic projections to the ventral pallidum (VP), then VP sends GABAergic projections to the VTA. Briefly, the NAc, VP, and VTA form the key component of the ventral basal ganglia, among which, NAc is the first input, VTA is the output of the ventral basal ganglia and VP is the relayed nucleus. But the fact is different subtypes of neurons in these nuclei intricately interact with each other, playing a positive or negative role in regulating several fundamental behaviors. Previous studies have clearly shown that dopaminergic neurons in the VTA promote arousal through NAc, however, how do

the ventral basal ganglia integrate inputs and outputs in regulating arousal and related motivated behaviors are still poorly understood. In this study, our focus, in particular, is on the key role of the ventral basal ganglia in regulating arousal. Furthermore, we also recovered that the modified arousal by the ventral basal ganglia manipulation is related to motivation/depression. These findings will help us to understand how sleep disorders are associated with several mental diseases.

Functional analysis of neural network regulating circadian sleep-wake rhythms

Arisa Hirano, International Institute for Integrative Sleep Medicine, University of Tsukuba

Sleep-wake cycle and many other biological rhythms with a period of 24 hours are regulated by internal body clock system. The master circadian clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus in mammals. The mechanism of the circadian oscillation at the molecular level in each SCN neuron has been well characterized. However, it is still largely unknown how physiological rhythms (i.e., sleep/wake rhythms) are systematically regulated at the neural circuit levels. Here, we performed retrograde tracing analysis of neurons in ventral lateral preoptic area (VLPO), which is known to contain sleep-active neurons. We found that input neurons included SCN neurons, which is also confirmed by the anterograde tracing assay. Functional assay by using pharmacogenetics indicated that activation of SCN neurons especially at night time induced sleep through activation of VLPO. On the other hand, activation during light phase had no effect on mouse locomotor activity. Considering the previous studies showing that SCN neural activity is higher during subjective daytime than night in mice, activated SCN neurons in the light phase induces POA activity and trigger sleep behavior in physiological condition. The sleep-wake rhythms are largely affected by the neurotoxin expressed in SCN neurons projecting to VLPO, although the molecular rhythms of PER2::LUC in the SCN are still observed in these mice. This suggested that the SCN subpopulation projecting the sleep center is necessary for output of sleep-wake rhythms but not for the clock oscillation itself and output of other biological rhythms.

Ca^{2+}-dependent/independent hyperpolarization pathways in sleep regulation

Shoi Shi, Department of Systems Pharmacology, University of Tokyo

Sleep is a physiological phenomenon that is widely conserved throughout the animal kingdom. Although we are beginning to understand the neuronal and biochemical nature of sleep regulation, questions remain about how sleep amount is controlled and how sleep is homeostatically regulated. Beyond its importance in basic physiology, understanding sleep in molecular level will provide a new therapeutic target in sleep disorder (e.g., insomnia). Thus, one of the primary goals of sleep research is to answer a question that how sleep duration is regulated. To address this challenge, we combined mathematical analysis and comprehensive KO study. We developed a series of simple computational models of cortical neurons with multiple channels and receptors. By using mean-field approximation, these mathematical models succeeded in recapitulating the cortical electrophysiological characteristics of slow-wave sleep (SWS firing pattern) and wakefulness.

In order to validate the essential channels for SWS firing pattern, we performed comprehensive bifurcation and detailed mathematical analyses against these mathematical models, which predicted that a part of Ca2+ channels and K+ channels play a role in generating the electrophysiological characteristics of SWS firing pattern. The predicted mechanism is as follows: 1) During the bursting phase of SWS firing pattern, Ca2+ enters mainly through NMDA receptors and voltage-gated Ca2+ channels to increase the intracellular Ca2+ concentration. 2) The transition from bursting to silent phase occurs when the intracellular Ca2+ concentration reaches a certain threshold, which activates Ca2+-dependent K+ channels. 3) In the silent phase, Ca2+ exits through Ca2+-pump/exchangers to decrease the intracellular Ca2+ concentration. 4) The transition from silent to bursting phase occurs when the intracellular Ca2+ concentration decreases, which inactivates the Ca2+-dependent K+ channels. These results lead to a hypothesis that these channels play a role in the regulation of sleep duration. To test this hypothesis experimentally, we comprehensively generated and analyzed KO mice of these predicted channels, and analyzed their sleep phenotypes. As a result, we identified a series of genes in the Ca2+-dependent/-independent hyperpolarization pathways play a role in regulation of sleep duration.

No need to sleep if you should drink and eat

Mathias Treier, Max Delbrück Center for Molecular Medicine

Why we sleep is still a mystery. Hunger and thirst are potent stimuli that suppress sleep. Indeed, terrestrial animals like elephants and giraffes that extensively need to forage for water/food sleep very little without negative consequences. Food/water seeking is a complex physiological response to metabolic demands that requires an increased state of wakefulness, arousal and locomotory activity. We have identified a neuronal network in mice that is sufficient to elicit and maintain food/water foraging for days without sleep. In contrast, deletion of the genetic components encoding this innate behavior lets mice fall asleep upon food deprivation. Our findings suggest that the amount of sleep depends on the balance between metabolic demand and water/food availability and is set for each species individually according to its habitat.

Symposium 43: Understanding, Modulating and Enhancing Sleep Process with Novel Neurotechnologies and Models

Summary

The theme of this workshop focuses on the applications of multi-modal brain imaging and advanced non-invasive neurotechnologies in the diagnosis and treatment of sleep disturbances. As such, this workshop will address the recently discovered neurophenotypes from large-scale neuroimaging studies with multi-modality imaging methods, as well as the potential utilities and workflows when using these findings to guide brain-based interventions (i.e., personalized medicine). In this workshop, we will endeavor to foster exchange and collaboration between researchers working at different fields, including cognitive psychology, neuroinformatics, computational and clinical neuroscience. By fostering exchange between neuroscientists, engineers and clinicians, this workshop will address several topics for the collaborations between researchers working on related research, and to draw inspiration for interdisciplinary and intermodal interactions during the workshop. This workshop will be ideal for junior researchers to discuss their work with the experts from different fields, in either Lightening Round Presentations or interactive Q&A sessions, which allows this workshop to provide a unified framework for educating and promoting new ideas and in-depth collaborations.

Learning Objectives

1. Identify and differentiate the main types of sleep disturbances in development, normal ageing and age-related neurodegenerative diseases.
2. Outline cutting-edge and evidence-based brain stimulation treatments for sleep disorders
3. Describe non-pharmacological treatments for sleep disorders.
4. Discuss recent breakthroughs in neuroimaging, neurology, and brain stimulation which influence management of patients with sleep disturbances.
5. Examine the role of transcranial brain stimulation in the diagnosis, characterization, and management of sleep disturbances in neurodegenerative diseases.

Target Audience

Neurologists, Psychiatrists, Physicians, Rehabilitation, Medicine, Neuroscience Nurses, Neurosurgery Nurses, Nurse Practitioners, Occupational Therapists, Respiratory Therapists, Dietitians, Radiology Technologists, Pharmacists, Rehabilitation and Pain Management Specialists, Physician Assistants, as well as other specialists interested in the fields of sleep medicine, brain stimulation and neuroscience.

In particular, this symposium will add tremendous value to residents and clinicians in training as well as fellows in multiple specialties, including sleep medicine, internal medicine, neurology, psychiatry and geriatrics.

Chairs

Hanna Lu, Jiahui Deng (Co-chair)

Transcranial brain stimulation, sleep quality and cognition: recent findings from randomized clinical trials
Hanna Lu (Hong Kong, China)
Disrupting sleep oscillations by transcranial alternating current stimulation in rem sleep impairs emotional memory consolidation
Jiahui Deng (China)
Sleep disorders and neurodegenerative diseases
Junliang Yuan (China)
Open-source software for advanced analysis of sleep EEG in clinical populations using MDD as an example
Frederik Weber (Netherland)
Trajectory of sleep and cognitive change: new insights from statistical modeling
Xi Ni (Hong Kong, China)

Transcranial brain stimulation, sleep quality and cognition: recent findings from randomized clinical trials

Hanna Lu, The Chinese University of Hong Kong

Objective: We aimed to investigate the effects of transcranial direct current stimulation (tDCS) on sleep quality and cognition in mild neurocognitive disorder due to Alzheimer's disease (NCD-AD) patients. Methods: A 12-week, double-blind, randomized controlled trial (Registration ID: ChiCTR-TRC-14005036) was conducted in 201 mild neurocognitive disorder due to Alzheimer's disease (NCD-AD) patients. All subjects were randomly assigned to receive a 4-week intervention of either a combination of tDCS and cognitive training, sham tDCS, or tDCS. Primary outcomes included sleep quality (measured by PSQI) and global cognition (measured by ADAS-Cog) at 4th week, 8th week and 12th week. Results: Compared to combined modality, mild NCD-AD patients who received tDCS only demonstrated prominent enhancement on sleep quality at 12th week (F=9.5, p= 0.003). Within the tDCS group (n=62), we defined poor sleepers as baseline PSQI total score>5 and good sleepers as PSQI total score≤5. After a 4-week course tDCS treatment, poor sleepers showed significantly enhanced sleep quality than good sleepers at 4th week (t=-2.41, p=0.02), 8th week (t=-2.7, p=0.01) and 12th week (t=-4.38, p<0.001). Meanwhile, poor sleepers had more cognitive gains than good sleepers across the follow-up observations, including global cognition measured by ADAS-Cog (4th week, t=-2.42, p=0.019; 8th week, t=-2.19, p=0.031). Conclusions: A 4-week course tDCS has significant positive effects on sleep quality and cognitive function in mild NCD-

AD patients with or without sleep disturbances.

Disrupting sleep oscillations by transcranial alternating current stimulation in REM sleep impairs emotional memory consolidation

Jiahui Deng, Peking University

Research demonstrates that emotional memories are preferentially retained across time. Notably, this effect appears to be enhanced by sleep. Selective effects of sleep on emotional memory have mostly been studied in the context of episodic memory. Transcranial alternating current stimulation (tACS) is a non-invasive brain stimulation technique that allows interaction with endogenous cortical oscillatory rhythms by means of external sinusoidal potentials. Whether transcranial alternating current stimulation in REM sleep could modulate emotional memory consolidation is less known.

Sleep disorders and neurodegenerative diseases

Junliang Yuan, Peking University Sixth Hospital

Sleep disorders are associated with increased risk of neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD). In this presentation, Dr. Yuan will systematically summarize the recent findings of the relationship between sleep disorders and neurodegenerative diseases.

Open-source software for advanced analysis of sleep EEG in clinical populations using MDD as an example

Frederik Weber, Donders Institute

SpiSOP (abrev. for Spindles Slow Oscillation and Power-spectral-density) is an open source tool supporting detection and reporting of spindle or slow oscillation events, their co-occurance or respective matching non-events and power (density) of specific spectra or frequency bands in pre-scored (sleep stages) EEG and MEG data as well as simple automatic EMG artifact detection. Most detection methods and annotations reported in sleep EEG research are covered and thus can be replicated by minor adaptions in the standard parameters.

Trajectory of sleep and cognitive change: new insights from statistical modeling

Xi Ni, The Chinese University of Hong Kong

Assessing and quantifying sleep quality and circadian cycle are well developed in clinical practice. Among the assessments, The Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire that assesses sleep quality over a 1-month time interval, which is the most popular tool using in clinical trials. However, if the intervention lasts for one month, then the score of PSQI represents the sleep quality before intervention (i.e., baseline) or not. In this presentation, advanced statistical modeling will be developed and discussed for the applications of PSQI in clinical trials.

Symposium 44: Sleep Status, Socio–Behavioral Factors, and Comorbidities in Korean Adolescents

Summary

Sleep is also essential for the maintenance of the mental and physical health of adolescents, even though their sleep durations tend to be shortened by maturational changes in circadian rhythms and competing academic and social demands. Some different facets of "sleep" may have a unique impact on adolescent health, including sleep problems, sleep duration, and sleep patterns. Sleep problems refer to having trouble falling or staying asleep; sleep duration refers to the length of sleep; and sleep patterns refer to the times youth go to sleep and wake up and the consistency of those patterns across weekdays and weekends. There are many adverse consequences of inadequate sleep as various parameters of different meaning. Not only that, but there are many researches showing significant associations between adolescent risk behaviors, such as substance use, and overall sleep problems have been illustrated in both cross-sectional and longitudinal research. This symposium is to be introduced as a survey of Korean adolescence. This study evaluated the sleep health status among Korean adolescents and its effects on daily life. The survey enrolled a total of 26,395 students from 75 middle schools (7th – 9th grade) and 75 high schools (10th – 12th grade) in 2011. Each school had approximately 30 students in each class, and 2 classes were randomly selected from each grade at each school to represent the overall population of that grade. Sleep problems, such as insufficient sleep amount, eveningness preference, snoring, and sleep apnea, were associated with obesity and depression. As well as, diverse aspects including sleep habits and sleep related environmental factors were associate with depression. Besides, various socio-behavioral factors were also associated with suggestive symptoms of insomnia and restless legs syndrome in adolescence.

Learning Objectives

1. Short sleep duration rather than late chronotype or social jet lag is associated with adolescent obesity
2. Relationship between diverse aspects of sleep such as morningness-eveningness preference, sleep apnea, and weekend catch-up sleep and depression in late adolescents
3. Suggestive symptoms of Insomnia and restless legs syndrome were related to a range of socio-environmental factors

Target Audience

1. Clinicians who participate current clinical practices of pediatric sleep medicine, such as neurologist, pediatrics, and psychiatrists
2. Students and other health care professionals seeking to increase their knowledge of sleep medicine and sleep research, such as psychologist and clinical nurse.

Chairs

Kwang Ik Yang

Sleep duration, chronotype, and obesity in adolescence
Jun-Sang Sunwoo (Korea)
Impact of sleeping habits and sleep-related environmental factors on depression in late adolescence
Dae Lim Koo (Korea)
Insomnia symptoms and its associated factors in adolescence
Soo Hwan Yim (Korea)
Socio-behavioral factors associated with suggestive symptoms of restless legs syndrome in adolescence
Jongkyu Park (Korea)

Sleep duration, chronotype, and obesity in adolescence

Jun-Sang Sunwoo, Seoul National University Hospital
Adolescents undergo rapid changes in sleep regulatory processes and increased external constraints with age, resulting in decreased sleep duration with circadian phase delay. The mechanisms by which inadequate sleep confers obesity risk during adolescence may be more complex but has been relatively less studied. Moreover, little is known about the effect of sleep timing alteration or misalignment on adolescent obesity. Therefore, we aimed to investigate sleep patterns, including sleep duration and sleep timing, of adolescents and to examine which sleep-related parameters are associated with a higher risk of adolescent obesity.

Impact of sleeping habits and sleep-related environmental factors on depression in late adolescence

Dae Lim Koo, Department of Neurology, Seoul Metropolitan Government Seoul National University Boramae Medical Center and Seoul National University College of Medicine
Adolescents tend to present shorter sleep duration during the night and delayed sleep phase. With these changes in circadian rhythms, environmental and psychosocial factors, such as early school start times and competing academic and social demands, may result in a higher prevalence of insufficient sleep in adolescents. In addition, adolescents are vulnerable to psychological and physical health problems, such as depressive mood and sleep disturbances. However, there is a lack of studies that examined the association between sleeping habits, sleep-related environmental factors and depression in late adolescents. We aimed to review the relationship between sleep associated parameters and depression in late adolescents.

Insomnia symptoms and its associated factors in adolescence

Soo Hwan Yim, Department of Neurology, Gangneung Asan Hospital, University of Ulsan College of Medicine

The amount of sleep time in Asian adolescents, including Korean students, is well known remarkably shorter than one in western countries. Until now, almost preceding studies have been conducted with focusing on the amount of sleep time. Study-related insomnia symptom in adolescents is relatively scarce. The factors that cause insomnia symptoms are capable to affect a range of aspects. For this reason, it is necessary to consider in-depth the social environments, such as unique teenage age's leisure and fierce entrance examination environment, to figure out the entire sleep status in Korean high school students. In this session, we will look into the prevalence of insomnia symptoms among Korean high school students and discuss various factors that influence them.

Socio-behavioral factors associated with suggestive symptoms of restless legs syndrome in adolescence

Jongkyu Park, Department of Neurology, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine

Asian adolescents experience a lack of quality and quantity of sleep in many related to their living environment, and various sleep-related symptoms appear. However, sleep studies targeting adolescence are insufficient, and studies to find factors related to sleep abnormalities are insufficient. We investigated the prevalence of adolescents for restless legs syndrome, a common type of sleep-related movement disorder, and investigated the association with socio-behavioral factor.

Symposium 45: High Altitude and Medicine

Summary

High altitude is defined as a place with an altitude over 1500 meters and hypobaric hypoxia as an important characteristic. People experiencing headache, nausea, vomiting and insomnia ascending to high altitude, and insomnia is one of the main complaints at high altitude. Previous studies found that lowlander have decreased sleep efficiency, increased central apnea and periodic breathing ascending to high altitude. The same findings were also found in OSA and COPD patients. Besides the lowlander ascending to high altitude, there are also a large number of people living at high altitude. Tibetans, Ethiopians and Andeans are the three main highland populations, they have developed different adaptations to high altitude. The also present different sleep and sleep-disordered breathing patterns at high altitude. In this symposium, we will invite high altitude experts from United States of American, Switzerland and China to share their research in the field of sleep in healthy participants, OSA and COPD patients at high altitude, the characteristics and sleep pattern difference between high altitude populations and also the effect of possible treatment on sleep-disordered breathing at high altitude. From this symposium, we could have an overview of sleep at high altitude and also the difference between different highland populations.

Learning Objectives

1.Sleep in healthy participants and OSA patients at high altitude

2.Adaptation difference among Tibetans, Ethiopians and Andeans

3.Characteristic of highland Tibetan and Han OSA patients and the effect of oxygen

Target Audience

Clinical doctors and researchers in the field of sleep medicine, high altitude medicine and respiratory medicine

Chairs

Xiangdong Tang

Sleep at high altitude

Konrad Bloch (Switzerland)

Healthy hypoxia: oxygen delivery characteristics of ethnic Tibetans

Cynthia Beall (USA)

Characteristic of 24-hour blood pressure changes in patients with obstructive sleep apnea-hypopnea syndrome in high altitude areas

Yunhui Lv (China)

The characteristics of highland OSA patients and the effect of oxygen supplementation

Lu Tan (China)

Sleep at high altitude

Konrad Bloch, Department of Respiratory Medicine, Sleep Disorders Center, University Hospital of Zurich

The presentation will focus on the sleep at high altitude, especially the sleep and breathing disturbance in healthy participants or OSA patients ascending to high altitude.

Healthy hypoxia: oxygen delivery characteristics of ethnic Tibetans

Cynthia Beall, Case Western Reserve University

Indigenous high-altitude residents provide insights into the physiology of hypoxia in the absence of pathology. Understanding the features of healthy hypoxia offers perspectives on illnesses associated with hypoxia at any altitude. This report presents phenotypic and genotypic information about traits associated with oxygen exchange (such as lung volume and pulmonary artery pressure) and oxygen transport (including cardiac output and hemoglobin concentration) in a sample of 430 ethnic Tibetan women, 46-86 years of age, native to and resident at > 3500m in Nepal. Together with previously published data, these data represent a successful pattern of adaptation to high-altitude hypoxia resulting from thousands of years of evolution and adaptation.

Characteristic of 24-hour blood pressure changes in patients with obstructive sleep apnea-hypopnea syndrome in high altitude areas

Yunhui Lv, Sleep Center of the First People's Hospital of Yunnan Province

Introduce the clinical study on the difference between the 24-hour blood pressure changes in patients with obstructive sleep apnea hypopnea syndrome (OSAHS) in high altitude areas and patients with OSAHS in plain areas

The characteristics of highland OSA patients and the effect of oxygen supplementation

Lu Tan, Sleep Medicine Center, West China Hospital, Sichuan University

The presentation will first focus on the demographic and polysomnography characteristic of Tibetan and Hans living at high altitude, and also the cardiometabolic risk difference between Tibetan and Han highland OSA patients. Moreover, the presentation will also focus on the effect of oxygen supplementation on highland Tibetan OSA patients.

Symposium 46: REM Sleep Behavioral Disorder (RBD) and Neurodegeneration

Summary

REM sleep behavior disorder (RBD) is regarded as a specific prodrome for synucleinopathy neurodegeneration as over 90% of RBD will eventually develop into synucleinopathy disorders, namely Parkinson's disease (PD), Dementia with Lewy bodies and Multiple System Atrophy within 15 years. However, the timing, type and prognosis of phenoconversion are hard to predict in patients with RBD. Longitudinal studies suggested that some risk factors and biomarkers, e.g., constipation, subtle motor dysfunction and EMG activity during REM sleep, are potential predictors of early phenoconversion. Other conditions or comorbidities, e.g., chronic obstructive pulmonary disease, and cancer, are predictors for life expectancy in converted subjects. In this case, accurate personalized prediction of phenoconversion and neuroprotective therapy during RBD or even pre-RBD stage is an important direction for future investigations. In this symposium, Prof. Liu Jun will talk about a novel neuroimaging biomarker of neurodegeneration in patients with RBD, while Dr. Zhou Junying will talk about the relationship between RBD and mortality. Among biomarkers, gut microbiota and peripheral inflammation are novel candidates for early prediction and intervention. Gut microbiota may play a critical role in the pathogenesis of synucleinopathy. For example, some proinflammatory bacteria were more abundant in PD patients, and similar changes of microbes were observed in PD and RBD patients when compared with normal controls. At the same time, accumulating evidences showed the levels of peripheral inflammatory cytokines increased in PD patients. In this symposium, Prof. KY Jung will talk about the relationship between RBD and inflammation, while Dr. Joanne Bei HUANG will talk about the evidences of microbiota involvement in RBD and early synucelinopathy. This proposed symposium is aimed to address the close relationship between RBD and neurodegeneration from the perspectives of clinical phenoconversion, prognosis and underlying pathophysiology. The symposium will help to enhance the understanding of the complex in the relationship between RBD and synucleinopathy.

Learning Objectives

1. Neuroimaging biomarker of neurodegeneration as a potential indicator of disease progression in RBD patients.
2. Identify the risk factors for the mortality of RBD patient
3. Have an overview of the inflammatory response in RBD
4. Conceptualize brain-gut-microbiota axis and its role in the pathogenesis of synuleinopathy

Target Audience

Professionals in sleep medicine, general physicians, neurology, psychiatry, geriatricians, students

Chairs

Yun Kwok Wing, Ky Jung (Co-chair)

Increased free-water in the substantia nigra in iRBD, a new neuroimaging biomarker
Jun Liu (China)
Mortality and RBD
Junying Zhou (China)
RBD and inflammation
Jin Sun Jun (Korea)
RBD and microbiota
Joanne Bei Huang (Hong Kong, China)

Increased free-water in the substantia nigra in iRBD, a new neuroimaging biomarker

Jun Liu, Department of Neurology, Shanghai Jiaotong University School of Medicine

Imaging markers that are sensitive to neurodegeneration in the substantia nigra are critically needed for future disease-modifying trials. Previous studies have demonstrated the utility of posterior substantia nigra free water as a marker of progression in Parkinson's disease. In this study, we tested the hypothesis that free water is elevated in the posterior substantia nigra of idiopathic rapid eye movement sleep behavior disorder, which is considered a prodromal stage of synucleinopathy. We applied free-water imaging to 32 healthy controls, 34 idiopathic rapid eye movement sleep behavior disorder patients and 38 Parkinson's disease patients. And 18 healthy controls and 22 idiopathic rapid eye movement sleep behavior disorder patients were followed up completing longitudinal free-water imaging. Free-water values in the substantia nigra were calculated for each individual and compared among groups. We tested the associations between posterior substantia nigra free water and uptake of striatal dopamine transporter in the idiopathic rapid eye movement sleep behavior disorder. Free-water values in the posterior substantia nigra were significantly higher in the idiopathic rapid eye movement sleep behavior disorder patients than in the healthy controls but significantly lower in the idiopathic rapid eye movement sleep behavior disorder patients than in the Parkinson's disease patients. In addition, we observed significantly negative associations between posterior substantia nigra free-water values and dopamine transporter striatal binding ratios in the idiopathic rapid eye movement sleep behavior disorder patients. Longitudinal free-water imaging analyses were conducted with a linear mixed-effects model and showed a significant group $\times$ time interaction in posterior substantia nigra, identifying increased mean free-water values in posterior substantia nigra of iRBD over time. These results demonstrate that free water in the posterior substantia nigra is a valid imaging marker of neurodegeneration in idiopathic rapid eye movement sleep behavior disorder, which has the potential to be used as an indicator in disease-modifying trials.

Mortality and RBD

Junying Zhou, Sleep Medicine Center, West China Hospital, Sichuan University

Mortality is one of the most robust and definitive endpoints in the assessment of outcome of a disease condition, which is considered as a gold standard of clinical performance. Previous studies have investigated an increased risk of mortality in neurodegenerative diseases, for example, there is a 2.2-fold increased risk of mortality in Parkinson's disease (PD). It is widely known that RBD is the prodromal stage of alpha-synucleinopathies and the majority of RBD will eventually develop neurodegenerative diseases including PD, dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). But it remains unclear 1) whether RBD per se leads to the increased mortality; 2) whether neurodegenerative diseases play a role in the mortality risk in RBD; 3) and whether there is any risk factor predicting mortality in RBD. We conducted an observational cohort study to determine the mortality and its risk factors in 205 patients with RBD by comparing to that of the general population in Hong Kong. Medical records and death status were systematically reviewed in the computerized records of the health care system. Standardized mortality ratio (SMR) was used to calculate the risk ratio of mortality in RBD with reference to the general population. Forty-three patients (21.0%) died over a mean follow-up period of 7.1 $\pm$ 4.5 years. We found the SMR was not increased in the overall sample, but the SMR was significantly increased in RBD patients who eventually developed neurodegenerative diseases. Furthermore, the mortality risk was significantly associated with age, living alone, chronic obstructive pulmonary disease, cancer, periodic limb movements during sleep, and development of neurodegenerative diseases and dementia. In summary, RBD per se was not associated with the increased mortality until neurodegenerative diseases were developed. The findings of the study could help further understanding of the disease burden and pathological process of RBD. Furthermore, it underscores the timely need of neuroprotective intervention in the early phase of RBD before the development of neurodegenerative diseases.

RBD and inflammation

Jin Sun Jun, Department of Neurology, Hallym University College of Medicine

Isolated REM sleep behavior disorder (iRBD) can be considered a prodromal synucleinopathy with a conversion rate of about 6% a year. While some patients with iRBD convert rapidly, others can remain free of Parkinson disease (PD), Dementia with Lewy bodies (DLB) or multiple system atrophy. iRBD which is a prodromal phase of PD considered to have multifactorial etiology involving genetic and environmental factors. Recently, neuroinflammation have considered to be one of the factors that affect the phenoconversion rate. A recent study on iRBD has revealed increased microglial activation in the substantia nigra along with reduced nigrostriatal dopaminergic function, providing insight into the role of neuroinflammation in iRBD. Systemic inflammation is known to be related to brain inflammation and neurodegeneration. Similarly, a few studies have shown the possibility of the association of peripheral inflammation with iRBD. Given the accessibility and practicality of using peripheral blood, measurement of inflammatory markers in

serum or plasma may be an attractive option to study and monitor the immune response in iRBD. The first study to investigate peripheral inflammatory cytokines including interleukin (IL)-1β, IL-2, IL-6, IL-10 and tumor necrosis factor (TNF)-α in 54 iRBD patients by Kim et al. suggest that there is a trend toward increased production of IL-10, but the role of peripheral inflammation in the phenoconversion remained unclear. These results were limited by cross-sectional study design and the use of prolonged release melatonin, which had anti-inflammatory properties, in several patients included in the study. Two recent prospective cohort studies showed significantly elevated level of TNF-α in iRBD compared with healthy controls. These studies supported the early involvement of peripheral inflammation in iRBD. TNF-α may be candidate marker of predictive of phenoconversion. In addition, one of novel biomarker studies for iRBD using liquid chromatography–mass spectrometry by Mondello et al. also showed altered protein profiles related to inflammation as well as protein profiles related to norepinepherinergic and dopaminergic systems. Further studies are warranted to confirm the role of peripheral inflammation especially TNF-α in the pathogenesis of neurodegeneration in iRBD.

RBD and Microbiota

Joanne Bei Huang, Department of Psychiatry, The Chinese University of Hong Kong

Recent studies revealed distinct composition of gut microbiota in subjects with Parkinson's disease (PD), including depletion of anti-inflammatory genera, enrichment of putative pathobionts and mucin-degraders (i.e., Akkermansia). Meanwhile, these microbial alterations revealed in PD were greatly associated with intestinal hyperpermeability, changes of microbial metabolites, immune system activation, and further correlated with enteric pathologic alpha-synuclein staining, which suggested the involvement of gut microbiota and microbiota-gut-brain axis in the pathogenesis of PD. Nonetheless, the roles of gut microbiota at the early stages of synucleinopathy, REM sleep behavior disorder (RBD) and their relatives, and its interactions with the prodromal markers of PD are still unclear. We investigated gut microbiota across the early stages of synucleinopathy, including 15 subjects with early PD, 80 RBD, 82 first-degree relatives of RBD (RBD-FDR), and 59 healthy controls, and further correlated the abundances of microbiota with clinical biomarkers. Intestinal disorders were diagnosed according to Rome-IV criteria. Fecal micorbial composition was generated by sequencing the third and fourth variable regions (V3-4) of the microbial 16S ribosomal RNA gene. We found that subjects with RBD showed comparable microbial composition and similar distribution of community types with early PD, while differed from those of control and RBD-FDR. Besides, 15 differential genera were revealed among four groups, in particular, relative abundance of anti-inflammatory genus, such as Fusicatenibacter and Faecalibacterium, were significantly decreased from control, RBD to early PD. Further association network of differential genera indicated that the strength of significant co-excluding interactions between genera enriched and depleted in RBD/early PD, was increased from control, RBD-FDR, RBD to subjects with early PD. Lastly, among all the biomarkers, constipation especially stool consistency was strongly

associated with differential genera and PD/RBD-related community types. In conclusion, alterations of gut microbial compostion and individual microbes, especially the decreased abundance of anti-inflammatory bacteria, already occurred at the early stages of synucleinopathy, namely subjects with RBD, which was strongly associated with constipation. This suggested that gut microbiota and related inflammatory pathways might play critical roles in the pathogenesis of synucleinopathies, and constipation is one of the potiential modifiable factors for early prevention of synucleinopathy.

Symposium 47: Sleep habits and sleep problems in children

Summary

Sleep problems (e.g., insomnia, obstructive sleep apnea) are common in children and may be linked to a constellation of negative outcomes. Sleep practices may also be an important factor to consider in the clinical management. This symposium will discuss the correlates and effects of co-sleeping, which is a common sleep practice in Asian culture, and will provide an update on the clinical management of common sleep problems in children. In particular, the latest evidence on adenotonsillectomy and non-invasive positive pressure ventilation (NPPV) for childhood OSA will be presented, followed by the discussion on the impacts and management of childhood insomnia in the context of neurodevelopmental disorders (ASD, ADHD).

Learning Objectives

1. To learn that co-sleeping patterns in children can be different according to sleep environment and cultural background.

2. To learn about the recent findings on the treatment effects of adenotonsillectomy for childhood OSA

3. To learn about the latest research and utility of NPPV for childhood OSA

4. To develop a transdiagnostic perspective on the role of sleep disturbances in the core features and comorbidities in children with ASD and ADHD, and to understand the importance to consider sleep disturbances in research and clinical practice of neurodevelopment disorders

Target Audience

Researchers, clinicians, and trainees (physicians, psychologists, nurses, nurse practitioners, polysomnography technicians and technologists)

Chairs

Shirley Xin Li, Aly Sooyeon Suh (Co-chair)

Co-sleeping, sleep environment, and mental health
Seockhoon Chung (Korea)
Effects of adenotonsillectomy on childhood OSA: subjective and objective outcomes from RCTs
Chun Ting Au (Hong Kong, China)
Non-invasive positive pressure ventilation in childhood OSA
Zhifei Xu (China)
Insomnia in children with ASD and management
Guanghai Wang (China)
Insomnia in children with attention deficit hyperactivity disorder (ADHD): impact and management
Xiao Li (Hong Kong, China)

Co-sleeping, sleep environment, and mental health

Seockhoon Chung, Department of Psychiatry, University of Ulsan College of Medicine, Asan Medical Center

Co-sleeping is a natural part of parenting in the Eastern culture. However, it may seem strange and possibly even dangerous to Western cultures, since co-sleeping, especially bed-sharing, is usually considered to increase the risk of sudden infant death syndrome. The differences in the prevalence of co-sleeping between Eastern and Western society may be rooted in differences in child-care philosophies, sleeping habits, and home architecture, physical differences in bedroom design, parenting style, or acceptance of co-sleeping. In addition, the sleep environment factors that influence children＇s sleep, and the relationship between co-sleeping and parenting stress and parents＇ mental health. A study done to identify the clinical features related to sleep environment of NREM-related parasomnia showed that 48.5% mothers experienced coldness while sleeping, and 64.7% parents had dysfunctional beliefs about their children＇s sleep. The large number of co-sleeping members, coldness mothers experienced while sleeping, and dysfunctional beliefs about their children＇s sleep may influence the NREM-parasomnia in children. Another survey conducted in 115 parents of preschool children revealed that the high score of parenting stress was significantly correlated with the frequency of a child sharing a bed with other children, and difficult child subcategory was correlated with the frequency of a child sharing a room with other children or sleeping in a too bright place. The high sleep problem of children was correlated with the high parenting stress, mother＇s young age and high PHQ-9 score. In the path analysis, sleeping in the same space with parents can induce sleep problems in the child, resulting in the mother perceiving the child＇s behavior as difficult. Also, the mother perceiving her child as difficult was found to correlate with the mother＇s insomnia. In this talk, the association among Co-sleeping, sleep environment, and mental health will be discussed.

Effects of adenotonsillectomy on childhood OSA: subjective and objective outcomes from RCTs

Chun-Ting Au, Department of Pediatrics, Faculty of Medicine, The Chinese University of Hong Kong

Adenotonsillar hypertrophy is the most common cause of obstructive sleep apnea (OSA) in children and adenotonsillectomy (AT) has been the first-line treatment of the condition. Evidence of the treatment effects of AT for childhood OSA was based on observational studies until recently, more and more RCTs have been published to evaluate its effect on improving OSA severity, symptoms, as well as the associated neurocognitive complications. As the subjects and their caregivers were impossible to be blinded to the treatment allocation, self- or parent-reported subjective outcomes were usually demonstrated to have substantial improvement after AT, whereas for those objective outcomes, the improvements were much as apparent with much less effect size. This talk will summaries the findings of recent RCTs in views of the differential effect of AT on subjective and

objective outcomes.

Non-invasive positive pressure ventilation in childhood OSA

Zhifei Xu, Respiratory Department, Beijing Children's Hospital; Capital Medical University

Adenotonsillar hypertrophy is most common cause of childhood obstructive sleep apnea (OSA), adenotonsillectomy (T&A) therefore is the first line treatment for children. Noninvasive positive pressure ventilation (NPPV) therapy should be considered in children who are not surgical candidates or have contraindications for T&A, and those who continue to have symptomatic residual OSA after T&A. NPPV may also be considered for children with severe pre-operative OSA, co-existing morbidities like cor pulmonale, morbid obesity, neuromuscular disorders and craniofacial abnormalities. The adherence to NPPV treatment in children is generally lower than that in adults and thus less experience with the application of this therapeutic option in children has been accumulated. This talk shares experience and discuss the compliance of NPPV in complicated OSA children.

Insomnia in children with ASD and management

Guanghai Wang, Department of Developmental and Behaviral Pediatrics, Pediatric Translational Medicine Institute, National Children's Medical Center -Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine

Sleep disturbances, particularly insomnia are very common in children with autism spectrum disorders (ASD), but the association with emotional/behavioral problems and autism symptoms, especially its diagnostic feature of social deficits has been limited investigated. In addition, the well-established cognitive-behavioral treatment for insomnia (CBTI) in typically developing children is promising for children with ASD, but relevant evidence requires scrutinize. The presentation is to discuss how and insomnia is associated with emotional/behavioral problems, and social deficits in children with ASD, as well as common techniques of CBT-I for management. And a transdiagnostic perspective will be provided to appreciate the role of sleep disturbances in the core feature and comorbidities in children with ASD, and highlight the importance to consider sleep disturbances in their research and clinical practice.

Insomnia in children with attention deficit hyperactivity disorder (ADHD): Impact and management

Xiao Li, Department of Psychology, The University of Hong Kong

Sleep disturbances are common in children with attention deficit hyperactivity disorder (ADHD), with prevalence rates ranging from 25% to as high as 73%. In children with ADHD, sleep disturbances can lead to excessive daytime fatigue and interfere with mood, attention, behavior, and physical health, all of which are critical for school performance and a good quality of life. Moreover, parents with an ADHD child with comorbid sleep disturbances are 2.7 times more likely to be clinically depressed, stressed, or anxious. Although sleep disturbances are very common

in individuals with ADHD, comorbid sleep disturbances are often overlooked and left untreated in ADHD populations. There is a pressing need for evidence-based behavioral interventions to treat sleep disturbances in children with ADHD. Some recent studies have examined the efficacy of behavioral interventions on sleep disturbances in children with ADHD, which showed improvements in sleep, inattentive symptoms, quality of life, daily functioning, and behavior. The presentation explores the impacts and management of sleep disturbances in children with ADHD. In the first part, an overview of the comorbidities between ADHD and a range of sleep disturbances, including insomnia, obstructive sleep apnea, circadian rhythm disturbances, and periodic limb movements during sleep, is presented. In the second part, we review recent observational and experimental findings examining sleep and functional outcomes in children with ADHD, along with a presentation of the results of two studies from our lab, that examine the impact of insomnia and circadian rhythms on behavioral and cognitive functioning. Finally, recent intervention work focused on treating sleep disturbances in children with ADHD are discussed. We also present the results of the effects of a brief parent-based sleep intervention on sleep symptoms, behavioral, and cognitive functioning as well as parental sleep and mental health in children with ADHD. Some possible future avenues of research in the field are listed.

Symposium 48: MCI and OSA: Common Problems in iRBD. How to Recognize and Manage It

Summary

Both mild cognitive impairment (MCI) and obstructive sleep apnea (OSA) are common comorbid condition and might be risk factor for synucleinopathies. It has been reported up to 50% of isolated REM sleep behavior disorder (iRBD) has cognitive decline to level of MCI. MCI is related to increased risk for especially dementia first synucleinopathy such as dementia with Lewy body (DLB). In the first half of this symposium, two speakers will present role of APOE, which is known to risk factor of Alzheimer disease, on cognition, and metabolic network according to cognitive function. OSA is very common comorbid condition in iRBD patients. It is well known REM sleep without atonia may be a protective factor for sleep disordered breathing in iRBD. However, little is known about impact of OSA on RBD symptomatology. Furthermore, there is scant data on the CPAP treatment in iRBD combined with OSA. Two speakers will present relationship between OSA and RBD, and show recent data on efficacy of CPAP treatment in iRBD with moderate to severe OSA.

Learning Objectives

1.Understand importance of cognition in iRBD

2.Cognitive related metabolic pattern in iRBD

3.Complex relationship between OSA and RBD

4.Usefulness of CPAP treatment in iRBD combined with OSA

Target Audience

Professionals in sleep medicine, general physicians, neurology, psychiatry, geriatricians, students

Chairs

Ki-Young Jung

Is APOE genotype associated with cognitive decline in iRBD?

Jun-Sang Sunwoo (Korea)

Metabolic pattern associated with cognition in RBD

Jung-Ick Byun (Korea)

Is REM sleep behavior disorder a friend or foe of obstructive sleep apnea?

Yu Jin Jung (Korea)

Improvement of nightmare with CPAP treatment in iRBD combined with OSA

Woo-Jin Lee (Korea)

Is APOE genotype associated with cognitive decline in iRBD?

Jun-Sang Sunwoo, Department of Neurosurgery, Seoul National University Hospital

The Apolipoprotein E (APOE) ε4 allele is the strongest genetic risk factor for Alzheimer disease. APOE ε4 is also associated with increased risk of dementia in Parkinson's disease (PD). Idiopathic rapid eye movement sleep behavior disorder (iRBD) is the strongest predictor of future development of α-synucleinopathy including PD and dementia with Lewy bodies. However, the effect of APOE genotype on cognitive function in patients with iRBD has not been studied. Therefore, in this study, we investigated the association between APOE genotype and cognitive performance in patients with iRBD.

Metabolic pattern associated with cognition in RBD

Jung-Ick Byun, Kyung Hee University Hospital at Gangdong

Idiopathic REM sleep behavior disorder (IRBD) is a high risk factor for development of cognitive impairment. Structural imaging study revealed wider cortical and subcortical abnormalities on magnetic resonance imaging (MRI) in patients with IRBD with MCI compared with those without cognitive deficit. (18)F-fluorodeoxyglucose Position emission tompgraphy (FDG-PET) regarding cerebral metabolism may allow earlier detection of the changes between the two groups. Moreover, metabolic covariance pattern associated with RBD can be identified.

Is REM sleep behavior disorder a friend or foe of obstructive sleep apnea?

Yu Jin Jung, Department of Neurology, Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea

REM sleep behavior disorder (RBD) is a parasomnia characterized by loss of muscle atonia during REM sleep, associated with complex motor enactment of dreams. Obstructive sleep apnea (OSA) is a relatively common sleep disorder characterized by repetitive episodes of upper airway obstruction while sleeping, which can result in hypoxemia and sleep fragmentation. Even though the nature of RBD and OSA is different, OSA may sometimes be accompanied by RBD symptoms. Accordingly, it is reasonable to distinguish these two sleep disorders in subjects with dream enactment behaviors. Although RBD and OSA share similar sleep phenomena, their association has yet to be elucidated. Herein, we draw attention to various RBD mimicking conditions, RBD combined with OSA, and the relationship between RBD and OSA. Furthermore, the clinical implications of OSA in neurodegeneration and the optimized management of RBD combined with OSA are also discussed.

Improvement of nightmare with CPAP treatment in iRBD combined with OSA

Woo-Jin Lee, Department of Neurology, Seoul National University Hospital

Background: When isolated rapid eye movement (REM) sleep behavior disorder (iRBD) is combined with obstructive sleep apnea (OSA), the pattern of temporal association between the apnea-hypopnea (AH) and REM without atonia (RWA) events might be related with the improvement of iRBD after continuous positive airway pressure (CPAP) treatment. We evaluated

the temporal association of RWA and AH during REM, and investigated its relation to the improvement of iRBD symptoms after continuous positive airway pressure (CPAP). Methods: From an institutional cohort of sleep disorders between January 2016 and October 2020, thirty-one patients (5 [16.1%] female, mean age of 66.6 ± 6.6 years old) with iRBD confirmed by overnight video-polysomnography (vPSG) and combined OSA with an apnea-hypopnea index (AHI) of ≥15/h, received CPAP treatment, and followed-up for at least six months were included. Along with gross vPSG parameters, mini-epoch based parameters, AH associated electromyography (EMG) activity ratio and AH associated EMG activity index, were used to evaluate the temporal association between the AH and the RWA events. Results: Twenty-three (74.2%) patients exhibited a clinical improvement of their iRBD symptoms after CPAP treatment (improvement group). An AH EMG activity ratio of ≥ 15% (Odd ratio [OR] 10.146, 95% CI 1.302–79.032, P=0.027) and an AH EMG activity index of ≥ 10% (OR 99.045, 95% CI 3.091–3173.908, P=0.009) were significantly associated with the clinical improvement after CPAP treatment, in each regression models adjusting age, sex, and dichotomized REM AHI. In eighteen patients who both presented with those factors, the probability of improvement of iRBD after CPAP was 17 (94.4%). Conclusions: Treatment of combined OSA can improve the symptoms of iRBD. Mini-epoch based analysis for the temporal association between the AH and the RWA events might be useful for predicting the improvement of iRBD symptoms after CPAP treatment.

Symposium 49: International Sleep Research Training Program & Scientific Work from ISRTP Trainees

Summary

World Sleep Society has developed the International Sleep Research Training Program (ISRTP). The overarching goal of the program is to prepare sleep trainees from various countries throughout the world for future leadership in basic and/or clinical sleep research. Prior to ISRTP, there was no formalized process to select the best international trainees whom would optimally benefit from a 1-year comprehensive training program. The ISRTP will provide an opportunity for such trainees, especially those in developing countries, to train at major academic institutions so they can acquire sleep research skills and observe management of patients with sleep disorders from experienced scientists and clinicians. In turn, the program will foster a cohort of future sleep research leaders who will keep the field of sleep research and medicine vibrant with their ideas, plans and goals. The trainees will be matched to sleep research mentors at host academic institutions. Each trainee must have funds to support his or her trainee year at the host institution. The program will provide trainees with travel funds to participate in two major international sleep meetings. Selection of trainees will be based on their research plans; plans to further research in their home country; English communication skills; motivation; educational level; and availability of continued mentorship in their home countries. Two classes of fourteenth young investigators from six countries have participated in the ISRTP. In this symposium, the organizing committee will introduce the scope of ISRTP. The trainees will talk about their research work during ISRTP.

Learning Objectives

1.Learn the opportunities of international sleep research training

2.Learn the benefit for trainees of ISRTP

3.Know the process to apply for ISRTP

4.Know the research work on OSA and narcolepsy by ISRTP trainees across different countries

Target Audience

Sleep physicians and researchers, Students, Mentors

Chairs

Allan O'Bryan, Leila Emami (Co-chair)

Introduction of International Sleep Research Training Program

Allan O'bryan (USA)

International Sleep Medicine and Research Training

Clete A. Kushida (USA)

Curriculum of International Sleep Research Training Program

Mike Mutschelknaus (USA)

The effect of armodafinil on sleep spindles in obstructive sleep apnea: secondary analysis of a randomized placebo-controlled trial

Leila Emami (Iran)

Heart rate variability during wakefulness as a marker of obstructive sleep apnea severity

Hua Qin (Germany)

Effect of obstructive sleep apnea and positive airway pressure therapy on cardiac remodeling as assessed by cardiac biomarker and MRI in non-obese and obese adults

Liyue Xu (China)

The role of mitophagy in the mechanism of genioglossal dysfunction caused by chronic intermittent hypoxia and the protective effect of adiponectin

Wenjing Wang (China)

The effect of apnea management on novel coronavirus infection: a study on patients with obstructive sleep apnea

Arezu Najafi (Iran)

Clinical and neurophysiological characteristics of 89 patients with narcolepsy- cataplexy from the Russian narcolepsy network

Andrey Golovatyuk (Russia)

Associations between affect and sleep among college students: results from mixed-effect models

Bingqian Zhu (China)

International Sleep Medicine and Research Training

Clete A. Kushida, Stanford University

Dr. Kushida will present on the current scope of international sleep medicine and research training. He will focus on opportunities for sleep medicine and research training in the United States, and also describe mechanisms by which trainees can observe and learn about sleep medicine and research in academic settings. Lastly, Dr. Kushida will discuss what the World Sleep Society's International Sleep Research and Training Program (ISRTP) can offer trainees to become international leaders within the fields of sleep medicine and research.

The effect of Armodafinil on sleep spindles in obstructive sleep apnea: secondary analysis of a randomized placebo-controlled trial

Leila Emami, Woolcock Institute of Medical Research, Research Center Amiralam Hospital

Curriculum of International Sleep Research Training Program

Mike Mutschelknaus, World Sleep Society

Possibilities for international collaboration in sleep medicine and research training have increased in the past few years. An overview of the field will be presented, followed by a description of a unique opportunity for young researchers, the International Sleep Research Training Program (ISRTP). The ISRTP curriculum will also be reviewed.

Oral presentation

youth investigator award

youth travel award

oral presentation

youth investigator award

Obstructive Sleep Apnea (OSA) Detection System Based on Fast Fourier Transform (FFT) Algorithm on Electrocardiogram

Fajar,Rifaldy、Jupri,Prihantini、Kurniastuti,Nana Indri

Yogyakarta State University

Objective: In this study, an Obstructive Sleep Apnea (OSA) disease detection system was created using the RR interval parameter. The design of this detection system uses backpropagation Artificial Neural Network (ANN) which is implemented using MATLAB software as a method in the classification of OSA determination. Methods: The steps taken to design an OSA disease detection system in this study included data collection, feature extraction, ANN training, ANN testing, and performance determination. The feature extraction stage was performed using the Fast Fourier Transform (FFT) mathematical algorithm process. The result of feature extraction was then carried out ANN training using 10% of the entire data and ANN testing using 90% of the total data. To get the best performance results, variations in segment length features, variations in OSA definition features, and variations in frequency composition features were performed. Results: The best performance results in this OSA disease detection system design were features that use a combination of frequency components 2, 5, and 6 with an OSA definition of 5% in the 90-segment length. This was shown from the results of ANN performance in the form of specialization, sensitivity, and best accuracy, with successive values of 79.3%, 84.6%, and 81.6%. Conclusions: In this research, system design has been made to detect OSA which is implemented in MATLAB software. The feature used in this detection system is the RR interval feature that has been transformed using the Fast Fourier Transform (FFT) operation. Based on the results of performance calculations, all values indicate a number exceeding 75% so that a system that can be said to be good in detecting is obtained.

youth travel award

Development of a classification method for sleep phenotypes – a method to draw a landscape of sleep phenotypes

Katori,Machiko1、 Shi,Shoi2,3、 Ueda,Hiroki.R1,2,3

1. Graduate School of Information Science and Technology，The University of Tokyo

2. Graduate School of Medicine，The University of Tokyo

3. Laboratory for Synthetic Biology，RIKEN Center for Biosystems Dynamics Research

Background: Genetic, physiological, and social factors diversify the sleep phenotypes of humans. Some categories of sleep phenotypes, such as morning person, social jetlag, and insomnia, are defined by diagnostic measurements based on polysomnography, sleep diaries, or questionnaires. However, even in the same category of insomnia, there is a variety of effective treatments and associated risks, making it challenging to provide appropriate treatment for sleep disorders based on current classification. Thus, a more sophisticated method for classifying sleep phenotypes in more detail is required. Methods: We applied a state-of-the-art sleep-wake classification algorithm with high specificity to convert over 100, 000 accelerometer data stored in the UK Biobank into sleep-wake data and performed the first effort to classify sleep phenotypes automatically. Results: We revealed 16 clusters, including lifestyle-related sleep phenotypes, such as social jetlag and phenotypes of shift/rotation workers, which were difficult to be captured from polysomnography measurements. In addition, we also defined seven insomnia-like sleep phenotype clusters. For example, we identified a cluster named "insomnia with short sleep duration and long-term awake". In this cluster, subjects show difficulty in falling asleep smoothly after mid-awake. Alternatively, the subjects in another cluster named "insomnia with short sleep duration and short- and long-term awake" show repeated awake and light sleep. Conclusions: These clusters have not been defined in the current insomnia diagnosis, suggesting the possibility to update the current major sleep classification guidelines. This detailed and quantitative division of insomnia was made possible by the algorithm with high specificity and comprehensive analysis of population data, showing the promising potential of our method for drawing the landscape of sleep phenotypes. By linking it with other information of different modalities such as present illness, past medical history, and mental conditions, the landscape could provide a more appropriate and accurate diagnosis of insomnia.

Prognostic effect of sleep–disordered breathing on hospitalized patients following acute heart failure

Ishiwata,Sayaki、Kasai,Takatoshi、Sato,Akihiro、Suda,Shoko、Matsumoto,Hiroki、Shitara,Jun、Yatsu,Shoichiro、Murata,Azusa、Shimizu,Megumi、Kato,Takao、Hiki,Masaru、Matsue,Yuya、Naito,Ryo、Daida,Hiroyuki、Minamino,Tohru

Department of Cardiovascular Biology and Medicine，Juntendo University Graduate School of Medicine

Background Identification of patients at risk of poor clinical outcomes following acute heart failure (AHF) is important. However, data are limited regarding the prognostic effect of sleep-disordered breathing (SDB) and its treatment with positive airway pressure (PAP) on the clinical outcomes of hospitalized patients following AHF. Objectives We aimed to investigate the prognostic effect of SDB, its treatment with PAP, and compliance with PAP treatment on clinical outcomes of such patients. Methods After the initial AHF improvement, overnight polysomnography was performed in hospitalized patients whose left ventricular ejection fraction was <50%. Patients were divided into groups based on whether they had SDB and received PAP treatment. Furthermore, SDB patients with PAP treatment were subdivided into more and less compliant groups. The incidence of deaths and re-hospitalizations due to heart failure was assessed. Results Overall, 241 patients were enrolled in the study, of which73% had SDB and 29% started PAP. At a median follow-up of 1.7 years, 89 clinical events occurred. In the multivariable analysis, compared with the non-SDB group, SDB without PAP treatment was associated with an increased risk of clinical events (hazard ratio [HR] 1.79, P=0.049), whereas SDB with PAP treatment was not (HR 0.78, P=0.582). Among SDB patients with PAP treatment, the more compliant group was also inversely associated with clinical events occurrence (HR 0.11, P=0.012). Conclusions: In hospitalized patients with AHF, untreated SDB was associated with worse clinical outcomes, which may be reversible by PAP treatment, but such potential may be suppressed in less compliant patients.

Sleep Problems and Heart Failure: A Bidirectional and Multivariable Two–sample Mendelian Randomization Study

Sizhi Ai1,6、 Jihui Zhang1,7、 Guoan Zhao6、 Xiaoyu Wang6、 Hon-Cheong So1、 Guohua Li6、 Jie Chen1、 Xiao Tan2、 Ningjian Wang3、 Xiangdong Tang4、 Jie Shi5、 Lin Lu5、 Yun-Kwok Wing1

1. The Chinese University of Hong Kong
2. Uppsala University
3. Shanghai Ninth People's Hospital，Shanghai JiaoTong University School of Medicine
4. West China Hospital，Sichuan University
5. National Institute on Drug Dependence，Peking University Sixth Hospital，Peking University
6. The First Affiliated Hospital of Xinxiang Medical University
7. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences

Importance: Observational studieshave suggested bidirectional associations between various sleep problems andheart failure (HF). However, the causality and direction of these associationsare unclear. In addition, there are some genetic overlaps across sleepproblems, but the independent effect of each sleep problem on HF risk remainsunknown.Objective: To assess the bidirectional and independent causalassociations of six common sleep problems with HF by using a 2-samplesingle-variable (SV), bidirectional, and multivariable (MV) Mendelianrandomization (MR) design.Design, setting and participants: We extracted summary-level data forsleep problems (i.e., insomnia, snoring, short and long sleep duration, daytimesleepiness, and daytime napping) and HF (47 309 cases/930 014 controls) asgenetic instruments at the genome-wide significance level ($P < 5 \times 10^{-8}$) from the largest published genome-wide associationstudies (GWAS). These GWAS were conducted among adults of European ancestry indifferent observational cohorts, including the UK Biobank (for sleep problems)and the Heart Failure Molecular Epidemiology for Therapeutic Targets (HERMES)Consortium (for HF). Random-effects inverse-variance weighted (IVW) method wasused as the main analyses. Other methods, such as weighted median, MR Egger,and MR–Pleiotropy Residual Sum and Outlier (MR-PRESSO), served as thesensitivity analyses to account for potential horizontal pleiotropy andoutliers.MAIN OUTCOMES AND MEASURES HF and six common sleep problems.Results: SVMR analyses showed no evidence supporting the causal effectsof HF on sleep problems, while there are strong evidence supporting the causaleffects of genetically predicted insomnia (odds ratio [OR], 1.07 per doublingof genetic liability for insomnia; 95% CI, 1.04 to 1.09; P < .001) anddaytime napping (OR, 1.54 per category increase for daytime napping; 95% CI,1.18 to 2.01; P = .002) on HF risk. No causal associations of other four sleepproblems with HF risk after adjustment for multiple comparison. In the MVMRanalyses, we found an independent effect of genetically predicted insomnia (OR,1.05 per doubling of genetic liability for insomnia, 95% CI, 1.02-1.09; P =.003) rather than daytime napping (OR, 1.28 per category increase

for daytimenapping, 95% CI, 0.90-1.81; P = .167) on HF risk.Conclusions and relevance: Although sleep problems are common amongpatients with HF, no causal evidence was found in the direction from geneticliability for HF to sleep problems. Among 6 common sleep problems tested, onlygenetically predicted insomnia and daytime napping were associated with anincreased risk of HF. However, MVMR analyses revealed that only geneticallypredicted insomnia is independently associated with HF, which suggested thatthe causal link between genetically predicted daytime napping on HF seems to bemediated by insomnia. Our findings suggested that the intervention of bothinsomnia and daytime napping may be promising strategies in the prevention ofHF, but insomnia shall be the primary one.

Prevalence of Sleep Disturbances and Its Associated Factors in Children with Autism Spectrum Disorder

c、Awang,Hamidin、Lim,Poh Ying、Shiang Yen Eow

Universiti Putra Malaysia

Objective: Sleep disturbances are common co-morbidities in children with Autism Spectrum Disorder (ASD). Alleviation of sleep problems is important to improve daytime functioning of children and reduce the burden of their caregivers. This study aimed to assess sleep disturbances and their associated factors among children with ASD in Malaysia. Methods: A cross-sectional study was conducted on 261 children (83.5% males and 16.5% females) aged 3-18 years old at nine autism intervention centers by using convenience sampling. A mother-administered questionnaire on sociodemographic background, parenting style, parental feeding practices, parenting stress, autism severity, and sleep disturbances was completed and on-site measurement of body weight and height of the children was conducted. Results: The means of bedtime and wake time of children with ASD in this study were 9.16 pm (SD=3 h 25 min) and 7.24 am (SD=1 h 12 min), respectively. The mean sleep duration was 9h 30min (SD=2 h 18 min), with 47.1% of children having a sleep duration less than 9 hours. The prevalence of potential clinical sleep disturbances among children with ASD was 90.3%, with the major sleep problem being bedtime resistance (73.9%). Multiple logistic regression results showed that perceived child weight (AOR=3.95, 95% CI=1.21, 12.88, p<0.05), parenting stress (AOR=0.98, 95% CI=0.95, 1.00, p<0.05), and satiety responsiveness (AOR=4.07, 95% CI=1.56, 10.63, p<0.05) were significantly associated with sleep disturbances among children with ASD. Conclusion: The high prevalence of sleep disturbances among children with ASD in this study was alarming. Educational programs involving child weight management and regulation of satiety should be organized for mothers to improve sleep habits of children.

Longitudinal examination of the directionality association between chronotype and insomnia

Cheung, Forrest Tin Wai1、Chan, Ngan Yin2、Chan, Wing Yan Joey2、Li, Xiao1、Zhang, Jihui3,4、Wing, Yun Kwok2、Li, Shirley Xin1,5、Forrest Tin Wai Cheung

1. The University of Hong Kong

2. Department of Psychiatry，The Chinese University of Hong Kong

3. Guangdong Mental Health Center， Guangdong General Hospital and Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China

4. Zhujiang Hospital，Southern Medical University/The Second School of Clinical Medicine，Southern Medical University，Guangzhou，Guangdong，China

5. The State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong

Objective: Evening chronotype and insomnia are common in youth and are often closely linked. However, the existing research on the causal relationship between chronotype and insomnia is limited. The current study aimed to examine the directionality of the association between chronotype and insomnia using a set of longitudinal community samples. Methods: Three hundred and thirty-seven youth participants (mean age at baseline = 21.5, SD = 2.52; % Female = 75.1%) completed the measures on insomnia severity (i.e., Insomnia Severity Index) and chronotype (i.e., mid-point of sleep derived from Munch Chronotype Questionnaire) at baseline and 12-month follow-up. A series of cross-lagged pathway analyses were tested to examine whether insomnia at baseline could predict chronotype at follow-up, or vice versa, or whether insomnia and chronotype are bidirectionally linked. Results: The chronotype to insomnia cross-lagged model was deemed to be the parsimonious best fitted model (Chi2 [1] = 0.005, p = .946, CFI = 1.000, SRMR= 0.001, RMSEA= 0.000; AIC = 6067.118). Greater tendency towards eveningness at baseline predicted more insomnia symptoms at 12-month follow-up (β = 0.317, p = .044). The alternative, insomnia to chronotype cross-lagged model was not supported (β = -0.00, p = .098). Conclusions: This current study provided evidence that there was a directional relationship between chronotype and insomnia, where evening chronotype leads to more insomnia problems. This directional relationship suggested the potential role of circadian preference in the aetiology of insomnia and highlighted the need to consider circadian factors in the clinical prevention and intervention of insomnia.

Abnormal dream–related brain network in patients with isolated REM sleep behavior disorder (RBD)

Cha,Kwang Su1、Sunwoo,Jun-Sang2、Jung,Ki-Young1、Kwang Su Cha

1. Seoul National University Hospital

2. Neurosurgery，Seoul National University Hospital

Objective: Isolated REM sleep behavior disorder (iRBD) is characterized by disinhibition of motor control facilitating dream enactment behaviors. It has been reported that decreased activity of posterior regions is associated with experiencing dreams, and increased neuronal bistability in the frontal regions leads to protecting the continuation of sleep (Siclari et al., 2017). Although electrophysiological abnormalities during sleep have been investigated, characteristics of the dream-related network in iRBD are still unknown. Therefore, we evaluated electroencephalography (EEG) functional connectivity during REM sleep to identify the characteristics of the dream-related network in patients with iRBD. Methods: Seep EEG data from 13 people with iRBD (mean age, 66.3 years; men, 84.6%) and 10 controls (mean age, 62.3 years; men, 70%) were analyzed. We estimated cortical source activities using sLORETA during N2 and REM sleep. For functional connectivity analysis, we calculated the weighted phase lag index (wPLI) and conducted a pixel-based permutation test to compare connection strength between the groups. wPLI was selectively applied for 8 ROIs (anterior cingulate cortex, lingual cortex, parahippocampal cortex, and precentral cortex), which has been known to be associated with dream-related cortical regions. To determine the dream-related functional connections, wPLI during the REM stage was normalized to the N2 stage. Results: Overall connectivity strength did not differ between the two groups in the delta, theta, and beta frequency bands. However, in the sigma frequency-band, the strength of functional connectivity between the left precentral and left lingual cortex was significantly increased in the iRBD group than the control group (iRBD: 0.96 ± 0.03, control: 0.92 ± 0.06). In the gamma frequency-band, functional strength between the left anterior cingulate and left lingual cortex was significantly increased in the iRBD group (iRBD: 1.02 ± 0.02, control: 1.00 ± 0.02). Conclusion: Hyper-excitability of brain network in the motor cortex and visual association cortex may be associated with the generation of dream-enacting behaviors in iRBD.

10–year Follow–up for Morbidities in Children with Obstructive Sleep Apnea

Patibat,Lucksanai、Preutthipan,Aroonwan

Pediatric pulmonary division，Ramathibodi Hospital Sleep Disorder Center，Faculty of Medicine，Ramathibodi Hospital，Mahidol University

Background: Obstructive sleep apnea (OSA) in children has been shown to be associated with cardiovascular, metabolic, and neurocognitive impairment. It is unclear which baseline parameters of the patients can predict these sequelae. Objectives: To determine long-term morbidities and factors affecting morbidities in children with OSA. Methods: We recruited children, aged 1-18 years, who underwent polysomnography (PSG) at Ramathibodi Hospital Sleep Disorder Center in 2008-2011. We retrospectively reviewed the medical records of these children to identify morbidities and time-to-event during 10 years follow-up after PSG. We used the Chi-square test to compare baseline parameters between subjects with and subjects without morbidities. Kaplan-Meier was used to compare time-to-event between various patients' characteristics and PSG parameters. Cox regression was used to analyze the hazard ratio of those parameters. Results: We obtained PSG and follow-up data of 115 children. The incidence of cardiovascular morbidity 12/115 (10.4%), metabolic and endocrine disease 27/110 (24.5%), and attention deficit hyperactivity disorder (ADHD) (n=11/112, 9.8%). Cardiometabolic morbidities were associated with obesity (HR 16.2; 95%CI 2.5, 13.9), Nadir SpO2 below 70% (HR 5; 95%CI 1.1, 5.8), desaturation $\geq$ 5% of total sleep time (TST) (HR 4.9, 95%CI 1.1, 6.2), and age $\geq$ 7 years old (HR 4; 95%CI 1.0, 4.4). Cardiovascular morbidity was associated with either apnea-hypopnea index (AHI) $\geq$ 10 events/hr (HR4.6; 95%CI 1.2, 24.8) or obesity (HR 6.9; 95%CI 1.7, 36.3). ADHD was associated with either SpO2 below 90% $\geq$ 5% of TST (HR 5.1; 95%CI 1.2, 14) or end-tidal CO2 > 50 mmHg $\geq$ 10% of TST (HR 5.4; 95%CI 1.3, 18.3). Conclusions: In children with OSA, obesity, severe long duration of desaturation, long duration of high EtCO2, and older age are associated with cardiometabolic morbidities. The severity of OSA (AHI $\geq$ 10 events/hr) and obesity may link to cardiovascular complications. Desaturation and/or hypoventilation are likely associated with ADHD.

Long term effects of insomnia prevention program in at–risk adolescents over a 3–year follow–up

CHAN,Rachel Ngan Yin1、 Li,Shirley Xin 2,3、 Zhang,Jihui1、 Yu,Mandy Wai Man1、 Tsang,Chi Ching1、 Wing,Yun Kwok1、 Rachel Ngan Yin CHAN

1. The Chinese University of Hong Kong

2. Department of Psychology，The University of Hong Kong

3. The State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong

Background: Our previous study has indicated that insomnia can be prevented in at-risk adolescents over 12-month follow-up. This study is the extension of the previous study with the aim to evaluate the long-term efficacy of the insomnia prevention program in at-risk adolescents over a 3-year period Methods: A total of 242 adolescents (mean age: 14.9 yrs) who had a positive family history and presented with sub-threshold insomnia symptoms were randomized to a 4 weekly group-based insomnia prevention program or non-active control group. They were followed up at post-intervention, 6-, 12-, 18-, 24, and 36-month after the intervention. Survival analysis was used to compare the cumulative incidence of insomnia disorder ($\geq$ 3 times per week) between the 2 groups. Intervention effects were compared using linear mixed models. Results: The follow-up rates at 18m, 24m, and 36m were 80%, 65%, and 60% respectively. The intervention group had a significantly lower incidence rate of insomnia disorder compared to the control group over the 3-year follow-up (Hazard Ratios = 0.42; p = 0.004) but the difference were not shown when chronic insomnia criteria were used. Significant interaction effect (P = 0.027) was observed in Insomnia symptoms (measured by insomnia severity index) with the intervention group having lower insomnia symptoms at 36 m follow up compared to the control group. However, other measures that have demonstrated significant effect at 12-month follow up including vulnerability to stress-related sleep disturbance (P = 0.12), daytime sleepiness (P = 0.58), and dysfunctional belief (P = 0.083) were not maintained over the 3-year periods. Conclusions: A brief 4 weekly group-based insomnia prevention program seems to have enduring benefits in insomnia symptoms over the long term. However, the effect on other functional outcomes and vulnerability factors gradually decayed, suggesting the need for a booster intervention to maintain the intervention effect.

Heart Rate Variability during Wakefulness as a Marker of Obstructive Sleep Apnea Severity

Qin,Hua1、Keenan,Brendan 3、Mazzotti,Diego3、Vaquerizo-Villar, Fernando4,11、Kraemer,Jan 6、Wessel,Niels6、Tufik,Sergio 8、Bittencourt,Lia 8、Cistulli,Peter9,13、Chazal, Philip de 9、Sutherland,Kate9,13、Singh,Bhajan 2,10、Pack,Allan 3、Chen,Ning-Hung 10、Fietze,Ingo1、Gislason,Thorarinn 5,12、Holfinger,Steven 7、Magalang,Ulysses 7、Penzel,Thomas1

1. Charité Universitätsmedizin zu Berlin

2. School of Human Sciences，University of Western Australia

3. Department of Medicine，University of Pennsylvania Perelman School of Medicine

4. Biomedical Engineering Group，Universidad de Valladolid

5. Department of Sleep Medicine，Landspitali University Hospital

6. Department of Physics，Humboldt Universität zu Berlin

7. Division of Pulmonary，Critical Care，and Sleep Medicine，The Ohio State University Wexner Medical Center

8. Departamento de Psicobiologia，Universidade Federal de São Paulo

9. Charles Perkins Centre，Faculty of Medicine and Health，University of Sydney

10. Division of Pulmonary，Critical Care Medicine and Sleep Medicine，Chang Gung Memorial Hospital

11. Centro de Investigación Biomédica en Red en Bioingeniería，Biomateriales y Nanomedicina，(CIBER-BBN)

12. Medical Faculty，University of Iceland

13. Department of Respiratory and Sleep Medicine，Royal North Shore Hospital

Objectives: Patients with obstructive sleep apnea (OSA) exhibit heterogeneous heart rate variability (HRV) during wakefulness and sleep. We investigated the influence of OSA severity on HRV parameters during wakefulness in a large international clinical sample. Methods: 1,247 subjects (426 without OSA and 821 patients with OSA) were enrolled from the Sleep Apnea Global Interdisciplinary Consortium. HRV parameters were calculated during a 5-minute wakefulness period with spontaneous breathing before the sleep study, using time-domain, frequency-domain and non-linear methods. Differences in HRV were evaluated among groups using analysis of covariance, controlling for relevant covariates. Results: Patients with OSA showed significantly lower time-domain variations and less complexity of heartbeats compared to individuals without OSA. Those with severe OSA had remarkably reduced HRV compared to all other groups. Compared to non-OSA patients, those with severe OSA had lower HRV based on SDNN (adjusted mean: 37.4 vs. 46.2 ms; $p < 0.0001$), RMSSD (21.5 vs. 27.9 ms; $p < 0.0001$), ShanEn (1.83 vs. 2.01; $p < 0.0001$), and Forbword (36.7 vs. 33.0; $p = 0.0001$). While no differences were found in frequency-domain measures overall, among obese patients there was a shift to sympathetic dominance in severe OSA, with a higher LF/HF ratio compared to obese non-OSA patients (4.2 vs. 2.7; $p = 0.009$). Conclusions: Time-

domain and non-linear HRV measures during wakefulness are associated with OSA severity, with severe patients having remarkably reduced and less complex HRV. Frequency-domain measures show a shift to sympathetic dominance only in obese OSA patients. Thus, HRV during wakefulness could provide additional information about cardiovascular physiology in OSA patients.

The Effect of Armodafinil on Sleep Spindles in Obstructive Sleep Apnea: Secondary Analysis of a Randomised Placebo–controlled Trial

Emami,Leila1、Marshall,Nathaniel S1、Chapman,Julia L.1,2、Cho,Garry1、Grunstein,Ronald R1,3、Yee,Brandon J1,3、D'Rozario,Angela L1,4

1. Woolcock Institute of Medical Research，World Sleep Society，Otolayngology Research Center Amiralam Hospital

2. School of Psychology，Faculty of Science，Brain and Mind Centre and Charles Perkins Centre，The University of Sydney，NSW，Australia

3. Royal Prince Alfred Hospital，Camperdown，NSW，Australia

4. School of Psychology，Faculty of Science，Brain and Mind Centre and Charles Perkins Centre，The University of Sydney，NSW，Australia

Introduction: Armodafinil has been trialed in OSA patients to promote wakefulness and simulated driving performance. We have previously completed a 6-month trial of 150mg of Armodafinil vs placebo in moderate-severe OSA patients not using CPAP (ACTRN# 12611000847910) observing that participants on Armodafinil learnt to perform better across a 90-minute driving simulator task faster than those on placebo. It is possible that this reduction in time-on-task decrement may have been due to increased learning on Armodafinil. Sleep spindles have previously been implicated in procedural learning and neuro-behavioural performance. We hypothesized that Armodafinil increases sleep spindle events during NREM sleep to enhance learning. Methods: Sixty three overweight severe OSA patients (mean BMI: 32.3kg/m2 (26.1-42.5); age 53.1years (28-71), 52 males) underwent overnight in-lab polysomnography at baseline (0 month) and at a 6 month follow-up. All-night EEG signals were analyzed using a previously validated automated spindle detection algorithm. EEG recordings were visually inspected by an experienced sleep physician (LE), who was blinded to drug allocation. To minimize the likelihood of type 1 error we selected three key spindle variables detected at Cz for analysis of change between 0 and 6 months: 1) total number of spindle events (11-16 Hz) in NREM sleep 2) density of slow spindles ($\geq$11 to $\leq$ 13Hz) per minute of NREM sleep, and 3) fast spindle density in NREM (>13 to $\leq$ 16Hz). Results: The change in total spindle count in NREM sleep (Armodafinil = 11.6 vs Placebo = -17.1, p = 0.57), fast spindle density (Armodafinil = 0.06 vs Placebo = -0.02, p = 0.63) and slow spindle density (Armodafinil = -0.00 vs. Placebo = -0.03, p = 0.74) were not

increased by Armodafinil. Conclusion: If Armodafinil enhances simulated driving performance in a way that suppresses time-on-task effects it does not appear to be through a sleep spindle enhancing mechanism. Armodafinil is probably not a pharmacological method of enhancing sleep spindles.

The Effect of Apnea Management on Novel Coronavirus Infection: A Study on Patients With Obstructive Sleep Apnea

Najafi,Arezu1、Sadeghniiat-Haghighi , Khosro 1、Akbarpour,Samaneh 1、Samadi ,Shahram 1、Rahimi,Besharat 2、Alemohammad, Zahra Banafsheh1

1. Occupational Sleep Research Center, Baharloo Hospital,Tehran university of medical sciences
2. Advanced Thoracic Research Center, Tehran University of Medical Sciences, Tehran, Iran

Objective: To assess the frequency of coronavirus disease-2019 (COVID-19) and the effect of obstructive sleep apnea (OSA) management on COVID-19 among patients with confirmed OSA. Design: Cross-sectional telephone interview survey. Setting: Academic sleep labs. Participants: Iranian adults aged ≥ 18 years old with confirmed OSA. Results: Among 275 participants with OSA, 20% (n = 55) were suspected to have a history of COVID-19 but without positive test, and 18% (n = 51) were included in the definite COVID-19 group according to their reported symptoms or confirmed positive test. Having severe OSA (apnea hypopnea index ≥ 30) was not associated with an increased risk of definite COVID-19, with an odds ratio (OR) of 2.31 (95% confidence interval (CI): 0.87-5.55) compared to those with mild OSA. Those without undergoing treatment for OSA had higher odds to develop definite COVID-19 (OR=2.43, 95%CI: 1.26-4.67) compared with those accepting treatment in definite COVID-19 group. Total sleep times (TSTs) were 354, 340, and 320 minutes in healthy, suspected, and COVID-19 groups, respectively; TST was associated with COVID-19 (P-value =0.04). Similarly, sleep efficiency (SE) scores were 75.7%, 74.2%, and 67.9% for the healthy, suspected, and COVID-19 groups, respectively (P-value =0.005); Beck Depression scores were 13.8, 13.0, and 17.7, respectively (P-value = 0.056). Conclusions: OSA as a proinflammatory condition with multiple comorbidities may contribute to develop COVID-19. Greater OSA severity, without treatment for OSA, and lower TST and SE were associated with increased COVID-19 prevalence among patients with OSA.

Clinical and Neurophysiological Characteristics of 89 Patients With Narcolepsy– Cataplexy from The Russian Narcolepsy Network

Golovatyuk,Andrey、*Kuts,Alexander*、*Poluectov,Michail*、*Zaharov,Alexey*、*Govzman,Vlada*、*Ponomareva,Irina*、*Yakupov,Eduard*、*Zavalko,Irina*、*Tihomirova,Olga*、*Sviriaev,Yuri*、*Yakovlev,Alexei*、*Poliakov,Alexander*、*Melnikov,Alexander*、*Bassetti,Claudio*

Russian Sleep Society

In the report results of collaboration work of 11 sleep centers will be present. In 2018 the Russian Nar c olepsy network was started by associate prof. Michail Poluektov and his team in Sechenov University with the supervision of C. Bassetti. The Ruassian narcolepsy network includes 11 sleep medicine centers from Moscow, Saint-Petersburg, Samara, Novosibirsk, Kazan, Chelyabinsk and Khabarovsk.The last population study about narcolepsy in Russia was provided by Novitskaya in 1991, and from this time the diagnosing of narcolepsy in Russia was improved. This work was aimed for studying demographic, clinical and neurophysiological data of patients with narcolepsy-cataplexy from Russia and compare them with the population recently reported by the European Narcolepsy Network.

Excessive Daytime Sleepiness: A Case Report of Cognitive Behavioral Therapy for Sleep Deprivation

Bui-Diem,Khue、*Nguyen,Binh-Thu*、*Thuy Le,Minh-An*、*Khue Bui-Diem*

University of Medicine and Pharmacy at Ho Chi Minh City，Vietnam

Excessive daytime sleepiness (EDS) is a troublesome symptom and leads to increasing risk of traffic and work-related incidents. The most frequent causes of EDS are obstructive sleep apnea, narcolepsy, restless leg syndrome, sleep deprivation, and usage of the sedative drugs. In sleep medicine, cognitive behavioral therapy (CBT) is used primarily for insomnia (CBT-I) but not for EDS. However, in this case, we have found the problem is behavioral sleep deprivation, therefore CBT-I was implemented for this case. This patient is a 20-year-old medical student. He forced himself to sleep less in order to have more time to study. He had 5 traffic accidents due to sleepiness, and drowsy in class every day about one year. There are no evidence of snoring or leg movement before and during sleep, or any usage of sedative medication in this patient. The baseline body mass index was 19.3 kg/m2. Other histories included seizure episodes in childhood and night awakenings with dreams (not nightmares), then falling asleep easily. The patient visited a neurologist to exclude epilepsy. Polysomnography had not been implemented yet due to economic issues. Clinically, we had less suspicion of other sleep disorders. We applied CBT-I to this patient for 8 sessions with the intervals every 1-3 weeks. At the two first visits, the Epworth Sleepiness Score (ESS) was 18, and mean Total Sleep Time (TST) was 5.75 hours/day via sleep diary. We added melatonin to make the bedtime earlier

as the patient expected. This patient had a 1.5-hour napping habit. We did not ask the patient to give up his napping, but required him to reduce it to 45 minutes gradually. After 3 months of CBT-I with melatonin, this patient reduced night awakenings and EDS (ESS=12), mean TST (6.9 hours/day). Through this case, we hope to contribute an effective tool to evaluate and treat EDS, especially in patients with sleep deprivation. However, it would be better if we had the data of polysomnography.

Comparison of anatomical and aerodynamic characteristics of the upper airway among edentulous mild, moderate and severe obstructive sleep apnoea patients

Hui Chen1,2,Emami Elham3,Yingguang Li4,Shaohua Ge1,Matthieu Schmittbuhl2,Gilles Lavigne2,Paul Van der Stelt5,Nelly Huynh2

1.School of Stomatology，Shandong University，Jinan，China

2.University of Montreal，Canada

3.McGill University，Canada

Objectives: To compare the differences in the anatomic and aerodynamic characteristics of the upper airway among mild, moderate, and severe edentulous obstructive sleep apnoea (OSA) patients using cone beam computed tomography (CBCT) images.Methods: 58 patients (19 mild OSA, 18 moderate OSA, and 21 severe OSA) were included in this clinical trial. NewTom5G CBCT scans were obtained from all edentulous OSA patients with denture in situ. Severity of OSA was assessed based on an overnight polysomnographic recording, also with denture in situ. The anatomical characteristics of the upper airway were determined using CBCT images. Computational models of the upper airway were reconstructed based on CBCT images. The aerodynamic characteristics of the upper airway were calculated based on these computational models[y1]. Results: Compared with mild and moderate edentulous OSA patients, the severe edentulous OSA patient has an hourglass-shaped upper airway. ($X2=3.13$, $P=0.051$). The severity of OSA, viz., AHI with denture in situ is significantly correlated with the length, shape, and minimum cross-sectional area (CSAmin) of the upper airway. During inspiration, the mean velocity of the airflow within the upper airway of the severe edentulous OSA patients (0.63 ± 0.24 m/s) was higher than that of mild (0.49 ± 0.23 m/s), and moderate (0.48 ± 0.14 m/s) OSA patients.Conclusions: Within the limitations of this study, we found that the severe edentulous OSA patients have an hourglass-shaped upper airway. During inspiration, the airflow travels faster in severe edentulous OSA patients than in mild, moderate OSA patients.

Keywords edentulism; obstructive sleep apnea; cone beam computed tomography; computational fluid dynamics;

A prospective study of sleep duration, snoring and risk of heart failure

Sheng Zhuang1,Zhe Huang2,Shue Huang4,Muzi Na3,Duanping Liao2,Shouling Wu2,Xiang Gaou

1.the Second Affiliated Hospital of Soochow University

2.Kailuan General Hospital，North China University of Science and Technology

3.Pennsylvania State University

4.University of California

Objective: To investigate whether self-reported nighttime sleep duration and snoring status were associated with incident heart failure (HF) in a large community-based cohort including approximately 100, 000 Chinese adults. Methods: Included were 93, 613 adults free of preexisting cardiovascular diseases. Sleep duration and snoring were assessed by a self-reported questionnaire. Incident HF cases were ascertained by reviewing medical records. Cox proportional hazards model was applied to calculate the hazard ratio (HR) and 95% confidence interval (CI) of the risk of developing HF. Mediation analyses were used to understand whether and to what extent hypertension or diabetes mediated the association between sleep duration, snoring and HF. Results: During a median follow-up of 8.8 years, we documented 1, 343 incident HF cases. Individuals with short sleep duration had a significantly higher risk of developing HF (adjusted hazard ratio, aHR was 1.24 for < 6 h/night, 95% CI 1.01-1.55; and aHR was 1.29 for 6.0-6.9 h/night, 95% CI 1.06-1.57), relative to those with 7.0-7.9 hours of sleep, after adjustment for several covariates. A similar 30% to 40% higher risk of incident HF in individuals reporting occasional or frequent snoring, relative to those who never or rare snore. No significant mediation associations were found between short sleep duration and incident HF through hypertension or diabetes. Conclusion: Individuals with short sleep duration and snoring were associated with a higher risk of HF.

Keywords sleep duration; snoring; heart failure; cohort study

Heterozygous SOD2 deletion deteriorated chronic intermittent hypoxia–induced lung inflammation and vascular remodeling through mtROS–NLRP3 signaling pathway

Shengyu Hao,Zilong Liu,Pan Jiang,Shanqun Li

Zhongshan Hospital，Fudan University

Oxidative stress caused by chronic intermittent hypoxia (CIH) is the hallmark of obstructive sleep apnea (OSA). Among the first line intervention towards oxidative stress is the dismutation of superoxide radicals, it is carried out by manganese superoxide dismutase (SOD2) in the mitochondria. In this study, wild-type (WT) and SOD2-heterozygous knockout (SOD2+/-) mice were both exposed to CIH or normoxic (Nor)

conditions. After 4 weeks, pulmonary artery pressure was measured, and the mice were processed to harvest either serum for cytokine assays or lungs for flow cytometry and histopathological studies. Herein, we showed that heterozygous deletion of SOD2 markedly deteriorated pulmonary remodeling and increased the oxidative stress, especially promoted the infiltration of macrophages in the lungs of CIH mouse. Moreover, in the intermittent hypoxia (IH)-treated RAW264.7 cells, SOD2 knockdown increased the nucleotide-binding domain-like receptor protein 3 (NLRP3) inflammasome activation accompanied with the IL-1β elevation and caspase-1 activity. Additionally, mitochondrial ROS (mtROS) scavenger mito-TEMPO abolished NLRP3 inflammasome activation in IH-treated RAW264.7 cells. Collectively, our results supported that SOD2 contributed to the pathogenesis of CIH-induced lung remodeling. Meanwhile, SOD2 knockdown exacerbates oxidative damage through assembly and activation of NLRP3 inflammasome in macrophages. SOD2 may be a novel therapeutic target for CIH-induced pulmonary inflammation and arteriole remodeling.
Keywords

Mesencephalic dopaminergic neurons are essential for modafinil induced arousal

Yan-Fei Yang,Zhi-Li Huang

Department of Pharmacology，School of Basic Medical Sciences，State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science，Institutes of Brain Science，Fudan University，Shanghai 200032，China

Modafinil is a potent wake-promoting agent that is prescribed to treat narcolepsy and has a low incidence of abuse. Although previous studies have shown that modafinil-induced arousal depends on the dopaminergic receptors and transporters, the specific dopaminergic population underlying this mechanism remained unclear. Here, we investigated the role of mesencephalic dopaminergic neurons in modafinil-promoted arousal. A dopamine indicator (dLight1.1) was employed to detect dopamine changes in the nucleus accumbens (NAc) and dorsal striatum (dStr). We specifically lesioned mesencephalic dopaminergic neurons via diphtheria toxin (DTA) in the dopamine transporter (DAT)-Cre mice. Then, the sleep-wake states were recorded to evaluate the effects of modafinil on arousal. Finally, the extent of DTA-induced lesions was determined by immunohistochemistry. Modafinil promptly increased dopamine levels in the NAc and dStr in a dose-dependent manner. Lesioning of dopaminergic neurons in the substantia nigra pars compacta (SNc) or ventral tegmental area (VTA) had no significant effects on physiological sleep-wake cycles. Modafinil (90 mg kg-1) increased continuous wakefulness for 355.3 min in control mice, however, these effects were slightly decreased by 6.7% in the SNc-lesioned mice, and were prominently diminished by 32.8% in VTA-lesioned mice ($P < 0.01$). Furthermore, the modafinil-induced arousal was completely blocked in the SNc-VTA-lesioned mice ($P < 0.01$), whereas lesions of the dorsal raphe nucleus did not alter it. Taken together, our findings indicate that mesencephalic dopaminergic neurons are essential for modafinil-induced arousal.
Keywords Modafinil, Midbrain, Dopamine, Sleep-wake cycle

GABAergic neurons in the lateral pontine tegmentum switch off REM sleep and facilitate REM–to–NREM transition

Zeka Chen,Hui Dong,Weiming Qu,Zhili Huang

Fudan University

Abstract: Rapid eye movement (REM) sleep followed non-REM (NREM) sleep several times during a typical night of sleep in humans. However, the neural mechanisms gating REM sleep and alternating with NREM sleep remain largely unknown. Here, we showed that the activity of most lateral pontine tegmentum GABAergic (LPTGABA) neurons was the lowest during REM sleep and was increased significantly during the transition from REM sleep to non-rapid eye movement (NREM) sleep by multichannel recording in vivo and fiber photometry. Activation of LPTGABA neurons completely suppressed REM sleep, promoted REM-to-NREM sleep transitions, and increased NREM sleep by optogenetics and chemogenetics, whereas inhibition or ablation of LPTGABA neurons both increased REM sleep and interrupted NREM sleep. In addition, chemogenetic manipulation or ablation of LPTGABA neurons powerfully gated REM-sleep rebound following REM-sleep deprivation. Furthermore, we found that LPTGABA neurons executed control of REM sleep via projections to glutamatergic neurons in the sublaterodorsal nucleus, a prominent REM-sleep promotor. Collectively, our findings reveal that LPTGABA neurons are essential for REM sleep suppression and REM-to-NREM sleep transitions in order to maintain continuity of physiological sleep.

Keywords GABA, lateral pontine tegmentum, REM-to-NREM sleep transition, optogenetics, sublaterodorsal nucleus, REM sleep deprivation

Effect of obstructive sleep apnea and positive airway pressure therapy on cardiac remodeling as assessed by cardiac biomarker and MRI in non–obese and obese adults

Liyue Xu1,Brendan Keenan2,David Maislin 2,Thorarinn Gislason3,Bryndis Benediktsdottir3,Sigrun Gudmundsdóttir 3,Marianna Gardarsdottir3,Bethany Staley2,Frances Pack 2,Xiaofeng Guo2,Yuan Feng4,Jugal Chahwala2,Pritika Manaktala2,Anila Hussein2,Maheshwara Reddy-Koppula2,Zeba Hashmath2,Jonathan Lee2,Raymond Townsend2,Richard Schwab2,Allan Pack2,Samuel Kuna2,Julio Chirinos2

1.Peking University
2.University of Pennsylvania
3.University of Iceland
4.Southern Medical University

Objectives: It is unknown whether obesity modifies the effect of obstructive sleep apnea (OSA) and positive airway pressure (PAP) therapy on cardiac remodeling and N-Terminal pro-brain natriuretic peptide (NT-proBNP) levels. Methods: We compared NT-proBNP and cardiac magnetic resonance imaging in adults without OSA (n = 56) and non-obese (n = 73; body mass index [BMI] < 30kg/m2) and obese (n = 136; BMI≥30kg/m2) adults with OSA. We also investigated these traits in non-obese (n = 45) and obese (n = 78) participants with OSA adherent to 4-months of PAP treatment. At baseline, left ventricular (LV) mass to end-diastolic volume ratio, a measure of LV concentricity, was greater in both non-obese and obese participants with OSA compared to those without OSA. Participants with OSA and obesity exhibited reduced phasic right atrial (RA) function. Results: No significant differences in baseline NT-proBNP were observed across groups. The effect of PAP treatment on NT-proBNP and left atrial volume index (LAVI) was significantly modified by obesity. In non-obese participants, PAP therapy was associated with a decrease in NT-proBNP (p < 0.0001) without a change in LAVI, whereas in obese participants, PAP was associated with an increase in LAVI (p = 0.006) without a change in NT-proBNP. Conclusions: OSA was associated with LV concentric remodeling independent of obesity and RA dysfunction in participants who were obese. PAP treatment was associated with reduced NT-proBNP in non-obese participants with OSA, but LA enlargement in obese participants with OSA, suggesting that PAP-induced reduction in BNP release (which is known to occur during obstructive apnea episodes) may lead to volume retention in obese participants with OSA.

Keywords obstructive sleep apnea, obesity, positive airway pressure, N-Terminal pro-brain natriuretic peptide

The NAergic locus coeruleus–ventrolateral preoptic area neural circuit mediates rapid arousal from sleep

Yue Liang1,Wu Shi2,Anfeng Xiang2,3,Dandan Hu3,Ling Zhang2,3,Liecheng Wang1

1. Department of Pharmacology，School of Basic Medical Sciences，Anhui Medical University
2. The First Rehabilitation Hospital of Shanghai，Tongji University School of Medicine
3. Key Laboratory of Spine and Spinal Cord Injury Repair and Regeneration of Ministry of Education，Orthopaedic Department of Tongji Hospital，School of Medicine，Tongji University

Objective: Locus coeruleus (LC) in the brain stem has long been reported to play an important role in promoting arousal. Early studies have shown that the fibers in LC projects to VLPO and noradrenalin (NA) excites sleep-related neurons in VLPO. However the role of NAergicLC-VLPO pathway in modulating wakefulness remains unclear.Method: Cortical electroencephalography combined with optrode recording were used to examine the activity of LC NAergic neurons at different stages of sleep. The activation of LC-NA neuron was manipulated chemogenetically for the study of their role in wakefulness. Anterograde and retrograde viral tracing approaches were used to determine the connection between LC and VLPO brain regions. Optogenetic manipulation combined with cortical electroencephalography recording were used to examine the circuit of NAergicLC-VLPO in arousal regulation. Optrode recordings in VLPO uncovered the activity of VLPO neurons during different sleep stages. Electrophysiological recordings in vitro were used to tested the receptor mechanisms in response to NA on VLPO neurons.Results:1. LC noradrenergic (NAergic) neurons exhibit high activities during wakefulness, while suppressing these neuronal activity causes a reduction in wakefulness.2. LC NAergic neurons directly project to ventrolateral preoptic area (VLPO) and optogenetic activation of NAergicLC-VLPO neural circuit promotes arousal.3. Optrode recordings in VLPO uncovered two functionally distinct neuronal populations in response to the optogenetic activation of LC NAergic neurons, sleep-active neuron and wake-active neuron.4. Electrophysiological recordings revealed that NA inhibited sleep-active neurons of VLPO through α2-receptors and activates waking-active neurons of VLPO through α1-receptors and β-receptors.Conclusion: Together, our studies have demonstrated that the neural circuit of NAergicLC-VLPO induces the rapid transition from NREM sleep and REM sleep to wakefulness and maintain wakefulness through two types of VLPO neurons by activating different adrenergic reptors.

Keywords

Anti–Streptococcal antibodies in Chinese patients with type 1 narcolepsy

Qidi Ding,Jing Li,Fulong Xiao,Chi Zhang,Xiaosong Dong,Fang Han

Peking University People's Hospital

Background: Narcolepsy type 1 (NT1) is considered to be an autoimmune disease, and streptococcal infection may be an environmental trigger. However, previous studies from Asian narcolepsy patients did not reveal elevated anti-streptolysin O [ASO]. The aim is to investigate whether large sample of Chinese patients with NT1 have an increase in antistreptococcal antibody titers. Methods: A total of 214 narcolepsy patients and 360 healthy controls were recruited. All patients were DQB1*0602 positive with clear-cut cataplexy or had low CSF hypocretin-1. Participants were tested for ASO and anti-DNAse B [ADB]. These patients were divided into five groups according to disease duration, including 29 patients less than 3 months; 25 from 3 months to 1 year; 40 from 1 to 3 years; 61 from 3 to 10 years and 59 patients over 10 years. The comparison was also made between children and adults with age-matched controls, respectively. Results: There were no significant differences between patients and healthy controls in regard to both ASO ≥ 200 IU (19.2% vs. 16.9%, p = 0.50) and ADB ≥ 480IU (9.8% vs. 10.3%, p = 0.86). For children narcolepsy patients, ASO positive rates (19.8% vs. 18%, p = 0.68) and ADB positive rates (10.4% vs. 12%, p = 0.72) had no differences compared to age matched controls. No difference was observed in adult narcolepsy patients either, with ASO positive rates (18.5% vs. 13.8%, p = 0.39) and ADB positive rates (9.3% vs. 5.3%, p = 0.42) compared to age matched controls, respectively. ASO and ADB positive rates had no significant differences among different disease duration groups (p = 0.55 and 0.9, respectively). Conclusion: Streptococcus infection reflected by the increase of ASO and ADB levels was not found in Chinese patients with type 1 narcolepsy, additional triggers for narcolepsy need to be addressed in this population.

Keywords Narcolepsy, cataplexy, Streptococcus

The exploration of pathogenesis and treatment of catathrenia from the perspective of maxillofacial structures

Min Yu1,Zeliang Hao1,Liyue Xu2,Yongfei Wen2,Fang Han2,Xuemei Gao1

1.Peking University School and Hospital of Stomatology

2.Peking University People's Hospital

Objectives: Catathrenia（nocturnal groaning）is a rare sleeping disorder. Its pathogenesis and treatment remain unknown. This study aimed to explore the pathogenesis and treatment of catathrenia from the perspective of maxillofacial structures. Methods: A consecutive of thirty patients (aged 16 to 67 years) diagnosed with catathrenia by audio-polysomnography participated in the study. They underwent standard

clinical evaluations. The acoustic characteristics of groaning sounds were analyzed. Informed choices were made by patients to take cone beam computed tomography (CBCT) of upper airway. A custom-fit mandibular advancement device (MAD) was made for each patient. And audio-polysomnography was repeated with MAD emplacement for objective evaluation of efficacy. Results: A total of 12 males and 18 females completed the study. Compared to normal reference values in upper airway measurements, patients with catathrenia had broader retro-palatal airway space, lower mandibular plane, higher hyoid bone and shorter tongue length. The fundamental frequency of groaning episodes could be defined. And groaning had rhythmic or semi-rhythmic waveform and harmonics. With the insertion of MAD, approximately 70% of the patients reported improvement in sleep quality and decreased nocturnal groaning noises. And the groaning episodes decreased significantly with MAD emplacement in audio-polysomnography, from a median of 5.8 to 2.8/hour of sleep (p=0.014). Conclusions: Patients with catathrenia have distinctive characteristics in maxillofacial structures. Groaning sounds could originate from vocal cord based on acoustic analysis. And MAD could be considered as a treatment option for catathrenia.This study was supported by National Natural Science Foundation of China (grant number 81670082).
Keywords

Mendelian randomization reveals no causal association between daytime napping and Parkinson's disease

Hongliang Feng1,2,Sizhi Ai3,Yue Liu1,2,Lulu Yang1,2,Xinru Chen1,Jiajin Zhou1,Jihui Zhang1,3,4

1. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，China.

2. Guangdong Cardiovascular Institute，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，China.

3. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin，Hong Kong SAR，China.

4. Zhujiang Hospital，Southern Medical University，The Second School of Clinical Medicine，Southern Medical University，Guangzhou，China.

Objective: Epidemiological studies have suggested that daytime napping predicts the onset of Parkinson's disease (PD). However, it is unclear whether daytime napping is a risk factor or a manifestation of the PD disease process. Therefore, this bidirectional Mendelian randomization (MR) study aimed to clarify the direction and causal nature of the relationships between daytime napping and PD. Methods: We used publicly available summary statistics from genome-wide association studies on daytime napping and PD. The inverse-variance weighted (IVW), MR-Egger, weighted-median, and weighted-mode were used to investigate both the direction and causal nature of the relationships between daytime napping and PD. We also conducted the pleiotropy, heterogeneity, and leave-one-out sensitivity tests to further tesify the MR

assumptions. Results: The was no causal relationship between daytime napping and PD, as suggested by the IVW method (daytime napping to PD: IVW: β = -0.44, P = 0.14; PD to daytime napping: IVW: β = 0.005, P = 0.45). These associations were further supported by other MR methods (all P β > 0.05). The pleiotropy tests found no significant pleiotropy effects (all P > 0.05). In addition, there was no significant heterogeneity (all P > 0.05). The leave-one-out sensitivity analyses indicated that the results were not driven by a specific SNP. Conclusions: These findings suggest that daytime napping is neither a risk factor nor a disease-process marker of PD.

Keywords Mendelian randomization; Daytime napping; Parkinson's disease; Causal association

Bidirectional Associations Between Sleep Problems and Psycho–behavioral Problems in Preschool Children

Wen Li,Guanghai Wang,Tingyu Rong,Zijing Wang,Min Meng, Fan Jiang

Shanghai Children's Medical Center affiliated with Shanghai Jiao Tong University School of Medicine

Objectives: Psycho-behavioral problems are common in preschool children. Multiple studies have indicated the cross-sectional and longitudinal associations between child sleep problems and psycho-behavioral problems. However, the interplay between child sleep and different types of psycho-behavioral problems in preschoolers is controversial. We aimed to explore the potential bidirectional associations between preschoolers' sleep and internalizing and externalizing problems. Methods: Participants included 20,324 preschoolers from the Shanghai Children's Health, Education and Lifestyle Evaluation-Preschool (SCHEDULE-P) in Shanghai, China. They were initially assessed in November 2016 and were reassessed in April 2018 and April 2019. Sleep disturbances were assessed by the Children's Sleep Habits Questionnaire (CSHQ). Child psycho-behavioral problems were assessed by the Strength and Difficulties Questionnaire (SDQ). Cross-lagged path models were used to calculate the associations between child sleep and psycho-behavioral problems. Results: The 20,324 children enrolled in 2016 had a mean (SD) age of 3.73 (95% CI, 3.72-3.74) years, and 52.43% (95% CI, 51.46%-53.39%) were male. In 2019, 17,233 children (84.8%) were retained. Significant bidirectional associations were detected between child sleep problems with both internalizing and externalizing problems during preschool period. Sleep was a significant driver of later internalizing problems (standardized coefficient, 0.071 [95% CI, 0.056-0.086] to 0.079 [95% CI, 0.064-0.094]) and externalizing problems (standardized coefficient, 0.054 [95% CI, 0.040-0.067] to 0.054 [95% CI, 0.040-0.068], and the reverse associations were also significant for internalizing problems (standardized coefficient, 0.031 [95% CI, 0.017-0.045] to 0.056 [95% CI, 0.040-0.072]) and externalizing problems (standardized coefficient, 0.055 [95% CI, 0.041-0.068] to 0.074 [95% CI, 0.059-0.089]). The cross-sectional associations between child sleep and psycho-behavioral problems were attenuated but remained significant across the follow-up. Conclusions: These results suggest that future studies should investigate whether implementing sleep intervention decreases the occurrence of preschoolers' psycho-behavioral problems.

Keywords

The role of mitophagy in the mechanism of genioglossal dysfunction caused by chronic intermittent hypoxia and the protective effect of adiponectin

Wenjing Wang1、Yina Zhu1、Xilong Zhang2

1. The Second Affiliated Hospital of Nanjing Medical University (The Second Clinical Medical College of Nanjing Medical University，The Second Red Cross Hospital of Jiangsu Province)
2. Jiangsu Provincial People's Hospital

Purpose: Dysfunction of the genioglossus muscle is important in the pathogenesis of obstructive sleep apnea due to chronic intermittent hypoxia (CIH). Mitochondrial impairment resulting from hypoxia is mitigated by mitophagy to avoid cell apoptosis in cardiomyocytes. This project was designed to explore the effects of CIH on mitophagy in the genioglossus muscle and the impact of adiponectin (Ad). Methods: 180 male SD rats were randomly divided into 3 groups (normal control (NC], CIH, and CIH + Ad groups), with 60 rats in each group observed for 5 weeks. Comparisons of serum Ad levels, mitochondrial structure and function, mitophagy, and cell apoptosis in the genioglossus were made at different time points. Results: (1) The CIH group was significantly different from the NC group as follows: During the first 3 weeks, serum Ad levels, the reactive oxygen species (ROS), relative proteins and mRNA of mitophagy, autophagy biomarker LC3-II, and autophagosomes increased, while during the last 2 weeks, most parameters decreased. (2) There was no difference among the 3 groups in mitochondrial structure and function-associated mRNA during the first 3 weeks, while damaged mitochondrial structures developed during the last 2 weeks. Exacerbation of apoptosis was also detected in the last 2 weeks. (3) All of the damage was partially alleviated in the CIH + Ad group in contrast to CIH group at the end of this study. Conclusion: Disturbances of genioglossal mitophagy could be related to damaged mitochondrial structure and function induced by CIH, which could be alleviated by supplementation of exogenous Ad via increasing mitophagy.

youth travel award

Personality Trait and Its Association with Conversion to Neurodegenerative Disease in Idiopathic Rem Sleep Behavior Disorder

ZHOU,Li1、WANG,Jing 1、LIU,Yaping1、HUANG,Bei1、ZHANG,Jihui2,4、CHAU,Steven Wai Ho1、LI,Shirley3、CHAN,Joey Wing Yan1、WING,Yun Kwok1

1. Li Chiu Kong Family Sleep Assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin Hospital，N.T.，Hong Kong，China

2. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China

3. Department of Psychology，The University of Hong Kong，Shatin，Hong Kong，China

4. Zhujiang Hospital，Southern Medical University/ The Second School of Clinical Medicine，Southern Medical University

Background: Patients with Parkinson's disease (PD) were described to harbour a typical personality trait characterized by introverted, industrious, rigid, and lack of novelty-seeking. It remains unclear whether the similar personality trait would be found in idiopathic rapid eye movement behavior disorder (iRBD), a prodromal stage of PD, and whether the personality trait may predict the future conversion to α -synucleinopathies. Objective: To investigate the personality trait and its predictive value in future conversion to clinically diagnosed α -synucleinopathies in iRBD patients. Methods: Ninety-five video-polysomnography confirmed iRBD patients and 64 age- and sex-matched controls were recruited at baseline. All subjects completed personality assessment with NEO five-factor inventory (NEO-FFI). Ninety-one iRBD patients were prospectively followed up with a mean duration of 6.1 years and α -synucleinopathies were clinically diagnosed during the follow-up. Results: Less extraverted personality trait was associated with iRBD (adjusted β = -1.76, 95% CI = -3.40 ~ -0.12, p = 0.035), but not neuroticism, openness, agreeableness, and conscientiousness. During the follow-up, twenty-three iRBD patients (25.3%) developed clinically diagnosed α -synucleinopathies. More neuroticism (adjusted hazard ratio (HR) = 1.14, 95% CI=1.04-1.24, p = 0.005), less extravertion (adjusted HR = 0.88, 95% CI = 0.81-0.96, p = 0.006), and less agreeableness (adjusted HR = 0.86, 95%CI = 0.75-0.98, p = 0.026) were associated with an increased risk of phenoconversion in iRBD patients. Conclusion: Being more neurotic, less extraverted, and less agreeable in iRBD patients were associated with a higher risk of conversion to clinically diagnosed α -synucleinopathies. Our findings suggested that personality trait might serve as a prodromal marker of iRBD phenoconversion.

Effectiveness of E–based Cognitive Behavioral Therapy for Insomnia on Improving Sleep and Mental Health in Chinese Youths with Insomnia and Subclinical Depression: a Randomized Control Trial

Chen,Si-Jing1、Que,Jian-Yu 、Shi ,Le、Zhang,Ji-Hui2,5、Li,Shirley Xin 3,6、Chan,Ngan Yin 1、Tsang,Chi Ching1、Huang,Wei-Zhen4、Lu,Lin、Wing,Yun Kwok1、Si-Jing Chen1

1. Li Chiu Kong Family Sleep Assessment Unit，Department of Psychiatry，The Chinese University of Hong Kong，Hong Kong SAR，China

2. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China

3. Department of Psychology，The University of Hong Kong，Hong Kong SAR，China

4. Zhujiang Hospital，Southern Medical University/ The Second School of Clinical Medicine，Southern Medical University，Guangzhou，Guangdong，China

5. The State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong，Hong Kong SAR，China

Objective: As increasingevidence has suggested a reciprocal relationship between depression andinsomnia, the intervention targeting insomnia may become a potentiallypromising approach to prevent depression in youths. Thus, we aimed to evaluatethe efficacy of e-based cognitive behavior therapy for insomnia (e-CBT-I) onimproving insomnia and preventing depression in youths.Methods: This was a randomized controlled trial conducted in Chineseyouths (aged 15-25 years) with insomnia disorder and subclinical depressivesymptoms. Eligible participants were randomly assigned (1:1) to 6-week e-CBT-Ior e-based health education (e-HE). Assessments were conducted at baseline,post-intervention, 6-month and 12-month follow-up. The primary outcomesincluded insomnia and depression at both symptomatic and disorder levels.Outcomes were examined by the mixed model repeated measures ANOVA and generalizedestimating equations. This trial has been registered in ClinicalTrials.Gov(NCT04069247).Results: Currently, 397 participants were randomly allocated to e-CBT-Igroup (n = 198) or e-HE group (n = 199). The preliminary results based on theinitial sample of 142 participants (e-CBT-I: n = 74; e-HE: n = 68) showed thatyouths in the e-CBT-I group had significant reductions in insomnia anddepressive symptoms at post-treatment compared with the control group, and theeffect of e-CBT-I on insomnia symptoms lasted for 6-month (Cohen's d = 0.29).In addition, youths receiving e-CBT-I were at lower risk of having persistentinsomnia (OR: 0.47, 95% CI: 0.26–0.85), clinically significant depression (OR:0.33, 95% CI: 0.14–0.77) and anxiety (OR: 0.26, 95% CI: 0.09–0.72) atpost-treatment and 6-month follow-up. There were also significant group andtime interactions favoring e-CBT-I for DBAS-16, rMEQ, sleep efficiency, andsleep onset latency.Conclusions: The preliminary results suggested that e-CBT-I is effectivein improving sleep and mental health among youths with insomnia and subclinicaldepression, and e-CBT-I may serve as a potential intervention for preventingdepression in high-risk youths.

Craniofacial Phenotyping By Photogrammetry In Hong Kong Chinese Prepubertal Children With Obstructive Sleep Apnea

Yuen,Hoi Man、 Au,Chun Ting、 Chan,Kate Ching-ching、 Li,Albert Martin

The Chinese Univerisity of Hong Kong

Objective: This study aimed to examine the craniofacial phenotype of Hong Kong Chinese prepubertal children with and without OSA using a quantitative photographic analysis technique. We hypothesized the children with different OSA severities would have different craniofacial measurements. Methods: This was a prospective cross-sectional study. Chinese children aged 5-12 years old, suspected to have OSA were recruited from our sleep clinic. Frontal and profile photos were taken for craniofacial phenotyping based on Lee et al photogrammetry method. Polysomnography (PSG) was performed and defined subjects into 3 sleep-disordered breathing (SDB) groups: non-OSA group (obstructive apnoea hypopnoea index (OAHI) <1/h), mild OSA (OAHI between 1/h and 5/h), and moderate-to-severe (MS) OSA (OAHI ≥5/h). Group comparisons were performed using Chi-square, one-way ANOVA and Kruskal-Wallis tests for categorical, normal and skewed continuous variables respectively. Results: This study included 89 subjects (mean age: 8.2 ± 1.57 years, 66 males). Non-OSA, mild OSA and MS OSA groups included 32, 30, and 27 subjects respectively. There was no significant difference in anthropometric data between groups. Increased OSA severity in SDB groups showed an increasing trend in maxillary-mandibular relationship angle (p=0.006), and decreasing trends in anterior mandibular height (p=0.020), and upper to lower face height ratio (p=0.065). Our findings on the maxillary-mandibular relationship angle cohered with that in Caucasian children reported by Sutherland et al (2020). Conclusion: Craniofacial features obtained by photogrammetry were significantly different between SDB groups in prepubertal children. Maxillary-mandibular relationship angle was a feature that was found in both Asian and Caucasian OSA children.

Alerting Network Alteration in Idiopathic Rapid Eye Movement Sleep Behavior Disorder Patients with Mild Cognitive Impairment

Jeong,El1、 Cha,Kwang Su2、 Sunwoo,Jun-Sang3、 Jung,Ki-Young2、 El Jeong

1. Interdisciplinary Program in Bioengineering，College of Engineering，Seoul National University，Seoul，South Korea

2. Department of Neurology，Seoul National University Hospital，Neuroscience Research Institute，Seoul National University College of Medicine，Seoul，South Korea

3. Department of Neurosurgery，Seoul National University Hospital，Seoul，South Korea

Objective: It is reported that idiopathic REM sleep behavior disorder (iRBD) is associated with alteration of

attention, executive functions, and visuospatial abilities. In addition, it is known that about half of the iRBD patients have mild cognitive impairment (MCI). The aim of this study was to explore the differences between iRBD patients with MCI and ones without MCI. Methods: 14 healthy controls (HC), 24 iRBD patients without MCI (iRBD-nMCI), and 24 iRBD patients with MCI (iRBD-MCI) were recruited. The attention network task (ANT) was used to assess three attention network effects (alerting, orienting, and executive control). Event-related potentials (ERPs) and behavioral performances were recorded during the ANT. EEG data were recorded using 60 scalp electrodes. ERP N1 and P3 components were used to assess the three attention network effects. Results: In comparison with HC, iRBD-nMCI showed similar neuropsychological, behavioral, and ERP results. On the other hand, iRBD-MCI showed an overall decline in cognitive domains and the alerting effect impairment [HC (no cue: -0.17 $\pm$ 1.10 μV vs. center cue: -0.66 $\pm$ 1.18 μV, p=0.043); iRBD-nMCI (no cue: -0.33 $\pm$ 1.07 μV vs. center cue: -0.77 $\pm$ 1.16 μV, p=0.014); iRBD-MCI (no cue: 0.07 $\pm$ 0.86 μV vs. center cue: -0.20 $\pm$ 0.99 μV, p=0.130)]. Compared to iRBD-nMCI, iRBD-MCI showed impairment in executive function and verbal memory domains and responded slower when performing the ANT. Although it was not significant, there was a trend that the iRBD-nMCI showed better performances and larger ERP response in ANT than the HC. Conclusions: Our results suggest that the attention network particularly alerting component is impaired when MCI occurs in iRBD patients. On the other hand, attention network and cognition may be maintained because of the compensatory mechanism in iRBD patients.

Subjective and Objective Sleep–Wake Patterns on Weekdays and Weekends in Offspring of Parents with Bipolar Disorder

LEI,Binbin1、Feng,Hongliang2、Yang,Lulu2、Liu,Yaping1、Tsang,Chi Ching1、Chen,Jie1、Song,Weidong3、Jiang,Chao4、Chan,Wing Yan Joey1、Wing,Yun-Kwok1、Zhang,Jihui2,5

1. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong
2. Guangdong Mental Health Center，Guangdong Provincial People＇s Hospital，Guangdong Academy of Medical Sciences
3. Shenzhen Nanshan Center for Chronic disease control
4. Shenzhen Fuyong People's Hospital
5. Zhujiang Hospital，Southern Medical University/ The Second School of Clinical Medicine，Southern Medical University

Background: Sleep-wake pattern alteration is one of the markers of bipolar disorder. The instability of the sleep-wake pattern might precede the onset of depressive symptoms in bipolar disorder. Sleep-wake pattern abnormalities have been identified in the high-risk offspring. However, there were limited studies comparing the sleep-wake patterns on weekdays and weekends with both subjective and objective measurements among

offspring of parents with bipolar disorder. Methods: Totally, 212 case offspring and 200 control offspring were recruited in the high-risk offspring cohort. Subjective sleep-wake patterns on weekdays and weekends were evaluated by the questionnaire, and objective sleep-wake patterns were measured by Actigraphy. The Generalized Estimating Equation model was used to analyze the subjective and objective data. Results: Compared to the control offspring, case offspring had significant later bedtime on weekdays ($22:54 \pm 1.04$ vs. $23:39 \pm 3.28$), weekend ($23:29 \pm 1.06$ vs. $00:25 \pm 3.09$), and holiday (23.36 ± 1.18 vs. $00:22 \pm 3.00$), according to the questionnaire. Subjective rise-time in weekday of case offspring was later than control offspring ($6:50 \pm 1.12$ vs. $7:20 \pm 1.23$). In terms of objective data on weekdays, case offspring presented a significantly shorter sleep time during the rest period (6.95 ± 1.8 vs. 6.42 ± 1.67) and an earlier start time of active period ($06:12 \pm 2.58$ vs. $05:29 \pm 4.16$) than control offspring. On weekdays and weekends, case offspring had more daytime sustained inactivity bouts than control offspring (weekday: 1.73 ± 1.21 vs. 2.38 ± 1.49; weekend: 2.01 ± 1.36 vs. 2.61 ± 1.95). All adjusted $p < .05$. Conclusion: Bipolar offspring presents a distinctive sleep-wake pattern, including shorter sleep duration, early wake-time, and late rise-time on weekdays, and more inactivity bouts in the active period on weekdays and weekends. Further cohort studies are warranted to determine whether the sleep-wake pattern alteration predicts the conversion of bipolar disorder in the high-risk population.

Relationships of social jetlag with poor mental health, emotional and behavioral problems, and daytime sleepiness among adolescents: a cross–sectional study in Hong Kong

Chen,Xie1、 Li, Shirley Xin2、 Zhang,Ji Hui3、 Tsang,Chi Ching1、 Li,Albert Martin1、 Wing,Yun Kwok1、 Chan,Ngan Yin1

1. The Chinese University of Hong Kong，Hong Kong，China
2. The University of Hong Kong，Hong Kong，China
3. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China

Social jetlag, the discrepancy between the internal biological clock and external social activity timing, is common in adolescents. Although some data have suggested the association of social jetlag with general health repercussions, there were few studies exploring the effect of social jetlag on mental health. Our study aimed to investigate social jetlag in relation to general mental health, emotional and behavioral problems, and daytime sleepiness in adolescents. The study included 4973 adolescents in Hong Kong. Social jetlag was estimated by the absolute difference between the midpoint of sleep time of weekends and weekdays. Chronotype was determined by the reduced version of the Morningness-Eveningness Questionnaire (rMEQ). Insomnia was assessed by the Insomnia Severity Index (ISI). Daytime sleepiness was assessed by the

Pediatric Daytime Sleepiness Scale (PDSS). The mental health outcome was assessed by the General Health Questionnaire (GHQ-12), while emotional and behavioral problems were assessed by the Strengths and Difficulties Questionnaire (SDQ). Binary logistic regression and restricted cubic spline regression analyses were applied to examine the predicting function of social jetlag, with potential confounding variables adjusted. The results showed 50.9% of the study participants had social jetlag for more than 2 hours. It was observed that social jetlag had a U-shape nonlinear relationship with poor general mental health, a probably J-shape relationship with emotional and behavioral problems, and a strong linear relationship with daytime sleepiness. Meanwhile, eveningness and social jetlag had an interaction on mental health and daytime sleepiness. Both short and long social jetlag were risk factors for poor mental health. Irregular sleep-wake patterns may contribute to the nonlinear relationship. Our study suggested a pervasive adverse effect of social jetlag on poor mental health, emotional and behavioral problems, and daytime sleepiness. Interventions for reducing social jetlag and keeping healthy and regular sleep-wake habits are needed for preventing mental health problems in adolescents.

Respiratory profiling of community–dwelling individuals many years after polio infection

Xiao Li1,5、Meng Wang5、Qidi Ding2、JingYu Wang2、Ting Sun5、YunLiang Sun2、Yan Yu5、XiaoSong Dong2、Jing Li2、Long Zhao5、XueLi Zhang2、JinXian Wu3、LiJuan Ren1、ChangJun Lv1、Kingman P. Strohl4、Fang Han2

1. the university of Hong Kong
2. Department of Pulmonary Medicine，Peking University People's Hospital，Beijing，China;
3. Department of Pediatrics，DongYang People's Hospital，DongYang，China
4. Division of Pulmonary，Critical Care and Sleep Medicine，Department of Medicine，Case Western Reserve University，and Cleveland Louis Stokes VA Medical Center，Cleveland，OH
5. Department of Pulmonary and Critical Care Medicine，Binzhou Medical University Hospital，BinZhou，China

Objective: To determine the presence of respiratory impairment in community-living subjects with a history of poliomyelitis. Methods: In a study conducted from July 2013-December 2015, we used a national database to recruit individuals in China with a known prior poliomyelitis infection > 25 years previously. They were assessed by overnight oximetry to collect the number/hr of drops in oxygen saturation >4% (ODI4), chest x-ray (CXR), spirometry and maximal voluntary ventilation (MVV), and Epworth Sleepiness Scale (ESS). Those who had an ODI4 ≥ 5/hr with sleep apnea-related symptoms were randomly selected to undergo overnight polysomnography (PSG) in sleep clinics. Results: A total of 298 subjects (age 47.8 ± 6.7, 71.1% males) completed overnight oximetry. As defined by ODI4 ≥ 5/hr, the frequency of sleep-disordered breathing (SDB) was 37.2% (n = 111);of the whole sample, 9% (n = 27) had an ODI4 ≥ 15/hr. ESS was within the normal

range, but was higher in patients with SDB compared with those without (6.8 $\pm$ 5.0 vs. 5.2 $\pm$ 4.0, p < 0.01) . Scoliosis on the CXR was present 26.1% of those with SDB and 14.4% of those without (p = 0.038). Spirometry and MVV were similar between those with vs. those without SDB. Thirty-four participants with an ODI4 $\geq$ 5/hr completed PSG. Thirty (88.2%) had an apnea hypopnea index (AHI) $\geq$ 5/hr, twenty-five (73.5%) had an AHI $\geq$ 15/hr. None of the participants met the diagnostic criteria for central sleep apnea. A strong positive correlation was found between ODI4 and AHI (r = 0.802, p<0.001). Conclusion: Mild (37.2%) and to a smaller extent moderate-severe (9%) SDB and PSG confirmed OSA are present many years after surviving poliomyelitis. In most, sleepiness is low but scoliosis is often present. It needs to be aware of the potential impact of SDB and post-polio sequelae in the aging population worldwide.

The relationship of drug dream phenomenon, drug withdrawal and religiosity among muslim amphetamine–type stimulant patients during recovery period in Klang Valley, Malaysia

Hamizi,Muhammad Asqalani1、 Rashid,Rusdi Abd 1,3、 Hutagalung,Fonny Dameaty2

1. Universiti Malaya Centre for Addiction Science Studies，Universiti Malaya，Malaysia

2. Department of Educational Psychology & Counselling，Universiti Malaya，Malaysia

3. Sleep Disorder Society Malaysia，Malaysia

Drug abuse is a global burden. The recovery journey requires a lot of resources and comprehensive strategies were needed in order for this effort to be effective. Since this is a complex issue, it needs to be viewed from multiple angle which is an eclectic perspective of biopsychosocial-spiritual paradigm rather than solely on biomedical approach. Ex-drug user experienced drug dream phenomenon during withdrawal period. Some patient complained that they＇re having craving sensation after the dream occurs and some other reported otherwise. The effect of drug dream towards patient is remain unsolved among dream researchers. The type of drug dream imageries and its various contents might trigger the mesocorticolimbic dopamine pathway and may contribute to drug cravings after awakening. Social support and religious factor may be an important moderator that reducing and even inhibit drug relapse to take place if the patient reported the occurrence of stimulating drug dream. The objective of this study is to find the relationship of drug dream phenomena, drug withdrawal and religiosity activities among amphetamine-type stimulant patients during recovery period in Klang Valley, Malaysia. This research was divided into two phases. First, a stratified sampling of cross-sectional study was conducted among patients across various stages of drug recovery period. Validated self-administered questionnaires of sleep quality, drug dream content, addiction severity, drug withdrawal, quality of life and religiousity will measured. Then, a focus group from each strata of withdrawal period will be selected to compare the EEG pattern of recalled dream memory in contrast to the baseline. The expected outcome and findings of this research would integrate an additional layer into the holistic coping mechanism

of biopsychosocial-spiritual paradigm. It would be beneficial to prevent patients from relapsing after experiencing drug dream phenomena.

Home Sleep Apnea Testing with telemedicine in asymptomatic healthy persons

Cao,Can1、He,Zhongming2、Thomas,Penzel3、Han,Fang4

1. Technical University of Berlin

2. Karamay Central Hospital

3. Charite University Medicine

4. Peking University People's Hospital

Background: Due to the simplicity of use and the low cost, Home Sleep Apnea Testing (HSAT) is used increasingly to diagnose obstructive sleep apnea (OSA), while polysomnography (PSG) is time and cost-consuming. This study aimed to evaluate the usage of HSAT with telemedicine between asymptomatic healthy individuals and patients with a high pretest probability of moderate to severe OSA.Methods: 31 subjects aged from 16-81 years were recruited to perform an HSAT with telediagnostic. Before undergoing an HSAT, questionnaires, including the Epworth Sleepiness Scale (ESS), the Insomnia Severity Index (ISI), the Patient Health Questionnaire (PHQ-9), and the Generalized Anxiety Disorder (GAD-7), and the medical record of each volunteer were collected. Based on this survey, the volunteers for studies of circadian physiology were segmented into two groups: an ostensibly healthy group and a patient group. The volunteers were educated in the correct application of the device. After that, they started the recording at home when they went to sleep as usual. The data were collected and then uploaded to the server of the manufacturer. The reports were analyzed by licensed physicians.Results: Only one subject terminated the recording due to the inadaptation of wearing the device. In the rest 30 subjects, seven subjects were identified as OSA patients according to the HSAT results. The portable monitor (PM) device provides a feasible solution for the diagnosis of unrecognized OSA. The accuracy of the device may be limited when used in old patients with frequent sleep fragments. Three subjects repeated HSAT for four nights. The Night-to-Night differences in sleep stages, AHI, sleep efficiency and mean SpO2 are insignificant. Conclusions: HSAT using the tested device provides reliable information for evaluating sleep disorders in asymptomatic healthy persons. The tested device is capable of remotely diagnosing OSA, HSAT with telemedicine for one night is reliable.

Association of COVID–19 related traumatic events with suicidal thoughts among Wuhan hospital workers: the mediating role of nightmares

Jianyu Que1,Le Shi1,Sijing Chen2,Yi Zhong1,Ping Wu3,Siwei Sun1,Zhongchun Liu4,Zhou Zhu5,Jingyi Fan6,Yu Lu7,Bo Hu8,Han Xiao9,Zhisheng Liu9,Guofu Huang7,Yi Li10,Yu Hu8,Gaohua Wang4,Wei Wang5,Maosheng Ran11,Yanping Bao3,Jie Shi3,Lin Lu1

1.Peking University Sixth Hospital

2.Chinese University of Hong Kong

3.National Institute on Drug Dependence，Peking University

4.Renmin Hospital of Wuhan University

5.Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology

6.Zhongnan Hospital of Wuhan University

7.Wuchang Hospital

8.Union Hospital of Tongji Medical College of Huazhong University of Science and Technology

9.Wuhan Children＇s Hospital

10.Wuhan Mental Health Center

11.University of Hong Kong

Objective: Trauma experience may increase the risk of suicidal thoughts. This study aimed to examine the association of COVID-19-related traumatic events exposure with suicidal thoughts and the mediating roles of sleep disturbances (symptoms of nightmares and insomnia severity) among hospital workers in the most affected area by COVID-19. Methods: A total of 16,220 hospital workers in Wuhan city were recruited via an online platform from May 27, 2020, to Jul 31, 2020. Participants completed a self-reported questionnaire to evaluate the number of COVID-19 related traumatic events, the frequency of nightmares, insomnia severity, suicidal thoughts, symptoms of depression and anxiety, and demographic characteristics. Bias-corrected bootstrap mediation analysis was used to examine the indirect effects of trauma experience on suicidal thoughts through nightmare frequency and insomnia severity when controlling for psychological status and demographics. Results: Of the sample, 13.3% reported having suicidal thoughts in the past month. COVID-19-related traumatic events exposure was associated with insomnia, nightmares, and suicidal thoughts. Pathway analyses showed that the relationship between the number of COVID-19 related traumatic events and suicidal thoughts was fully mediated by the frequency of nightmares, but not insomnia severity, after adjusting for demographic characteristics and symptoms of depression and anxiety. Conclusions: Suicidal thoughts are prevalent among hospital workers from the most affected area by COVID-19. The association of trauma experience with suicidal thoughts was fully mediated by the frequency of nightmares. Identification and intervention of nightmares may have important implications for reducing the risk of suicidal thoughts. Keywords COVID-19; insomnia; nightmares; suicidal thoughts; mediation

The glutamatergic neurons in the lateral periaqueductal gray regulate rapid eye movement sleep and wakefulness associated defensive behaviors

Lei Li1,Yiqun Wang1,Wenying Liu1,Sébastien Arthaud2,Pierre-Hervé Luppi2,Zhili Huang1

1. Fudan University
2. SLEEP Team，CNRS UMR 5292，INSERM U1028，Faculté de Médecine RTH Laennec，Centre de Recherche en Neurosciences de Lyon (CRNL)，Université Claude Bernard Lyon 1，7 rue Guillaume Paradin，Lyon 69008，France

The periaqueductal gray (PAG) is a major target of sleep-wake regulation and defensive responses to danger that rely on arousal state. Previous studies suggest the lateral periaqueductal gray (lPAG), an important part of the PAG, also involved in sleep-wake regulation. However, the role and mechanism of the lPAG in sleep—wake regulation remain poorly understood. In the present study, we sought to elucidate the specific role of lPAG glutamatergic neurons in controlling sleep-wake behaviors in mice. Fiber photometry revealed that the population activity of lPAG glutamatergic neurons was increased during physiological transitions from non-rapid eye movement (non-REM, NREM) and REM sleep to wakefulness. Moreover, optogenetic activation of lPAG glutamatergic neurons induced immediate transitions from NREM sleep to wakefulness, and chemogenetic stimulation promoted arousal, with increased freezing behaviors. Furthermore, chemogenetic inhibiton of lPAG glutamatergic neurons reduced REM sleep. Patch-clamp, tracing, and immunohistochemistry revealed that lPAG glutamatergic neurons project to the locus coeruleus (LC), sublaterodorsal tegmental nucleus (SLD) and ventral gigantocellular reticular nucleus (GiV). Furthermore, optogenetics showed that activation of their efferents to the LC drive wakefulness. Taken together, these results indicate that glutamatergic neurons in the lPAG are required for wakefulness associated with defensive behaviors and REM sleep.

Keywords lPAG, arousal, freezing behaviors, REM sleep

Sub–cultural comparison in Chinese preschoolers' sleep

Qiuye Lan1,2,Huilian Zhu1,Albert Martin Li2

1.Sun Yat-sen University

2.Department of Paediatrics，Faculty of Medicine，The Chinese University of Hong Kong

Background: Preschoolers are vulnerable to the effects of sleep problems. Previous cross-cultural studies underscored the problem of inadequate sleep among Chinese children. China shares 13% of the world's childhood population. There is an increasing need for a better understanding of the modifiable factors that affect children's sleep in this population. Methods: Guangzhou (GZ) and Hong Kong (HK) preschoolers were recruited to conduct a sub-cultural comparison. The parent-completed questionnaire provided information on socioeconomic status (SES), children's and parental sleep information. Results: A gender- and age-matched sample of 2412 children was included (639 from GZ and 1773 from HK). More mothers in GZ work full-time (84.7% vs 49.3%). There is no difference observed in average daily sleep duration and weekday sleep duration. HK children tend to have later bedtime on both weekdays (22:08 $\pm$ 0:48 vs 21:54 $\pm$ 0:32) and weekends (22:36 $\pm$ 0:51 vs 22:11 $\pm$ 0:32). Guangzhou children's wake time is much earlier throughout the week (weekdays: 7:05 $\pm$ 0:16 vs 7:56 $\pm$ 0:57; weekends: 8:00 $\pm$ 0:41 vs 8:45 $\pm$ 1:02). HK children had short daily outdoor play. Structural equation modeling (SEM) was used to analyze relationships in children's sleep, daily activities, parental sleep, parental knowledge and SES. Maternal sleep duration was the strongest predictor for the children's sleep duration indicated by a standardized regression weight (SRW) of 0.24, followed by consistent bedtime (SRW = 0.17). Parental knowledge and bedtime routines play an important part in their children's consistent bedtime. Physical activity and paternal sleep duration were also related with children's sleep. Conclusions: Although no difference in average sleep duration between HK and Guangzhou children, the late bedtime in HK children and early wake time in Guangzhou children is an interesting contrast. Modifiable factors for short sleep duration including parental knowledge, parental behaviors, children's daily activities, and bedtime routines.

Keywords Sub-cultural, sleep patterns, preschooler

Disrupted small–world networks are associated with decreased psychomotor vigilance after total sleep deprivation

Jing Qi1,Bozhi Li1,Ying Zhang2,Bei Pan3,Yuhong Gao1,Hao Zhan3,Yong Liu4,Yongcong Shao5,Xi Zhang1

1.Chinese PLA General Hospital

2.The Eighth Medical Center of the General Hospital of People's Liberation Army

3.Airforce Medical Center，PLA

4.Brainnetome Center，Institute of Automation，Chinese Academy of Sciences，Beijing

5.School of Psychology，Beijing Sport University，Beijing

Objective: To explore the topological changes in brain functional networks and their associations with cognitive performance after 36 hours of total sleep deprivation (TSD). Methods: We investigated the topological properties of brain functional networks derived from resting-state magnetic resonance imaging of 30 healthy men in rested wakefulness (RW) state and after 36 hours of TSD. In the predefined sparsity threshold range, both global and nodal network properties were evaluated based on graph theory analysis, including clustering coefficient, degree, shortest path length, global efficiency, local efficiency, and small-world property. Cognitive performance was assessed using the psychomotor vigilance test (PVT) before and after TSD. We compared topological properties between the RW and TSD states at both the global and nodal levels. Furthermore, Pearson's correlation analyses were conducted to explore the association between altered network properties and the mean response time of PVT in the TSD state. Results: Data from 26 participants were analyzed. At the global level, the brain functional networks in the TSD state showed a significantly lower small-world coefficient than RW, with higher local efficiency but lower global efficiency. At the nodal level, the altered regions were selectively distributed in frontoparietal networks, sensorimotor networks, temporal regions, and salience networks. These topological changes were further associated with worse PVT performance elicited by TSD. Conclusions: The topological properties of brain functional networks were disrupted following TSD. Further, TSD may affect cognitive function by altering the topology in the frontoparietal, sensorimotor, temporal, and salience networks.

Keywords

Association of BST1 polymorphism with idiopathic restless legs syndrome in Chinese population

Yumeng Huang,Jianfang Ma,Pei Wang,Qi Luo

Shanghai Jiao Tong University Medical School Affiliated Ruijin Hospital

Background: Parkinson's disease (PD) and restless legs syndrome/William Ekbom disease (RLS/WED) are both common movement disorders. Based on their clinical overlap, association studies of PD and RLS/ WED have been conducted for many years. Objective: To investigate whether the genetic risk factor of PD was also associated with RLS/WED. Methods: We included 102 idiopathic RLS/WED patients and 189 matched controls from southeast China. Clinical data included the International Restless Legs Syndrome Study Group rating scale, the subtype of RLS/WED symptoms (painful or other discomforts), comorbidities, the pregnancy history of female patients, Hamilton Depression Scale (HAMD), and Pittsburgh Sleep Quality Index (PSQI) questionnaire. Risk gene analysis between RLS/WED and control groups including 21 SNPs (single nucleotide polymorphism) was conducted. Genotyping was done by Sanger sequencing. Results: We found that rs4273468 polymorphism of BST1 gene increased the risk of idiopathic RLS/WED patients in the Southeastern Chinese population ($P < 0.001$, OR = 2.85, p = 0.019 after Bonferroni correction). Moreover, the haplotype of G-G (rs4698412-rs4273468) was significantly associated with Chinese RLS/WED patients ($P < 0.001$). Conclusion: BST1 may contribute to the development of RLS/WED. Further studies on larger cohorts are needed to confirm it.

Keywords

Interaction between Night Shift Work and MTNR1B rs10830963 on the incidence of prostate cancer in the UK Biobank

Lulu Yang1,Jie Chen2,Jihui Zhang1

1. Guangdong Provincial People's Hospital
2. Li Chiu Kong Family Sleep Assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin，Hong Kong SAR，China

Objectives: To examine whether an interaction between night shift work and MTNR1B rs10830963 on prostate cancer risk among male participants from the UK Biobank cohort. Methods: This was a prospective cohort study based on the UK biobank. A total of 133,416 male participants resident in United Kingdom and recruited between 2006 and 2010 were included into the current study. Data on prostate cancer diagnosis was obtained from cancer register in UK Biobank and newly developed prostate cancer was defined as the outcome. Night shift exposure was assessed at baseline. MTNR1B rs10830963 SNP was amongst the directly genotyped SNPs of the UK Biobank. Results: The mean (SD) age of 133416 participants at the initial recruitment was 53.13 (7.34) years old. The mean (SD) follow-up period is 7.76 (1.16) years. During the

follow-up period, 2646 participants had incidental prostate cancer. There was an interaction between night shift work and rs10830963 variant on the outcome (p=0.008). Among non-night shift workers, compared with those who carry CG/GG genotype, no significant association with prostate cancer was observed for ones who carry CC genotype (HR: 1.02, 95% CI: 0.94 - 1.10) after adjusting for age. For night shift workers, those with CC genotype had a significantly increased prostate cancer risk (HR: 1.18, 95% CI: 1.00 – 1.41), whereas a significantly reduced risk for ones with CG/GG genotype (HR: 0.80, 95% CI: 0.64 – 0.99). These findings largely unchanged even after adjustment for a series of potential confounding factors, including sociodemographics, lifestyle behaviors, obesity, snoring, sleep duration, chronotype, and family history of prostate cancer. Conclusions: Night shift work may predispose towards prostate cancer for people with CC genotype, but not CG/GG genotype. These data have great implications for public health to reduce the risk of prostate cancer.

Keywords night shift; gene; circadian rhythm; prostate cancer

Observe the therapeutic effect of EEG–Based biofeedback on 82 patients with insomnia

Huicong Wang,Penghui Song,Yuping Wang,Yue Hou

Xuanwu Hospital，Capital Medical University

Background: Insomnia is the most common sleep disorder in the clinic, and the vast majority of patients are accompanied by anxiety and tension. Electroencephalography (EEG) biofeedback therapy is a new method for the treatment of related mental diseases after drug and physical therapy. EEG information is fed back to the subjects to regulate their EEG activities with subjective consciousness, so as to achieve the purpose of treatment and regulation. This study was to observe the clinical effect of EEG biofeedback therapy on insomnia and to explore its possible mechanism. Methods: 82 patients with insomnia in Xuanwu Hospital were selected for EEG biofeedback treatment. The training site was CZ point. The specific implementation methods were as follows: two minutes of EEG were collected before and after the training, and the α wave and electromyography (EMG) training were performed for 30 minutes, once every other day, 10 times as a course of treatment. BDI, s-stai, t-stai and PQRI were used to evaluate before treatment and after one course of treatment. Spss26.0 was used for statistical analysis. Results: The score of PQRI after treatment was significantly lower than that before treatment ($P < 0.001$), and the score of PQRI after 10 times of biofeedback treatment was significantly lower than that after 5 times of treatment ($P < 0.001$). The scores of BDI, s-stai and t-stai after treatment were significantly lower than those before treatment ($P < 0.001$). Conclusions: Biofeedback therapy has a good effect on patients with insomnia. The possible mechanism is that the α wave indicating relaxation increases, while the β wave indicating alertness and the θ wave indicating deep sleep decrease after treatment. Biofeedback can relax patients' nerves and muscles well, help them enter a state of soberness and relaxation, relieve tension and anxiety, and improve the symptoms of insomnia.

Keywords

Changes of gut microbiota in patients with type 1 narcolepsy

Ruirui Zhang1,Shenghui Wang2,Yingying Bai2,Pengfei Xu1,2,Hongju Zhang1,2

1.People's Hospital of Henan University

2.Henan Provincial People's Hospital

Objective: To explore the characteristics of gut microbiota in patients with type 1 narcolepsy (NT1), and to provide new ideas for its diagnosis and treatment. Methods: Fecal samples from 20 NT1 patients and 16 healthy control (HC) patients in our hospital were collected to extract DNA from the samples. PCR primers were used to amplify the V3-V4 region on 16S rDNA, and then sequencing was conducted. Finally, bioinformatics analysis was performed on the two groups of samples. Spearman correlation analysis was performed between different gut microbiota and clinical indicators. Results: There was no significant difference in Alpha and Beta diversity between NT1 group and HC group (P>0.05). There were significant differences in phylum, class, order, family, genus, species and OTU between the two groups (P<0.05). The relative abundance of intestinal Tenericutes, Coriobacteriia, Mollicutes, Coriobacteriales, Mollicutes_RF39, Barnesiellaceae, Blautia, Barnesiella, Bilophila, Lactococcus and Ruminiclostridium_5 in the NT1 group was lower than that in the HC group (P<0.05). The relative abundance of intestinal Megamonas and Klebsiella in NT1 group was higher than that in HC group (P<0.05). Lefse analysis showed that Klebsiella was the main contributor to NT1. Correlation analysis showed that Megamonas in NT1 group was negatively correlated with nocturnal awakening times (P=0.031, R=-0.483). Klebsiella was negatively correlated with Epworth sleepiness scale score (P=0.032, R=-0.481). Barnesiella was positively correlated with body mass index (P=0.048, R=0.447). Barnesiella and Barnesiellaceae were negatively correlated with the level of hypocretin (P=0.045,0.020; R=-0.453, -0.514), and positively correlated with the number of sleep onset REM periods (P=0.006,0.001; R=0.591,0.700). Coriobacteriia/Coriobacteriales was negatively related to the Hamilton Depression Scale scores (P = 0.026, R = 0.496). Conclusion: Partial changes in the gut microbiota of patients with NT1 may be related to hypocretin levels and NT1-related symptoms. Larger longitudinal multi-omics studies are needed to elucidate the causal relationship between NT1 and gut microbiota and the possible role of gut microbiota in the pathogenesis of NT1.

Keywords

Effects of titrated mandibular advancement on obstructive sleep apnea severity

Yanyan Ma,Min Yu,Xuemei Gao

Peking University School and Hospital of Stomatology

Objectives The treatment outcome of oral appliances for obstructive sleep apnea (OSA) can be influenced by the mandibular protrusion amounts. Therefore, this study aimed to search for the optimal mandibular

advancement amounts and identify potential influencing factors by titration of an adjustable device. Methods Forty-two patients aged 41.5 ± 9.0 years who were diagnosed with OSA were prospectively recruited. The mandible advancement amount was adjusted from 0 mm with a daily increment of 0.5 mm, monitored by a type III home sleep testing until the apnea-hypopnea index (AHI) was reduced to the lowest. Rhinospirometry, rhinomanometry, and magnetic resonance imaging were used to observe the change of respiratory function and upper airway dimensions. Results A significant dose-dependent relationship was found between the mandibular protrusion and treatment outcome from 0mm to approximately 70% of the maximal mandibular protrusion (MMP). The changing curves plateaued after that. Besides, the improvement of AHI brought by increased mandibular protrusion was more obvious in severe OSA. The optimal mandibular advancement amounts for patients with mild, moderate, and severe OSA were 3.5 ± 1.8 mm ($38.6\pm19.4\%$ MMP), 5.8 ± 1.9 mm ($62.9\pm18.8\%$ MMP), and 5.9 ± 2.2 mm ($68.8\pm15.6\%$ MMP), respectively. Regression analysis revealed that the factors influencing optimal mandibular protrusion included soft palate length and change of maximal lateral dimension of the total upper airway with mandibular advancement. Further protrusion brought more lateral expansion of the velopharynx, whereas the change in nasal ventilation was not significant. Conclusions The dose-dependent effect of titrated mandibular advancement on treatment efficacy of oral appliance became pronounced as the OSA severity increased. And this dose-dependent relationship existed mainly within 70% MMP. The mandibular protrusion should be more personalized to each patient.

Keywords

Abnormal striatal–cortical networks contribute to the attention/ executive function deficits in idiopathic REM sleep behavior disorder: A resting state functional MRI study

Yingying Bai,Hongju Zhang,Shuai Chen,Shenghui Wang,Zhonglin Li,Jiewen Zhang

Henan Provincial People's Hospital

Introduction: The structural and functional damages of the striatum were evident in idiopathic REM sleep behavior disorder (iRBD). With the research on iRBD deepens, cognitive impairment in iRBD is getting increasing attention. However, the mechanism of cognitive impairment in idiopathic RBD (iRBD) was poorly understood. Methods: Neuropsychological assessment were carried out in 20 polysomnographies (PSGs) confirmed iRBD patients and 22 normal controls. Both regional homogeneity (ReHo) and seed-based functional connectivity (FC) rs-fMRI analyses were applied to explore the FC abnormalities and its association with cognition in iRBD patients. Positive ReHo clusters were set as seeds for further FC analysis. Results: iRBD patients presented cognitive deficits in attention/working memory, executive function, immediate memory, and visuo-spatial ability. ReHo analysis revealed abnormal spontaneous brain activities

in the striatum (right caudate, left pallidum and bilateral putamen) in iRBD. FC analysis showed decreased striatum-related FCs in the frontal, temporal, occipital lobes, thalamus, anterior cingulate gyrus, as well as decreased intrinsic FCs between bilateral putamen and between caudate and pallidum. Deficits in attention/ working memory, executive function, and immediate memory were associated with abnormal striatal-cortical FCs including frontal, temporal and anterior cingulate cortices. Conclusions: Functional changes of striatum and cognitive impairment in iRBD were reconfirmed in the present study. Abnormal striatal-cortical networks, especially the striatal-frontal network, contribute to the attention/executive function deficits in idiopathic REM sleep behavior disorders.

Keywords

Semi–supervised residual attention network for sleep staging

Chuanhao Zhang1,Fang Han2,Yuan Zhang1

1.Southwest University

2.Peking University People's Hospital

Purpose: Polysomnography (PSG) analysis, as a standard approach for sleep disorder diagnosis, also take key effects on automatic sleep staging process. However, many existing computer-aided methods heavily rely on the labeled data supervising. The annotation of all-night data for diverse patients is both time-consuming and challenging even for the experienced physicians. Hence, there is an urgent need for developing efficient classification method without many labels training. Method: We propose a novel hybrid residual attention convolutional neural network for automatic sleep staging. The pseudo label with adversarial semi-supervised training scheme is combined to solve the insufficient labeled data problem. A multi-scale attention loss is proposed to detect the fine-grained feature representation from coarse-to-fine stages. The residual connection utilized in our top-down architecture can mitigate the risk of overfitting. When the hybrid feature extractors catch enough low-level spot features, a contractive classifier is adopted to output the final prediction. Results: The proposed model was validated on a 13-subject dataset. Our pipeline achieved 0.77 accuracy, 0.73 precision, 0.76 sensitivity, 0.74 f1-score and kappa coefficient of 0.7, respectively. Compared with several state-of-the-art methods, the obtained results verify that our model performed more efficiently than other semi-supervised models. Conclusions: Due to the development of semi-supervised learning, many AI assisted technologies are no longer limited by data labeling. With much less labeled training samples, deep learning models can also achieve promising results. It can both free the labor of physicians and mitigate the time consuming of patients simultaneously. The introduction of attention mechanism not only increases the interpretability of the model but also helps physicians to diagnose more efficiently. Our approach also improves the machine classification performance closer to the gold standard in clinic.

Keywords: Sleep staging, convolutional neural network, multi-scale attention

Causal Association of Benzodiazepines Target Genes with Dementia: A Mendelian Randomization Study

Yue Liu1,2,Xinru Chen3,Sizhi Ai4,Hongliang Feng1,2,Lulu Yang1,2,Jiajin Zhou5,Jihui Zhang1,3

1. Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences
2. Guangdong Cardiovascular Institute，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，China.
3. The First School of Clinical Medicine，Southern Medical University，Guangzhou，China
4. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin，Hong Kong SAR，China.
5. Medical School & Affiliated Hospital，Kunming University of Science and Technology，The First People's Hospital of Yunnan Province，Yunnan，China.

Objectives: The association between the administration of Benzodiazepines and the risk of dementia remains controversial in observational studies. Therefore, current study aimed to estimate the potential causal effect of benzodiazepines on dementia. Methods: Expression levels of Benzodiazepines target genes (including gamma-aminobutyric acid (GABA) receptors and translocator protein(TSPO)) served as proxies for drug exposure and mendelian randomization (MR) instruments. The inverse-variance weighted (IVW), MR-Egger, weighted-median, and weighted-mode were applied to assess the causal association between single-nucleotide variant polymorphisms (SNPs) and drug target gene expression from existing expression quantitative trait loci (eQTL) data in blood and brain regions, and the SNPs-dementia association from published case-control genome-wide association studies. Results: Higher expression of TSPO gene in blood was associated with an increased risk of dementia (β =0.282, p=0.01), but not associated with risk of Alzheimer's disease (AD) (β =0.086, p=0.56). In addition, higher expression of GABRA1 and GABRA3 genes in caudate were associated with a higher risk of dementia (β =0.725, p=0.03 and β =0.436, p=0.02 respectively) but no causal relationship was detected between gene expression of GABA receptors and AD. No significant pleiotropy effects (all P > 0.05) or heterogeneity (all P > 0.05) was observed in the study. Conclusions: Findings suggest a causal association of higher messenger RNA of TSPO and GABA receptor α isoforms with dementia risk. These findings warrant greater pharmacovigilance and further investigation into the effect of Benzodiazepines on dementia symptoms in elderly with insomnia.

Keywords benzodiazepines , drug target, dementia, mendelian randomization

Validation of a Contact–free Device for the Diagnosis of Patients with Obstructive Sleep Apnea

Ruiling Liang,Chenyang Li,Fang Han

Peking University People's Hospital，Beijing，China

Study Objectives: To evaluate the value of a contact-free device used to diagnose obstructive sleep apnea (OSA) in Chinese adults. Methods:130 Chinese adults (mean±standard deviation age 49.7±17.4 years,70% males,body mass index 28.2±5.0 kg/m2) underwent an overnight in-laboratory polysomnogram(PSG) with a contact-free device, Sara.The Sara recordings were scored using automated analysis and the PSG recordings were scored according to recommended guidelines by independent technicians. Results: The total sleep time M[Q1,Q3] was 523.67(497.50,542.64) minutes on Sara recording, and 408.25(364.25,462.50) minutes on PSG (P<0.001).The apnea-hypopnea index (AHI) M[Q1,Q3] was 15.83(6.18,27.49) events/h on Sara recording, and 18.25(6.15,35.68) events/h on PSG (P=0.009). The AHI on Sara correlated significantly with AHI on PSG (r=0.645, P<0.001). Bland-Altman analysis of AHI on Sara versus PSG showed a mean difference (95% confidence interval) of -5.7(-40.5,29.2).Based on a threshold of AHI≥5 events/h, Sara had 83.81% sensitivity,92% specificity,97.8% positive predictive value and 57.5% negative predictive value compared to PSG. Using an AHI≥15 events/h, Sara had 88.16% sensitivity,74.07% specificity. Using an AHI≥30 events/h, Sara had 64.86% sensitivity, 91.40% specificity. Conclusion: Sara has a good diagnostic value for adult OSA patients and there is close agreement between Sara and PSG.

Keywords apnea-hypopnea index,contact-free device,polysomnogram, obstructive sleep apnea

Protective role of mesenchymal stem cells transfected by miRNA–378a–5p in phosgene inhalation lung injury

Yubei Qu1,Jie Shen2

1.Zhongshan Hospital

2.Jinshan Hospital

Objective: Our previous study revealed that expressions of 6 miRNAs were significantly increased in phosgene-induced lung injury. This study aimed to found the miRNA having the most significant effect on hepatocyte growth factor (HGF) expression in mesenchymal stem cells (MSCs) among the six ones, and investigate whether the transfected MSCs with this miRNA had a better therapeutic effect than untreated MSCs alone. Methods:In order to select the most effective miRNA, MSCs were co-cultured with miRNA mimics or selected miRNA inhibitor for 24h and 48h respectively. Then, HGF expression in culture supernatant and the treated MSCs was detected by ELISA and Western blotting respectively.. The selected miRNA was transfected to MSCs. Then these MSCs were given to rats suffering from phosgene-

induced lung injury. The pathological indexes of lung injury were tested. Expressions of inflammatory cytokines, including TNF-α, IL-6, IL-1β and IL-10, were assayed by ELISA. SP-C mRNA level was tested by RT-PCR, andVE-CAD expression was tested by Western blot. Results:We found that miRNA-378a-5p was the most effective miRNA increasing HGF expression among the six miRNAs. After transfection of MSCs with miRNA-378a-5p inhibitor, HGF expression in MSCs was decreased. Compared with untreated MSCs, MSCs transfected with miRNA-378a-5p exhibited more significant decreases in lung injury score, white blood cell count, and protein content and restored respiratory indexes. Meanwhile, expressions of TNF-α, IL-6, IL-1β were decreased while IL-10, SP-C, and VE-cadherin were increased. Conclusions: MSCs transfected with miRNA-378a-5p were more effective in treating phosgene-induced lung injury by repairing the secretion function of alveolar epithelial cells and improving the permeability of vascular endothelial cells compared with the untreated MSCs.

Keywords

Pinocembrin ameliorates intermittent hypoxia–induced neuroinflammation through BNIP3–dependent mitophagy in a murine model of sleep apnea

Linjing Gong1,Xu Wu1,Lei Zhu1

1.Zhongshan Hospital，Fudan University

2. Fudan University

Purpose: Intermittent hypoxia (IH) caused by obstructive sleep apnea (OSA) leads to neuroinflammation. Pinocembrin has been shown to have neuroprotective effects, while the therapeutic functions under IH condition are still unknown. Methods: An OSA model was established by CIH exposure inside custom-made chambers. C57BL/6 mice were intraperitoneally injected with pinocembrin (40 mg/kg, i.p.) or vehicle (PBS containing 5% povidone; i.p.), and the changes of behavior on mice were detected by Morris Water Maze test. Immunohistochemical staining, western blotting, immunofluorescence assays and immunoprecipitation were used to investigate the association between NLRP3 inflammasome and BNIP3-dependent mitophagy. The mitochondrial morphology and mitophagosomes were detected under transmission electron microscope. The detrimental effects of IH were tested by annexin V-FITC/PI staining, Mito SOX Red staining and JC-1 mitochondrial membrane potential assay. Results: In this study, our observations in vivo indicated that administration of pinocembrin can restore spatial learning as well as memory ability, and reduce neuronal apoptosis and hippocampal inflammation. Pinocembrin treatment significantly inhibited formation of NLRP3 inflammasome, infiltration of microglia and enhanced BNIP3-mediated mitophagy in hippocampus of IH mice. Additionally, our in vitro results show that pinocembrin protects microglial cells against IH-induced cytotoxicity (such as mtROS and NLRP3 inflammasome) by activating BNIP3-dependent mitophagy

through the JNK-ERK signalling pathway. Conclusions: Taken together, our preliminary experiments suggest that mtROS and NLRP3-mediated inflammation play key roles in the pathogenic processes driven by IH-induced microglia in OSA patients, which can be offset by pinocembrin-enhanced mitochondrial autophagy. Overall, these findings demonstrate that pinocembrin is a potential therapeutic agent for OSA-associated neuroinflammation.

Keywords

NLRP3 inflammasome mediates chronic intermittent hypoxia–induced renal injury implication of the microRNA–155/FOXO3a signaling pathway

Xu Wu,Linjing Gong, Shanqun Li

Zhongshan Hospital，Fudan University

Purpose: As the foremost pathophysiological change of obstructive sleep apnea (OSA), chronic intermittent hypoxia(CIH) contributes to continued deterioration in renal function. Nucleotide‑binding domain like receptor protein 3 (NLRP3) inflammasome is a multiprotein complex that triggers innate immune responses to infection and cellular stress through activation of caspase‑1 and maturation of inflammatory pro-interleukin-1β cytokine. Emerging evidence indicates that inhibition of the NLRP3 inflammasome ameliorates renal injury. Nevertheless, it is uncertain whether NLRP3 inflammasome participates in CIH‑induced renal injury. The molecular mechanisms modulating NLRP3 inflammasome activation remain to be elucidated. METHODS: A model of OSA was established by CIH exposure inside custom-made chambers, and then the NLRP3−/− and wild-type (WT) male mice on C57BL/6 background were euthanized at 5 wk following CIH exposurement. The CIH-induced renal structure damage was evaluated by H&E staining and TUNEL assay. The level of NLRP3 inflammasome activity was investigated through immunohistochemistry, immunofluorescent staining and western blot analysis. The oxidative stress biomarkers, SOD and MDA, were also examined in renal tissues. The underlying mechanisms of action of NLRP3 inflammasome under IH were examined in vitro using HK-2 cells via Western blotting, flow cytometry, qRT-PCR and luciferase assay. RESULTS: Compared with wild‑type mice, NLRP3 knockout mice dramatically protected them from kidney injury, as indicated by the restoration of creatinine levels, lessened histopathological alterations, and the suppression of macrophages infiltration stained with F4/80. NLRP3 deficiency notably reversed CIH‑induced oxidative stress (malondialdehyde and superoxide dismutase), concomitantly with the abrogated apoptosis‑related proteins and proinflammatory signaling pathway. Consistently, NLRP3‑deficient tubular cells remarkably inhibited reactive oxygen species generation and NLRP3 inflammasome activation. Furthermore, our study revealed that microRNA‑155 (miR‑155) was augmented in the renal tissue and HK‑2 cells exposed to CIH. In addition, we investigated the role of miR‑155 in the regulation of NLRP3

inflammasome. Inhibition of miR‑155 suppressed the CIH‑induced NLRP3 inflammasome activation in renal tubular cells, whereas overexpression of miR‑155 promoted oxidation and enhanced NLRP3 pathway. CONCLUSIONS: Collectively, we demonstrated that miR‑155 might be a positive‑regulator of NLRP3 pathway by inhibiting the targeted FOXO3a gene. These results established a link between the miR‑155/FOXO3a pathway and the NLRP3 inflammasome, suggesting pharmacological blockage of NLRP3 could be a potential therapeutic strategy for OSA‑associated chronic kidney disease.
Keywords

Independent component analysis and graph theoretical analysis in patients with narcolepsy

Fulong Xiao,Fang Han
Peking University People's Hospital

Objective: To evaluate resting-state functional connectivity and topological properties of brain networks in patients with narcolepsy compared with healthy controls. Methods: Resting-state fMRI was performed in 26 adult patients with narcolepsy and 30 matched healthy controls. MRI data were first analyzed by group independent component analysis, then a graph theoretical method was applied to evaluate the topological properties in the whole brain. Small-world network parameters and nodal topological properties were measured. Altered topological properties in brain areas between groups were selected as region-of-interest seeds, then the functional connectivity among these seeds was compared between groups. Correlation analysis was performed to evaluate the relationship between the severity of sleepiness and functional connectivity or topological properties in the patients with narcolepsy. Results: Compared with healthy controls, the patients with narcolepsy exhibited significantly decreased functional connectivity within the executive and salience networks, along with increased functional connectivity in the bilateral frontal lobes within the executive network. There were no differences in small-world network properties between patients and controls. The altered brain areas in nodal topological properties between groups were mainly in the inferior frontal cortex, basal ganglia, anterior cingulate, sensory cortex, supplementary motor cortex, and visual cortex. In the correlation analysis, nodal topological properties in the putamen, anterior cingulate, and sensory cortex as well as functional connectivity between these regions were correlated with the severity of sleepiness among patients with narcolepsy. Conclusions: Altered connectivity within the executive and salience networks were found in patients with narcolepsy. Functional connection changes between the left frontal cortex and left caudate nucleus may be one of the parameters describing the severity of narcolepsy. Changes in the nodal topological properties in the left putamen and left posterior cingulate, and changes in functional connectivity can be considered specific indicators for evaluating the severity of narcolepsy.
Keywords Narcolepsy, Functional connectivity, Independent component analysis, Graph theory

The effects of improvements of sleep problems throughout kindergarten on executive function: A latent change score analysis

Xiaoning Sun,Guanghai Wang,Fan Jiang

Shanghai Children's Medical Center affiliated to Shanghai Jiao Tong University School of Medicine

Objective: Executive function (EF) refers to a set of neurocognitive skills involved in goal-directed problem solving, and is a key predictor for long-term cognitive and social developmental outcomes. Meanwhile, the importance of sleep in neurocognitive development has been revealed. Considering children's rapid maturation during the kindergarten years, the current study examined the association between sleep problem as well as its changes throughout kindergarten with EF at graduation. Method: With stratified random sampling approach, we recruited 992 kindergarteners from 191 kindergartens in Shanghai, China. Children's sleep problems were assessed with the Children's Sleep Habit Questionnaire (CSHQ) at the entrance (T1), middle (T2), and graduation (T3) of kindergarten. At T3, with the Behavior Rating Inventory of Executive Function (BRIEF-2), we obtained scores on the EF domains of inhibition, emotional control, shifting, working memory, and planning. Results: Stepwise linear regression models revealed that, taking into consideration children's gender, parents' education level, and household income, there are significant associations between sleep problems at T1, T2, and T3 with all five domains of EF skills (inhibition, shifting, emotional control, working memory, and planning) at graduation of kindergarten. Latent change score analysis revealed that, from T1 to T3, the more children's sleep improves throughout kindergarten, the better children's inhibition (b=.16, p<.01), emotional control (b=.20, p<.001), working memory (b=.17, p<.01), and planning skills (b=.18, p<.01) are at T3, but not shifting (b=.12, n.s.). Further analyses indicated both T1-T2 and T2-T3 sleep improvements are significant predictors of better inhibition, emotional control, working memory, and planning, whereas only T1-T2 sleep improvements significantly predicts better shifting at T3. Conclusion and implication: Taking a developmental perspective, improvements of sleep problems throughout kindergarten are predictive of better EF at graduation of kindergarten. Our results provided an important empirical foundation for the promising effects of sleep interventions in promoting neurocognitive developmental outcomes.

Keywords Sleep Problems, Executive Function, Kindergarten, Latent Change Score Analysis

Neuromodulation of the histaminergic nervous system on HN in CIH conditions

Liang Xie,Shanqun Li
Zhongshan Hospital，Fudan University

Objective: Hypoglossal nucleus (HN) controls the movement of genioglossus (GG) muscle via hypoglossal motoneurons (HMNs). Dysfunction of GG muscle leads to airway occlusion and occurrence of obstructive sleep apnea (OSA). Histamine produced by tuberomammillary nucleus (TMN) has a potent excitatory action on GG muscle activity. The aim of the study was to investigate the role histaminergic neurons plays in the regulation of HMNs. Methods: C57BL/6 mice were exposed to chronic intermittent hypoxia (CIH) for 3 weeks to resemble OSA. The histamine H3 receptor (H3R) antagonist ciproxifan was applied to increase histamine concentration in the brain. Histamine levels and GG activity were measured by liquid chromatography–tandem mass spectrometry (LC-MS/MS) and electromyogram (EMG) separately. We separated HN and TMN and applied RNA-Sequencing to analyze them at transcriptome levels. The pathways of the differential genes were analyzed by the Kyoto Encyclopedia of Genes and Genomes. Results: Significant decline of histamine and GG activity induced by CIH exposure could be ameliorated by ciproxifan. In HN, the pathway of histamine metabolism was down-regulated, and the cholinergic, serotoninergic, dopaminergic, glutamatergic pathways were up-regulated. In the group of normoxia+ciproxifan, the cholinergic, glutamatergic, dopaminergic, and serotoninergic pathways were up-regulated. In the group of CIH+ciproxifan, the cholinergic, glutamatergic, serotoninergic, dopaminergic and GABAergic pathways were up-regulated. While, in the TMN of the CIH group, the cholinergic, GABAergic, serotoninergic and glutamatergic pathways were up-regulated. In the normoxia+ciproxifan group, the serotoninergic and cholinergic pathways were up-regulated. In the CIH+ciproxifan group, the glutamatergic pathway was down-regulated. Conclusions: This investigation revealed that negative effects on the HN and TMN caused by CIH could be partly ameliorated by ciproxifan. Histaminergic nervous system could regulate the HMNs via the cooperation with the glutamatergic, serotoninergic, cholinergic, dopaminergic and GABAergic pathways. This study might open new perspectives for the development of the pharmacological treatment for OSA.

Keywords

Ten years follow–up：the correlation between obstructive sleep apnea syndrome and hypertension, diabetes disease in Han and Uygur nationality

Qinglong Zhang1,Xuelong Jiang1,Dongmei Chen1,Shilin Ma1,Jianping Li1,Meirong Han1,Juan Shi1,Min Li1,Zhongming He1,Fang Han2

1.Karamay Central Hospital of Xinjiang

2.Peking University People's Hospital

Objective: To explore the association of obstructive sleep apnea syndrome (OSAS) with hypertension and diabetes mellitus (DM). Methods: A total of 1,331 subjects was screened for OSAS from October 2008 to October 2018. All the subjects underwent the portable sleep monitoring at home. Seventy-five subjects were lost of follow-up. Among the 1,256 elderly subjects,820 (55.2%) were confirmed to have OSAS, including 532(54.0%) males and 724(46.0%) females. A total of 470 Han patients with OSA and 350 Uygur patients with OSA were included into case group. The other 436 heathy subjects were categorized as control group, including164 Han patients with OSA and273 Uygur patients with OSA. Annual medical examinations including blood pressure, blood sugar. The end point of the study was incident hypertension or DM. Results: During the 10-year follow-up, compared with the control group, patients with OSAS had higher prevalence of hypertension (12.7% vs 8.0%) (P<0.05) and higher prevalence of diabetes than the non-OSAS group (5.6% vs 3.2%) (P<0.05) respectively. Conclusions: Patients with OSAS were more likely to develop hypertension and diabetes. OSAS may be an independent risk factor for hypertension, diabetes.
Keywords Sleep apnea-hypopnea syndromes；Hypertension；Diabetes mellitus; Follow up

Psychological reactions and insomnia in adults with mental health disorders during the COVID–19 outbreak

Qimeng Sun1,Qingsong Qin2,Maria Basta3,Baixin Chen1,Yun Li1

1.Shantou University Mental Health Center

2.Shantou University Medical College

3.Heraklion University Hospital

Objective: The 2019 coronavirus disease (COVID-19) has disrupted millions of lives and commerce. We aimed to investigate psychological reactions and insomnia during the COVID-19 outbreak in adults with mental health disorders (MDs). Methods: A self-reported psychological and sleep online survey was conducted in China between February 5th to 19th, 2020. A total of 244 adults with MDs and 1116 controls matched for age, gender and sites were included. Worsened symptoms of anxiety, depressive and insomnia

were defined when severity levels shifted to a more severe category from pre-COVID-19. Results: During the COVID-19 outbreak, we found significantly increased prevalence of anxiety (MDs: 54.9% vs. 49.6%, controls: 25.5% vs. 14.3%), depression (MDs: 63.9% vs. 61.5%, controls: 29.9% vs. 21.2%) and insomnia (MDs: 66.0% vs. 57.8%, controls: 31.5% vs. 24.8%) compared to pre-COVID-19 period (all P-value < 0.001). Furthermore, adults with MDs had higher odds for developing COVID-19-related stress (OR = 3.41, 95% CI 2.49 ~ 4.67), worsened anxiety (OR = 1.95, 95% CI 1.38 ~ 2.76), depression (OR = 2.04, 95% CI 1.43 ~ 2.93) and insomnia (OR = 2.22, 95% CI 1.53 ~ 3.21) during the COVID-19 outbreak compared to the controls. Moreover, higher COVID-19-related stress and lower levels of pre-COVID-19 anxiety, depressive and insomnia symptoms were predictors for worsened anxiety, depression and insomnia in adults with MDs, respectively. Conclusions: Our findings suggest that adverse psychological reactions and insomnia are more pronounced in adults with mental health disorders during the COVID-19 outbreak, thus more attention need to be paid to this issue.

Keywords

Prevalence and prediction of metabolic syndrome in patients who consult otolaryngologists for symptoms of obstructive sleep apnea

Wenbin Guo1,2,3,Yupu Liu1,2,3,Jian Guan1,2,3,Hongliang Yi1,2,3,Hongmin Wu1,2,3,Shankai Yin1,2,3

1. Department of Otorhinolaryngology Head and Neck Surgery，the Sixth People's Hospital Affiliated to Shanghai Jiaotong University
2. Shanghai Key Laboratory of Sleep Respiratory Disorders
3. Institute of Otorhinolaryngology，Shanghai Jiaotong University

Objective: To Explore the prevalence of metabolic syndrome in patients who consult otolaryngologists for symptoms of obstructive sleep apnea (OSA); and to develop a model to predict metabolic syndrome with easily accessible questionnaire and anthropometry indices. Methods: Participants were enrolled from 7,834 unrelated consecutive individuals with suspected OSA assessed with polysomnography (PSG) tests by otolaryngologists in Shanghai Jiao Tong University Affiliated Sixth People's hospital, from January 2007 to December 2018. Questionnaire information, anthropometric measurements, polysomnographic variables, and biochemical indicators were collected for each participants. Metabolic syndrome was defined according to the Chinese guideline for the management of dyslipidemia. Its overall prevalence, gender-specific and body mass index (BMI)-specific prevalence was explored. In addition, stratified sampling was used to divide participants' data into the training set (75%) and the validate set (25%). A prediction model for metabolic syndrome was created with questionnaire and anthropometry indices in the training set, and its performance (C statistics, sensitivity, specificity, etc.) was evaluated in the independent validate set ("hold-out" method). Gender-specific and BMI-specific model were also created and compared. Result: A total of 5,047 adults were

enrolled in this study, including 4135 males and 912 females. The overall prevalence of metabolic syndrome was 44.3%, gender-specific prevalence was 48.7% for males and 24.5% for females, and BMI-specific prevalence was 14.8% for those <24kg/m2, 45.5% for those 24-27.9kg/m2, and 65.5% for those ≥28kg/m2. Gender-specific and BMI-specific prediction models for metabolic syndrome failed to outperform the non-gender-specific model, which yield a C statistics of 0.82 (0.793-0.840), a sensitivity of 0.87, a specificity 0.60, a positive predictive value of 0.63, and a negative predictive value of 0.86, and an overall accuracy of 0.72. The indices included in the predicting model were age, Epworth Sleepiness Scale score, smoking status, drinking status, history of diabetes, history of hypertension medication, body mass index, neck circum ference, waist to hip ratio, and mean arterial pressure. Conclusion: Metabolic syndrome was highly prevalent in patients with OSA symptoms. A predicting model including several easily accessible indices could help detect the presence of metabolic syndrome, which might be beneficial to the comprehensive treatment for patients with OSA.

Keywords: Obstructive sleep apnea; metabolic syndrome; prediction model; subgroup analysis

Diurnal Autonomic Cardiovascular Regulation in Pediatric Narcolepsy with Cataplexy

Jingyu WANG, Fang HAN

Peking university people's hospital

Primary narcolepsy with cataplexy (NC) is caused by a peptide deficiency in the lateral hypothalamus, which connects to autonomic centers in the brain. We hypothesized that heart rate (HR) and blood pressure (BP) regulation are altered in pediatric Narcolepsy with cataplexy. Values and circadian rhythmicity of 24-hour ambulatory systolic (SBP) and diastolic (DBP) blood pressure and HR were compared between 50 NC patients (40 males, 10 females; mean age 10.4 ± 3.5 years (M+/-SD, range 5-17years) and 100 age-sex-BMI matched controls, and between before and after stimulant medication. Compared to controls, patients with NC had a lower diurnal SBP (-6.5mmHg; p=0.000) and higher HR (+11.0bpm; p=0.000), particularly evident in the daytime, but comparable DBP. With methylphenidate (18mg sustained release at 8 AM) patients with NC had an even higher SBP (+4.6mmHg, p=0.015), DBP (+3.3 mmHg, p=0.005), and HR (+7.1 bpm, p=0.028), but with comparable nighttime values to untreated patients. Methylphenidate did not change the amplitude of variation in cardiovascular values across 24-hours. In conclusion, pediatric patients with NC have a downregulated BP profile, and overnight non-dipping, cardiovascular profile, but higher in HR. Methylphenidate in NC patients increased waketime BP towards control values but further elevated HR values.

Keywords Blood pressure, Circadian rhythmicity, Hypocretin, Narcolepsy.

The association between corporal punishment and sleep disturbances in preschooler: a 3–year prospective cohort study

Zijing Wang,Tingyu Rong,Wen Li,Min Meng,Fan Jiang,Guanghai Wang

Shanghai Children's Medical Center affiliated with Shanghai Jiao Tong University School of Medicine

Background: Previous studies have consistently concluded that corporal punishment (CP) has both short-term and long-term effects on negative outcomes in childhood. However, few studies have examined whether CP is associated with the risk of developing sleep disturbances among preschoolers. Methods: This 3-year prospective cohort study obtained data from the Shanghai Children's Health, Education and Lifestyle Evaluation, Preschool (SCHEDULE-P), a cohort study of newly enrolled in kindergartens. Data on CP experiences were included in the study, along with sleep variables derived from the Children's Sleep Habits Questionnaire (CSHQ) completed by the parents. Logistic regression was used to calculate the risk of sleep disturbances in relation to exposure to corporal punishments both before, and after, adjusting for confounders. Results: The sample of 15687 participants included 5675 (48.70%) females, with a mean (SD) age of 3.73 (0.29) years. In those with sleep disturbances at wave 3, 35.38% experienced corporal punishment, while in those without sleep disturbances, the incidence was 26.99%. Exposure to CP during any of the waves of preschool was associated with increased odds of sleep disturbances at wave 3, and effect sizes were greater for exposure to CP exposure at wave 3 (OR,1.76;95%CI, 1.56-1.99; p< .001). We observed an increasing effect size with exposure to a greater number of time-points of CP exposure. Conclusion: These findings suggest that CP is associated with an increased risk of sleep disturbances in preschoolers. This study provides pediatricians and families a new picture of the outcomes associated with CP so that they can move beyond CP to the incorporation of positive parenting behaviors with the potential to encourage healthy child trajectories.

Keywords

Oxygen Desaturation Rate as a Novel Intermittent Hypoxemia Parameter in Severe Obstructive Sleep Apnea is Strongly Associated With Hypertension

Jing Xu1,Zili Meng1,Xilong Zhang2

1.Huai'an First People's Hospital

2.The First Affiliated Hospital of Nanjing Medical University

Objectives: To investigate the effects of different intermittent hypoxemia (IH) properties on blood pressure (BP) and short-term blood pressure variability (BPV) in patients with severe obstructive sleep apnea (OSA). Methods: Nocturnal BP was continuously monitored by measuring pulse transmit time. Apnea-related systolic BP elevation values were used to reflect BPV. Beat-to-beat RR interval data were incorporated in

polysomnography for heart rate variability analysis. The LF/HF band ratio was used to reflect sympatho-vagal balance. The rate of SpO2 decrease was counted as the change in the percentage of SpO2 per second after obstructive apnea and expressed as the oxygen desaturation rate (ODR). Severe OSA subjects (n=102) were divided into two groups according to the median ODR: faster ODR (FODR group: ODR>0.37, n=50) and slower ODR (SODR group: ODR≤0.37, n=52). Results: A significantly higher level of systolic BP (SBP) was observed in the FODR group compared with SODR group (awake SBP 149.9±18.3 vs.131.8±15.6 mm Hg; asleep SBP: 149.6±19.9vs.128.7±15.6 mm Hg; both p < 0.001). Compared with SODR group, the FODR group showed higher level of short-term BPV (15.0±4.8 vs. 11.6±3.6 mm Hg; p<0.001), and a higher prevalence of hypertension (74.0% vs. 26.9%; p<0.001). Multiple linear regression analyses revealed that ODR, assessed by △ SpO2/△ t, demonstrated the strongest association with both BP and short-term BPV after adjusting for BMI, FRC, ERV and baseline SpO2. Correlation analysis showed that ODR was positively correlated with the LF/HF band ratio (r=0.288, p=0.003). Conclusions: ODR, a novel hypoxemia profile, was closely associated with the elevation of BP and BPV in patients with severe OSA. FODR might be associated with enhanced sympathetic activity.

Keywords Oxygen desaturation rate; blood pressure variability; intermittent hypoxemia; obstructive sleep apnea; hypertension

Characteristics of objective sleep and its related risk factors among Parkinson's disease patients with and without restless legs syndrome

Sun,Shuyu1、 Ren, Jiafeng 1、 Zhao,Xianchao 1、 Cheng,Jinxiang 1、 Wu,Chengji 2、 Zhou,Junying 1,3,4、Su,Changjun1、 Shuyu Sun

1. The second affiliated hospital of Fourth Military Medical University

2. Basic Medical School of Fourth Military Medical University，

3. Sleep Medicine Center，West China Hospital，Sichuan University

4. Department of Neurology，West China Hospital，Sichuan University

Objectives: This study aimed to investigate the objective sleep characteristics and its related risk factors among Parkinson's disease (PD) patients with and without restless legs syndrome (RLS). Methods: A total of 125 patients with PD who underwent overnight polysomnography (PSG) were consecutively recruited. Eighty-one patients including 27 PD with RLS (PD-RLS) and 54 PD without RLS (PD-NRLS) were included in the final analysis after 1:2 propensity score matching. Demographic, clinical, and polysomnographic data were compared between PD patients with and without RLS. The risk factors of sleep quality were examined using the multiple linear regression model. Results: The prevalence of RLS among PD patients was 28.0% (35/125). PD-RLS group had a higher score of the Unified Parkinson Disease Rating Scale (UPDRS) III than the PD-NRLS group. In addition, PD-RLS patients had significantly shorter total sleep time, poorer

sleep quality, decreased stage 3 duration, longer wake after sleep onset, and higher arousal index than those without RLS (all p < 0.05). In the multiple linear regressions models, PD duration (β = -0.363, 95% CI: -0.652 to -0.074; p = 0.016), UPDRS-III (β = -0.356, 95% CI: -0.641 to -0.071; p = 0.016) and periodic limb movement index (PLMI) (β = -0.472, 95% CI: -0.757 to -0.187; p = 0.002) were specifically found to be the risk factors influencing sleep quality in PD-RLS patients, and the UPDRS-III (β = -0.347, 95% CI: -0.590 to -0.104; p = 0.006) and HAMD scores (β = -0.343, 95% CI: -0.586 to -0.100; p = 0.007) were significantly associated with sleep quality after adjustment of confounding factors in PD-NRLS patients, respectively. Conclusions: PD-RLS patients have more disturbed and fragmented sleep in objective sleep architecture than PD-NRLS patients. Notably, our findings indicate that PLMI is the risk factor influencing the objective sleep quality in PD patients with RLS.

Gut microbiota modulates the inflammatory response and cognitive impairment induced by sleep deprivation

Wenhao Chen1、Zhong Wang1、Suxia Li2、Yanbin Ji3、Zhe Wang1、Ximei Zhu1、Jie Shi2、Lin Lu1,2,4

1. Peking University Sixth Hospital
2. National Institute on Drug Dependence and Beijing Key Laboratory of Drug Dependence，Peking University
3. Qilu Hospital of Shandong University
4. Peking-Tsinghua Center for Life Sciences and PKU-IDG/McGovern Institute for Brain Research，Peking University

Objective: Sleep deprivation (SD) is increasingly common in modern society, which can lead to the dysregulation of inflammatory responses and cognitive impairment, but the mechanisms remain unclear. Emerging evidence suggests that gut microbiota plays a critical role in the pathogenesis and development of inflammatory and psychiatric diseases, possibly via gut microbiota-brain interactions and neuroinflammation. Methods: The present study investigated the impact of SD on gut microbiota composition and explored whether alterations of the gut microbiota play a causal role in chronic inflammatory states and cognitive impairment that are induced by SD. Results: We found that SD induced gut dysbiosis, inflammatory responses, and cognitive impairment in humans. Moreover, the absence of the gut microbiota suppressed inflammatory response and cognitive impairment induced by SD in germ-free (GF) mice. Transplantation of the "SD microbiota" into GF mice activated the Toll-like receptor 4/nuclear factor-κB signaling pathway and impaired cognitive function in the recipient mice. Mice that harbored "SD microbiota" also exhibited increases in neuroinflammation and microglial activity in the hippocampus and medial prefrontal cortex. Conclusions: These findings indicate that gut dysbiosis contributes to both peripheral and central inflammatory processes and cognitive deficits that are induced by SD, which may open avenues for potential interventions that can relieve the detrimental consequences of sleep loss.

Relationships between a range of inflammatory biomarkers and subjective sleep quality in chronic insomnia patients: A clinical study

Ping Zhang、*Guihai Chen*

Chaohu Hospital of Anhui Medical University

Objective: Insomnia is associated with inflammation. However, previous studies have only explored a few inflammatory factors in insomnia patients, while the associations with other kinds of inflammatory factors remain unclear. The aim of this study was to examine whether associations exist between chronic insomnia disorder (CID) and overlooked inflammatory factors (serum amyloid-A [SAA], tumor necrosis factor [TNF]-α, granulocyte-macrophage colony-stimulating factor [GM-CSF], and regulated on activation and normal T cell expressed and presumably secreted [RANTES]). Methods: A total of 65 CID patients (mean age, 41.37 ± 12.12 years, 58.5% female) and 39 sex- and age-matched good sleeper (GS) controls (mean age, 42.15 ± 14.28 years, 51.3% female) participated in this study. They completed a baseline survey to collect data on demographics, depression, anxiety, and sleep, followed by blood sample. Results: The CID group had higher serum levels of SAA, TNF-α, and GM-CSF and a lower level of RANTES than GS group. In the Spearman's correlation analysis, SAA and GM-CSF positively correlated with the PSQI and AIS scores. After controlling for sex, HAMD-17 score, and HAMA-14 score, the partial correlation analysis showed that GM-CSF was positively correlated with PSQI score ($P < 0.05$). Further stepwise linear regression analyses showed that GM-CSF was positively associated with the PSQI and AIS scores, while RANTES was negatively associated with them ($P < 0.05$), and SAA was positively associated with just the AIS score. Conclusions: The serum levels of inflammatory mediators (SAA, TNF-α, and GM-CSF) were significantly elevated and the level of RANTES was significantly decreased in CID patients and, to some extent, the changes are related to the severity of insomnia. These findings may help us to improve interventions to prevent the biological consequences of CID by inhibiting inflammation, thereby promoting health.

Self–reported Sleep Characteristics Associated with Dementia Among Rural–dwelling Chinese Older Adults

Rui Liu1、Shi Tang1,2、Chengxuan Qiu1,2,3、Yifeng Du1,2

1. Shandong Provincial Hospital，Cheeloo College of Medicine，Shandong University

2. Shandong Provincial Hospital Affiliated to Shandong First Medical University

3. Karolinska Institutet-Stockholm University

Background: Sleep characteristics associated with dementia are poorly defined and their associations stratified by demographic factors and APOE genotype among older adults in rural China are unclear. Objective: To examine the associations of self-reported sleep characteristics with dementia and global cognitive function among rural-dwelling Chinese older adults, and to explore whether the associations were different when being stratified by demographic factors and APOE genotype. Methods: This population-based cross-sectional study included 4641 participants (age ≥65 years, female 57.0%) living in rural China. Sleep parameters were measured using the Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale. Dementia and Alzheimer's disease (AD) were diagnosed based on international criteria. Data were analyzed using multiple logistic and general linear regression models. Results: A total of 172 participants were diagnosed with dementia (115 with AD). The multivariable-adjusted odds ratios (OR) of dementia were 1.85 (95% CI, 1.20-2.85) for sleep duration ≤4 hours/night and 1.71 (95% CI, 1.12-2.62) for sleep duration >8 hours/night, compared with sleep duration of 4-8 hours/night. The multivariable-adjusted odds ratios (OR) of dementia were 1.60 (95% CI, 1.14-2.26) for low sleep efficiency and 1.64 (95% CI, 1.04-2.59) for excessive daytime sleepiness (EDS). Short sleep duration, low sleep efficiency, and EDS were significantly associated with AD (multi-adjusted OR range: 1.70-1.99; p<0.05). The associations of sleep duration with dementia and AD were evident mainly among young-old adults (65-74 years) and APOE e4 allele carriers. Among dementia-free participants, these sleep characteristics were significantly associated with a lower MMSE score (p<0.05). Conclusion: Self-reported sleep disturbances in dementia are characterized by short or long sleep duration, low sleep efficiency, and EDS, especially among young-old people and APOE e4 carriers.

The association between BTBD9 polymorphism and sleep parameters within OSA patients

Gao,Zhenfei1,2,3、Liu,Feng1,2,3、Wang,Fan1,2,3、Li,Niannian1,2,3、Guan,Jian1,2,3、Yi,Hongliang1,2,3、Yin,Shankai1,2,3

1. Department of Otolaryngology-Head and Neck Surgery，Shanghai JiaoTong University Affiliated Sixth People's Hospital
2. Otolaryngology Institute of Shanghai JiaoTong University
3. Shanghai Key Laboratory of Sleep Disordered Breathing

Objective: sleep fragmentation is a main pathophysiology feature of obstructive sleep apnea (OSA), but the underlying mechanism is poorly understood. BTBD9 is a risk factor of Restless leg syndrome and plays an important role in sleep-wake regulating. The aim of our work was to investigate the association between a variant in BTBD9(rs117733138) from our GWAS and sleep-related parameters. Methods: We performed GWAS on SSHS (n=20590) consisting of all suspected cases admitted to Shanghai Sixth People's Hospital from January 2011 to June 2019. Both the cases and controls underwent whole night polysomnography and anthropometry profiles. Affymetrix human genome-wide SNP array 6.0 (SNP6.0) and Affymetrix AxiomTM genome-wide CHB array plate were used for genotyping. Results: We found the distribution of rs117733138(G>A) had no significant difference between patients with OSA and the controls, however, several wake-related sleep parameters were significantly associated the genotype of BTBD9 in patients with OSA. Patients with this variant had lower sleep efficiency and decreased duration of sleep (β =-0.032, 95%CI -2.276--0.147; β =-0.029, 95%CI -3.683--0.022, P=0.047), and more frequent awakening time (β =0.052, 95%CI 0.017-2.258) during sleep period despite this variant had little effect on structure of sleep (P>0.05). Conclusions: Our study results showed that BTBD9 (rs117733138) polymorphisms was associated with the awakening in patients with OSA. It is urgent to explore the mechanism underlying that how this variant contributed to sleep regulation.

oral presentation

Clinical characteristics of sleep disorders in patients with vestibular migraine

Jun Wu1,Chunling Liu1,Haitao Yu1,Hui Li1,Yanlu Jia1,Defu Zhang2
1.The Second Affiliated Hospital of Zhengzhou University，Zhengzhou，China
2.The Affiliated Hospital of Binzhou Medical University，Yantai，China

Objective: To study and analyze the sleep quality and sleep structure of patients with vestibular migraine (VM). Methods: In this cross-sectional case-control study, the Pittsburgh Sleep Quality Index (PSQI) questionnaire and polysomnography (PSG) were used to compare the clinical characteristics of sleep disorders in 49 patients with VM, 52 patients with migraine, and 54 controls. Results: The VM, migraine, and control groups did not significantly differ in terms of age or sex (all P > 0.05). Compared with the migraine and control groups, the VM group had a higher incidence of poor sleep quality (x^2 = 36.618, p < 0.01) and greater severity of poor sleep quality (p < 0.01). Furthermore, the VM group showed reduced sleep efficiency (p < 0.01) and reduced proportions of REM and slow wave (N3) sleep (p ≤ 0.01). Conversely, sleep latency (p = 0.01) and REM latency (p = 0.04) were prolonged, and proportions of light sleep phases (N1, p < 0.05 and N2, p < 0.01) and the micro-arousal index (p = 0.03) were increased. The migraine group had significantly higher apnea hypopnea index (AHI) and periodic leg movement (PLMI) indices than the VM group. Conclusions: Our findings suggest an effect of VM on sleep structure and an association with migraine. Similar to migraine, VM affects the sleep regulation centers and causes structural sleep disorders. Keywords

Association among serum leptin, orexin, and ghrelin levels and indices related to sleep monitoring in patients with obstructive sleep apnea–hypopnea syndrome

Huiwen Tan1,Li Xiao2,Yue Yu3,Yin Zeng1,Yishu Liu1

1.Sheng Jing Hospital，China Medical University

2.Sleep Medical Center，Sheng Jing Hospital，China Medical University

3.Emergency Department，Sheng Jing Hospital，China Medical University

Objective: To improve the clinical assessment of obstructive sleep apnea-hypopnea syndrome (OSAHS) by observing changes in the serum concentrations of leptin, orexin, and ghrelin in affected patients and their correlations with metabolic and sleep-monitoring indicators. Methods: We enrolled 58 patients with obstructive sleep apnea-hypopnea syndrome at our hospital in 2018. Polysomnography and fasting arteriovenous blood tests were performed. The blood oxygen saturation, partial pressures of oxygen and carbon dioxide, and the levels of blood glucose, lipids, leptin, orexin, and ghrelin were measured in each patient. We used Spearman's correlation to analyze the correlations between the indicators and the severity of the disease; significant factors were further analyzed with orderly logistic regression. Results: The Apnea-Hypopnea Index negatively correlated with the minimum oxygen saturation, and positively correlated with body mass index; neck, waist, and hip circumferences; total arousals, arousals longer than 15 seconds, arousal index, and total recorded time when the oxygen saturation below 90% (T90%). Leptin concentration negatively correlated with the partial pressure of oxygen and positively correlated with body mass index, waist circumference, hip circumference, and bedtime systolic blood pressure. Ghrelin concentration negatively correlated with bedtime systolic and diastolic blood pressure. Orexin negatively correlated with bedtime. Only T90% was found to be a significant independent influence factor of OSAHS severity. Conclusions: Factors such as hypoxia and obesity interact to promote the increase of leptin concentrations in patients with obstructive sleep apnea-hypopnea syndrome, inducing leptin resistance and the onset of metabolic disorders. T90% features promise as a simple, effective indicator of the condition's severity and high-risk groups.

Keywords Obstructive Sleep Apnea Hypopnea Syndrome, leptin, orexin, ghrelin, PSG.

Sleep–related painful erection: A case report and review of literature

Jiangtao Xu

Sleep Medical Center，Affiliated Xiamen Humanity Hospital of Fujian Medical University

A case of sleep related painful erection treated with lorazepam was reported. The literature was reviewed from the aspects of epidemiology, pathogenesis, clinical manifestation, auxiliary examination, diagnosis, and treatment. Case report: a 45 years old male patient was hospitalized because of recurrent penile distention and pain during night sleep for 10 years. The patient wakes up 3-5 times every night due to penile erectile distention pain, accompanied by head pain. After waking up each time, he must get out of bed to walk in the living room, watch TV, or pee, and the symptoms will last for 15-30 minutes. Sexual desire and sexual function are normal, and erection during the day is not uncomfortable. PSG showed that the sleep latency was 24 min, REM latency was 230 min, sleep efficiency was 67%, wake up three times due to erectile pain. Lorazepam was taken orally (0.5 mg once a night) and given psychological guidance. After 3 months, the symptoms disappeared and the treatment was stopped. 3 years later, the patient was followed up by telephone. The patient woke up once every 2-3 weeks because of erectile swelling and discomfort, without penile pain, without getting out of bed to move, and could go to sleep, so no further treatment or taking any medicine.

Keywords sleep related painful erection; case report; review

Chronic sleep deprivation promotes appetite via attenuation of LepRb–mediated signal pathways and disruption of circadian clock regulation in hypothalamus of adolescent rats

Qi Sun1,Yang Liu1,2,Wei Wei1,Dan Wu1,Ren Lin1,Deliang Wen1,2,Lihong Jia1
1.School of Public Health，China Medical University
2.Institute of Health Science，China Medical University

Objectives: The sleep duration of adolescents continues to decline in recent twenty years. Sleep insufficiency is one of the important risk factors for obesity, but its mechanism is not clear yet.the regulatory mechanisms involving hypothalamus of appetite and circadian clock were studied in sleep deprived rats. Methods: 14 rats at the age of 7 weeks were randomly divided into two groups (7 rats per each group):Sleep deprivation group were exposed to sleep deprivation for 4 weeks while control group had normal sleep cycles. The body weight gain, the food intake and water consumption, and serum leptin levels were generated, and the gene or protein expressions of regulating appetite and energy metabolism via leptin receptor signaling and circadian clock in hypothalamus were assessed. Results: Chronic sleep deprivation increased the food intake and induced weight gain in adolescent to young adult rats starting from week 2 . Phosphorylation of Janus kinase

2 (JAK2)/Signal transducer and activator of transcription 3 (STAT3) signal was decreased, while the serum leptin level and leptin receptor expression levels were unchanged. Besides, insulin receptor substrate (IRS)/ phosphoinositide 3-kinase (PI3K)/AKT/mTOR and forkhead box O1 (FoxO1) signal pathways were also compromised. Moreover, the reduction of expression of core clock genes in sleep deprivation groupversus control were also identified. Conclusions: Chronic sleep deprivation induced hyperphagic behaviors, attenuated leptin receptor mediated signal pathways and disturbed circadian clock regulation in hypothalamus of adolescent to young adult rats.

Keywords Sleep deprivation, Appetite, Hypothalamus, LepRb signal pathway, Circadian clock

Self–reported snoring patterns predict cardiovascular events in high–risk patients with obstructive sleep apnea: post–hoc analyses of the SAVE study

Jingwei Li,Craig Anderson

First Hospital Affiliated to the Chinese PLA General Hospital，Beijing，China.

Background: The relation of snoring to risks of stroke and other major cardiovascular (CV) events is uncertain. Objective: We aimed to determine associations of snoring patterns and major CV events in relation to obstructive sleep apnea (OSA), among participants of the international Sleep Apnea cardiovascular Endpoints (SAVE) trial. Methods: Post-hoc analyses of the SAVE trial, which involved 2, 687 patients with co-existing moderate-severe OSA and established coronary or cerebral CV disease, who were randomly allocated to continuous positive airway pressure (CPAP) treatment plus usual care or usual care alone, and followed up for a median 3.5 years. Associations of self-reported snoring patterns (frequency and loudness) and breathing pauses collected on the Berlin questionnaire at baseline and multiple times during follow-up, and adjudicated composites of CV outcomes (primary, CV death, non-fatal myocardial infarction, non-fatal stroke, and hospitalization for unstable angina, heart failure, or transient ischemic attack; and separately of cardiac and cerebral events), were evaluated in time-dependent Cox proportional hazards models adjusted for various confounders including apnea-hypopnea index. Results: Increase (per category) of snoring frequency (adjusted hazard ratio [HR] 1.10, 95% confidence interval [CI] 1.02-1.20; P = 0.015), loudness (HR 1.16, 95% CI 1.06–1.27; P = 0.001), and breathing pauses (HR 1.16, 95% CI 1.08–1.25; P < 0.001) at any timepoint during follow-up were each associated with the primary composite CV outcome. These associations were driven by significant associations for cerebral rather than cardiac events, and positive interactions between the three snoring patterns for cerebral events. There is no significant interaction between CPAP treatment and snoring variables for cerebral events. Interpretation: Snoring in OSA patients with established CV disease is associated with greater risks of cerebral but not cardiac events, independent of CPAP treatment and frequency of apnea and hypopnea events.

Keywords

A meta–analysis of the association between sleep duration and type 2 diabetes mellitus

Huapeng Lu1,Qing He 2,Xiaoting Li 1,Peipei Liu 3,Qinling Yang 1,Boyan Tian 1,Yi Lv 1,Jin Li 2,Xuemei Zheng1

1.First Affiliated Hospital of Xi'an Jiaotong University

2. Xi'an Jiaotong University

3.HanDan Central Hospital

Objective: To systematically review the cross-sectional studies on the relationship between sleep duration and type 2 diabetes mellitus (T2DM) in adults. Methods: Web of Science, PubMed, Scopus, Embase, Cochrane Library (Issue 12, 2029), CNKI, WanFang, VIP, and CBM were searched from inception to Dec. 2019. All cross-sectional studies on the relationship between sleep duration and T2DM in adults were included. According to the inclusion and exclusion criteria, two authors independently assessed the literature and extracted the data. Publication bias was evaluated. Sensitivity and meta-analyses were conducted with RevMan 5.3. Results: A total of 23 studies were collected, involving 312805 participants. The prevalence of T2DM was 9.8% in the short sleep duration group (t ≤ 6h), 6.2% in the normal sleep duration group (6h < t < 9h), and 9.8% in the long sleep duration group (t ≥ 9h). The meta-analysis showed that short sleep duration was associated with a higher risk of T2DM than that of normal sleep time [RR = 1.47, 95%CI (1.34-1.61), P ＜ 0.001]. In subgroup analysis, the risk of T2DM was increased in male with short sleep time [RR = 1.45, 95% CI (1.11-1.89), P = 0.006] and female [RR = 1.30, 95% CI (1.05-1.61), P = 0.01]. The meta-analysis showed that long sleep duration was associated with a higher risk of T2DM than that of normal sleep time [RR = 1.38, 95%CI (1.26-1.51), P ＜ 0.001]. In subgroup analysis, the risk of T2DM was increased in males with short sleep time [RR = 1.22, 95%CI (1.06-1.39), P = 0.005] and females [RR = 1.47, 95%CI (1.19-1.80), P = 0.0003]. Conclusion: The findings suggest that long sleep duration or short sleep duration can increase the risk of T2DM. Future longitudinal study is warranted to further clarify these relationships.
Keywords sleep duration; type 2 diabetes mellitus; Meta-analysis

The impact of symptom severity on health–related quality of life in patients with narcolepsy

henyang Li1,Shaomei Shang1,Fang Han2

1.Peking University School of Nursing

2.Peking University People's Hospital

Objective: To assess the symptom severity and its correlation with health-related quality of life (HRQoL) in patients with narcolepsy type 1 (NT1). Methods: In this cross-sectional study, a total of 174 patients with

NT1 were recruited. They also completed the Narcolepsy Severity Scale (NSS) and European Quality of Life-5 Dimensions Questionnaire (EQ-5D) including five dimensions (EQ-5D utility values) and a visual analog scale (EQ-5D VAS). The relation between severity of symptoms and HRQoL dimensions was assessed by Pearson correlation analyses. Logistic regression was used to identify the significant predictors of HRQoL. Nomogram was established based on results of independent predictors factors on logistic regression analyses. Results: The scores for NSS, EQ-5D utility values and EQ-5D VAS were 29.89 ± 10.08, 0.78 ± 0.09 and 64.30 ± 19.84 in patients with NT1 respectively. NSS score showed a significantly correlation with self-care ($r = 0.157$, $P < 0.05$), usual activities ($r = 0.236$, $P < 0.01$), pain/discomfort ($r = 0.174$, $P < 0.05$), anxiety/depression ($r = 0.2$, $P < 0.01$) and EQ-5D utility values ($r = -.261$, $P < 0.01$). EDS (excessive daytime sleep), cataplexy, hallucinations, paralysis and disrupted nocturnal sleep (DNS) were significant associated to EQ-5D VAS (r ranged from $-0, 154$ to -0.354, $P < 0.05$). As for the pentad symptoms, EDS (OR = -0.297, 95% CI -1.892- -0.634) and DNS (OR = -0.16, 95% CI -0.7307- -0.446) were predictors of HRQoL. Regards the NSS scores logistics regression analysis indicated NSS (OR = -0.360, 95% CI -0.979- -0.438) and treated (OR = 0.215, 95% CI 3.567-16.188) were predictors of the metrics of HRQoL. The C-indices of the nomogram was 0.726 (95% CI 0.686-0.766). Conclusions: For Chinese patients with NT1, the severity of symptoms could disrupt self-care and usual activities and increase pain/discomfort and anxiety/depression. EDS, DNS and treatment were the significant factors to predict the HRQoL. NSS score could be used for predicting HRQoL in patients with NT1, but with modest precision.

Keywords Narcolepsy, health-related quality of life, symptom assessment

Weekday and weekend sleep deprivation is associated with recurrent nightmare in adolescents: a cross–sectional study

Yiqi Lin1,2,Jinzhuang Wen1,2,Haozheng Fu2,1,Nanzeng Zhao1,2,Xiwu Yong1,2,Yingwu Si2,Chaowei Shi1,2

1.Fujian Provincial Hospital

2.Fujian Medical University

Objective: Our study aimed to investigate the association between sleep deprivation and parasomnias including nightmare and sleepwalking in Chinese adolescents. Methods: A total of 19,229 high school students aged 10-20 years in Fuzhou were invited to complete questionnaires regarding sleep duration, parasomnias including nightmare and sleepwalking, and emotional problems. Subjects with sleep deprivation (SD) defined as sleeping less than 8 hours either on weekdays or on weekends were categorized into three groups: weekday SD, weekend SD, and habitual SD. Results: The prevalence of recurrent nightmare was significantly higher for subjects with SD (SD vs non-sleep deprivation (NSD): 7.6% vs 3.7%, $P < 0.05$). In all subjects, habitual SD was associated with the highest risk of recurrent nightmare (Odds ratio (OR) = 2.19, 95% Confidential interval (95% CI) = 1.73-2.75, $P < 0.001$), followed by weekday SD (OR = 2.06, 95% CI =

1.64-2.61, P < 0.001) and weekend SD (OR = 1.45, 95% CI = 1.01-2.08, P = 0.045). However, no significant association was found between sleepwalking and sleep deprivation (P > 0.05). In further age-based (10-13/14-17 years) and sex-based subgroup analyses, the findings were consistent except that association between weekend SD and recurrent nightmare disappeared among subjects aged 14-17 or among girls. Conclusions: Our study suggests a significant association between recurrent nightmare and sleep deprivation either on weekdays or on weekends in adolescents, which was stronger with more deprivation episodes. No significant association was found between sleepwalking and sleep deprivation.

Keywords

Do psychiatric patients experience more psychiatric and sleep symptoms during the COVID–19 pandemic and lockdown? A case–control study with service and research implications for immunopsychiatry

Fengyi Hao1,Wanqiu Tan3,2, Xiaojiang Jiang13,Roger S McIntyre4,Bach Tran5,6, Jiaqian Sun7,Zhisong Zhang8,Roger Ho9,10,Cyrus Ho11,Wilson Tam12

1. The First People&'s Hospital of Chongqing Liang Jiang New Area

2. The China-Singapore (Chongqing) Demonstration Initiative on Strategic Connectivity Think Tank

3. Institute for Health Innovation and Technology (iHealthtech)，National University of Singapore

4. Mood Disorders Psychopharmacology Unit，University Health Network，University of Toronto

5. Bloomberg School of Public Health，Johns Hopkins University

6. Institute for Preventive Medicine and Public Health，Hanoi Medical University

7. Department of Psychological Medicine，Yong Loo Lin School of Medicine，National University of Singapore

8. Faculty of Education，Huaibei Normal University

9. Institute for Health Innovation and Technology (iHealthtech)，National University of Singapore

10. Department of Psychological Medicine，Yong Loo Lin School of Medicine，National University of Singapore

11. Department of Psychological Medicine，National University Health System

12. Alice Lee Centre for Nursing Studies，National University of Singapore

13. Department of Neurology，Daping Hospital，Army Medical University

Objective: This study aimed to assess and compare the immediate stress and psychological impact experienced by people with and without psychiatric illnesses during the peak of the coronavirus disease 2019 (COVID-19) epidemic with strict lockdown measures. Methods: Seventy-six psychiatric patients and 109 healthy control subjects were recruited from Chongqing, China. They completed a survey on demographic

data, physical symptoms during the past 14 days and a range of psychiatric symptoms using the Impact of Event Scale-Revised (IES-R), Depression, Anxiety and Stress Scale (DASS-21) and Insomnia Severity Index (ISI). IES-R measures PTSD symptoms in survivorship after an event. DASS-21 is based on a tripartite model of psychopathology that comprises a general distress construct with distinct characteristics. Results: The mean IES-R, DASS-21 anxiety, depression and stress subscale, and ISI scores were higher in psychiatric patients than healthy controls ($p < 0.001$). Serious worries about their physical health, anger and impulsivity, and intense suicidal ideation were significantly higher in psychiatric patients than healthy controls ($p < 0.05$). More than one-third of psychiatric patients might fulfill the diagnostic criteria for post-traumatic stress disorder (PTSD). More than one-quarter of psychiatric patients suffered from moderately severe to severe insomnia. Respondents who reported no change, poor or worse physical health status and had a psychiatric illness were significantly more likely to have higher mean IES-R, DASS depression, anxiety and stress subscale scores and ISI scores ($p < 0.05$). Conclusions: This study confirms the severity of negative psychological impact on psychiatric patients during the COVID-19 epidemic with strict lockdown measures. Understanding the psychological impact on psychiatric patients during the COVID-19 pandemic has the potential to provide insight into how to develop a new immunopsychiatry service. Further research is required to compare pro-inflammatory cytokines between psychiatric patients and healthy controls during the pandemic.

Keywords Anxiety; COVID-19; Coronavirus; Depression; Epidemic; Immunopsychiatry; Insomnia; Lockdown; PTSD

Sleep disturbance and its neurophenotypes in seniors with different cognitive status

Hanna LU1,Vincent C. T. MOK2,Timothy C. Y. KWOK3,Winnie Chu Chiu WING4,Linda Chiu Wa LAM1

1. The Chinese University of Hong Kong
2. Department of Neurology，The Chinese University of Hong Kong
3. Department of Medicine & Therapeutics and School of Public Health，The Chinese University of Hong Kong
4. Department of Imaging and Interventional Radiology，The Chinese University of Hong Kong

Background: Sleep disturbances and cognitive changes co-occur in late adulthood. We aimed to investigate the sleep quality and its associations with neurophenotypes in elderly with different cognitive statuses in Hong Kong. Methods: A community-based survey was conducted in 269 cognitively normal (CN) adults and 227 neurocognitive disorders (NCD) patients. Sleep disturbance was assessed with the Pittsburgh Sleep Quality Index (PSQI). A neuropsychological battery was used to assess the main domains of cognitive function, including attention, memory, executive function. Structural magnetic resonance imaging was used to measure the cortical thickness with surface-based morphometry analysis in a subsample (n = 52). Results:

NCD patients showed worse sleep quality (6.31 vs. 5.65) and a higher prevalence of sleep disturbance (51.5% vs. 42.7%) than CN adults. Within CN adults, worse sleep quality was correlated with decreased quality of life (r = -0.202, p = 0.001). Meanwhile, except for the quality of life, worse sleep quality was related to poorer cognitive function, processing speed (measured by trail making test, r = 0.144, p = 0.041) in particular, in NCD patients. Using age, sex, and years of education as covariates, PSQI total score was decreased cortical thickness of left transverse temporal gyrus (TTG) (r = -0.366, p = 0.009). Conclusions: The prevalence of sleep disturbance is varied in seniors with different cognitive statuses. Specific cognitive profiles, encompassing processing speed, are related to sleep quality in individuals with an early-stage neurodegenerative disorder. The morphometric underpinning of sleep quality may be used to guide non-invasive neuromodulation targets for sleep management.

Keywords Sleep disturbance; normal ageing; neurocognitive disorder; cognition; cortical thickness

A quantitative and qualitative study on the neuropsychiatric sequelae of acutely ill COVID–19 inpatients in isolation facilities

Fengyi Hao1, Wilson Tam2,Xiaoyu Hu3,Wanqiu Tan4,Xiaojiang Jiang5,Roger S McIntyre6,Travis Quek7,Bach Xuan Tran8,9, Zhisong Zhang10, Hai Quang Pham11,12,Cyrus S H Ho13,14,Roger C M Ho7,15

1. The First People's Hospital of Chongqing Liang Jiang New Area
2. Alice Lee Centre for Nursing Studies，National University of Singapore
3. First Affiliated Hospital of Chongqing Medical University
4. National University of Singapore (Chongqing) Research Institute
5. Department of Neurology，Daping Hospital，Army Medical University
6. Mood Disorders Psychopharmacology Unit，University Health Network，University of Toronto
7. Department of Psychological Medicine，Yong Loo Lin School of Medicine，National University of Singapore
8. Institute for Preventive Medicine and Public Health，Hanoi Medical University
9. Bloomberg School of Public Health，Johns Hopkins University
10.Faculty of Education，Huaibei Normal University
11.Institute for Global Health Innovations，Duy Tan University
12.Faculty of Medicine，Duy Tan University
13.Department of Psychological Medicine，Yong Loo Lin School of Medicine，National University of Singapore
14.Department of Psychological Medicine，National University Health System
15.Institute for Health Innovation and Technology (iHealthtech)，National University of Singapore

Objective: This study examined the neuropsychiatric sequelae of acutely ill patients with coronavirus disease

2019 (COVID-19) infection who received treatment in hospital isolation wards during the COVID-19 pandemic. Methods: Ten COVID-19 patients who received treatment in various hospitals in Chongqing, China, ten age- and gender-matched psychiatric patients, and 10 healthy control participants residing in the same city were recruited. All participants completed a survey that collected information on demographic data, physical symptoms in the past 14 days and psychological parameters. Face-to-face interviews with COVID-19 patients were also performed using semi-structured questions. Results: Among the COVID-19 patients, 40% had abnormal findings on the chest computed topography scan, 20% had dysosmia, 10% had dysgeusia, and 80% had repeated positivity on COVID-19 reverse-transcription polymerase chain reaction testing. The COVID-19 and psychiatric patient groups were significantly more worried about their health than healthy controls (p = 0.019). A greater proportion of COVID-19 patients experienced impulsivity (p = 0.016) and insomnia (p = 0.039) than psychiatric patients and healthy controls. COVID-19 patients reported a higher psychological impact of the outbreak than psychiatric patients and healthy controls, with half of them having clinically significant symptoms of posttraumatic stress disorder. Conclusions: The findings suggest that both COVID-19 patients and psychiatric patients had higher levels of depression, anxiety and stress than healthy controls. Three themes emerged from the interviews with COVID-19 patients: (i) The emotions experienced by patients after COVID-19 infection (i.e., shock, fear, despair, hope, and boredom); (ii) the external factors that affected patients' mood (i.e., discrimination, medical expenses, care by healthcare workers); and (iii) coping and self-help behavior (i.e., distraction, problem-solving and online support). The future direction in COVID-19 management involves the development of a holistic inpatient service to promote immune and psychological resilience.

Keywords COVID-19 patients; isolation wards; neuropsychiatric sequelae

Impaired sleep quality and its relative factors of health care workers at the beginning of the COVID–19 epidemic: a longitudinal follow–up study

Xiaolong Zhao1,2,Jiangang Fan1,2,Bin Li1,2,Ning13, Xiao1,2,Chuan1,2, Dong,Gang He1

1.Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital

2.Otolaryngology Head and Neck Surgery

3.Health Management Center

Background: Health care workers for the 2019 coronavirus disease (COVID-19) screening are at risk of occupational exposure to the virus, which may have an impact on their sleep quality. But the working factors associated with the change in sleep quality remain unclear. Methods: In February 2020, health care workers participating in the screening of fever patients in Sichuan Provincial People's Hospital were asked to fill in a set of questionnaires, including demographic information, work-related factors. The Pittsburgh Sleep

Quality Index (PSQI) was used to assess the sleep quality before and one month after participating in the fever clinic work. Linear regression was used to analyze the risk factors of sleep quality changes before and after the fever clinic work. Results: A total of 116 doctors and 99 nurses participated in this study. Before the fever clinic work, the frequency of night shifts is 4.99 per month. The number increased to 14.78 ± 6.69 days per month during the one-month work in fever clinic. There was significant increase in the total score and multiple components of PSQI during the one-month work in fever clinic (all $P < 0.05$). Linear regression showed that the changes of PSQI and multiple components were significantly related with the number of working days, working years, and the psychological pressure of fear of COVID-19 (all $P < 0.05$). Conclusions: The sleep quality of medical staff participating in COVID-19 screening was decreased in a short period of time. Reasonable work arrangement is helpful to ensure a certain sleep quality.

Keywords Coronavirus disease 2019 (COVID-19), Sleep disorders, Relative factors, Health care workers.

Identification of Potential Risk Genes and the Immune Landscape in Lacrimal Gland Using Sleep Deprivation–Induced Dry Eye Model

Xi Chen,Jing Zhuang

Zhongshan Ophthalmic Center，Sun Yat-Sen University

Sleep deprivation (SD) is a common public health problem associated with many diseases, and it＇s a key factor associated with dry eye syndrome. Accumulating evidence indicates that the pathogenesis of this specific type of dry eye involves immune-related and inflammatory phenomena of lacrimal glands. An understanding of SD-related lacrimal immune regulatory mechanisms would help develop new immunotherapeutic targets of dry eye syndrome. Based on high-throughput transcriptome sequencing data from SD mouse model using a＇stick over water＇method and untreated mice, 242 common differentially expressed immune-related genes (IRGs, containing 185 upregulated and 57 downregulated) were obtained, which were associated with＂cell chemotaxis＂,＂regulation of mononuclear cell proliferation＂etc. Four hub genes, including CD28, SEMA4A, BMP10 and KLRK1 were identified on protein-protein interaction network analysis. Lasso regression analysis showed that the area under the curve values of four hub IRGs were all above 0.95 for distinguishing SD-induced dry eye mouse model. In addition, the relative proportions of 2 subtypes of immune cells, namely, γ delta T cells and M1 macrophages were significantly dysregulated in the SD-related lacrimal samples. These findings may shed light on the development of novel immune biomarkers and target therapy of SD-induced dry eye syndrome.

Keywords

Analysis of the characteristics of sleep–disordered breathing in children with neuromuscular diseases

Qin Yang,Yuejie Zheng,Feiqiu Wen,Yanmin Bao

Shenzhen Children's Hospital

Objective: To analyze the characteristics of sleep-disordered breathing (SDB) in children with neuromuscular disease (NMD), and to improve the awareness of diagnosis and treatment of NMD with SDB. Methods: A retrospective analysis was performed for the 18 children with NMD who had finished polysomnography (PSG). Related data were collected for analysis, including demographic characteristics, daily and nocturnal symptoms of SDB, the incidence of OSA, pulmonary function, and End-tidal carbon dioxide partial pressure (PetCO2). Important sleep parameters and respiratory events were compared with those of the non-NMD group (control group). Results: In the NMD group, 16 cases (89%) had SDB-related daily and nocturnal clinical symptoms, and the youngest age of symptoms was one year old. The total sleep time and sleep efficiency in the NMD group were significantly lower than those in the control group ($P < 0.05$), The NMD group showed significantly lower proportion of REM sleep and more obstructive apnea-hypopnea events than their controls (all $P < 0.05$). Compared with control group, NMD group had decreased oxygen level and lower oxygen saturation in the REM stage (all $P < 0\ 05$). In our study, 17 cases (94%) of NMD with SDB were diagnosed as OSA, and the lung function and PetCO2 of all the cases were normal. Conclusions: The proportion of SDB in children with NMD is high. SDB can be found in the early stage of NMD, which results in damages of sleeping structure, declining sleep efficiency. The major respiratory events are obstructive type. Most hypoxia events occur during the REM stage.
Keywords

STAT6 deficiency ameliorates severity of intermittent hypoxia induced pulmonary hypertension by decreasing Th2–inducing cytokines

Shengyu Hao,Pan Jiang,Shanqun Li,Liu Zilong

Zhongshan Hospital，Fudan University

Obstructive sleep apnea (OSA) is commonly linked with higher prevalence and mortality of pulmonary hyperattention (PAH). Immune response is involved in pulmonary artery (PA) remodeling and the OSA-related diseases. However, the immunological factors associated with OSA-induced PAH remain unrevealed. Signal transducer and activator of transcription 6 (STAT6) belong to an important signaling pathway of modulating immune response. Nonetheless, little is known regarding the STAT6 phosphorylation

(p-STAT6) status in OSA-induced PAH mouse model. Chronic intermittent hypoxia (CIH) is the key pathological process in OSA. In this study, we employed CIH model to model OSA and investigated the role of STAT6 in CIH-induced PAH. We found obvious PA remodeling and PAH in CIH-induced mice, as measured by increased RVSP, RV/LV+S and morphological comparison at baseline and after CIH. These changes were accompanied by increasing p-STAT6 phosphorylation in lung and increased p-STAT6+ IL-4-producing T cells, in CIH treated WT mice. STAT6 deficiency (STAT6-/-) dramatically ameliorated PAH and PA remodeling in CIH-induced PAH mouse models. We also observed that STAT6 deficiency suppressed T helper 2 (Th2) related immune response, including IL-4 and IL-13 secretion. CIH-increased IL-17+CD4+T cells were also ameliorated in STAT6-/- mouse. Furthermore, STAT6 knockdown reduced proliferation and oxidative stress in IL-4 treated human PA smooth muscle cells (HPASMCs). These data demonstrate the critical role of STAT6 in the pathogenesis of CIH-induced PAH via regulating Th2-inducing cytokine production.

Keywords obstructive sleep apnea, chronic intermittent hypoxia, pulmonary hypertension, immune response

The influence of intra–family conflict on mental health problems in Chinese adolescents: the longitudinal mediating role of sleep problems

Shuo Wang,Xuliang Shi,Zihan Li,Anqi Wang,Lin Jiang

College of Education，Hebei University，Baoding，Hebei，China

Objectives: This study investigated the mediating role of poor sleep quality in the effect of intra-family conflict on mental health problems for adolescents using a three-year longitudinal study. Methods: In this study, we recruited 932 (age at baseline: 13.25 ± 0.66 years) adolescents from two junior high schools in Guangzhou city. The Family Environment Scale Chinese Version (FES-CV), the Pittsburg Sleep Quality Index (PSQI), the Depression Self-Rating Scale (DSRS), the Screen for Child Anxiety Related Emotional Disorders (SCARED), and the Strengths and Difficulties Questionnaire (SDQ) were used as assessments tools. The intervals were 12 months apart. Results: After adjusting for sleep quality, mental health problems, and family demographics at wave 1 (T1), the T1 intra-family conflict was correlated with internalizing symptoms (including anxiety symptoms and depression symptoms) at wave 3 (T3) and externalizing symptoms at wave 3 (T3). The T2 sleep quality was related to the intra-family conflict at wave 1 (T1), internalizing symptoms (including anxiety symptoms and depression symptoms) at wave 3 (T3) and externalizing symptoms at wave 3 (T3). The T1 intra-family conflict significantly positively predicted sleep quality at wave 2 (T2), and T2 sleep quality played a complete mediating role in the influence of T1 intra-family conflict and internalizing symptoms (including anxiety symptoms and depression symptoms) at wave 3 (T3). T2 sleep quality completely mediated the association between T1 intra-family conflict and

externalizing symptoms at wave 3 (T3). In addition, this mediation of sleep quality was consistent across gender. Conclusions: Sleep quality was an important mediator in explaining the relationship between intra-family conflict and mental health problems in adolescents. Prevention and intervention programs aimed at improving their sleep quality may be critical to prevent mental health problems when adolescents are involved in family conflict.

Keywords intra-family conflict, sleep quality, mental health, longitudinal study, adolescent

Nucleus accumbens neurons expressing dopamine D1 receptors modulate states of consciousness in sevoflurane anesthesia

Weiwei Bao1,2,Wei Xu1,Wenxian Li2,Zhili Huang1

1. Department of Pharmacology，School of Basic Medical Sciences，Fudan University Shanghai，China
2. Department of Anesthesiology，Eye & ENT Hospital，Fudan University，Shanghai，China

Objective: Although general anesthesia (GA) enables patients to undergo surgery without consciousness, the precise neural mechanisms underlying this phenomenon have yet to be identified. In addition to many studies over the past two decades implicating the thalamus, cortex, brainstem, and conventional sleep–wake circuits in GA-induced loss of unconsciousness (LOC), some recent studies have begun to highlight the importance of other brain areas as well.Methods: Population activities of nucleus accumbens (NAc) dopamine D1 receptor (D1R)-expressing neurons in response to sevoflurane anesthesia were determined via a combination of in vivo fiber photometry and polysomnographic recordings. The effects of specific activation or inhibition of NAcD1R neurons on sevoflurane GA were measured by using the chemogenetic" designer receptors exclusively activated by designer drugs" approach. Optogenetic methods combined with polysomnographic recordings were used to explore the effects of transient activation of NAcD1R neurons during the sevoflurane maintenance phase or deep anesthesia states with burst-suppression oscillations. Results: Population activities of NAcD1R neurons began to decrease before sevoflurane-induced LOC and gradually returned after recovery of consciousness. Chemogenetic activation of NAcD1R neurons delayed induction of and accelerated emergence from sevoflurane GA, whereas chemogenetic inhibition of NAcD1R neurons exerted opposite effects. Transient activation of NAcD1R neurons induced significant cortical activation and behavioral emergence during continuous steady-state GA with sevoflurane or deep anesthesia state with constant and stable burst-suppression oscillations.Conclusions: NAcD1R neurons modulated states of consciousness associated with sevoflurane GA and may represent an area for targeting GA-induced changes in consciousness and ameliorating related adverse effects.

Keywords consciousness, dopamine D1 receptor, general anesthesia, nucleus accumbens, sevoflurane

Control of wakefulness by lateral hypothalamic glutamatergic neurons

Lu Wang,Zhi-li Huang

Department of Pharmacology，School of Basic Medical Sciences，Shanghai Medical College of Fudan University

The lateral hypothalamus (LH) plays a key role in the maintenance of cortical activation and wakefulness. In the LH, the two main neuronal cell populations consist of excitatory glutamatergic neurons and inhibitory GABAergic neurons. Recent studies have shown that inhibitory LH GABAergic neurons are wake-promoting. However, the mechanism by which excitatory LH glutamatergic neurons contribute to sleep-wake regulation remains unclear. Using fiber photometry, we demonstrated that LH glutamatergic neurons exhibited high activities during both wakefulness and rapid eye movement sleep. Chemogenetic activation of LH glutamatergic neurons induced an increase in wakefulness that lasted for 6 h, whereas suppression of LH glutamatergic neuronal activity caused a reduction in wakefulness. Brief optogenetic activation of LH glutamatergic neurons induced an immediate transition from slow-wave sleep to wakefulness, and long-lasting optogenetic stimulation of these neurons maintained wakefulness. Moreover, we found that LH-locus coeruleus/parabrachial nucleus and LH-basal forebrain projections mediated the wake-promoting effects of LH glutamatergic neurons. Taken together, our data indicate that LH glutamatergic neurons are essential for the induction and maintenance of wakefulness. These results presented here may advance our understanding of the role of LH in the control of wakefulness.
Keywords lateral hypothalamus, glutamatergic neurons, wakefulness, fiber photometry, optogenetics

Paraventricular hypothalamic nucleus are essential for arousal promotion and maintenance

Chang-Rui Chen1,Yu-Heng Zhong1,Shan Jiang1,Zan Wang2,Wei-Min Qu1,Zhi-Li Huang1

1. Department of Pharmacology，School of Basic Medical Sciences; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science，Institutes of Brain Science，Fudan University，Shanghai，200032; China.
2. Department of Neurology，The First hospital of Jilin University，Changchun，130000; China.

Adequate wakefulness is fundamental for proper daytime functioning. Clinical observations indicate that the paramedian region of the hypothalamus is a critical node for controlling wakefulness. However, the specific nucleus and neural circuitry for this function remain unknown. Here, we found that inhibition of PVHvglut2 neurons induced 3-h increase of NREM sleep. Chemogenetic activation of PVHvglut2 neurons potently induced 9-h wakefulness, and PVHCRH neuronal activation also exerted

wakefulness. Photostimulation of PVHvglut2→ parabrachial complex/ventral lateral septum circuits immediately drove transitions from NREM to wakefulness. Furthermore, using in vivo fiber photometry or multichannel electrophysiological recordings in mice, we find arousal-dependent increases in population activity of PVHvglut2 neurons. Most importantly, ablation of PVHvglut2 neurons dramatically led mice to hypersomnia-like behaviors. These results demonstrate that PVHvglut2 neurons are essential for physiologic arousal in the hypothalamus.

Keywords PVH; glutamatergic neurons; hypersomnia; neural pathway; optogenetic approach; chemogenetic approach

Medial parabrachial nucleus is essential in controlling wakefulness in rats

Qi Xu1,2,Wei-Min Qu2,Zhi-Li Huang2

1. Department of Physiology，School of Basic Medical Sciences，Anhui Medical University，Anhui 230032，China.
2. Department of Pharmacology，School of Basic Medical Sciences; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science，and Institutes of Brain Science，Fudan University，Shanghai，200032，China.

Patients with brainstem stroke often show symptoms such as dizziness, decreased level of consciousness, and even coma, suggesting that there is an essential nucleus located in the brainstem that controls arousal. Activation of the parabrachial nucleus (PB) in the brainstem promoted wakefulness for hours in rats, indicated an important role of the nucleus in controlling arousal. However, the sub-regions of the PB in regulating sleep-wake cycle is still unclear. Here, we employed chemogenetics and optogenetics strategies, and found that only activation of the medial part of PB (MPB), but not the lateral part, induces continuous wakefulness for 10 h without sleep rebound in neither sleep amount nor the power spectra. Optogenetic activation of glutamatergic MPB neurons in sleeping rats immediately woke rats, with the shortest awaking latency of 2.75 s in animals whose MPB neurons were bilaterally stimulated at 5 ms/ 20 Hz. Furthermore, optogenetic activation of glutamatergic MPB axons in the basal forebrain (BF) or lateral hypothalamus (LH), but not the ventral medial of thalamus also induced an immediate transition from sleep to wakefulness, and remarkably increased wakefulness 2-3 fold. Most importantly, chemogenetic inhibition of PB neurons decreased wakefulness for 10 h. Conclusively, these findings indicate that the glutamatergic MPB neurons are essential in controlling wakefulness, and that MPB-BF and MPB-LH pathways are the major neuronal circuits.

Keywords chemogenetics; glutamatergic neurons; optogenetics; parabrachial nucleus; rat; wakefulness

The impact of hypoxia on sleep, fatigue and cognition: study on sleep wearable device

Jing Xu1,2,Xi Zhang1,Bozhi Li1,2,Jing Qi1

1. The Secondary Medical Center，National Clinical Research Center for Geriatric Disease，Chinese PLA General Hospital

2. Medical School of Chinese PLA

Objectives: To investigate the effect of hypoxia on sleep, subjective fatigue, and cognitive performance. Methods: Twenty plain-natives completed the baseline evaluation at 50m and an acute hypoxia exposure at 3750m. Sleep was assessed using a wearable watch device that recorded sleep duration, deep sleep time, light sleep time, wake after sleep onset, awakening, and nap time. Digital edition of the Epworth Sleepiness Scale (ESS) and the Multidimensional Fatigue Inventory (MFI) were used to assess sleepiness and fatigue symptoms, respectively. Cognitive performance was assessed by psychomotor vigilance task (PVT), Digit Symbol, Pursuit Aiming, and Benton Visual Retention, which were from the World Health Organization-recommended Neurobehavioral Core Test Battery (NCTB). Results: A total of 20 healthy plain-native individuals (37 $\pm$ 7 years; 8 females) were included. For the first night of hypoxia exposure, the total sleep time was 5.75 $\pm$ 0.92 hours, significantly declined from 6.35 $\pm$ 0.95 hours at the baseline. Deep sleep time (P = 0.002) and deep sleep proportion (P = 0.005) were also significantly declined. It is noteworthy that wake after sleep onset and awakenings increased at the second night of hypoxia exposure, from 0.27 $\pm$ 0.37 hrs to 1.47 $\pm$ 1.82 hrs and from 0.78 $\pm$ 0.53 hrs to 2.14 $\pm$ 1.64 hrs, respectively. Compared with the baseline, ESS and FMI showed a higher score during the hypoxia exposure. In addition, 5 min PVT increased from 458.58 $\pm$ 53.92 ms to 502.22 $\pm$ 59.39 ms. Pursuit Aiming declined and recovered to the baseline level at the 7th day. Conclusions: Acute hypoxia exposure may result in a decrease in total sleep time, deep sleep time and proportion, and an increase in wake after sleep onset and awakenings. Cognitive performance like digital, figure and visual memory, attention, and motor steadiness may be also affected. A 7-day-acclimatization recovered cognitive impairments, but did not fully restore sleep, somnolence, or fatigue impairments.
Keywords hypoxia, sleep quality, fatigue, cognitive performance

Abnormal cerebral white matter structural network topology and its correlation with cognitive behavioral abnormalities in narcolepsy type 1

Kunlin Ni,Bing Yu,Xiao Li

Shengjing Hospital of China Medical University

Objective: In the current study we investigated topological abnormalities of the cerebral white matter (WM) networks in narcolepsy type 1 (NT1) patients and its relationship with their cognitive abnormalities using diffusion tensor imaging (DTI) technology. Methods: The Beijing version of the Montreal Cognitive Assessment (MoCA-BJ) and DTI were applied in 30 patients with NT1 and 30 age-matched healthy controls. The DTI study was also performed by a 3T MRI system. The DTI data were then applied to establish a whole-brain white matter network for all subjects, and the topological characteristics of the white matter structural network were analyzed by a graph-theoretic approach. The topological parameters were compared between NT1 patients and controls. The correlation between topological parameters and the MoCA-BJ scores was also analyzed. Results: The MoCA-BJ scores were lower in NT1 patients than in controls ($P < 0.05$). NT1 patients had significantly lower global efficiency and small-world attributes of their WM network when compared to controls ($P < 0.05$). The global efficiency of the WM structural network was correlated with MoCA-BJ scores in NT1 patients ($P < 0.05$). Conclusions: The abnormal topological characteristics of the WM structural brain network in NT1 patients may be associated with their cognitive impairment.

Keywords cognitive dysfunction, graph theory analysis, narcolepsy type 1, diffusion tensor imaging

GABAergic neurons in the lateral pontine tegmentum facilitate REM–to–NREM transition

Ze-Ka Chen,Hui Dong,Wei-Min Qu,Zhi-Li Huang

Department of Pharmacology，School of Basic Medical Sciences; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science，Institutes of Brain Science，Fudan University.

Rapid eye movement (REM) sleep followed non-REM (NREM) sleep several times during a typical night of sleep in humans. However, the neural mechanisms gating REM sleep and alternating with NREM sleep remain largely unknown. Here, we showed that the activity of most lateral pontine tegmentum GABAergic (LPTGABA) neurons was the lowest during REM sleep and was increased significantly during the transition from REM sleep to non-rapid eye movement (NREM) sleep by multichannel recording in vivo and fiber photometry. Activation of LPTGABA neurons completely suppressed REM sleep, promoted REM-to-NREM sleep transitions, and increased NREM sleep by optogenetics and chemogenetics, whereas inhibition

or ablation of LPTGABA neurons both increased REM sleep and interrupted NREM sleep. In addition, chemogenetic manipulation or ablation of LPTGABA neurons powerfully gated REM-sleep rebound following REM-sleep deprivation. Furthermore, we found that LPTGABA neurons executed control of REM sleep via projections to glutamatergic neurons in the sublaterodorsal nucleus, a prominent REM-sleep promotor. Collectively, our findings reveal that LPTGABA neurons are essential for REM sleep suppression and REM-to-NREM sleep transitions in order to maintain continuity of physiological sleep.

Keywords GABA, lateral pontine tegmentum, REM-to-NREM sleep transition, optogenetics, sublaterodorsal nucleus

Electroencephalographic activity and cognitive function in middle–aged patients with obstructive sleep apnea before and after continuous positive airway pressure treatment

Jianhua Wang1,2,Rui Chen2
1.Zigong Third People's Hospital
2.The Second Affiliated Hospital of Soochow University

Objective: To investigate the effect of continuous positive airway pressure (CPAP) on sleep electroencephalogram (EEG) activity in patients with obstructive sleep apnea (OSA) and to examine the correlation between quantitative EEG changes and cognitive function. Methods: A total of 69 men and 11 women with an average age of 39.6 ± 7.7 years old who had first visits with snoring as their main complaint were recruited. All of them completed sleep questionnaires, neurocognitive tests, and night polysomnography (PSG). The patients in the OSA group also completed the second night of PSG monitoring under CPAP after pressure titration. A power spectrum analysis of EEG was used, and the correlation between the frequency powers of EEG and the scores of the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Mini-Mental State Examination (MMSE), and the Montreal Cognitive Assessment (MoCA) was further analyzed. Results: There were statistically significant differences in the absolute power of EEG in channel C3 between the OSA groups (before and after CPAP treatment), and between OSA group before CPAP and control group (all $P < 0.05$). Compared with control group, the delta/alpha power ratio (DAR) and the (delta + theta)/(alpha + beta) power ratio (the slowing ratio, TSR) of the OSA group before CPAP were higher ($P < 0.05$). The DAR and TSR of the OSA patients decreased significantly after CPAP. ESS scores were correlated with parameters such as respiratory-related microarousal index (RRMAI), apnea hypopnea index (AHI), and the average absolute power of delta, DAR, and TSR ($P < 0.05$). Conclusions: Patients with OSA have greater slow frequency EEG activity during sleep than control group. CPAP treatment reversed the slow frequency EEG activity in patients with OSA. These results suggest that slow frequency EEG activity may be used as a biomarker to assess the degree of daytime sleepiness in OSA patients.

Keywords

Clinical efficacy and cost–effectiveness analysis of telemedicine in obstructive sleep apnea (OSA): a randomized controlled trial

Mengyuan Pi,Fang Han

Peking University People's Hospital

Objective: To explore the clinical efficacy, patient satisfaction, and cost-effectiveness of the telemedicine management model in adult patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) compared with the conventional outpatient medical management model. Methods: The subjects were recruited from patients for OSAHS assessment in the sleep clinic due to snoring. Patients were randomly assigned to the telemedicine group (Group A) and outpatient group (Group B). Both groups completed the home sleep apnea test (HSAT), Auto-adjusted positive airway pressure (APAP) treatment, and 1-week, 1-month, and 3-month follow-up. Participants in Group A had to adjust the pressure and take the ventilator in the outpatient clinic, and the rest of the communication was done by telephone/video/mail; the subjects in Group B were the same as the routine outpatient procedure, except the first week call for follow-up. Subjects filled out questionnaires for the first visit, 1-month follow-up, and 3-month follow-up, and recorded the time/economic costs incurred during the visit. APAP data was received through wireless transmission. Results: A total of 130 subjects were included in the study and each with 65 cases. There were 61 and 64 successful HSAT subjects in Group A and Group B and 50 and 48 subjects received APAP treatment, 35 cases and 38 cases completed the 3-month follow-up. ESS score of Group B was 11.21 $\pm$ 5.29 changing to 5.46 $\pm$ 4.15 points, Group A changed from 10.43 $\pm$ 5.03 points to 7.42 $\pm$ 4.88 points. The change in ESS scores in Group B was significantly greater than that in Group A (p = 0.0131). At 3 months, the compliance of the subjects in Group A improved slightly, and there was no significant difference compared with Group B (54.5 $\pm$ 27.6% vs 61.5 $\pm$ 24.9%, p = 0.261). Participants Group B cost much more than Group A, respectively 1506.3 $\pm$ 423.8 Yuan and 995.8 $\pm$ 361.9 Yuan. The difference in quality-adjusted life years (QALYs) between the two groups was very small (Group A vs Group B: 0.0661 vs 0.0672). Conclusions: The clinical effectiveness of telemedicine is not inferior to the conventional model and telemedicine is much more cost-effective than the conventional outpatient model. Keywords Obstructive sleep apnea-hypopnea syndrome; Telemedicine; Auto-adjusted positive airway pressure

Clinical research of comprehensive treatment of sleep apnea syndrome with traditional Chinese medicine

Guiling Fu

Beijing Changing Hospital of Chinese and Western Medicine

Objective: To evaluate the efficacy of traditional Chinese medicine (TCM) comprehensive therapy in the treatment of sleep apnea syndrome (SAS). Methods: Eighty-two SAS patients who met the inclusion criteria were randomly divided into two groups: the TCM group (n = 41) and control group (n = 41). The control group was treated with continuous positive airway pressure (CPAP). The observation group was treated with traditional Chinese medicine, oral Chinese medicine, acupuncture, massage, and acupuncture points. Both groups were treated for 2 weeks. Polysomnography (PSG) was used to evaluate the various stages of sleep, including total sleep time, hypopnea time, < 90% oxygen saturation time. Results: The total effective rate of the TCM group and control group were 90.2% and 70.7%, respectively. The difference in total effective rate between the two groups was statistically significant ($x2$ = 4.970, P = 0.026). After treatment, the sleep time (, t = 3.556) of the treatment group was significantly longer than that of the control group (5.5 $\pm$ 0.7 vs. 5.0 $\pm$ 0.6 hrs, P < 0.01). The hypoventilation time (45.1 $\pm$ 9.5 vs. 50.2 $\pm$ 10.1 min, P < 0.05) and < 90% oxygen saturation time (19.8 $\pm$ 9.6 min vs. 25.4 $\pm$ 10.1 min, P < 0.05) of the TCM group were significantly lower than those of the control group. Conclusions: Then comprehensive TCM therapy may alleviate the clinical symptoms of SAS patients, by increasing sleep duration and improving sleep quality.
Keywords Sleep apnea syndromes; Acupuncture therapy; Tui Na therapy; Auricular plastertherapy; CPAP

The correlation between sleep apnea and early neurological deterioration in acute ischemic stroke

Wei Liu

Beijing Haidian Hospital

Objective: To explore the association between sleep apnea (SA) and early neurological deterioration (END) in ischemic stroke patients. Methods: Clinical data of ischemic stroke patients who were admitted to our stroke unit within 72 hours of symptom onset were collected consecutively. Apnea-hypopnea index (AHI) was assessed with a portable respiratory monitor. Moderate to severe SA was defined as an AHI of greater than or equal to 15 per hour. Based on the END within 7 days, all the patients were divided into END group and non-END group. Binary Logistic analysis was performed to analyze the association between SA and END. Results: A total of 247 ischemic stroke patients were enrolled in the study. Among them, 88 patients (35.6%) had moderate to severe SA and 35 patients(14.2%) worsened during the 7 days after inclusion. Binary logistic analysis showed that NIHSS (OR = 1.106, 95%CI: 1.007-1.216, P = 0.036) and moderate to

severe SA (OR = 2.992, 95%CI: 1.407-6.361, P = 0.004) were significantly related to END. Conclusions: The findings suggest that SA may be a risk factor for the END in acute ischemic stroke.

Keywords

CB1 receptor antagonist rimonabant protects against chronic intermittent hypoxia–induced renal injury in rats

Li Zhao2,Tao Liu1,Zhan-jun Dou2,Mei-ting Wang2,Zi-xuan Hu2,Bei Wang1

1.The Second Hospital of Shanxi Medical University

2.Shanxi Medical University

Objective: Obstructive sleep apnoea (OSA) induced chronic kidney disease is mainly caused by chronic intermittent hypoxia (CIH). Our study investigate the mechanism underlying CIH-induced renal damage and whether the cannabinoid receptor 1 (CB1R) antagonist rimonabant (Ri) alleviates CIH-induced renal injury. Methods: Male Sprague-Dawley rats were randomly divided into five groups: one normal control (NC) group, two chronic intermittent hypoxia (CIH) groups, and two CIH+Ri groups. Rats in the NC groups were exposed to room air, while the CIH groups were exposed to a CIH environment for 4 weeks (4w CIH group) and 6 weeks (6w CIH group), respectively. Additionally, rats in the CIH+Ri groups were administered 1.5 mg/kg/day Ri for 4 weeks (4w CIH+Ri group) and 6 weeks (6w CIH+Ri group), respectively. In the renal tissues, the morphological alterations were examined via haematoxylin eosin staining (HE) and periodic acid schiff (PAS) staining, CB1R, Fis1, Mfn1, and p66Shc expression was assessed through western blot and immunohistochemistry，and the mitochondrial ultrastructural changes in kidney sections were assessed by electron microscopy.Results: CB1R expression in the 4w and 6w CIH groups was significantly elevated, and further increased with prolonged hypoxia; however, Ri prevented the increase in CIH-induced CB1R expression. Fis1 and p66Shc expression in the CIH groups were increased, but Mfn1 expression decreased. Ri decreased Fis1 and p66Shc expression and increased Mfn1 expression. Renal damage in the 4w or 6w CIH+Ri group was evidently improved compared with that in the 4w or 6w CIH group. CB1R expression was positively correlated with Fis1 and p66Shc and negatively correlated with Mfn1. Meanwhile, electron microscopy showed that mitochondrial fission in tubulars was associated with the expression of CB1R. Conclusion: CIH causes endocannabinoid disorders and induces abnormal mitochondrial dynamics, resulting in renal injury. Treatment with CB1R antagonists reduces CIH-induced renal damage by inhibiting dysregulated renal mitochondrial dynamics.

Keywords chronic intermittent hypoxia; cannabinoid receptor system 1;renal injury；mitochondrial dynamics

Abnormal sleep–wake behaviors in ovariectomized mice

Surong Yang,Yu-Dong Yan,Shi-Yuan Tao,Zhi-Li Huang

Department of Pharmacology，School of BaMedical Sciences; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science

The estrogen hormone deficiency may happen by surgery or undoubtedly by aging. Among the menopausal symptoms, sleep disturbances are a common and recurring condition that has been self-reported in 40%–60% of perimenopausal women. Sleep is an active process in which memories undergo consolidation and integration into long-term storage and plays a critical role in regulating emotion. Therefore, the improvement of sleep dysfunction may help relieve or prevent psychological symptoms like cognition impairments and depression in women following menopause. However, the objective sleep characteristics in postmenopausal women have not been well known. In this study, a surgery-induced menopausal mouse model was utilized by bilateral ovariectomies (OVXs). At approximately two weeks after OVXs, mice were implanted with the electroencephalogram (EEG) and electromyogram (EMG) electrodes. One week later, EEG/EMG recordings wereconducted. During the active phase, compared with ovary-intact mice, the OVX mice had a remarkable decrease in wakefulness and an increase in both total non-rapid eye movement (non-REM, NREM) and REM sleep. The OVX mice had more REM sleep episodes and conversions between NREM and REM sleep. On the contrary, during the inactive phase, OVX mice showed no significant differences in the amount of wakefulness or NREM sleep compared with sham mice. However, OVX mice showed a remarkable decrease in REM sleep during the inactive phase and had fewer REM sleep episodes with a longer duration between 2 and 4 min. These results suggest that the mice with removed ovaries had sleep disturbances in a time-of-day-dependent manner, with a marked increase of NREM and REM sleep during the active phase and a decrease of REM sleep during the inactive phase.
Keywords

Gender differences in the Clinical and Polysomnographic Characteristics among Patients with Comorbid Obstructive Sleep Apnea and Insomnia

Rong Zhou,Yang Zhang,Zhoulong Yu,Wei Sun

Peking University Sixth Hospital，Peking University Institute of Mental Health，NHC Key Laboratory of Mental Health (Peking University)，National Clinical Research Centerfor Mental Disorders (Peking University Sixth Hospital)

Objectives: To investigate gender differences in clinical symptoms and polysomnography among patients with comorbid obstructive sleep apnea (OSA) and insomnia, and to explore the correlation between apnea

hypopnea index (AHI)/oxygen saturation and serum sex hormone levels. Methods: 311 patients with insomnia were retrospectively analyzed and the medical chart was reviewed if AHI ≥ 5 times/hour. The demographic information, Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression rating scale (HAM-D), sex hormone results, and polysomnography (PSG) results were collected. The parameters of different gender groups were analyzed and correlation between PSG parameters and serum sex hormone levels was analyzed. Results: Of the 311 insomnia patients who underwent a diagnostic PSG, 139 were diagnosed of having OSA (AHI ≥ 5/hour). Female patients had significantly higher HAM-A [15.5 (10, 22) vs 10 (4, 18), P = 0.006] and HAM-D score [16.5 (12, 24) vs 11 (5, 19.25), P < 0.001], lower AHI [8.9 (6.2, 13.5) vs 12.0 (7, 22.2), P < 0.001], higher mean oxygen saturation (95.1 ± 1.5 vs 94.3 ± 3.0, P = 0.043), lower proportion of N1 stage [10.7 (7.6, 15.0) vs 13.7 (8.9, 19.6), P = 0.013] and fewer snoring events [10.0 (0.5, 111.5) vs 143.0 (5.0, 244.0), P = 0.031] compared with male patients. Correlation analysis showed that in female patients, serum FSH was negatively correlated with lowest oxygen saturation (r = -0.346, P = 0.031), and estradiol was positively correlated with average oxygen saturation (r = 0.484, P = 0.002). Conclusions: For patients with comorbid OSA and insomnia, females may have a higher level of depression and anxiety, fewer snoring events; while males have higher AHI, lower mean oxygen saturation, and higher percentage of N1 sleep. The proportion of comorbid OSA is high in patients with insomnia, and the symptoms of OSA are atypical, especially in women.

Keywords obstructive sleep apnea, insomnia, gender difference, sex hormone

Clinical manifestations and sleep structure in children with sleep apnea–hypopnea syndrome at different ages

Xueyun Xu,Yuqing Wang

Children's Hospital of Suzhou University

Objective To analyze the clinical and sleep structure characteristics of OSAHS in preschool and school-age children.Method We enrolled 123 children diagnosed with OSAHS through polysomnography from December 2016 to November 2019 in the Department of Respiratory at the Children's Hospital of Soochow University. The 313 children diagnosed with snoring during the same period were selected as the control group. The two groups of children were divided into preschool and school age groups according to their ages, and clinical data and PSG results were collected.Results The night and day symptoms of OSAHS children in preschool and school age were more significant than those in the control group（P <0.05）. The sleep structure of preschool and school-age children with OSAH is different from that of the control group: the proportion of preschool children with OSAHS in REM stage is higher than that in control group, the proportion of stage NREM1 in school-age OSAHS children was higher than that in the control group, while the proportion of stage NREM3 was lower（P <0.05）. The TST and sleep efficiency of school-age children with OSAHS were lower than those of preschool children with OSHAS, the proportion of NREM2 stage

increased, the proportion of NREM3 stage decreased, and ODI increased. AHI was positively correlated with the proportion of NREM2 stage sleep in preschool children (r=0.217, p=0.043), and negatively correlated with the proportion of REM stage (r=-0.220, p=0.040). BMI was negatively correlated with the NREM3 stage in school-age children (r=-0.429, P =0.009).Conclusion The clinical manifestations of OSAHS children are different from those of PS children, and vary by age. The changes of sleep structure in school-age OSAHS children were more obvious than those in pre-school children. The changes of sleep structure in preschool-age and school-age OSAHS children were respectively related to AHI and BMI

Keywords

Digital Cognitive Behavioral Therapy for insomnia: A systematic review and meta–analysis of randomized controlled trials

Yueying Wang,Mu Yunping,Zhu Bingqian

Shanghai Jiao Tong University，School of Nursing

Objective: This systematic review aimed to evaluate the effect of digital Cognitive Behavioral Therapy for insomnia (dCBT-I) for the treatment of insomnia in Chinese adults, and thereby provide further evidence for the management of insomnia. Methods A systematic search was performed in 10 electronic databases including CNKI, Wanfang, PubMed, and Embase. Only randomized controlled trials conducted in the Chinese population were included. Two independent investigators performed study selection, data extraction, and quality appraisal. Revman 5.4 was used for meta-analysis. Results: Seven studies consisting of 957 participants were included. Five studies were analyzed using meta-analysis. Based on the analyses, at the end of the treatment (6-8weeks), compared with medication treatment, dCBT-I resulted in better sleep efficiency (WMD = 4.63%, 95%CI, 0.63%-8.63%), sleep onset latency (WMD = -12.2min, 95%CI, -20.5min - -3.9min), and wake after sleep onset (WMD = -17.2min, 95%CI, -30.3min - -4.1min). Sleep duration and psychological factors (anxiety and depression) did not differ between the two methods. Similarly, compared with those who received no active treatment, those receiving dCBT-I showed better sleep efficiency (WMD = 8.94%, 95%CI, 1.64%-16.24%), sleep onset latency (WMD = -14.7min, 95%CI, -27.6min - -1.8min), insomnia severity (WMD = -3.7, 95%CI, -6.6 - -0.9), and over sleep quality (WMD = -2.2, 95%CI, -3.0 - 1.4). Additionally, dCBT-I and traditional CBT-I resulted in similar improvements in sleep. Conclusions: Currently, dCBT-I was delivered via various forms and platforms in China. Overall, dCBT-I can effectively improve sleep quality among Chinese adults with insomnia. Additional studies using both objective and subjective measurements of sleep are warranted to examine the long-term effect of dCBT-I.

Keywords

Are anti–inflammatory cytokines associated with cognitive impairment in patients with comorbid insomnia and depression? a clinical study

Shuo He1,Xi-Xi Chen2,Wei Ge1,Shuai Yang1,Jun-Tao Chen1,Jing-Wen Niu1,Lan Xia3,Gui-Hai Chen1

1.The Affiliated Chaohu Hospital of Anhui Medical University
2.The First Affiliated Hospital of Anhui Medical University
3.The Second Affiliated Hospital of Anhui Medical University

Background: To explore the relationship between serum levels of frequently overlooked anti-inflammatory cytokines and cognitive function in patients with comorbid insomnia and depression (ICD). Methods: A total of 42 ICD patients, 63 chronic insomnia disorder (CID) patients, and 42 healthy control subjects were enrolled in the study. The Pittsburgh Sleep Quality Index and Hamilton Depression Rating Scale were used to assess sleep quality and depression severity, respectively. The Montreal Cognitive Assessment scale (MoCA) and Nine-Box Maze Test (NBMT) were used to assess cognitive function. Serum levels of anti-inflammatory interleukins (IL-1RA, IL-4, IL-5, IL-10, IL-13, and IL-28A), transforming growth factor (TGF)-β1, granulocyte-macrophage colony-stimulating factor, interferon-γ, and the chemokine regulated upon activation, normal T cell expressed and secreted (RANTES) were measured by enzyme-linked immunosorbent assay. Results: The ICD group had significantly more errors in the spatial reference task (H = 2.55, Ps = 0.03) and spatial working memory task (H = 5.67, Ps < 0.01) of the NBMT, as well as lower levels of IL-1RA (H = −2.85, Ps = 0.01), IL-4 (H = −3.28, Ps < 0.01), IL-5 (H = −3.35, Ps < 0.01), IL-10 (H = −4.46, Ps < 0.01), and IL-28A (H = −2.75, Ps = 0.02) than control subjects. A partial correlation analysis showed that the level of one or more of IL-4, IL-5, IL-10, IL-13, and TGF-β1 was positively correlated with cognitive function (MoCA score and/or performance in spatial memory task) in ICD patients. Limitations: Lack of an objective assessment tool for sleep quality and small sample size. Conclusion: Immune dysfunction, as reflected by altered anti-inflammatory IL levels in serum, may contribute to cognitive dysfunction in ICD.

Keywords Insomnia; Depression; Comorbidity; Cytokine; Cognition

Evaluation of a Non–contact Ultra–wideband Bio–radar Sleep Monitoring Device for Screening of Sleep Breathing Disease

Zhijing Wei,Wei Wang,Jiahuan Xu,Wenyang Li

The First Hospital of China Medical University

Purpose Ultra-wideband bio-radar (UWB) is a new non-contact technology that can be used for the screening of obstructive sleep apnea (OSA). However, little information is available regarding its reliability. This study aimed to evaluate the effectiveness of UWB and to determine whether and how UWB could provide a novel and reliable method for the primary screening of sleep-related breathing disorders.Methods Subjects with suspected OSA from the sleep center of the First Hospital of the China Medical University assessed over the period of September 2018 to April 2019 were enrolled in the study. Three detection methods were simultaneously used, including the Stop-Bang questionnaire (SBQ), UWB, and standard polysomnography (PSG). The data were analyzed using a fourfold table, receiver operating characteristic curves, Spearman rank correlation coefficients, Bland-Altman plots, and epoch-by-epoch analysis.Results Sixty-seven patients participated in the study including 56 males and 11 females. The mean age was 43 ± 11 years, the mean body mass index was 27.78 ± 4.82 kg/m2, and the mean SBQ score was 4.78 ± 1.56. The apnea-hypopnea index (AHI) (r=0.82, p<0.01) and min arterial oxygen saturation (r=0.80, p<0.01) of the UWB were positively correlated with those obtained from the PSG. UWB performed better than SBQ, as indicated by the larger area under the curve (0.85 vs. 0.632). The sensitivity and specificity of the UWB-AHI were good(100%, 70%, respectively).Conclusions UWB performs well in the screening of OSA and can provide reliable outcomes for the screening of OSA at the primary level.

Keywords Bio-radar, Ultra-wideband, Monitoring technology, Obstructive sleep apnea, Screening.

Characteristics of overnight changes of obstructive apnea episodes in patients with obstructive sleep apnea hypopnea syndrome

Jianqing Wang1,Zhao Dan1,Wang Yan1,Cao Jie1,Chen Baoyuan1,Li Shuo1,Guo Hengjuan1,Zhang Jing1,Zhu Lei2

1.Tianjin Medical University General Hospital

2.Tianjin Medical University Cancer Hospital

Objective: To compare the overnight trend of the duration of obstructive apnea events in patients with obstructive sleep apnea hypopnea syndrome (OSAHS), and to explore the adaptability of the body to the pathophysiological consequences of periodic apnea disorders and its potential mechanism. Methods: A retrospective analysis was made of 89 snoring patients who underwent polysomnography (PSG) in the Sleep Center of Tianjin Medical University General Hospital from October 2018 to December 2019. According to

the apnea hypopnea index (AHI), the patients were divided into non-OSAHS group (N = 10), mild OSAHS group (N = 15), moderate OSAHS group (N = 29) and severe OSAHS group (N = 35). The total recording time of the whole night was divided into 4 stages averagely, and the trends of the average apnea duration (MAD) and the longest apnea duration (LAD) with sleep duration in each group were compared, in addition, the apnea times-duration variation curve was drawn for fitting analysis. Results: The levels of MAD and LAD in patients with severe OSAHS were significantly higher than those in patients with non-OSAHS, mild OSAHS and moderate OSAHS ($P < 0.05$). The MAD and LAD of all subjects in the third and fourth period were significantly higher than those in the first period ($P < 0.05$). At the beginning of sleep period (the number of obstructive apnea episodes from 1 to 31), the average MAD of each apnea increased by 0.22s and then increased by 0.04s, which slowed down by 5.5 times. Conclusions: The MAD and LAD in patients with OSAHS gradually prolonged with the passage of sleep periods, especially in patients with severe OSAHS. Patients with OSAHS may have a variety of adaptation mechanisms to repeated hypoxic attacks, and this adaptation is phased. Patients with severe OSAHS show the most complete form of change, suggesting that their pathophysiological changes were the most serious.

Keywords

The level of carbon dioxide is the determinant of successful non–invasive ventilation pressure titration in patients with non–hypercapnic primary central sleep apnea: a case report

Xuejiao Han,Dan Zhao,Jianqing Wang,Yan Wang,Lixia Dong,Baoyuan Chen
Tianjin Medical University General Hospital

Primary central sleep apnea (CSA) is classified as non-hypercapnic CSA. Due to high loop gain, lower carbon dioxide (CO_2) reserve and so on, these patients intermittently hyperventilate resulting in hypocapnia during sleep. Thus, it is important to monitor nocturnal CO_2 level is for these patients. We report a female patient who complained of snoring, apnea, and excessive daytime sleepiness, and was diagnosed with non-hypercapnic primary CSA. With the monitoring of transcutaneous partial pressure of carbon dioxide ($PtcCO_2$), manual non-invasive ventilation (NIV) pressure titration was performed with continuous positive airway pressure, bi-level positive airway pressure, and adaptive servo-ventilation (ASV) mode for three nights, respectively. Only ASV mode can keep the $PtcCO_2$ stable above the apneic threshold (approximately 40 mmHg), thereby eliminate central apnea events successfully. It is concluded that the level of CO_2 is the determinant of successful NIV pressure titration in patients with non-hypercapnic primary CSA.

Keywords

High Flow Nasal Cannula Therapy for Obstructive Sleep Apnea in Adults

Yan Hu1,Fang Han2

1.Pekin University International Hospital

2.Perkin University People's Hospital

Background: Obstructive sleep apnea hypopnea syndrome (OSAHS) is characterized by the aggravation of upper airway constriction or obstruction, which is associated with a high incidence of various metabolic diseases and high mortality. Continuous positive airway pressure (CPAP) is now recommended as the first-line therapy for OSAHS, but its application is limited by its unsatisfactory patient tolerance. Previous studies showed that high flow nasal cannula (HFNC) could improve some OSAHS patients` symptoms. Therefore, the aim of the present study is to evaluate the effect of HFNC on OSAHS within a larger cohort and to study the details of its therapeutic characteristics. Methods: HFNC was performed in a wide spectrum of OSAHS severity patients. A full night's usage of the device was evaluated with polysomnography. Subgroups were divided by different treatment response criteria to find the effect of this device. Results: Fifty-six patients were enrolled: Age 45.59 ± 12.47 years, BMI 26.67 ± 3.11 kg/m2 and AHI 26.93 ± 14.69 events/h at baseline. AHI was significantly decreased ($p < 0.05$) after HFNC treatment. Transformation mechanism was found in the subgroups with different treatment responses. The elderly patients with mild to moderate OSAHS achieved a better response rate. Conclusions: HFNC can be used to treated OSAHS patients, especially for those elderly patients with mild to moderate severity. This study found the transformation mechanism of HFNC. HFNC could be an alternative treatment when patients cannot be tolerated with CPAP.
Keywords

Long non-coding RNA MALAT1 affects intermittent hypoxia-induced endothelial injury by regulating miR-142-3p/HMGB1

Mengxue Chen1,Lida Chen2,JIanchai Huang1,Aiming Zeng1,Jiefeng Huang1,Qichang Lin1,3

1. the First Affiliated Hospital of Fujian Medical University
2. Zhangzhou Affiliated Hospital of Fujian Medical University
3. Fujian Provincial Sleep-disordered Breathing Clinic Center，Fuzhou，Fujian Province，People's Republic of China.

Background: OSA is a risk factor for atherosclerosis. Long non-coding RNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is closely related to endothelial cell functions. However, the role of MALAT1 in intermittent hypoxia (IH)-induced endothelial injury has not yet been studied. The aim of the present study was to investigate the function of MALAT1 in IH-induced endothelial injury and its

underlying regulatory mechanism. Methods: To mimic the effect of OSA, human umbilical vein endothelial cells (HUVECs) were treated with IH. The expression levels of MALAT1 and miR-142-3p were measured using qRT-PCR. The expression levels of apoptosis-associated proteins were measured by western blot. Cell Counting Kit-8 (CCK-8) was performed to detect cell ability. Dual-luciferase reporter assay was used to confirm the relationships among MALAT1, miR-142-3p, and high mobility group box (HMGB)1. Results: IH treatment significantly reduced cell viability but enhanced cell apoptosis in HUVECs. Concomitantly, MALAT1 was significantly upregulated in IH-treated HUVECs. Further experiment showed that MALAT1 knockdown augmented IH-induced injury of HUVECs. Dual-luciferase reporter assay revealed a direct interaction between MALAT1 and miR-142-3p. In addition, inhibition of miR-142-3p reversed damage effects of MALAT1 knockdown on IH-treated HUVECs. Finally, miR-142-3p directly interacted with HMGB1 and the inhibition of HMGB1 protein expression mediated by MALAT1 knockdown was reversed by miR-142-3p inhibitor. Conclusions: IH resulted in increased expression of MALAT1 in HUVECs. MALAT1 knockdown augmented IH-induced injury of HUVECs. MALAT1 exerted its effects on IH-treated HUVECs via miR-142-3p/HMGB1.

Keywords obstructive sleep apnea; intermittent hypoxia; MALAT1; miR-142-3p; endothelial injury; apoptosis

Comparison of The Cognitive Impairment Between Children with OSAHS and Primary Snoring using Das– Naglieri Cognitive Assessment System

Adwoa Takyiwaa Gyabaah1,2, Brett Lyndall Singh1,2,Xue Hao Qiu1,2,Jia Yun Tu1,2,Jia Yi Chen1,2, Zhi Lin Li1,2, Yuan Ai Li1,2, Chun Yan Ma1,2, Zhi Jie Li1, Xu Chen1, Qin Ling3, Xiaohong Cai1,2

1. THE 2ND AFFILIATED HOSPITAL AND YUYING'S CHILDREN HOSPITAL OF WENZHOU MEDICAL UNIVERSITY

2. The Second School of Medicine，Wenzhou Medical University，Wenzhou，P. R. China

3. The center of Cognitive and Sleeping，The people's hospital of Guangxi Zhuang autonomous region，Nanning，China.

Objective: To compare the severity of sleep disorders and hypoxia between children with obstructive sleep apnea-hypopnea syndrome (OSAHS) and children with primary snoring (PS) by the quantitative evaluation of cognitive function with the Das–Naglieri Cognitive Assessment System (DN-CAS). Methods: 129 children were enrolled and divided into two groups: OSAHS and PS groups, after undergoing all-night polysomnography (PSG). An age and sex-matched control group of 55 healthy children also underwent the study. The cognitive function of the children was evaluated by the DN-CAS applying the Planning, Attention, Simultaneous processing, and Sequential processing scales. Results: The comparison of the PSG

parameters in the OSAHS group and PS group clearly indicated that sleep disruption and apneic events were far higher in the OSAHS group. Significant differences were seen in planning scores, attention scales, sequential processing scales, and total scale scores in the DN-CAS across the 3 groups (P <0.05), but there was no difference in the scores of the simultaneous processing scale. The Planning test scores of PS and OSAHS groups were significantly lower than those of control group; with a more obvious reduction in the OSAHS group compared to the PS group. The attention scores and total scores of the OSAHS group were significantly lower than those of the control group, and the successive scores of the PS group were higher than those of control group. Conclusion: Both children with OSAHS and PS have cognitive process defects as detected by DN-CAS. Children with PS are mainly characterized by planning dysfunction. On the other hand, children with OSAHS have both planning and attention deficits hence OSAHS children suffer a more severe form of cognitive impairment than PS children.

Keywords OSAHS, PS, DN: CAS, PASS

Is accurate titration necessary for successful treatment of OSA ?

Yan Chen,Lu Wang,Yingxin Wu,Qishan Wei,Yuanming Luo

Guangzhou Medical University

Background: Automatic continuous positive airway pressure (Auto-CPAP) has a similar compliance as fixed-CPAP, although AutoCPAP is usually 2-3cmH2O higher than fixed-CPAP. We therefore hypotheses that accurate titration may not be necessary for successful treatment of OSA Methods: We used a questionnaire to assess subject comfort and treatment acceptance in 65 participants, including 34 healthy subjects and 31 patients with OSA, under different CPAP level (4-20cmH2O). Respiratory muscle activities were recorded with surface electromyography (sEMG) to quantify the respiratory load at each level of CPAP. End inspiratory lung volume (EILV), end expiratory lung volume (EELV), tidal volume (VT) and minute ventilation (VE) were also measured. Results: There was no significant difference in subject comfort and treatment acceptance when CPAP pressure was lower than 10cmH2O in healthy subjects and lower than 14cmH2O in patients with OSA. Expiratory muscle EMG become obvious only when CPAP above 12cmH2O. Both EILV and EELV increased significantly with increasing CPAP but VT changed little over the different pressure. Conclusions: CPAP pressure higher than the pressure for elimination OSA should not decrease acceptance if CPAP pressure is equal or lower than 10 cm H2O .

Keywords continuous positive airway pressure, obstructive sleep apne, acceptable range

Analysis of miRNA expression profile in lung tissue of intermittent hypoxia rat model

Zhijuan Liu,Ai Li,Yongxia Li

The Second Affiliated Hospital of Kunming Medical University

Objective To screen out key miRNAs in intermittent hypoxia rat model and explore the biological roles of their downstream target genes as well as the related regulatory pathways. Methods 50 adult male Wistar rat were randomly divided into 5 groups, namely 5% oxygen concentration group (IH1), 7.5% oxygen concentration group (IH2), 10% oxygen concentration group (IH3), 12.5% oxygen concentration group (IH4), and negetive control group (NC). Rats with intermittent hypoxia received intermittent hypoxia for 8 hours daily for 12 weeks. miRCURY LNA miRNA PCR Panel were used to analyze the expression profile of miRNAs from lung tissues. Analyzed the common miRNAs of IH1 to IH4 groups. The miRbase database identified the conservation of these miRNAs. Funrich software was used to analyze the target genes, their biological function and pathway of the common miRNAs in the IH1 to IH4 groups. Results The miRNAs chip analysis showed that there were a large number of differentially expressed miRNAs in the lung tissues of IH1 to IH4 groups. Intersection of the expression profiles of the miRNAs of the IH1 to IH4 groups yielded 10 common miRNAs, such as hsa-miR-122-5p，hsa-miR-30c-2-3p, and so on. There were 929 target genes of 10 common miRNAs and mainly distributed in the nucleus, followed by the cytoplasm. The molecular function was mainly the activation of transcription factors, and the biological process focuses on cell interaction and signal transduction. Two of the significant signaling pathways may play a role in the pathophysiological process of intermittent hypoxia. Conclusion There were specific miRNAs in the lung tissue of rats under intermittent hypoxia at different concentrations, and 10 common miRNAs in the IH1 to IH4 groups, their target genes may play a key role in the pathophysiological process of OSA through two signaling pathways.
Keywords

How does tongue strength training increase upper airway stability in rats?

Hong Huang,Wei Wang,Wenyang Li,Hongyu Jin

The First Affiliated Hospital of China Medical University

Tongue strength training (TST) has been shown to decrease the apnea-hypopnea index in some patients with obstructive sleep apnea (OSA). However, how TST modulates the central regulation of genioglossus and influences the stability of the upper airway remains unknown. Sixteen adult male Sprague-Dawley rats were randomly assigned to the normal control (NC) and TST groups. The TST group underwent 8-week

progressive resistance tongue exercise training. Transcranial magnetic stimulation (TMS) responses and EMG activities were contumeliously recorded for 2 hours on days 0, 14, 28, and 56 in both groups. Critical pressure (Pcrit) was measured on days 0,14, 28, and 56. The TST group showed shorter TMS latency and higher genioglossus EMG activity, which lasted from 5 to 80 min after training on day 56 of training, than the NC group. The TST group showed significantly lower Pcrit on days 28 and 56 of training than the NC group (-4.07±0.92 vs. -3.12±0.77 cmH2O, P< 0.05, -4.66±0.74 vs. -3.07±0.38 cmH2O, P< 0.01). This study revealed that an 8-week TST could gradually increase corticomotor excitability of genioglossus, elevate the genioglossus EMG activity, and ultimately enhance the stability of the upper airway. Moreover, improved neuromuscular excitability occurred prior to the enhanced upper airway stability. These findings provide a theoretical framework for TST as a promising treatment for OSA patients.

Keywords

Impact of sleep quality on post–stroke anxiety in stroke patients

Meijuan Xiao,Guiqian Huang, Liang Feng, Xiaoqian Luan,Qiongzhang Wang,Wenwei Ren,Siyan Chen,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Objective: To explore whether poor sleep is associated with post-stroke anxiety (PSA) in Chinese patients with acute ischemic stroke (AIS) and to verify whether poor sleep is a predictor of PSA. Methods: A total of 327 patients with AIS were enrolled and followed up for one month. Sleep quality within one month before stroke was evaluated using the Pittsburgh Sleep Quality Index (PSQI) at admission. The patients were divided into the poor sleep group (PSQI > 7, n = 76) and good sleep group (PSQI ≤ 7, n = 251). One month after stroke, patients with obvious anxiety symptoms and a Hamilton Anxiety Scale score greater than 7 were diagnosed with PSA. Results: Eighty-seven patients (26.6%) were diagnosed with PSA. Compared to the good sleep quality group, the incidence of PSA in patients with poor sleep quality was higher (42.1% vs 21.9%, P = 0.001). Poor sleep quality is more common in patients with PSA (35.6% vs 18.8%, P = 0.001). A logistic regression analysis indicated that poor sleep quality was significantly associated with PSA (OR: 2.265, 95% CI: 1.262 - 4.067, P = 0.003). After adjusting for conventional and identified risk factors, poor sleep quality was found to be independently associated with PSA (OR: 2.676, 95% CI: 1.451 - 4.936, P = 0.001). Conclusions: Poor sleep quality before stroke was associated with PSA and may be an independent risk factor of PSA one month after AIS onset

Keywords

The Month of Birth Distribution of Type 1 Narcolepsy Patients: A 20–year Cohort in China

Jingjing Guo,Fang Han,Liyue Xu,Xiaosong Dong,Chi Zhang,Fulong Xiao

Peking University People's Hospital

Objectives: To elucidate environmental factors associated with narcolepsy, we aimed to assess the seasonal effect on birth pattern in Chinese patients with narcolepsy, and to further analyze whether this effect is different among patients with onset date before, during and after 2009 H1N1 pandemic. Methods: A total of 1942 patients with birth data information and diagnosed as narcolepsy cataplexy were included in this study. The birth month and seasonal effect of 1064 patients born from 1970 to 2000 was compared to controls (n=2,028,714) from the general population. Furthermore, birth season effect in 1373 patients with definite disease onset month were compared among patients with onset date before (n=595), during (n=325), and after (n=453) H1N1 pandemic. Results: Patients with narcolepsy had a significantly different seasonality of birth month from the general population (p = 0.027). The monthly distribution of birth yielded a peak in November (odds ratio = 1.23 [95%CI,1.01-1.49]) and a trough in April (odds ratio = 0.68 [95 %CI,0.52-0.88]). No significant difference was observed in the birth month across patients with onset dates before, during and after the H1N1 pandemic (p = 0.603). Conclusions: An excess of births in November and a decrease of birth was observed in April in Chinese patients with narcolepsy, and this effect maintained before, during and post by 2009 H1N1 pandemic.

Keywords autoimmune, birth month, onset month, narcolepsy, seasonality

The effect of Intelligent patient–controlled analgesia system on high–quality nursing service of labor analgesia

Xiaoyan Qian

Aviation General Hospital of Medical University

Objective: To explore the effects of intelligent patient-controlled analgesia system on high-quality nursing service of labor analgesia. Methods: 400 primiparas who were waiting for labor analgesia in our hospital from September 2017 to February 2018 were enrolled and randomly divided into two groups: artificial supervision group (n = 200) and intelligent management group (n = 200). The parameters of the patient-controlled epidural analgesia (PCEA) pump were set to the first load of 12ml, the continuous background dose of 0.1ml / kg, the locking time of 12min, the single dose of 6ml /kg /h, and the limit of 30ml /h. The artificial supervision group needed regular on-site follow-up and the delivery room nurses to assist in observation; while the intelligent management group used the intelligent patient control system to directly connect with the anaesthesia nurse's mobile phone on the basis of the original patient-controlled analgesia, so as to monitor the operation of the analgesia pump from time to time and change the passive

service into active service. In the course of the experiment, the VAS and HAMA of 15min, 30min, 60min, 120min, 180min and 240min, and the fault treatment time of the two groups were recorded at the beginning of admission, before the delivery of 3cm, immediately after the delivery analgesia treatment, and post-treatment, and the nursing satisfaction of the parturients was evaluated 24 hours after delivery. Results: After labor analgesia, the VAS and HAMA scores in the intelligent management group were significantly lower than those in the manual supervision group at 60min, 120min, 180min and 240 min, ($P < 0.05$). The fault handling time (8 ± 2 min) in the intelligent management group was significantly lower than that in the artificial supervision group (13 ± 1.3 min), and the maternal nursing service satisfaction in the intelligent management group (94.2%) was significantly higher than that in the manual supervision group (86%) ($P < 0.05$). Conclusion: On the basis of the effect of PCEA on labor analgesia, the intelligent management group realizes real-time management of analgesia process through internet of technology combined with artificial intelligence operation, changed passive service into active service, reduced the failure rate of analgesia pump, which was of great significance to maintain the effectiveness and stability of analgesia effect, relieved maternal anxiety and improved patient nursing satisfaction, so as to improved high-quality nursing service. Keywords Intelligent patient-controlled analgesia system; Labor analgesia; PCEA; VAS; HAMA.

Effect of Respiratory Training in the Treatment of Shivering after Laparoscopic Surgery under General Anesthesia

Xiaoyan Qian

Aviation General Hospital of Medical University

Background: Shivering is one of the common complications after general anesthesia with different incidence rate in different researches. Both domestic and international studies have shown that pharmacotherapy is one of the principal modes of treatment for post-operative shivering including tramadol, pethidine and dexmedetomidine. However, studies about the non- pharmacotherapy for the treatment of post-operative shivering are still lacking. Respiratory training, however, can improve oxygen consumption and reduce the occurrence of hypoxemia. Therefore, the previous study was performed: (1) To analyze the effects and influences of commonly used general anesthesia drugs on patients with shivering. (2). The therapeutic effects and adverse reactions of medicines in the treatment of shivering on postoperative shivering. (3). The comparison of blood gas analysis indexes between pre- and post- treatment for shivering; (4). the action time, effective time and cost-effect of common drugs in the treatment of shivering. The previous results showed that respiratory training can improve the clinical symptoms of shivering after laparoscopic surgery under general anesthesia. Therefore, the present study is taken. Objective: To detect the effects of respiratory training and drug intervention in the treatment of shivering after laparoscopy under general anesthesia. Methods: One hundred and thirty-two patients with shivering after laparoscopic Surgery under general anesthesia were selected from April 2019 to December 2019. All participants were divided into two groups According to the double-blind random number table method: respiratory training group (n=66) and drug

intervention group (n = 66). A comprehensive search of literature showed that the shivering could be treated with tramadol, pethidine and dexmedetomidine, while our medicine team is routinely use dexmedetomidine for treating shivering. According to the medical advice after the patients entered the recovery room, 0.5ug/kg dexmedetomidine was given intravenous injection. The shivering grades were recorded at the beginning (T0), 5min latter (T1), 10 min latter (T2), and 15min latter (T3) after the patients entered the recovery room. Moreover, the nausea, vomiting, bradycardia and excessive sedation during the experiment were recorded. Results: The remission rate of shivering in the respiratory training group (T1: 30.30%, T2: 69.69) was higher than that in drug intervention group (T1:12.12%, T2:33.33%) at T1 and T2 and lower than that in drug intervention group at T3 (respiratory training group: 77.27%, drug intervention group: 95.45%). But the result didn't have statistical significance at T1 (P>0.05). There were significant differences between two groups at T2 and T3 (P<0.05). The adverse reactions were also observed and recorded. The difference about the rate of nausea, vomiting, bradycardia, sedation were statistically significant compared with the respiratory training group. Conclusion: Breathing training can effectively reduce medical costs and the proportion of drug use, which is conducive to the promotion of DRG payment.

Keywords

Effect of oral management on respiratory system of both doctors and patients during perianesthetic period: a normative study of specialty nursing in anesthesiology department

Xiaoyan Qian

Aviation General Hospital of China Medical University

Background Oral management is a common clinical nursing procedure to alleviate patient discomfort. However, oral management of patients with endotracheal intubation under preoperative and intraoperative general anesthesia has not been studied. Objective To supplement the development of oral care standards applicable to patients in the perianesthetic period based on the existing extended oral care management practices. Methods compared with various existing oral care methods and mouthwash, mint and lime healthcare mouthwash were selected and operated by oral spray method. A total of 200 patients undergoing endotracheal intubation anesthesia under general anesthesia were investigated and randomly divided into control group (n=28), saline group (n=80), experimental group (n=92). The oral bacteria culture of patients before and after endotracheal intubation under general anesthesia, bacteria culture in oral and outside the mask of anesthesiologists, oral situation and satisfaction survey of patients, length and cost of hospitalization of each group were observed. Results Before and after endotracheal intubation under general anesthesia, oral bacteria culture of patients in each group was significantly different (P<0.05). There was no significant difference in the bacteria culture results in oral and outside the mask of the anesthesiologists. The oral environment of patients, the satisfaction survey of patients, length of stay and cost were statistically

significant. Conclusion Healthcare mouthwash combined with oral spray management achieves a two-way protection between patients and medical workers and improves the quality of work during the perianesthetic period.

Keywords perianesthetic period, oral management, endotracheal intubation, respiratory inflammatory.

The timing of CPAP benefits on Circulating Biomarkers for OSA patients

Yi Wang1,2,Yingni Lin1,2,Liyue Zhang1,2,Chuanxiang Li 1,2,3,Shiqi Li1,2,Liu Zhang1,2,Hongpeng Li1,2,Ning Li1,2,Yongjie Ding1,Qingyun Li1,2

1. Department of Respiratory and Critical Care Medicine，Ruijin Hospital，Shanghai Jiao Tong University School of Medicine
2. Institute of Respiratory Diseases，Shanghai Jiao Tong University School of Medicine
3. Wuhan Third Hospital -Tongren Hospital of Wuhan University，Respiratory and Critical Care Medicine

Background: Continuous positive airway pressure (CPAP) is the first-line therapy for moderate-to-severe obstructive sleep apnea. Specifying timing of CPAP benefits on OSA-related biomarkers will help to assess the efficacy of CPAP and to optimize the treatment strategies. Objective: To evaluate the time signature of circulating biomarkers (ie, (C-reactive protein (CRP); tumor necrosis factor-α (TNF-α); fasting blood glucose (FBG); fasting insulin (FINS); low-density lipoprotein (LDL); high-density lipoprotein (HDL); total cholesterol (TC) and triglyceride (TG).response to CPAP treatment on obstructive sleep apnea. Methods: Pubmed and Embase database were searched. Data were extracted from 75 included studies by two independent reviewers. A meta-analysis was conducted using a random-effect (or fixed-effect) model and standardized mean difference (SMD) model. According to CPAP duration, studies were divided into three subgroups: short-term (less than 3 months), mid-term (3~6months), and long-term (greater than or equal to 6 months). Results: Circulating biomarkers improved by short-term treatment included CRP [SMD: 0.75(CI:0.24, 1.26; P=0.004)], TNF-α [SMD: 0.48(CI:0.10, 0.86; P=0.014)], LDL [SMD: 0.39(CI:0.17, 0.60; P=0.000)], TG [0.39(CI:0.17, 0.60; P=0.000)]; Those improved by mid-term treatment included HDL[SMD: -0.25(CI: -0.50, -0.01; P=0.044)]; TC [SMD: 0.17(CI: 0.02, 0.32; 0.025)]; Only CRP, LDL, HDL, TC were further improved by long-term CPAP. For glucose metabolism, our analysis found that CPAP could only effectively reduce FBG of OSA patients with high baseline blood glucose level and CPAP failed to produce statistical change on FINS at any time point. Conclusion: The results imply that there exists the time signature of circulating biomarkers in response to CPAP treatment on OSA. Short-term benefit can be achieved for some biomarkers such as CRP, TNF-α, and LDL, while HDL and TC may need longer duration. Specifying timing of CPAP benefits on OSA-related biomarkers will help to assess the efficacy of CPAP, to improve the adherence to CPAP, and to optimize the treatment strategies.

Keywords

Effect of Long–term CPAP on AHI in Patients with Comorbid OSA and Cardiovascular Disease

Yilu Cheng1,3,Qiong Ou1,Baixin Chen4,R. Doug McEvoy5,Kelly A. Loffler5,Yanxia Xu1,3,Miaochan Lao1

1. Department of Sleep Center，Department of Pulmonary and Critical Care Medicine，Guangdong Provincial People＇s Hospital/Guangdong Academy of Medical Sciences/Guangdong Provincial Geriatrics Institute，Guangzhou 510080，China
2. School of Medicine，South China University of Technology，Guangzhou 510080，China
3. Shantou University Medical College，Shantou 515000，China
4. Adelaide Institute for Sleep Health，Flinders Health and Medical Research Institute，Flinders University，GPO Box 2100，Adelaide SA 5001
5. Guangdong Second Province General Hospital，Guangdong Province Emergency Hospital，Infectious Diseases，Guangzhou 510080，China

Background: Continuous positive airway pressure (CPAP) treatment has an immediate positive effect on breathing during sleep. However, whether these effects are strictly transient, or have a sustained impact on underlying disease severity is unclear. Objective: To determine whether long-term CPAP treatment of obstructive sleep apnea (OSA) alters underlying severity of sleep disordered breathing. Methods: We studied SAVE study participants who were recruited at Guangdong Provincial People＇s Hospital, China. Participants were aged 45-75 years with a history of cardiac or cerebrovascular disease. Moderate-severe OSA was confirmed by home sleep apnea testing (HSAT). Participants were randomized to receive CPAP plus standard cardiovascular care (CPAP Group) or standard care alone (UC Group) and followed for several years. At the study conclusion, surviving participants were invited to repeat HSAT. Baseline to end-of-study changes in OSA in the two groups were compared by independent samples t-tests. Linear mixed models were used as an adjusted analysis to confirm the effect of CPAP on apnea-hypopnea index (AHI) and nadir oxygen saturation (SpO2). Results: 102 adults were recruited (51 per group) and followed for 48.0 ± 14.5 months. Daily CPAP usage in the CPAP group was 4.1 ± 1.9 h. AHI decreased from baseline to end-of-study in both CPAP and UC groups (-5.0(-12.5,2.0), P=0.000; -4.0(-12.5,1.5), P=0.007, respectively), with no between-group difference (P=0.453). Similarly, there was no between-group difference in change in ODI (CPAP vs UC, P=0.851). There was an improvement in nadir SpO2 from baseline to end-of-study in the CPAP but not UC group ($2.3\%\pm6.1\%$, P=0.011 and $-0.7\%\pm7.6\%$, P=0.511, respectively; between-group difference P=0.032). Conclusion: Long-term CPAP use in patients with comorbid OSA and cardiovascular disease did not result in clinically significant changes in AHI or ODI, but showed a small positive effect on nadir SpO2. Keywords

Angiotensin–(1–7) rescues chronic intermittent hypoxia–aggravated TGF–β –mediated airway remodeling in murine and cellular models of asthma.

Jianping Zhou,Qingyun Li

Ruijin Hospital，Shanghai Jiao Tong University，School of Medicine

Renin-angiotensin system (RAS) is involved in TGF-b–mediated epithelial-to-mesenchymal transition (EMT) and is responsible for airway remodeling in refractory asthma. Obstructive sleep apnea (OSA), which affects RAS activity, is a risk factor for refractory asthma. We aimed to investigate how chronic intermittent hypoxia (IH), the main pathophysiology of OSA, exacerbates asthma and whether Ang-(1–7) protects against chronic IH–induced airway remodeling in asthma. We exposed ovalbumin (OVA)-challenged asthma mice to chronic IH and observed that chronic IH aggravated airway inflammation and collagen deposit in OVA-challenged mice. Compared with the OVA group, the OVA + chronic IH group had a lower expression level of epithelial marker E-cadherin and higher expression levels of mesenchymal markers a-smooth muscle actin and collagen IV in airway epithelia, accompanied with activation of TGF-b/Smad pathway. These changes were reversed by the administration of Ang-(1–7). Consistently, Ang-(1–7) mitigated chronic IH–induced activation of TGF-b–mediated EMT in lipopolysaccharide-treated bronchial epithelial cells in a dose-dependent manner, which was blocked by Ang-(1–7)–specific Mas receptor antagonist A779. Taken together, Ang-(1–7) rescued chronic IH–aggravated TGF-b–mediated EMT to suppress airway remodeling, implying that RAS activity is involved in the mechanisms of OSA-related airway dysfunction in asthma. Keywords

Vertical facial types and age–related changes in adenoids and tonsils

Xin Huang,Xiaoqing Li,Xuemei Gao*

Peking University School and Hospital of Stomatology

Objective: To compare the size of adenoids and tonsils in children and adolescents with different vertical facial types. Methods: The present retrospective cross-sectional study was conducted among 378 consecutive orthodontic patients (138 boys and 240 girls, aged 3 to 18 years). Lateral cephalometric radiographs were obtained before orthodontic treatment. Standard cephalometric examinations were conducted to compare the size of adenoids and tonsils in five age groups: kindergarten, lower grades of primary school, upper grades of primary school, junior high school and senior high school. The sample were further divided into hyperdivergent group (HG) and normodivergent group (NG) according

to vertical facial types. Comparisons between HG and NG were carried out using Student's t-test. Comparisons among five age groups were examined using Student's t-test with the Bonferroni method (p < 0.0125). Results: In junior high school, adenoids in HG were significantly larger than those in NG. (p =0.007). However, there was no statistical difference in adenoids between HG and NG in other age groups and no statistical difference in tonsils at all ages. Significant reduction of adenoid size appeared in middle school in NG. By contrast, the adenoid size did not reduce until high school in HG. Tonsil size reduced in upper primary school both in HG and NG. Conclusion: Vertical facial types correlate well with adenoid size but not with tonsil size. Adenoids were larger in patients with hyperdivergent facial pattern when compared with those with normodivergent facial pattern especially in the age of junior high school. Patients with hyperdivergent facial pattern may undergo longer periods of adenoid hypertrophy. This work was supported by National Program for Multidisciplinary Cooperative Treatment on Major Diseases (PKUSSNMP-201902).

Keywords Vertical facial types, adenoids, tonsils, age.

Eosinophils are more strongly relevant to allergic sensitization than basophils in pediatric adenotonsillar hypertrophy

Juanjuan Zou1,Yan Yang1,2,Yan Wang1,2,Yanzhong Li1,2

1.Qilu Hospital of Shandong University，department of ENT

2.National health Commission，Key Laboratory of Otorhinolaryngology

Objective: The relationship between eosinophils/basophils and allergic sensitization was not clear in pediatric adenotonsillar hypertrophy（ATH）. The objective of this study is to investigate the relationship between eosinophil/basophil counts and peripheral specific IgE levels, and identify the common allergens in children with ATH. Methods: We initially screened 1,031 consecutive children who underwent adenotonsillectomy in our department from 2018 to 2019, and finally included 676 children. The eosinophil count, basophil count and levels of specific IgE were collected. Correlations between two quantitative variables were assessed using the Pearson or Spearman coefficient. Logistic regression analyses were performed to evaluate the odds ratios (ORs) for atopy after controlling for age, sex, vitamin D, BMI and visiting season. Results: Both the eosinophil and basophil counts in atopic participants were significantly higher compared to non-atopic participants. The eosinophil count correlated with the levels of IgE specific to all allergens, and eosinophilia was independently associated with all tested atopy allergens other than atopy to dander after multivariate adjustment. Additionally, the basophil count correlated with the IgE levels specific to A. alternate and food mix, and basophilia was still significantly associated with atopy to food mix after multivariable adjustment. Furthermore, among allergic participants, D. farina was the most prevalent allergen, followed by food mix, D. pteronys sinus and A. alternata. Conclusion: In conclusion, eosinophils were more relevant to allergic sensitization than basophils, with eosinophils being significantly associated

with all tested atopy allergens apart from dander, and basophils being associated with atopy to food mix. Furthermore, D. farinae was the most prevalent allergen and may be indicative of desensitization therapy.
Keywords

Study of Nasal Continuous Positive Airway Pressure on Cognitive Dysfunction and Multimodal Brain Magnetic Resonance Changes in Patients with Severe OSAHS

Qun Lv,Qinxia Zhang

The Affiliated Hospital of Hangzhou Normal University

Objective: This study was to observe the effect of nasal continuous positive airway pressure (nCPAP)on improving cognitive function in patients with OSAHS based on ReHo index of rs-fMRI, and to observe its clinical efficacy combined with cognitive function assessment scale. Methods: 20 patients with severe OSAHS diagnosed by PSG and 20 healthy adults were included. MoCA, ESS and rs-fMRI were performed before treatment in both groups. The patients with severe OSAHS received nCPAP treatment for more than 4 hours per night for 3 months, and then received PSG examination, scale evaluation and rs-fMRI scanning again. Results: Compared with healthy control group, the MoCA score of OSAHS group before treatment was significantly lower, and negatively correlated with AHI and ODI. The ESS score of OSAHS group before treatment was significantly higher, and positively correlated with AHI and ODI. After 3 months of nCPAP treatment, ESS score of OSAHS group was significantly lower than that before treatment, MoCA score was significantly higher than that before treatment, especially in visual space and executive function, attention, language, delayed recall. (2) ReHo value: Compared with healthy control group, the ReHo value in right angular gyrus, precuneus and left parahippocompalgyrus, middle frontal gyrus of OSAHS group decreased, and the ReHo value in right posterior cerebellar lobe increased. After 3 months of nCPAP treatment, the right precuneus, temporal lobe, posterior cingulate gyrus and left limbic lobe increased in OSAHS group. (3) ReHo value of right posterior cerebellar lobe was positively correlated with MoCA score in OSAHS group and healthy control group. ReHo value of right precuneus was positively correlated with AHI and negatively correlated with MoCA score in OSAHS group before and after nCPAP treatment. Conclusion: Patients with severe OSAHS generally have cognitive dysfunction, and the structure and function of several brain regions have abnormal changes. After 3 months of nCPAP intervention, the cognitive function of patients with severe OSAHS was significantly improved, and increase of Reho in some brain regions was closely related to the severity of the disease and the improvement of cognitive function.
Keywords

Lactobacillus rhamnosus GG improves sleep deprivation induced– intestinal barrier dysfunction

Xiaoqi Pang,Bingqian Zhou,Bangmao Wang,Hailong Cao

General Hospital of Tianjin Medical University

Background /Objectives: Sleep deprivation (SD) is a serious and worldwide health hazard. Along with research going deep, microbiota-gut-brain axis has emerged as a key of psychological and intestinal diseases. Sleep deprivation is inextricably linked to gut microbiota disorder, even intestinal diseases. Here we aimed at identifying probiotic could improve sleep deprivation induced-intestinal barrier dysfunction. Methods: Heat-killed/live Lactobacillus rhamnosus GG (LGG) was supplemented to adult C57BL/6 male mice subjected to sleep deprivation stress, while the control group and the sleep deprivation group underwent PBS gavage as contrasts. All mice were given PBS or heat-killed/live LGG for 10 consecutive days, and continuous sleep deprivation by using a modified multiple platform water bath for the last 3 days. Behavioral tests were applied to measure anxiety-like behavior after SD. Gut microbiota, structural and functional integrity of the gastrointestinal barrier were investigated. We further assayed the impact of SD on a host function by evaluating inflammation and anti-oxidation action. Results: SD induced microbial dysbiosis as noted by significant perturbations in Firmicutes/Bacteroidetes ratio, alpha- and beta-diversity were significantly altered. Furthermore, both heat-killed and live LGG increased the number of goblet cells and Muc2 positive cells in villi. Additional changes were noted that live-LGG decreased the elevation in serum levels of inflammatory cytokines, and increased the expression of targets associated with the intestinal barrier. We also observed an increase of antioxidant ability in SD mice receiving live-LGG. The results of behavioral tests showed that live-LGG had no effect in the elevated plus maze, but significantly improved motor activity in the open field test after sleep deprivation. Conclusions: LGG could improve sleep deprivation induced-intestinal barrier dysfunction via regulating gut microbiota, providing a better understanding of microbiota-gut-brain axis.

Keywords sleep deprivation, Lactobacillus rhamnosus GG, intestinal barrier, brain-gut axis, gut microbiota

Clinical Subtypes of Chinese with Obstructive Sleep Apnea: a cluster analysis

Jingjing Guo,Fang Han,Chi Zhang,Liyue Xu,Xiaosong Dong,Chenyang Li

Peking University People's Hospital

Objective: To cluster Chinese with obstructive sleep apnea (OSA) based on clinical symptoms. Methods: Using data of 927 patients with mild to severe OSA (apnea-hypopnea index [AHI] >5 events per hour) recruited from the Department of Respiratory & Critical Care Medicine Peking University People's

Hospital, we performed a latent class analysis based on 18-item self-reported symptom variables and 3 kinds of comorbidities. The optimal clustering number was defined based on the minimal bayesian information criterion (BIC) value. Results: The optimal cluster number among all OSAHS patients was 6, the 6 clusters can be defined as"lack of typical symptom","minimal symptom","excessive sleepiness","disturbed sleep","upper airway symptoms dominant"and"sleepiness with disturbed sleep". Both 4 and 5 clusters solutions are optimal for clustering patients with moderate to severe OSAHS (n=713). (labeled as disturbed sleep, minimal symptoms, excessive sleepiness with upper airway symptoms, upper airway symptoms dominant and sleepiness dominant). We additionally performed cluster analysis in the mild OSAHS population (n=259). 3 clusters were identified, which were labeled as"minimal symptom","sleepiness with insomnia","upper airway symptoms dominant". Conclusions: The clinical symptom subtypes of OSAHS in Chinese population are similar with those of Caucasians which were reported by research before. Clusters exist in mild OSAHS as well.

Keywords Chinese population, obstructive sleep apnea, disease subtypes, latent cluster analysis

Clinical case of late–onset central hypoventilation with hypothalamus dysfunction: further consideration of ventilation support in ROHHAD syndrome

Rui Zhao1,Xiaosong Dong1,Yinghui Gao2,Fang Han1

1 Department of Pulmonary and Critical Care Medicine，Peking University Peoples'Hospital，Beijing，China.

2. PKU-UPenn Sleep Center，Peking University International Hospital，Beijing，China

Objective: Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) is a rare but life-threatening disorder in childhood. Here we firstly reported 2 cases of Chinese children with ROHHAD and more than 5-years follow-up. Case presentation: Case 1: A 5-year-old girl was suspected of ROHHAD with rapid weight gain, breathing cessation, hypoventilation, central hypothyroidism, hyperprolactinemia, decreased height velocity and negative PHOX2B sequencing results. The presented symptoms, laboratory and sleep-related findings met the diagnostic criteria of ROHHAD syndrome. During the 5 years'follow-up, with progressive deterioration to the respiratory center, hypoxemia (PO2 below 60mmHg) and hypercapia (TcPCO2 above 50 mmHg) still appeared in the N3 sleep stage with poor response to the ventilation. Case 2: A 5-year-old Chinese boy was admitted with rapid-onset obesity, daytime sleepiness, snore, and syncope after dyspnea and cyanosis, he was diagnosed obstructive sleep apnea hypopnea with his first admission. The patients suffered tonsillectomy and start BiPAP ventilation. When he was twelve, his dyspnea and cyanosis deteriorated after pneumonia infection and accompanied with frequent central sleep apnea. A brain magnetic resonance imaging was performed to demonstrate the evidence of giant medullary glioma (2.2*5.5cm). PHOX2B mutation was not found. The boy was diagnosed with

ROHHADNET syndrome, however, his progressively enlarged tumor prevented him from surgery and finally occur sudden death at night after an upper airway infection. Discussion: For ROHHAD, early recognition, application of noninvasive ventilation, regular follow up including PSG, TcPCO2 test, and titration will help improvement of the quality of life and the outcomes. Brain MRI is crucial for child presenting central sleep apnea/hypopnea. Successful management of these patients requires multidisciplinary care.

Keywords Child, ROHHAD syndrome, Sleep disordered breathing, Nocturnal hypoventilation, PHOX2B

The Prevalence of Sleep Apnea in Different Ethnic People of the Karamay Community

Qinglong Zhang1,Xuelong Jiang1,Dongmei Chen1,Min Li1,Juan Shi1,Zhongming He1,Fang Han1,2

1.Karamay Central Hospital of Xinjiang

2.Peking University People's Hospital

Objective: To investigate the prevalence of sleep-apnea of Han, Uygur and Kazak people in Karamay City community. Methods: During the period from Jan 2016 to Sep 2019, 2722 people were included in the sleep center of Karamay Central Hospital, respiration and pulse oximeter was performed, 1745 males and 977 females were involved., including 2062 of Han people, 564 of Uygur, and 96 of Kazakh, with the average age is 54 ± 14 years. And Han were 54 ± 14 years, Uygur were 54 ± 12 years, Kazakh were 52 ± 11 years, all the people completed the Berlin Questionnaire and Sleepiness Scale. The physical examination included height, weight, neck circumference,abdominal circumference. . Apnea-hypopnea index (AHI), the mean nocturnal oxygen saturation (MSaO2%), the nadir oxygen saturation (LSaO2) and the number of desaturations >4%per hour (ODl4) were calculated. Results: old, gender were matched among Han, Uygur and Kazakh people, the Body mass index [(26.6 ± 3.9) kg/m2 vs (28.7 ± 4.6) kg/m2 versus $29.0\pm4.2)$ kg/m2], abdominal circumference [(95 ± 20)cm versus (100 ± 13) cm versus (101 ± 11)], the number of desaturations $\geq$ 4% per hour (ODI4) [(16.2 ± 15.7)/h vs (12.4 ± 10.1) /h versus (11.7 ± 10.5) /h], the lowest SaO2 (LSaO2%) [(79.8 ± 10.5)% vs (81.9 ± 8.7)% vs (82.7 ± 9.1)%,] respiratory disorder index(RDI) [(21.7 ± 19.0)/h versus (16.4 ± 15.8) /h versus (14.9 ± 14.7) /h],and apnea index [(16.6 ± 10.9) /h versus (11.4 ± 5.3) /h versus (11.8 ± 5.5) /h] were significantly different (P<0.05). According to the apnea index $\geq$10 /h, the prevalence of sleep Apnea-hypopnea in Han,Uygur and Kazakh populations were 57.8% (1162/2722) versus 13.0% (229/2722) versus 2.1% (35/2722) respectively. The prevalence of sleep apnea in male and female were 38.0% (1035/2722) versus 14.4% (391/2722) respectively (P<0.05). Conclusion: There are difference that the prevalence of sleep-apnea among HAN, Uygur and Kazakh, Han people were higher than Uygur and kazakh, Uygur were higher than Kazakh, males were higher than females.

Keywords

Long sleep duration and unusual apnea–hypopnea index associated with mild cognitive impairment in older adults: a population–based study

Shi Tang,Rui Liu,Yifeng Du

Shandong Provincial Hospital

Objective: We sought to characterize the association between sleep structure and mild cognitive impairment among rural-dwelling older adults in China. Methods: This population-based study included 2141 participants (age ≥60 years, 54.7% women) in rural China. In March 2018-November 2019, data were collected via face-to-face interviews, clinical examinations, and psychological test. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), and the complete cardiopulmonary coupling (CPC) analysis. Cognitive function was evaluated using a comprehensive neuropsychological test battery. Cognitive impairment was defined as mild cognitive impairment (MCI) according to the DSM-IV criteria. Data were analyzed using logistic regression models. Results: Of the 2141 participants, 538 were defined with cognitive impairment. compared to the 1573 controls with normal, had more less deep and rapid eyes movement (REM) sleep, as well as higher intrasleep wake, and higher sleepiness scores. In the logistic regression analysis after adjustments for confounding variables, long sleep duration (total sleep time>8h), excessive daytime sleepiness (ESS>10 scores), and unusual apnea hypopnea index (AHI) were independently associated with MCI. Conclusions: Cognitive impairment in older adults is associated with excessive daytime sleepiness and sleep disordered breathing.
Keywords

Ring pulse oximeter for screening obstructive sleep apnea syndrome (OSAS): A novel wearable sleep apnea testing system

Rui Zhao,Jianbo Xue,Xiaosong Dong,Bing Zhou,Zhancheng Gao,Fang Han

Peking University Peoples' Hospital

Objective: A novel ring pulseoximetry (MegaRing) was designed focusing on photoplethysmography, automated signal processing in oxygen desaturation and sleep/wake analysis. This study aimed to evaluate the ability of MegaRing to diagnose obstructive sleep apnea in Chinese adults. Methods：201 Chinese Han subjects were recruited, with 69.7% males, mean age 48.3±15.1 years, mean BMI 27.5±4.7 kg/m2 and mean AHI 27.1±23.9 events/h. All participants underwent simultaneously polysomnography (PSG) and MegaRing testing in the sleep lab. Sleep duration, oxygen desaturation index(ODI), mean oxygen saturation(MSpO2), and saturation impair time below 90% (SIT90) were derived from an automated

algorithm of the MegaRing and manually scored PSG. The Ring_ODI3 is calculated as total 3% oxygen desaturation events*60/ total analyzed time in minutes. Results: The total sleep time (TST) derived from PSG had no significant difference with the total analyzed time (TAT) calculated from MegaRing, 388.6±64.5 vs 386.9±69.4 minutes (P=0.761). The ODI3 was 23.3±23.4 events/h on PSG and 20.4±21.8 events/h on MegaRing (P<0.0001), with an intraclass correlation coefficient(ICC) of 0.901. SIT90 and Mean heart rate between two methods had no statistical difference, and MSpO2 level of MegaRing was slightly higher than PSG, 95.3%(94.1%-96.6%) vs 95.0%(93.0%-96.0%), P<0.0001. When evaluating the validity of MegaRing as a diagnostic tool for screening OSA patients, Ring_ODI3 had a strong correlation (r=0.905, p<0.0001) and close agreement with PSG_AHI (Bland-Altman analysis: Mean Difference 6.7, 95%CI -13.2 to 26.6 events/h). Using a threshold of AHI ≥5 events/h, the ring pulse oximeter can reach 82.8% sensitivity, 84.4% specificity, 0.907 area under the curve (AUC). Conclusion: This ring pulse oximetry can detect OSAS with reasonable reliability. The system is a reliable and comfortable choice for OSAS screening test.

Keywords obstructive sleep apnea syndrome, pulse oximetry, polysomnogram; home sleep apnea test

Loss of dorsolateral nigral hyperintensity on 3.0T MRI and its correlation with motor function in idiopathic rapid eye movement sleep disorder

BingXin Song1,Xuan Zhang2,JingYi Ye1,YaQin Huang1,Rong Xue1
1.Tianjin Medical University General Hospital
2.Tianjin Medical University General Hospital Airport Site

Background:Idiopathic rapid eye movement sleep disorder (iRBD) is not an isolated clinical disease due to the high risk of transforming into α-synuclein diseases, such as Parkinson's disease (PD), Dementia with Lewy Bodies (DLB) and Multiple System Atrophy (MSA). As a result of the high incidence of PD，iRBD mainly converts to PD. Before the appearance of motor symptoms, the neuron degeneration of nigrosome-1 in PD already existed and manifested as the "swallow tail sign" disappearing in Susceptibility weighted imaging（SWI）. Studies have confirmed that patients with iRBD presented substantia nigra-striatum lesion and motor function decline. Objective: We aimed to qualitatively analyze the findings of the disappearance of dorsolateral nigral hyperintensity（DNH）in patients as the degeneration of nigrosome-1 with iRBD by tSWI、SWI and T2* sequence of 3.0T MRI, and to analyze the correlation of this imaging with the motor function of iRBD. Methods: 29 iRBD patients and 28 healthy volunteers were included and taken 3.0 T MRI. We collected their basic information and motor function scores, including the Unified Parkinson's disease Rating Scale part III (MDS-UPDRSIII) score, the alternate tapping test, 3-Metre Timed-Up-and-Go test and Flamingo balance test. Results: The dorsolateral nigral hyperintensity（DNH）disappeared in about 63% (12/29) iRBD patients, of which 4 cases were unilateral defect and 8

cases were bilateral defect. The proportion was significantly higher than the HC group(P<0.05).In the iRBD group, subjects with disappearance of DNH scored lower in the alternate tapping test than subjects with DNH (P<0.05). Conclusion: iRBD patients had a higher incidence of DNH Loss on tSWI sequence and SWI sequence、T2*WI sequence,which may be related to the loss of dopaminergic neurons and iron deposition of nigrosome-1.Loss of DNH may reflect the decrease of motor function in iRBD patients.

Keywords Idiopathic Rapid-eye-movement sleep Behavior Disorder ,dorsolateral nigral hyperintensity

Comparison of cephalometric measurements between simple snoring and obstructive sleep apnea: a retrospective study

Yanlong Chen,Liping Huang,Xuemei Gao

Department of Orthodontics，Peking University School and Hospital of Stomatology

Background: Snoring and obstructive sleep apnea (OSA) are defined as two different severity kinds of sleep disordered breathing (SDB). Currently, the data concerning the craniofacial characteristics of subjects who snore but do not exhibit OSA are limited. The study aimed to compare the differences of craniofacial and pharyngeal anatomy between groups of OSA and snoring subjects. Methods: A total of 51 patients (30 males, 21 females) were enrolled in this study. There were 34 patients (20 males, 14 females) in the OSA group, with an average age of 42.18 ± 10.37 year, body mass index (BMI) as 24.49 ± 2.81 kg/m2 and apnea-hypopnea index (AHI) as 25.65 ± 16.36 /h. The snoring group was matched with OSA group by age, gender and BMI, which included 17 patients (10 males, 7 females) with the average age, BMI, AHI of 42.29 ± 11.04 year, 24.49 ± 2.81 kg/m2, 1.75 ± 1.47 /h, respectively. All participants undergone overnight polysomnography (PSG) and lateral cephalograms. Differences of craniofacial structure, upper airway and its surrounding tissues between two groups were then evaluated. Paired T-test was practiced on all coordinates we collected and a two-sided p-value of <0.05 was considered to be statistically significant. Results: The OSA group showed smaller bony nasopharynx (PNS-R: 21.44 ± 2.62 vs 23.14 ± 2.30, P = 0.034) and lower hyoid position (H-MP:17.28 ± 5.30 vs 13.73 ± 6.45, P = 0.041). Pearson correlation showed that AHI was negatively correlated with posterior airway space (PAS) and mandible length (MAN) and positively correlated with hyoid position(H-MP). Multiple linear regression results showed that after adjusting for confounding factors, AHI was correlated with PAS (β = -0.427, t = -3.635, P = 0.001) and H-MP (β = 0.415, t = 3.533, P = 0.001). Conclusions: While the cephalometric measurements of snoring patients resembled those with OSA, some differences in soft tissue and hyoid orientation were apparent. OSA subjects may demonstrate a gradation trend in the size of the airway and its associated structures.

Keywords

A preliminary study of coronary vascular remodeling in patients with obstructive sleep apnea–hypopnea syndrome and coronary heart disease

Min Xu1,Huai De1,2,Ben Shan1

1.The Affiliated Huaian Hospital of Xuzhou Medical University

2.Department of E.N.T，the Affiliated Huaian Hospital of Xuzhou Medical University

Objective: To investigate the characteristics of left anterior descending coronary artery remodeling in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) and coronary heart disease. Methods: The clinical data of 40 patients with OSAHS and coronary heart disease (CHD) treated in our hospital from February 2014 to October 2018 were analyzed retrospectively. All patients underwent high-resolution coronary CT angiography. According to the remodeling index, the patients were divided into positive remodeling (PR) and negative remodeling (NR) groups. The quantitative indexes of blood vessels and plaques and the characteristics of vascular lesions were compared between the two groups. Results: The area of the narrowest wall, the area of plaque and the maximum thickness of plaque in PR group were higher than those in NR group (P＜ 0.05). The proportion of plaque roughness and slightly low density soft plaque in PR group was significantly higher than that in NR group (P＜ 0.05), but there was no significant difference in stenosis rate between the two groups (P＞ 0.05). Conclusion: Plaque characteristics of positive remodeling of the left anterior descending branch in patients with OSAHS are associated with coronary heart disease, which may indicate that this type of plaque has a higher risk and need more attention from clinicians. Keywords

Comprehensive treatment of moderate and severe OSAHS with low temperature plasma radiofrequency assisted multi plane simultaneous operation of upper airway

De Huai1,Min Yin2,Xilong Zhang3,Jing Shang1,Min Xu4

1.Affiliated Huai'an Hospital of Xuzhou Medical University and Huai'an Second People's Hospital

2.Department of Otorhinolaryngology，the First Affiliated Hospital of Nanjing Medical University

3.Department of Respiratory Diseases the First Affiliated Hospital of Nanjing Medical University

4.Department of Radiology，Affiliated Huai'an Hospital of Xuzhou Medical University and Huai'an Second People's Hospital

Objective   To explore clinical effect and application value of modified UPPP with low-temperature plasma and selective nasal cavity vasodilatation with tongue volume reduction for OSAHS. Methods   A

retrospective analysis was made on clinical data of 184 patients with serious OSAHS in the nose throat department of Huai'an Second People's Hospital from June 2014 to March 2018. These patients were divided into two groups according to surgery methods, observation group [y1] and control group, each of 92 patients. The patients in observation group accepted modified UPPP with low-temperature plasma and selective nasal cavity vasodilatation with tongue root volume reduction on the basis of fully preparation for surgery, while the patients in the control group accepted normal treatment. The clinical effect, operative complications, postoperative relapse and other indexes of the two groups were compared. Result   After 6 months of follow-up, the general effective rate of the observation group and control groups were 83.7% and 65.2% respectively, the difference was statistically significant（$p<0.05$）. Besides, the complication occurrence rate of observation group is also lower than that of control group. Conclusion   The effect of modified UPPP with low-temperature plasma and selective nasal cavity vasodilatation with tongue volume reduction is satisfactory for patients with moderate and severe OSAHS after enough preparation. So it is valuable to advocate clinically. However, more than one year's long-term efficiency needs to be further observed! For the severe OSAHS of IV type and all upper airway obstruction,it is still suggested that CPAP is the main comprehensive treatment, and if the CPAP cannot be tolerated, and the staging operation is more appropriate.

Keywords

Characteristics of attentional network in children with sleep disordered breathing

Yunxiao Wu1,Yan Wang2,Changming Wang3,Rui Song2,Dandi Ma1,Yuanjie Zhang1,Li Zheng1,Zhifei Xu1,Xin Ni1

1.Beijing Children's Hospital，Capital Medical University

2.Institute of Psychology，CAS

3.Xuanwu Hospital，Capital Medical University

Objective: To evaluate the attentional network function in children with sleep-disordered breathing and to identify related factors of attentional function. Methods: This was an observational study. Children with habitual snoring admitted to the Sleep Center, Beijing Children's Hospital were recruited to this study between May 2020 to December 2020. All children aged 6-10 years old and of them 45 were boys and 18 were girls. All subjects underwent an overnight polysomnography (PSG), as well as Attention Deficit Hyperactivity Disorder (ADHD) Diagnostic Scale and an attentional network test adapted to children (child-ANT). All subjects were grouped into primary snoring (20 cases), mild (22 cases) and moderate-to-severe OSA (21 cases) group according to the obstructive sleep apnea hypopnea index (OAHI). Results: In total, 63 children were included in the analysis. There were no significant differences in age, gender or body mass index among PS, mild and moderate-to-severe OSA group (all P >0.05). The score for group B items of

ADHD Diagnostic Scale of moderate-to-severe OSA group were significantly higher than those of PS (P<0.05) and mild OSA group (P<0.01). The efficiency of alerting network was higher and the efficiency of orienting network was lower in the mild OSA group than those in healthy control group (P=0.011, 0.032). Compared with healthy control group, moderate-to-severe OSA group had lower efficiency of executive control network (P=0.017). The efficiency of executive control network was significantly correlated with mean oxygen saturation (r=-0.317, P=0.011). Conclusions: The function of attentional network was impaired in children with sleep-disordered breathing. Children with mild OSA mainly showed excessive activation of alerting network and reduced efficiency of orienting network. Children with moderate-to-severe OSA mainly showed decreased efficiency of executive control network. Hypoxia may be the main risk factor of attention function. Keywords

The establishment and application of a follow–up system for the CPAP intervention＇s impact on OSAHS patients＇ cognitive function based on REDCap

Chenyang Li,Huajun Xu,Xinyi Li,Hongliang Yi,Jian Guan,Haibo Shi,Shankai Yin
Shanghai Sixth People＇s Hospital

Objective: To explore the clinical application of the REDCap database in the follow-up system of continuous positive airway pressure (CPAP) on the cognitive function of patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). Methods: We constructed a follow-up system for the CPAP intervention impact on OSAHS patients＇ cognitive function based on the REDCap database and collected basic information, medical history, PSG, MoCA test, MMSE test, neurobehavioral test, MRS, fMRI, behavioral test and other information for each subject at four time points (initial enrollment, first month, sixth months and twelfth months). We summarized the usage of this follow-up system in our hospital＇s Otorhinolaryngology-Head and Neck Surgery Department from January 2020 to March 2021. Results: The follow-up system could achieve subject＇s electronic data collection, multi-user and multi-site information entry, data screening, data export and analysis, quality control and permission setting, construction of follow-up calendar, etc. 74 OSAHS patients under CPAP intervention and 74 OSAHS patients without CPAP intervention were enrolled for a randomized controlled study and their data was collected by this system. Conclusions: The establishment of the follow-up system for the CPAP intervention impact on OSAHS patients＇ cognitive function based on the REDcap database supports the project management. Its easy tracking management and maintenance could provide a convenient, efficient, safe and standardized data management tool for medical researchers to carry out related investigations and research.
Keywords

Moderating Effect of BMI on the Relationship between Sympathetic Activation and Blood Pressure in Males with Obstructive Sleep Apnea

Baixin Chen1,2,Yun Li1,2

1.Shantou University Medical College

2. Shantou University Mental Health Center，Shantou University

Background: Sympathetic activation is a primary mechanism mediating increased blood pressure (BP) in obstructive sleep apnea (OSA). However, the relationships between overweight/obesity, sympathetic activation and BP in OSA are not well-understood. We hypothesized that increased sympathetic drive is associated with increased BP in normal weight, but not in overweight/obese males with OSA. We therefore examined the effects of body mass index (BMI) on the association between sympathetic activation and BP in males with OSA. Methods: We studied 115 males with OSA recruited consecutively from clinic. Twenty-four-hour urinary norepinephrine was used to assess sympathetic activation. Blood pressure was measured both in the evening and in the morning. Hypertension was defined based on either BP measurements or an existing diagnosis. Linear and logistic regressions were conducted to examine the associations between sympathetic activation and both BP and risk of hypertension. Results: We found that 24-hour urinary norepinephrine levels were associated with systolic and diastolic BP (SBP, β =0.157, p=0.082; DBP, β =0.212, p=0.023) and mean arterial pressure (MAP, β =0.198, p=0.032) after adjusting for confounders. Interestingly, these associations were modified by overweight/obesity. After adjusting for confounders, increased 24-hour urinary norepinephrine levels were significantly associated with elevated SBP (β =0.454, p=0.012), DBP (β =0.399, p=0.041), and MAP (β =0.432, p=0.023) in normal weight, but not in overweight/obese patients (all p>0.2). Similar findings were observed in the associations between 24-hour urinary norepinephrine levels and hypertension. Conclusion: Sympathetic activation is associated with elevated BP in normal weight but not in overweight/obese males with OSA, suggesting that BMI may moderate the association between sympathetic activation and BP in males with OSA.

Keywords Obesity; Overweight; Sympathetic Activation; Blood Pressure; Hypertension; Obstructive Sleep Apnea

Impact of dual orexin receptors antagonist on mice behaviors and depression in chronic intermittent hypoxia conditions

Qinhan Wu
Zhongshan Hospital，Fudan University

Obstructive sleep apnea (OSA) is a increasingly prevalent sleep disorder characterized by recurrent episodes of decreased or absent inspiratory airflow during sleep, resulting in chronic intermittent hypoxia (CIH). Psychological and personality changes are often reported in patients with OSA. Orexin produced in lateral hypothalamus (LH) are implicated in obesity, locomotor and anxio-depression. To analysis the impact of CIH and orexinergic neuro system on behaviors, C57BL/6 mice were exposed to chronic intermittent hypoxia (CIH) for 3 weeks to resemble OSA, and suvorexant was applied as dual orexin receptors antagonist. Orexin level in LH was measured by radio-immunofluorescence analysis. Tail suspension test, forced swimming test, and sucrose preference test were used to assess depression in mice. HomeCage Scan was used to analysis nocturnal activities of mice. Factor analysis was used to separate the 28 activities into meaningful groups. Our analysis indicated that CIH downregulated the expression of orexin A in LH of mice, and suvorexant aggravated the decrease of orexin A. The immobility time of tail suspension test and forced swimming test was prolonged after CIH treatment. Percentage of sucrose preference was decreased by CIH. The administration of suvorexant reversed the extension of immobility time and the decrease of sucrose preference percentage induced by CIH. CIH increased the frequency of most nocturnal activities during wake period, especially high and moderate physical activity, while decreased the frequency of eating. Suvorexant partially reversed the increase of physical activities induced by CIH, while aggravate the decrease of eating behavior. In conclusion, CIH induces depression and increase nocturnal physical activities in mice, and suvorexant, a dual orexin receptors antagonist, could reverse these changes induced by CIH. CIH could inhibit eating behavior of mice, and the inhibition was probably achieved through the inhibition of the orexinergic neuro system.
Keywords

Compromised Dynamic Cerebral Autoregulation in Patients with Central Disorders of Hypersomnolence

Yanan Zhang,Fang Deng,Ran Zhang,Qi Tang,Zan Wang,Yi Yang
The first hospital of Jilin University

Objective: We aimed to investigate the dynamic cerebral autoregulation (dCA) in patients with central disorders of hypersomnolence during wakefulness. Methods: Thirty-six patients with central disorders of hypersomnolence were divided into three groups according to polysomnography and multiple sleep latency

test results: the idiopathic hypersomnia group (IH), narcolepsy type 1 without rapid-eye-movement sleep behavior disorder group (NT1-RBD), and narcolepsy type 1 with rapid-eye-movement sleep behavior disorder group (NT1+RBD), with 12 patients in each group. Twelve sex- and age-matched healthy controls were recruited. We assessed the Epworth sleepiness scale (ESS) and dCA of all subjects. dCA was assessed by analyzing the phase difference (PD) using transfer function analysis. The ESS and dCA were analyzed before and after standardized treatment in 24 patients with narcolepsy type 1. Results: The overall PD of the IH, NT1-RBD, and NT1+RBD groups were lower than that of the control group (P <0.001). There were no significant differences of the overall PD between the NT1-RBD and NT1+RBD group (P >0.05). The ESS scores decreased and the overall PD increased after treatment in 24 patients with narcolepsy type 1 (P < 0.001). Multivariable analysis showed that mean sleep latency in multiple sleep latency tests was independently associated with impaired overall PD (P < 0.05). Conclusions: The dCA is impaired in patients with central disorders of hypersomnolence. The impairment of dCA occurs irrespective of NT1-RBD/+RBD. The ESS score and dCA improved in patients with narcolepsy type 1 after medication treatment. The mean sleep latency in multiple sleep latency test was independently associated with impaired dCA.
Keywords

Effectiveness of inhalation therapy with Taxus chinensis sustained release granules in Chronic Insomnia Disorder

Zan Wang,Jiannan Zhu,Qingqing Sun,Yudan Lv,Jie Zhu
the first hospital of Jilin University

Objective: To evaluate the sleep quality of patients with chronic insomnia disorder before and after inhalation therapy with Taxus chinensis sustained release granules (TCSRG), and to explore the effect of inhaling TCSRG on chronic insomnia disorder (CID). Methods: Twenty patients with CID were required to record their sleep diary, and to fill in Pittsburgh sleep quality index (PSQI) scale and the insomnia severity index (ISI) scale. Besides, patients were performed polysomnography (PSG) before and after inhalation therapy with TCSRG. The changes of total sleep time, sleep latency and efficiency, and wake after sleep onset (WASO) in a diary as well as scores of PSQI scale and ISI scale were compared before and after treatment by TCSRG. In addition, the alterations of sleep parameters in PSG including sleep latency and microarousal index were monitored before and after treatment. Results: Compared with before treatment, the sleep latency and WASO were significantly shortened after treatment, and the total sleep time was longer. Furthermore, the total scores of PSQI and ISI after treatment were significantly reduced after treatment. PSG results showed that the sleep latency and microarousal index after treatment were significantly reduced. Conclusions：Inhalation of TCSRG improved the subjective sleep quality and insomnia symptoms of patients with CID. However, due to some limitations of the study, Further studies are vital to confirm the effectiveness of TCSRG in a large sample.
Keywords

Application of Sleep Disorders patients：based on arterial spin labeling imaging and 23Na MRI

Jiao Jiang1,2,Ying Li2

1.Dalian Medical University

2.Xingcheng People's Hospital

Objective: Patients with sleep disorders(SD) have high rates of comorbid white matter lesions (WMLs) with different stages, which are attributed to cerebral small vessel disease. This study aimed to evaluate the WM TSC and WM CBF in patients with sleep disorders and to explore the correlation of the TSC and CBF with the extent of small vessel disease. Methods：From January 2017 to December 2020, 41 subjects with SD were recruited in the Department of Neurology, SuBei Hospital. Sociodemographic data were collected at baseline. All subjects were assessed by Mini-Mental State Examination (MMSE). Besides, they underwent magnetic resonance imaging (MRI) and were measured the relative blood flow in 116 brain regions quantitatively by using 3D-ASL and 3D-23NaMRI technology. Fazekas white matter scale was used to evaluate the periventricular and deep white matter lesions, which range from mild to severe CBF and TSC values of 116 brain regions were analyzed by MRICRON post-processing software. Statistical significance was tested by the Student t-test. Results: For patients with Fazekas grade I (n = 21) and Fazekas grade II/III (n = 20), there were no statistically significant differences in baseline data. There was a positive correlation between the TSC in WM and the Fazekas grade(r = 0.48, p < 0.001). There was a negative correlation between the CBF in WM and the Fazekas grade (p < 0.05). Conclusion: ASL and 23Na MRI parameters can observe 116 cerebral perfusion blood flow and tissue sodium concentration changes. In addition, CBF and TSC of SD patients may be neuroimaging markers to detect and monitor progression in the future.
Keywords

A CBCT study of hyoid bone position in different age females

Wanxin Zhang,Xuemei Gao

Peking University School and Hospital of Stomatology

Objective: To investigate the differences of the hyoid bone position in different age females. Methods: Thirty-four adult female outpatients who underwent large-field CBCT scans at Peking University Hospital of Stomatology since October 2015 were included. The patients were divided into a young group (n=12,18 to 29 years), a middle-aged group (n=12,50 to 59 years), and an older group (n=10,≥70 years). Dolphin 11.95 (Patterson Dental Supply Inc, Chatsworth, Calif) was used to axially determine the three-dimensional CBCT images of all patients, the sagittal (H-sagittal) and vertical (H-vertical) distances of the uppermost anterior point of the hyoid bone (H-point) from the point of the pterygoid saddle (S-point) were measured

in the median sagittal plane for the three groups. A one-way ANOVA was used to compare the H-sagittal and H-vertical in the three groups and a difference of P<0.05 was considered statistically significant. A linear regression analysis was performed on the position of the hyoid bone in the different age groups. Results: H-sagittal were statistically significant among the three groups (p=0.012), while H-vertical were not (p=0.641). Linear regression of hyoid bone position across age groups revealed that the sagittal distance of hyoid increased progressively with age (r=0.488, p=0.003), while there was no significant change in vertical position (r=0.092, p=0.604). Conclusion: The sagittal distance of the uppermost anterior point of the hyoid bone from the point of the pterygoid saddle increased with age in adult females, while the vertical distance did not change significantly.

Keywords

Effects of sleep structure in children with obstructive sleep apnea hypopnea syndrome

Yuqing Wang,Yaxuan Geng, Xueyun Xu,Yanyu He,Yuting Jiang, Meng Lv,Zhihui Wang

Children's Hospital of Soochow University

Objectives: To explore the characteristics of sleep structures of children with obstructive sleep apnea hypopnea syndrome (OSAHS). Methods: Children who had visited the outpatient department of respiratory in Children's Hospital of Soochow University for symptoms such as "snoring during sleep and/or mouth breathing" were enrolled. Polysomnography (PSG) was completed. Results: A total of 607 cases were included in this study. There were 133 children (21.9%) in the OSAHS group and 474 (78.1%) children in the PS group. Compared with PS group in sleep structure, the proportion of N1 stage, respiratory-related micro arousal index, spontaneous micro arousal index, and micro arousal index in REM stage were higher among the OSAHS group, while the proportion of N2 stage was lower. Compared with the school-age children with OSAHS in sleep structure, it showed that TST, sleep efficiency, the proportion of N3 sleep, and the proportion of REM sleep were higher than ones in the preschool children with OSAHS, and the number of awakenings, the proportion of N2 sleep, ODI, AHI, and the respiratory-related micro arousal index were lower. TST, sleep efficiency, and spontaneous micro arousal index were negatively correlated with BMI. The proportion of N1 sleep and respiratory-related micro arousal index were positively correlated with AHI. The proportion of N1 sleep and respiratory-related micro arousal index were positively correlated with ODI. Conclusions: There are differences in sleep structures among children with OSAHS of different ages, which has a great impact on school-age children. The proportion of N1 sleep and respiratory-related micro arousal index were positively correlated with AHI and ODI. TST, sleep efficiency, and spontaneous micro arousal index were negatively correlated with BMI.

Keywords

Diagnostic accuracy of the Berlin questionnaire and therapeutic effect of nasal continuous positive airway pressure in OSAHS patients with glucose metabolic dysfunction

Linjing Gong1, Xu Wu1,Shanqun Li1

1.Zhongshan Hospital，Fudan University

2. Fudan University

Purpose: Obstructive sleep apnea-hypopnea syndrome (OSAHS) is associated with alterations in glucose metabolism. Berlin Questionnaire (BQ) is a useful tool to identify the high-risk group for OSAHS. However, its validity in patients with glucose metabolic dysfunction remains unclear. Our study aims to examine the diagnostic efficacy of BQ in detecting OSAHS in patients with glucose metabolic dysfunction and explore the effect of nasal CPAP on glucose metabolism. Methods: Patients with glucose metabolic dysregulation were required to complete BQ and then recruited for a polysomnogram (PSG). The diagnostic accuracy of BQ and the relationships between the normal glucose tolerance (NGT), elevated fasting blood glucose (IFG), impaired glucose tolerance (IGT), and diabetes mellitus (DM) groups were analyzed. Subsequently, subjects with both OSAHS and glucose dysregulation further received CPAP treatment and then called for OGTT. Changes in AHI and glycemic parameters were used to the efficacy of CPAP. Results: Glycosylated hemoglobin and insulin levels were statistically different between the high-risk and low-risk groups according to BQ. For diagnosis of OSAHS among subjects with glucose metabolic dysfunction, the sensitivity and specificity of BQ were 72.84% and 66.67% when AHI cut-off values are set at 5. Furthermore, CPAP therapy could effectively reduce blood glucose, HOMA-IR, and insulin levels. Conclusions: BQ is an effective and economical screening method for OSAHS patients with glucose metabolic dysfunction. For better management, treatment with CPAP is feasible to improve their glycemic parameters.
Keywords

NLRP3 deficiency protects against intermittent hypoxia–induced neuroinflammation and mitochondrial ROS by promoting the PINK1–Parkin pathway of mitophagy in a murine model of sleep apnea

Xu Wu,Linjing Gong,Shanqun Li

Zhongshan Hospital，Fudan University

Purpose: Obstructive sleep apnea (OSA) associated neurocognitive impairment is mainly caused by chronic intermittent hypoxia (CIH)-triggered neuroinflammation and oxidative stress. Previous study has demonstrated that mitochondrial reactive oxygen species (mtROS) was pivotal for hypoxia-related tissue injury. As a cytosolic multiprotein complex that participates in various inflammatory and neurodegenerative

diseases, NLRP3 inflammasome could be activated by mtROS and thereby affected by the mitochondria-selective autophagy. However, the role of NLRP3 and possible mitophagy mechanism in CIH-elicited neuroinflammation remain to be elucidated. Methods: A mouse OSA model was established by CIH exposure inside custom-made chambers. The changes of behavior in NLRP3−/− mice and aged-matched controls on C57BL/6 background were evaluated by contextual fear conditioning test. We assessed hippocampal NLRP3 expression through immunohistochemical staining and immunoblotting analysis. The numbers of activated microglia and the levels of autophagic activities in cortex and hippocampus were evaluated by immunofluorescence analysis. Moreover, the levels of biomarkers of oxidative stress in hippocampus were also explored. In vitro experiments, we established an IH model using BV2 microglial cells. The detrimental effects of IH on BV2 cells were tested by annexin V-FITC/PI staining, Mito SOX Red staining and JC‑1 mitochondrial membrane potential assay. Western blotting and immunofluorescence assays were used to investigate the relationship between the inhibition of NLRP3 inflammasome and Parkin-dependent mitphagy activation. Results: Compared with wild‑type mice, NLRP3 deficiency protected them from CIH-induced neuronal damage, as indicated by the restoration of fear-conditioning test results and amelioration of neuron apoptosis. In addition, NLRP3 knockout mice displayed mitigated microglia activation elicited by CIH, concomitantly with elimination of damaged mitochondria and reduction of oxidative stress levels (malondialdehyde and superoxide dismutase). Elevated LC3 and beclin1 expressions were remarkably observed in CIH group. Besides, NLRP3 deficiency could further enhance the CIH-induced autophagy and mitophagy activities in mice hippocampus tissues. In vitro experiments, intermittent hypoxia (IH) significantly facilitated mitophagy induction and NLRP3 inflammasome activation in microglial (BV2) cells. Moreover, IH enhanced the accumulation of damaged mitochondria, increased mitochondrial depolarization and augmented mtROS release. Consistently, NLRP3 deletion elicited a protective phenotype against IH through enhancement of Parkin-mediated mitophagy. Furthermore, Parkin deletion or pretreated with 3MA (autophagy inhibitor) exacerbated these detrimental actions of IH, which was accompanied with NLRP3 inflammasome activation. Conclusions: In summary, these results revealed that NLRP3 deficiency acted as a protective promotor through enhancing Parkin-depended mitophagy in CIH-induced neuroinflammation. Thus, NLRP3 gene knockout or pharmacological blockage could be a potential therapeutic strategy for OSA-associated neurocognitive impairment.

Keywords

Performance of brief ICF–sleep disorders and obesity core set in obstructive sleep apnea patients

Liang Xie,Shanqun Li

Fudan University Zhongshan Hospital

Background: Clinical questionnaires are mainly applied as screening tools for identification of the Obstructive sleep apnea (OSA) patients. Little attention has been paid to assess the body functions and

health status of the patients. International Classification of Functioning, Disability and Health (ICF) was designed for better understanding and describing functioning and disability of patients. This study adopted the Brief ICF-Sleep Disorders and Obesity Core Set to evaluate the impairment of functioning and health status of OSA patients. Methods: A total of 592 participants were enrolled in this cross-sectional study. Data were collected using Brief ICF-Sleep Disorders and Obesity Core Set Polysomnography was performed and basic characteristics of the patients were recorded. Results: The scores for the component Body Functions and Code b130, b134, b140, b440, b530, s330, d160, d240, d450 of the two core sets were significantly different among the patients divided by apnea-hypopnea index (AHI) or oxygen saturation (SaO2) nadir, but the frequency of code s330, d160, d240, d450 was low. The Body Functions component of the both sets were closely related to neck circumference (NC), body mass index (BMI), apnea-hypopnea index (AHI) of the OSA patients. Body Functions of the Brief ICF-Sleep Disorders performed better with a threshold of 4 with sensitivity, specificity and area under the receiver operating characteristic curve (AUC) as 0.62, 0.74, 0.68(AHI $\geq$ 5), 0.69, 0.63, 0.66 (AHI $\geq$ 15), 0.75, 0.56, 0.66 (AHI $\geq$ 30), 0.56, 0.70, 0.63 (SaO2 nadir$\leq$90%), 0.67, 0.66, 0.66 (SaO2 nadir<85%), 0.71, 0.59, 0.65 (SaO2 nadir<80%), respectively. Conclusion: The Body Functions component of both two sets could be an evaluation tool of impairment of body functions for OSA patients. The Brief ICF-Sleep Disorders Body Functions component performed better with a threshold of 4 and might provide a new insight for physicians to assess OSA patients.
Keywords

Effects of daytime hypercapnia on memory and executive function in patients with obstructive sleep apnea hypopnea syndrome

Huaman Wu,zhijun Wang , chaohong Cheng,Jing Wang ,Qiaojun Wang ,Rui Chen
the Second Affiliated Hospital of Soochow University

Objective: To investigate the effects of daytime hypercapnia on memory and executive function in patients with obstructive sleep apnea hypopnea syndrome (OSAHS). Methods: This prospective study recruited patients complaining of snoring and diagnosed with OSAHS at the sleep center of the Second Affiliated Hospital of Soochow University from August 2019 to November 2020. A total of 123 patients who met the inclusion and exclusion criteria were included, and they were divided into the normocapnic group(n=79) and the hypercapnic group(n=44) according to the daytime transcutaneous partial pressure of carbon dioxide (PtcCO2) test Clinical data was collected. All patients underwent a daytime PtcCO2 test and overnight polysomnography (PSG). Besides, they were scored for their memory and executive function by using Logical Memory Test (LMT), Digit Span Test (DST), and Cambridge Neuropsychological Test Automated Battery (CANTAB), which includes Motor Screening (MOT), Pattern Recognition Memory (PRM), Spatial Recognition Memory (SRM), Spatial Span (SSP), Spatial Working Memory (SWM). Fast Fourier transform was used to analyze the frequency spectrum of the electroencephalograph signal captured

during non-rapid eye movement and rapid eye movement (REM) stages, to obtain the power spectral density of δ, θ, α and β bands in frontal, central and occipital regions. The clinical data, PSG parameters, and the test scores of their memory and executive function between the two groups were compared. Binary logistic stepwise regression was conducted to identify risk factors of memory impairment in OSAHS patients. Finally, the electroencephalograph characteristics of OSAHS patients with daytime hypercapnia were studied to further analyze the possible mechanism of memory and executive function decline in OSAHS patients with daytime hypercapnia. Results: The incidence of daytime hypercapnia among patients with OSAHS was 35.77%. The snoring history in years in the hypercapnic group was longer than that in the normocapnic group (P<0.05). There were no significant differences between the two groups in other general clinical characteristics. Compared with the normocapnic group, the apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and percent of the total time of oxygen saturation at thresholds <90% (TS90) in the hypercapnic group were higher (all P <0.05), while other PSG parameters exhibited no significant differences. There were no statistically significant differences in the immediate logical memory and PRM immediate accuracy rate between the two groups. However, compared with the normocapnic group, the delayed logical memory, verbal working memory, graphic visual delay memory, spatial visual memory, spatial working memory, and strategy application ability were worse in the hypercapnic group, as shown by lower delay LMT scores, lower DST- backward scores, lowest accuracy of delay PRM, lower accuracy of SRM, and lower SSP scores (P <0.05), and higher between errors, total errors, and strategy scores (P <0.01) of SWM in the hypercapnic group. Binary logistic stepwise regression showed that PtcCO2 ≥45mmHg [OR=3.109 (1.438, 6.720), P=0.004] was an independent risk factor for poor performance in delayed LMT. The risk factors for poor DST-forward scores were age [OR=1.116 (1.042, 1.196), P=0.002] and LSaO2 [OR=0.959 (0.926, 0.993), P=0.020]. The risk factors for poor DST-backward scores were PtcCO2 ≥45mmHg [OR=3.055 (1.359, 6.868), P=0.007] and BMI [OR=1.132 (1.005, 1.275), P=0.041]. PtcCO2 ≥45mmHg [OR=3.190 (1.338, 7.606), P=0.009; 3.941 (1.806, 8.599), P=0.001, respectively] was an independent risk factor for the accuracy of SRM and SSP scores. In addition, PtcCO2 ≥45mmHg [OR=3.238 (1.503, 6.972), P=0.003; 2.985 (1.378, 6.466), P=0.006; 2.785 (1.243, 6.238), P=0.013, respectively] was an independent risk factor for poor performance in between errors, total errors and strategy scores in SWM. In the NREM stage, the δ band power density in the frontal area and occipital area in the hypercapnic group were higher than the ones in the normocapnic group (P<0.05), while the power density of other bands showed no statistically significant differences between the two groups. In the REM stage, there were no statistically significant differences in the power density of all the bands in all brain areas between the two groups. After adjusting for age, sex, and BMI, the power density of the δ band in the frontal area in the NREM stage was positively correlated with PtcCO2 (r=0.239) and negatively correlated with delay LMT scores (r=-0.189), DST- forward scores(r=-0.139), and the accuracy of SRM(r=-0.201). All above correlations were statistically significant (P <0.05). Conclusion: About one-third of OSAHS patients were complicated with daytime hypercapnia，and the snoring history in years in the hypercapnia group was longer. Daytime hypercapnia has a negative impact on memory and executive function in OSAHS patients, as manifested by their decreased logical memory,

verbal and spatial working memory, and strategy application ability, though it had no impact on their visual memory ability. OSAHS patients with daytime hypercapnia showed increased slow wave activities in the brain, which may result in impaired memory and executive function.

Keywords Sleep apnea, obstructive, hypercapnia, memory, executive function

PM 2.5 exposure aggravates chronic intermittent hypoxia–induced myocardial injury via AMPK–PGC1α pathway mediated mitochondrial oxidative damage and apoptosis

Guiling Xiang,Shanqun Li

Zhongshan Hospital，Fudan University

Recent evidence suggests that exposure to air pollution may be a contributing risk factor for obstructive sleep apnea (OSA). While obstructive sleep apnea syndrome (OSAS), air pollution exposure have been respectively associated with increased risk of cardiovascular mortality. The effect of air pollution exposure to cardiac injury among patients with OSAS is still unclear. Thus, it is important to clarify the effects of OSAS and air pollution exposure on myocardial injury, and identify the underlying responsible molecular mechanisms. Chronic intermittent hypoxia (CIH) is one of the key pathological changes of OSA. We established CIH-induced OSAS models in H9c2 cells incubated with PM 2.5 (0-500 μg/mL). In this study, we revealed that PM 2.5 markedly aggravated the CIH-induced myocardial injury. In vitro study we verified that PM 2.5 aggravated CIH-induced mitochondrial dysfunction, apoptosis, and oxidative stress via the inhibition of AMPK and downregulation of PGC1α with its downstream signaling associated with mitochondrial homeostasis. These effects were reversed by treatment with metformin or overexpression of PGC1α in H9c2 cells. Moreover, PGC1α overexpression made no difference on the inhibition of AMPK phosphorylation in CIH-treated H9c2 cells incubatd with PM 2.5. Therefore, the inhibition of AMPK/PGC1α pathway may represent a potential mechanism for chronic intermittent hypoxia-induced myocardial injury aggravated by PM2.5 exposure via breaking the mitochondrial homeostasis and aggravating oxidative stress and apoptosis. Keywords

Is there a relationship between vasomotor symptoms and sleep–related problems among Chinese women in menopausal transition?

Di Zhao,Gaorong Lv ,Ping Li

Shandong University

Background: Sleep problems, such as difficulty initiating sleep, difficulty in maintaining sleep, and restless leg syndrome, are the common complaints reported among women during the menopausal transition.

Vasomotor symptom (VMS; i.e., hot flushes and night sweats) is strongly associated with sleep problems. However, the relationship between them has not been well explored. Objective: To examine risk factors associated with various sleep problems among midlife women and to identify the relationships between VMS and different sleep problems during the menopausal transition. Methods: This cross-sectional study involved 842 women aged 40 to 60 years who completed questionnaires on sleep problems (included six variables: difficulty initiating sleep, difficulty in maintaining sleep, restless leg syndrome, daytime sleepiness, having bad dreams, and subjective sleep quality) and VMS. Responses to questions about a confluence of potential risk factors were used to identify risk factors of different sleep problems. Binary logistic regression was used to analyze the relationships between VMS and different sleep problems. Results: Difficulty initiating sleep was more likely to be influenced by individual socio-demographic factors, lifestyles, and disease-related factors compared with the other five sleep problems. Restless leg syndrome was mainly relevant to age, chronic, and gynecological diseases. Of note, chronic and gynecological diseases were important risk factors for six sleep-related problems among women during the menopausal transition. Binary logistic regression showed that the odds ratios (OR) for the associations of VMS with sleep problems including restless leg syndrome, difficulty in maintaining sleep, difficulty initiating sleep, and subjective sleep quality were 1.526 (95% CI, 1.283-1.814), 1.486 (95% CI, 1.228-1.799), 1.321 (95% CI, 1.103-1.583), and 1.277 (95% CI, 1.056-1.545), respectively. Of these, the associations between VMS with daytime sleepiness and having bad dreams were not found (P > 0.05). Conclusions: VMS was related to certain sleep problems (restless leg syndrome, difficulty in maintaining sleep, difficulty initiating sleep, and subjective sleep quality) among Chinese women during the menopausal transition in our study, suggesting that it might be useful to improve sleep problems by relieving VMS.

Keywords Obstructive sleep apnea (OSA), noninvasive continuous positive pressure ventilation (CPAP), nasal mask, compliance, treatment effect.

Catathrenia phenomenon are common in obstructive sleep apnea

Yongfei Wen1,Feng Xu1,Xiaosong Dong2,Liyue Xu2,Yinghui Gao3,Wei Zhang3,Junjun Feng3,Mengjie Li3,Yongbo Yu3,Fang Han2

1.Cangzhou people's hospital
2.Peking University People's Hospital
3.Peking University International Hospital

Objective: To investigate the incidence of catathrenia in patients who completed polysomnography (PSG) test at two independent sleep centers and to explore the relationship between catathrenia and respiratory events through therapeutic responses. Methods: A retrospective study was conducted among subjects who completed PSG at Peking University People's Hospital and International Hospital sleep center from June to December 2018. A prospective study was conducted and patients who completed the PSG test from January

to March 2019 were recruited. Respiratory event-related catathrenia (RERC) was defined as follows: The groaning events occurred only after respiratory events and were closely related to respiratory events. Routine continuous positive airway pressure (CPAP) titration would be performed on patients and PSG data were collected when RERC was diagnosed Results: PSG data of 1123 patients were collected, including 741 males and 382 females. Aged 46.3 ± 14.0 years old. There were 865 OSA patients, of which 396 were severe OSA. RERC was found in 78 patients, The incidence of catathrenia was 19.40% in patients with severe OSA. The groaning index was positively correlated with AHI. Patients with RERC had significantly higher AHI (P < 0.001), BMI (P=0.001)，blood uric acid (P=0.003), hemoglobin (P=0.003), mean apnea time (P <0.001), central + mixed apnea index (P=0.001), and lower mean oxygen saturation during sleep (P <0.001), minimum oxygen saturation during sleep (P <0.001) than patients without groaning. Totally 26 patients with RERC performed PSG test when undergoing CPAP titration. The groaning index decreased from 32.1 ± 28.1 times/h to 0.1 ± 0.5 times/h (P=0.001), and 24 patients decreased to zero. Conclusion: RERC is common among patients with severe OSA. The groaning event is closely related to the obstructive respiratory event and can be mainly eliminated after CPAP treatment. The overshoot effect and hypocapnia caused by the overshoot effect might be the pathogenesis of secondary catathrenia.

Keywords Catathrenia, groaning, Obstructive sleep apnea, Breathing control, hypocapnia

Recursive Partitioning Analysis of Fractional Low–Frequency Fluctuations in Narcolepsy With Cataplexy

Fulong Xiao,Fang Han

Peking University People's Hospital

Objective: To identify narcolepsy related regional brain activity alterations compared with matched healthy controls and to determine whether these changes can be used to distinguish narcolepsy from healthy controls by recursive partitioning analysis (RPA) and receiver operating characteristic (ROC) curve analysis. Methods: Fifty-one patients who combined narcolepsy and cataplexy (26 adults and 25 juveniles) and sixty matched heathy controls (30 adults and 30 juveniles) were recruited. All subjects underwent a resting-state functional magnetic resonance imaging scan. Fractional low-frequency fluctuations (fALFF) were used to investigate narcolepsy induced regional brain activity alterations among adults and juveniles, respectively. Recursive partitioning analysis and Receiver operating curve analysis were used to evaluate the ability of fALFF values within brain regions in distinguishing narcolepsy from healthy controls. Results: Compared with healthy controls, both adults and juveniles with narcolepsy had lower fALFF values in bilateral medial superior frontal gyrus, bilateral inferior parietal lobule, and supra-marginal gyrus. Compared with healthy controls, both adults and juveniles with narcolepsy had higher fALFF values in the bilateral sensorimotor cortex and middle temporal gyrus. besides, juveniles with narcolepsy had higher fALFF in the right putamen and right thalamus compared with healthy controls. Based on RPA and ROC curve analysis, fALFF

differences in the right medial superior frontal gyrus can discriminate narcolepsy from healthy controls with a high degree of sensitivity (100%) and specificity (88.9%) among adult participants. The fALFF differences in the left superior frontal gyrus can discriminate narcolepsy from healthy controls with a moderate degree of sensitivity (57.1%) and specificity (88.9%) among juvenile participants. Conclusion: Compared with healthy controls, both the adult and juvenile with narcolepsy showed overlap brain regions in fALFF differences. Furthermore, we propose that fALFF value can be a helpful imaging biomarker in distinguishing narcolepsy from healthy controls among adults and juveniles.

Keywords narcolepsy, fMRI, fALFF, recursive partitioning analysis

Resting–state brain network topological properties and the correlation with neuropsychological assessment in adolescent narcolepsy

Fulong Xiao,Fang Han
Peking University People's Hospital

Objectives: To evaluate functional connectivity and topological properties of brain networks, and to investigate the association between brain topological properties and neuropsychiatric behaviors in adolescents with narcolepsy. Methods: A total of 26 adolescents with narcolepsy and 30 healthy controls were recruited. Resting-state functional magnetic resonance imaging and neuropsychological assessment were conducted. Functional magnetic resonance imaging data were analyzed in 3 ways. Group independent component analysis and a graph theoretical method were applied to evaluate topological properties within the whole brain. Besides, network-based statistics were used to compare region-to-region connectivity between groups. The relationship between topological properties and neuropsychiatric behaviors was analyzed with correlation analyses. Results: Sleepiness, depressive symptoms, and impulsivity were detected in adolescents with narcolepsy. Among adolescents with narcolepsy, functional connectivity decreased between regions of the limbic system and the default mode network and increased in the visual network. Adolescents with narcolepsy exhibited disrupted small-world network properties. Regional alterations in the caudate nucleus and posterior cingulate gyrus were associated with subjective sleepiness, and regional alterations in the caudate nucleus and inferior occipital gyrus were associated with impulsiveness. Remodeling within the salience network and the default mode network was associated with sleepiness, depressive feelings, and impulsive behaviors in narcolepsy. Conclusions: Alterations in brain connectivity and regional topological properties in adolescents with narcolepsy were associated with their sleepiness, depressive feelings, and impulsive behaviors.

Keywords narcolepsy, graph theory analysis, network-based statistics, sleepiness, depression, impulsivity

A case report of REM sleep behavior disorder, Behcet's disease, Sjogren's syndrome, and cognitive dysfunction

Fulong Xiao,Fang Han

Peking University People's Hospital

Background: Behcet's disease and Sjogren's syndrome is an autoimmune disorder from which many systems of the body can suffer. Here we reported a patient with a history of Behcet's disease and Sjogren's syndrome in which REM sleep behavior disorder (RBD) was then detected by polysomnographic (PSG) monitoring. Case presentation: A 68-year-old male patient with a history of Behcet's disease and Sjogren's syndrome was diagnosed with RBD by clinical examination and video-PSG. He also underwent a multiple sleep latency test and cerebral magnetic resonance imaging. The patient had a history of Behcet's disease for 20 years and Sjogren's syndrome for 2 years. The cerebral magnetic resonance imaging also suggested cerebral demyelination and mild cortical atrophy, with cognitive dysfunction by a score of 28 on the mini-mental state examination (MMSE) and a score of 22 on the Montreal cognitive assessment (MoCA). Conclusion: RBD is common in the elderly population and is significantly related to α-synucleinopathy. Combining the decline in neuro-cognition and mild cortical atrophy, the presentation of RBD in this patient indicates an underlying α-synucleinopathy neurodegenerative disorder in the future. Considering the role of inflammation in the pathogenesis of α-synucleinopathy and common shared HLA allelic genes in RBD and Sjogren's syndrome, it is suggested that a physiological process is related to neuroinflammation may be involved in the pathogenesis of RBD.
Keywords Behcet's disease; REM sleep behavior disorder; Sjogren's syndrome

The role of depression and anxiety in the relationship between poor sleep quality and subjective cognitive decline: exploring parallel, serial, and moderated mediation

Wenqi Xu,Lihua Lin,Shibin Wang,Fujun Jia

Guangdong Mental Health Center

Background: Poor sleep quality exacerbates subjective cognitive decline (SCD). Mental health may play an important role in the relationship, but the potential underlying mechanisms remain unknown. The present study aimed to explore the pathways linking poor sleep quality to SCD through the parallel, serial and moderated mediation effect of anxiety and depression in older Chinese adults. Methods: A cross-sectional study was conducted on older adult residents in Guangdong Province of South China from November 2020 to March 2021. A total of 717 adults aged 60 years and over were recruited for a face-to-face interview

on a range of demographics, socio-economic factors, lifestyle behaviors, sleep quality, SCD, depression, and anxiety. Parallel, serial, and moderated mediation models were used to examine whether anxiety and depression mediated the relationship between poor sleep quality and SCD. Results: Both direct and indirect effects of poor sleep quality on SCD were found. Anxiety and depression mediated the relationship between poor sleep quality and SCD (β Anxiety = 0.123, 95%CI: 0.079 to 0.173; β Depression=0.274, 95%CI: 0.200 to 0.348), respectively. Both indirect effect path (poor sleep quality→ anxiety→ depression→ SCD) and the alternative indirect effect path (poor sleep quality→ depression→ anxiety→ SCD) of the serial mediation model were significant (β a=0.052,95% CI: 0.026 to 0.084; β b=0.077, 95% CI: 0.033 to 0.128). Moderated mediation model revealed that the mediation of depression on the relationship between poor sleep quality and SCD was moderated by anxiety (β =0.318, 95% CI: 0.164 to 0.472). Conclusions: These findings highlight the role of depression and anxiety as mediators in the poor sleep quality-SCD linkage, which provides new insights into possible avenues for prevention and intervention on SCD through sleep-based treatments with a multi-faceted approach to psychiatric disorders.

Keywords

Effects of inflammation–associated KP on expression of apoptotic proteins Bcl–2 and Caspase3 in hippocampus after circadian rhythm disturbance in mice

Baoyan Wang,Wei Wu

General Hospital of Tianjin Medical University

Objective: Observe the pathological changes of colon tissue, TNF-α, IL-1β, IDO, Kyn, 3-HK in colon, blood and hippocampus of mice after continuous light exposure. The expression of apoptotic proteins Bcl-2 and Caspase3 in hippocampus; Further explore the possible transmission pathways of inflammatory signals and KP products between the brain and the intestinal tract, and the effect of KP on the expression of apoptotic proteins Bcl-2 and Caspase3 in the hippocampus. Methods: The model of circadian rhythm disturbance was established by continuous illumination.The pathological changes of colonic tissue were observed by HE staining.The levels of TNF-α, IL-1β, Kyn, 3-HK and IDO were detected by ELISA. The levels of Bcl-2 and Caspase-3 expression were detected by Western Blotting. Results: 1. Lymphocyte infiltration in lamina propria of mucosa was observed in colon of mice in LL group. The levels of TNF-α, Kyn and 3-HK in colon were significantly higher than those in LD group.2. Hippocampus TNF-α, IL-1β and Kyn in LL group were significantly higher than those in LD group.Blood levels of Kyn were significantly higher than those in LD group.3. The expression of Bcl-2 and Caspase3 in apoptotic eggs in mouse hippocampus was not significantly higher than that in LD group. Conclusion: 1. Inflammatory changes occurred in colon and hippocampus of mice after continuous light exposure, and the increased contents of Kyn and 3-HK may be

related to the activation of KP pathway under the effect of inflammation.2.KP associated with inflammation after continuous light exposure had little correlation with the expression of apoptotic proteins Bcl-2 and Caspase-3 in the hippocampus of mice.

Keywords

Hypercapnia and Hypoxemia in a Young Woman

Taoran Bi1,Jun Zhang1,Kingman Strohl2,Fang Han1

1.Peking University People's Hospital

2.Case Western Reserve University

A 28-year-old female developed chronic shortness of breath and fatigue. During an evaluation in a community hospital, she was stuporous on oxygen supplementation. Arterial Blood Gas (ABG) on room air indicated hypercapnic respiratory failure. Paradoxical thoracoabdominal movement on supine was observed. Nocturnal Polysomnography (PSG) and oximetry and transcutaneous carbon dioxide monitoring (PtcCO2) revealed severe sleep hypoventilation, which was the most remarkable in REM sleep. Severe sleep hypoventilation and paradoxical thoracoabdominal movement on supine led to clinical suspicion of diaphragms impairment which was revealed by fluoroscopy. Muscle biopsy, enzymatic test, and whole genome sequencing confirmed the diagnosis of late-onset Pompe disease. After treatment of nocturnal noninvasive BPAP, the parameters of repeated PSG, oximetry, and PtcCO2 on PAP, and daytime ABG on room air were significantly improved. After discharge from the hospital for one and half years, the patient continued nocturnal BPAP treatment at home. A remarkable improvement of clinical status and exercise capacity was self-reported. When being followed up in a local hospital, pulmonary function tests showed a slight improvement of ventilatory function. ABG on room air maintained normal. This case highlights the importance of the physical examination and testing in wake and sleep during the evaluation of such patients in regard to making a differential diagnosis and identifying the etiology. Nocturnal PSG, oximetry, and PtcCO2 during sleep can be important clues in the diagnosis of neuromuscular disorders with the involvement of respiratory muscles.

Keywords Glycogen storage disease type II, sleep hypoventilation, noninvasive ventilation

Sleep problems in children and adolescents recovered from COVID–19 in Wuhan, China

Anyi Zhang1,Han Xiao2,Le Shi1,Zhe Wang1,Yanping Bao3,Hong Mei2,Jie Shi3,Zhisheng Liu2,Jiajia Liu4,Lin Lu1,5

1. Peking University Sixth Hospital
2. Wuhan Children's Hospital
3. National Institute on Drug Dependence and Beijing Key Laboratory on Drug Dependence Research，Peking University
4. Peking University
5. Peking-Tsinghua Center for Life Sciences and PKU-IDG/McGovern Institute for Brain Research，Peking University

Objective: Coronavirus disease 2019 (COVID-19) is an ongoing global pandemic that has spread rapidly since the first outbreak was reported in December 2019. It has raised a large number of concerns regarding its impacts on sleep. This study aimed to assess the prevalence and risk factors for sleep problems in children recovered from COVID-19 in Wuhan, China. Methods: From July to September 2020, children and adolescents aged 4-18 years who recovered from COVID-19, were recruited in Wuhan Children's Hospital. The healthy controls were derived from the Wuhan birth cohort during the same period. The sleep problems in children and adolescents were assessed by the parent-reported Sleep Disturbance Scale for Children (SDSC). We also assessed the mental health status of caregivers by a self-report questionnaire. Logistic and linear regression analysis was conducted to identify risk factors. Results: 206 children aged 4-18 years were recruited for the final analysis, with 79 children (38.3%) recovered from COVID-19, and 127 children (61.7%) in the healthy control group. The prevalence of sleep problems in children and adolescents with previous COVID-19 infection was 17.7% (14 in 79), and 23.6% (30 in 127) in healthy controls (p = 0.315). While, the total score of SDSC in children recovered from COVID-19 was significantly lower than healthy controls (30.11±11.93 vs. 33.83±11.02, p = 0.024). We found that children's sleep problems were significantly associated with caregivers' post-traumatic stress symptoms (aOR = 9.52; 95%CI = 2.28, 39.82; p = 0.002) and depression symptoms (aOR = 5.61; 95%CI = 2.49, 12.67; p < 0.001). In the adjusted linear regression model, the score of SDSC in children was positively related to the score of Patient Health Questionnaire-9 (PHQ-9) assessing depression in caregivers (a β = 0.62, 95%CI = 0.20, 1.04; p = 0.004), and negatively related to the COVID-19 infection (a β = -3.41, 95%CI = -6.61, -0.21; p = 0.037) and male gender (a β = -3.32, 95%CI = -6.58, -0.07; p = 0.045). Conclusion: Sleep disturbances are common among children after the COVID-19 pandemic in Wuhan, China. We found sleep disturbances in hospitalized children were milder than healthy children quarantined at home, which might relate to the hospital's policy that one of the parents was allowed to accompany the hospitalized children. Our study underscores the need to provide timely and effective mental health related intervention and services for children and adolescents especially for girls and those quarantined at home, as well as their parents.

Keywords

Sleep Quality Measured with Odds Ratio Products in Narcolepsy Patients

Taoran Bi,Fang Han

Peking University People's Hospital

Objective: To evaluate sleep quality and architecture in patients with narcolepsy using the odds-ratio-product (ORP) and a continuous metric of sleep depth (0 = deep sleep; 2.5 = full wakefulness). Methods: This retrospective study recruited 55 patients with narcolepsy type 1 (NT1). Sleep quality and architecture were evaluated respectively by the ORP values of 30-second epochs and distribution in different ORP ranges. Results from 54 healthy volunteers were used as controls. Results: The mean NT1 ORPTRT, ORPN1, ORPN2, ORPN3, ORPNREM, and ORPREM were 1.11 ± 0.21, 1.31 ± 0.22, 0.87 ± 0.23, 0.47 ± 0.16, 0.88 ± 0.21, and 1.27 ± 0.27. and these of controls were 0.87 ± 0.21, 1.15 ± 0.18, 0.70 ± 0.17, 0.31 ± 0.09, 0.63 ± 0.13, and 0.91 ± 0.22 ($P<0.05$). These results indicated that patients with narcolepsy have lighter nighttime sleep than healthy controls. The mean post-arousal dynamics (ORP-9) of patients with narcolepsy was 1.20 ± 0.25 and the mean ORP-9 of controls was 0.89 ± 0.03 ($P<0.05$), which indicated poor stability and continuity in patients with narcolepsy. The distribution of 30-second epochs in different ORP ranges indicates a remarkable increase of transitional state and decrease of deep sleep and fully awake state in patients with narcolepsy. Conclusions: The sleep quality and architecture in patients with narcolepsy are poorer than healthy people.

Keywords Narcolepsy, Sleep Quality, Odds-ratio-product

A false alarm of polycythemia: obesity hypoventilation syndrome masquerading as erythrocythemia

Yanan Liu

Peking University First Hospital

Introduction: Obesity hypoventilation syndrome (OHS) with secondary polycythemia is complex and multifactorial involving various sleep problems and metabolic diseases. It is easily misdiagnosed since those clinical features are also common in erythrocythemia. Case presentation: We hereby reported a 39-year-old gentleman who presented to the hospital with erythrocytosis (HB 227g/dL). His erythropoietin (EPO) was markedly increased and bone marrow cytology suggested secondary polycythemia. He was overweight with daytime hypercapnia. His sleep polysomnography revealed severe obstructive sleep apnea-hypopnea syndrome (OSAHS), and he met a diagnosis of obesity hypoventilation syndrome (OHS). On admission, he was noted to have multi-organ dysfunction including respiratory failure and heart failure. The patient got improved with bi-level positive airway pressure therapy. Discussion: Obesity hypoventilation syndrome (OHS) is characterized by obesity, sleep disturbances, and daytime hypercapnia, which is also an

important pathogeny of secondary polycythemia. A nocturnal sleep study may be warranted in patients with unexplained polycythemia particularly when there is a combination of obesity and hypercapnia. When obese patients are diagnosed with OHS, they are often accompanied by multi-system organ dysfunction. Positive airway pressure (PAP) is also recommended as first-line therapy in patients with OHS, which can improve respiratory function and blood indexes. Most patients with OHS benefit from a multifaceted approach including lifestyle intervention, medication, and noninvasive ventilation therapy. Conclusion: This case highlights that polycythemia should not be ignored as a potential complication of OHS.

Keywords

Preoperative Application of Auto–CPAP on Obstructive Sleep Apnea Reduces Postoperative Complications in Patients Undergoing Heart Valve Replacement surgery

Ning Ding,Mei Su,Xilong Zhang
The First Affiliated Hospital of Nanjing Medical University

Objective: Obstructive sleep apnea (OSA) is common in patients referred for cardiac valve replacement (CVR) and associated with increased perioperative complications. Continuous positive airway pressure (CPAP) is the mainstay treatment for patients with OSA. We aimed to determine if perioperative auto-CPAP treatment decreases postoperative apnea hypopnea index (AHI) and length of ICU stay and decreases the postoperative heart and pulmonary complications in patients with OSA and valvular heart disease (VHD). Methods: Between December 2017 and December 2019, 223 VHD patients aged 18-75 years undergoing CVR were screened for OSA, and 34 patients with OSA were randomly assigned into CPAP treatment group (n=17) and non-CPAP treatment group (n=17). Patients in the CPAP treatment group received 7 days' CPAP + basic treatment (15 patients finished 7 days' treatment, with CPAP > 4 hours/night); patients in non-CPAP treatment group received 7 days' basic treatment. After one week's treatment, all the patients received cardiac valve replacement surgery. After surgery, all the patients were sent to the intensive care unit (ICU) and received mechanical ventilation. The postoperative PSG was conducted 1-3 days prior to discharge. The pre-and-postoperative sleep parameters were compared. Length of stay (including length of total hospital stay, length of preoperative stay, length of postoperative stay, and length of ICU stay), cardiac complications (including postoperative arrhythmia, pacemaker use, the first dose of dopamine in ICU, and first dose of dobutamine in ICU) and respiratory complications (reintubation, pneumonia, and length of mechanical ventilation) were assessed and compared between CPAP treatment and non-CPAP treatment groups. Results: There were no significant differences in baseline characteristics between the CPAP treatment group and non-CPAP treatment group. For CPAP treatment group, the AHI, AI, and ODI were significantly decreased, and mean and minimal SpO2 were significantly increased during CPAP treatment. The AHI, AI, and ODI were significantly decreased postoperatively compared with those preoperatively (baseline)

for both CPAP treatment group and non-CPAP treatment group. There were no significant differences for all the above parameters between CPAP treatment and non-CPAP treatment groups postoperatively. The length of postoperative ICU and hospital stay, as well as the length of mechanical ventilation, were all significantly reduced in CPAP treatment group compared with non-CPAP treatment group. However, there were no significant differences in length of total hospital stay, cardiac complications (including postoperative arrhythmia, pacemaker use, the first dose of dopamine in ICU and the first dose of dobutamine in ICU), and other respiratory complications (reintubation and pneumonia). Conclusions: Preoperative application of CPAP for OSA significantly decreased length of mechanical ventilation, postoperative stay in ICU and hospital, but failed to show any association with postoperative arrhythmia, pacemaker use, reintubation, and pneumonia.

Keywords

Transcutaneous Auricular Vagus Nerve Stimulation in the Treatment of Insomnia with Depression: a Retrospective Case Series

Yanan Zhao,Peijing Rong,Yu Wang,Shaoyuan Li,Yue Jiao,Shuai Zhang,Yu Chen, Jiakai He

Institute of Acupuncture and Moxibustion，CACMS

Objective: To investigate the effect of transcutaneous auricular vagus nerve stimulation (taVNS) on short-term clinical outcomes among patients with insomnia and depression, and to explore the potential mechanism of taVNS . Methods: This retrospective study enrolled 13 patients with insomnia and depression who were treated by taVNS. Therapeutic parameters were 30 mins each time, twice a day, 5 days a week, for 4 weeks. The Pittsburgh Sleep Quality Index (PSQI) and 17-item Hamilton Depression Rating Scale (17-HAMD) were used to evaluate before and after treatment. Sleep parameters, including total sleep time (TST), sleep latency period (SL), sleep efficiency (SE), REM time, and NREM time were recorded by Polysomnography(PSG). The changes of PSQI, 17-HAMD scores, and sleep parameters before and after treatment were observed, and the changes of β/δ ratio of sleep EEG spectrum were also analyzed. Results: After 4 weeks of treatment, the effective rate was 69.2%(9/13). Compared with before treatment, PSQI and 17-HAMD scores of patients with insomnia and depression significantly decreased after 4 weeks of treatment (P<0.01). Among PSG sleep parameters, REM time decreased significantly(P<0.05), and there were no statistical differences in TST, SL, SE, and NREM after treatment (P>0.05). However, all of them showed a trend of improvement. Homoplastically, there were no significant differences in the β/δ ratio of sleep EEG spectrum (P>0.05), but it also showed a downward trend. Conclusion: taVNS can significantly improve sleep and depressive symptoms. It can also increase TST, SE NREM, and decrease REM and SL, and adjust PSG objective sleep parameters in patients with insomnia and depression, which may be related to the reduction of excessive arousal in the cerebral cortex by taVNS. This exploratory trial lays the foundation for prospective randomized controlled trials of taVNS that regulates insomnia disorder combined with depression.

Keywords

The effect of mindfulness–based psychological intervention on sleep problem among lung cancer patients in the perioperative period

Gaorong Lv,Di Zhao,Ping Li

Shandong University

Background Sleep problems after surgery are common and are associated with increased symptom burden and poorer quality of life, even cancer progression and mortality. we recommend blockade of these responses during the perioperative period, as well as other low-risk, low-cost interventions. Methods A total of 140 patients with lung cancer who underwent surgery between March to December 2019 were screened for inclusion. They were grouped according to their ward, with 70 cases in each group. The patients in the control group were given routine care, and those in the intervention group received short-term mindfulness training (15 minutes) based on routine care. The revised sleep disorders and sleep quality components in the Pittsburgh Sleep Quality Index were used to evaluate the sleep problems of the patients on the 1st day before surgery, the day of the surgery, 1st, 3rd, 5th, 7th, and 14th days after surgery. Results The incidence of sleep problems(difficulty falling asleep, easy to wake up at night, wake up early, and bad subjective sleep quality) between the two groups were no statistical differences at baseline. Generalized estimation equation showed that the groups, time, and group $\times$ time effect of the incidence of these sleep problems were statistically significant. Furthermore, the Chi-square test showed that the incidences of sleep problems between the two groups were not different on the 1st day before surgery. There were no significant differences in the prevalence of being easy to wake up at night on the 3rd day after surgery, and poor subjective sleep quality on the 14th day after surgery, other sleep problems differed between the two groups at other points during the perioperative period. Conclusion Short and self-help mindfulness audio intervention could improve perioperative sleep problems in patients with lung cancer and can be widely used in clinical practice.

Keywords

The relationship between apolipoprotein E genetic polymorphism and metabolic syndrome in patients of OSAHS

Xinyi Li1,2,Huajun Xu1,2,Hongliang Yi1,2,Jian Guan1,2,Shankai Yin1,2

1.Shanghai Sixth People's Hospital

2.Shanghai Key Laboratory of Sleep Breathing Disorders

Background: Apolipoprotein E (APOE) is an important lipoprotein that is involved in lipid metabolism, while the relationship between APOE, insulin resistance, and metabolic syndrome in OSAHS is unclear. This study aimed to analyze the distribution characteristics of the three subtypes of APOE in OSAHS patients with

or without insulin resistance and metabolic syndrome and to explore the influence of APOE gene mutations on the metabolic disorders of OSAHS. Methods: A total of 4974 subjects who complained of snoring were consecutively enrolled in the study. Demographic, anthropometric, biochemical, and polysomnographic data were collected. APOE subtypes were classified according to APOE SNP rs429358 and rs741. The chi-square test was used to compare the ratios of APOE subtypes in each group of OSAHS patients with or without MetS and IR. Results: In OSAHS patients without MetS, the ratios of APOE E3/E3, E3/E4, E4 /E4 were 69.9%, 15.2%, 2.1%, and in OSHAS subjects with MetS were 66.5%, 17.5%, and 0.9%. The differences of the three genotypes were statistically significant (P =0.02, 0.01, 0.002, respectively). We found that E2/E3 in mild OSA with and without IR were 5.1% and 12.7% (P=0.03). The ratios of subjects containing ε2 with and without IR were 8.3% and 2.5% (P=0.004). In severe OSA, the ratios of E3/E3 with non-MetS and MetS were 71.25% and 67.2% (P=0.02). The ratios of E3/E4 were 14.6%, 17.4%, P=0.04. The ratios of subjects containing ε3with and without MetS were 82.3%, 84.3% (P=0.038). ε4 were 10.15% and 8.6% (P=0.042), ε4 carrier we also found that the ratio of 19.5% in the Mets which was higher than the ratio of 16.5% in the non-Met (P=0.039). Conclusions: The proportion of patients with MetS containing E4 is higher than that of subjects without MetS, suggesting that E4 may involve in the metabolic disorder caused by severe OSAHS. Keywords

Multiple genetic variations of chronic rhinosinusitis with nasal polyps are associated with respiratory parameters in men with obstructive sleep apnea

Xinyi Li1,2, Qianqian Zhang1,2,Haibo Ye1,2,Huajun Xu1,2,Hongliang Yi1,2, Jian Guan1,2, Shankai Yin1,2

1.Shanghai Sixth People's Hospital

2.Shanghai Key Laboratory of Sleep Breathing Disorders

Objective: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) have a higher risk of obstructive sleep apnea (OSA). However, the relationship between CRSwNP and OSA remains unclear. The aim of this research was to evaluate the associations of multiple single nucleotide polymorphism (SNP) variations in CRSwNP with sleep-related parameters among men with OSA. Methods: Eight CRSwNP SNPs in 2,320 participants were included. For each subject, the genetic risk score (GRS) was obtained based upon the cumulative effect of multiple genetic variants of CRSwNP. Bivariate correlation analysis was used to assess the relationship between CRSwNP genetic polymorphisms and polysomnography (PSG) parameters in men with OSA. Logistic regression analyses were used to assess the relationship between the risk of OSA and CRSwNP genetic polymorphisms. Results: In moderate OSA, rs28383314 was related to the oxygen desaturation index (ODI), and rs4807532 was positively associated with the microarousal index

(r=0.09, p=0.03; r=0.11, p=0.01, respectively). The CRSwNP GRS was positively correlated with the ODI and cumulative time percentage with SpO2 <90% in moderate OSA (r=0.13, p<0.001; r=0.1, p=0.01), and there was no association between the CRSwNP GRS and the risk of OSA (OR=1.007, 95%CI, 0.973-1.042, p=0.702). Conclusion: In patients with moderate OSA, single CRSwNP genetic variations correlated with sleep-related parameters, and the cumulative effects of CRSwNP genetic variations were associated with the hypoxic index. This suggests that CRSwNP might be a predisposing condition for sleep disorders in patients with moderate OSA.

Keywords

Factors related to sleep–disordered breathing in patients with acute stroke

Jihong He,Gangyu Ding,Xiaowen Li, Jingzhu Yao,Jianhua Xu

Central Hospital of Jiading District，Shanghai Medical College

Objective: There is a close relationship between stroke and sleep-disordered breathing. The cardiopulmonary coupling CPC technique was used to analyze the pattern of sleep apnea syndrome in patients with acute stroke, so as to provide relevant evidence for clinical treatment. Methods: A total of 500 patients with acute stroke were enrolled. CPC was used for nighttime sleep monitoring, OSA was defined as AHI＞ 5 times/h. OSA was divided into three grades according to AHI level. Multivariate correlation analysis was conducted between patients with acute stroke combined with severe OSA and patients without acute OSA, including gender, age, types of stroke, location of the stroke, and severity of disease (NIHSS score). Results: The incidence of OSA in patients with acute stroke was 69.2%, and the incidence of OSA in patients with hemorrhagic stroke was significantly higher than patients with ischemic stroke, with severe predominance (P ＜ 0.01). The severity of OSA in patients with acute stroke was correlated with gender, age, and stroke site (P＜ 0.01). Conclusions: The incidence of OSA in patients with acute stroke is high, and the incidence of hemorrhagic stroke is higher than ischemic stroke, and the proportion of sex, age, and the type of stroke site. Attention should be paid to early identification and intervention to improve the poor prognosis of stroke.

Keywords

Effect of high–fat diet on the respiratory function and diaphragm fiber types related with its mitochondrial mechanism in mice

Ning Li,Hong-Peng Li ,Ben-Yan Zhang ,Liu Zhang ,Ji-Min Shen ,Qing-Yun Li

Ruijin Hospital，Shanghai Jiaotong University of Medicine

Objective: Obesity related respiratory dysfunction is associated with impaired diaphragmatic function, but the

specific mechanism is not fully elucidated. The aim of the study is to explore the effects of high-fat diet (HFD) induced obesity on diaphragmatic fiber types and its mitochondrial mechanism in mice. Methods: Twenty male C57BL/6 mice were randomly divided into two groups, which were fed with normal diet (NFD) and HFD for 16 weeks, respectively. The parameters of respiratory function, lipid content of diaphragm, mitochondrial morphology and function were measured. Furthermore, the expression of proteins related to mitochondrial dynamics was also detected. Results: Compared with the NFD group, the tidal volume was significantly decreased by 34.2% (P=0.004 P<0.01) and the Penh value was increased by 18.7% (P<0.01) in the HFD group. The serum leptin level of the HFD group was significantly higher than that of the NFD group (0.36±0.26 ng/ml vs. 0.17±0.07ng/ml, P<0.05), while the soluble leptin receptor level was significantly lower (1.63±0.31ng/ml vs. 1.98±0.37ng/ml, P<0.001). The contents of triglyceride, total cholesterol and fatty acid in the diaphragm of HFD group were significantly higher than those of NFD group (P<0.001). A large number of neutral lipid droplets were also found by oil red O staining. Compared with the NFD group, the proportion of oxidative muscle fibers in the diaphragm of HFD group was significantly decreased (P<0.01). Electron microscopy showed disorder-arranged myofibrils, swelled mitochondria, and impaired cristae (some of them disappeared or even formed vacuoles). HFD significantly down-regulated the expression of mitochondrial fusion protein 2 and sarcoplasmic reticulum Ca2+-ATPase in diaphragmatic muscle, while up-regulated the mitochondrial fission related protein (all P<0.01). Conclusion: HFD induced obesity related respiratory function is associated with the decrease of oxidative muscle fibers and mitochondrial damage in diaphragm.

Keywords

Case Report: Niemann–Pick Type C with Sleep Disorders: Central Sleep Apnea and Daytime Sleepiness

Yimeng Zhang1,2,Yueyang Cheng1,2,Yuan Yuan1,2,Yi Zhai1,2,Xin Zhao1,2,Lidong Jiao1,2,Yue Hou1,2,Ning Li1,2,Shuqin Zhan1,2

1.Xuanwu Hospital of Capital Medical University

2.Beijing Key Laboratory of Neuromodulation

Objective：Niemann-Pick type C (NPC) is a set of autosomal recessive inheritance diseases that sheath phospholipids and cholesterol deposit in body organs. The manifestations are highly diverse, but sleep disorders are rarely reported in NPC. This paper reported 2 cases with NPC disease and sleep disorders and aimed to discuss clinical features and possible pathogenesis of sleep disorders in NPC patients. Methods：The sleep symptoms, polysomnography, and genetic characteristics of 2 patients with NPC were analyzed, and the related literature was reviewed to explore the possible pathological mechanism of sleep disorders in patients with NPC. Results：Case 1 was a young man with physical clumsiness, glossolalia, excessive sleepiness, and cataplexy. His polysomnography indicated severe central sleep apnea. Multiple sleep latency

tests(MSLT) suggested sleep latency on average was 3.9 minutes, 2 SOREMPs (sleep-onset REM period) were found five times. Case 2 was a child with cataplexy, intellectual impairment, and episodic jerking. The MSLT showed that there were 3 SOREMPs in 5 naps, and the mean REM latency was 2.3 minutes, and the mean sleep latency was 15.2 minutes, and orexin in cerebrospinal fluid was 45.61pg/ml. Two patients were diagnosed with Niemann Pick disease by bone marrow puncture and gene tests. Conclusions：Sleep disorders of patients with NPC significantly influence patient's life quality and are difficult to identify. In this paper, two patients suffered sleep disorders such as central sleep apnea, sleepiness, cataplexy, and other sleep disorders such as obstructive sleep apnea, REM sleep behavior disorder and restless leg syndrome have also been reported before. The mechanism may be related to sheath phospholipids and cholesterol deposit in brain tissue which is associated with sleep-wake regulating, but there is no enough evidence. The pathological mechanism needs to be discussed in the future.

Keywords

Application of a non–contact portable monitoring device for the diagnosis of obstructive sleep apnea: using impulse–radio ultra–wideband radar

Chen Feng1,Yan Wang1,Yanzhong Li1
1.Qilu Hospital of Shandong University
2.NHC Key Laboratory of Otorhinolaryngology

Objective: To study Impulse-radio ultrawideband (IR-UWB) radar technology against polysomnography (PSG) for sleep assessment. Methods: A total of 79 OSA patients were randomly divided into two groups. Forty patients in group A received both PSG and IR-UWB, and 39 patients in group B received both micromovement-sensitive mattresses (MSM) and IR-UWB. Pearson correlation and ROC curve were used to compare the measured data. Results: AHIPSG and AHIMSM were significantly correlated with AHIIR-UWB (r=0.91, p＝ 0.00; r=0.92, p＝ 0.00), and Bland-Altman analysis showed that the result consistency rate of AHIIR-UWB value against AHIPSG value and AHIIR-UWB value against AHIMSM value was very high (95.00%, 97.44%), and the consistency rate of diagnosis result was very high. The sensitivity and specificity of AHIIR-UWB compared with PSG were 70.40% and 89.90%. The area under the ROC curve was 0.915. Conclusions: IR-UWB has a high diagnostic value for adult OSA in terms of minimum blood oxygen saturation, average blood oxygen saturation, the average number of central sleep apnea, the average number of complex sleep apnea, average heart rate, sleep efficiency, REM sleep duration, average AHI，, etc. It is an economic and practical tool to evaluate objectively sleep.

Keywords

Regulation of breathing by leptin signaling in the nucleus tractus solitarii

Hongxiao Wei1,Fang Yuan1,2,Sheng Wang1,2
1.Department of Physiology，Hebei Medical University
2.Hebei Key Laboratory of Neurophysiology

Background: Sleep-disordered breathing (SDB) is characterized by abnormal breathing during sleep and consists of obstructive sleep apnea, central hypoventilation and obesity hypoventilation syndrome. It has been reported that deficiency in leptin signaling is closely associated with the onset and development of SDB in animal models and humans. Leptin, a peptide hormone derived mainly by white adipocyte, centrally facilitates breathing, suggesting that it is essential for central respiratory drive. However, the central target of leptin effect on breathing and the circuit mechanism remains poor understood. Objective: The present study aims to address whether leptin receptor b (LepRb)-expressing nucleus tractus solitarii (NTSLepRb) neurons potentiate central respiratory drive. Methods: Multidisciplinary approaches, including chemogenetics, optogenetics, on-target neural tracing, electrophysiology and Ca2+ imaging, were used to assess whether NTSLepRb neurons contribute to respiratory control. Results: Both chemogenetic and optogenetic stimulations of NTSLepRb neurons notably activate breathing. Moreover, stimulation of lateral parabrachial nucleus (LPBN)-projecting NTSLepRb neurons not only remarkably increases basal ventilation by a similar amplitude to all NTSLepRb neuron stimulation, but also activates the preBötzinger complex-projecting LPBN neurons. By contrast, ablation of LPBN-projecting NTSLepRb neurons notably eliminates the enhanced respiratory effect induced by NTSLepRb neuron stimulation. In brainstem slices, bath application of leptin rapidly depolarizes membrane potential, increases spontaneous firing rate and speed up Ca2+ transients in most of NTSLepRb neurons. Conclusions: Leptin potentiates breathing in the NTS via an NTS-LPBN-preBötzinger complex circuit. These findings help understand the pathogenic mechanism of SDB and provide new clues for precise intervention of these diseases.
Keywords: Sleep-disordered breathing; Respiratory center; Leptin; Neural circuit

Experience of being Bullied and Sleep Quality among Junior Middle School Students

Fangfang Duan1,Peipei Wang2
1.Beijing Jishuitan Hospital
2.Sanya Central Hospital (The Third People's Hospital of Hainan Province)

Objective: To explore the association between experience of being bullied and sleep quality among junior middle school students in Sanya City. Methods: An electronic survey was conducted to collect

the demographic information, Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and previous self-perceived being bullied in middle schools of Sanya City. T-test, $x2$ test, and Mann-Whitney U test were used to compare general demographic characteristics and sleep quality between subjects with and without being bullied experience. Binary Logistic regression was used to analyze the relationship between experiences of being bullied and sleep quality.   Results: A total of 2167 middle school students were included in the analysis, with a median PSQI score of 2.0 (1.0, 5.0), including 186 (8.6%) students with poor sleep quality (PSQI>7), 181 (8.4%) students with ISI score no less than 8 and 165 (7.6%) students had the previous diagnosis of insomnia. Totally, 125 (5.8%) students reported previous experience of being bullied. Univariate analysis showed that there were statistically significant differences in total PSQI score, total ISI score, and prevalence of insomnia between subjects with experience of being bulled and ones without (P <0.001). Logistic regression analysis after adjusting for potential confounding factors showed that self-perception as a bullying victim was significantly associated with poor quality of sleep (PSQI > 7) [OR (95% CI): 3.54 (2.23, 5.63)], high risk of insomnia (ISI≥8) [OR (95%CI): 4.95 (3.14, 7.81)] and clinically diagnosed insomnia [OR (95% CI): 2.76 (1.66, 4.61)] (P < 0.001).   Conclusions: Poor sleep quality and insomnia were prevalent among junior middle school students in Sanya City. The present results suggest that experience of being bullied might be a risk factor for poor sleep quality and insomnia among junior middle school students. Keywords

Obstructive sleep apnea and erectile dysfunction

Chen Feng1,2,Yan Wang1,2,Yanzhong Li1,2
1.Qilu Hospital of Shandong University
2.NHC Key Laboratory of Otorhinolaryngology

Objectives: (1)To investigate the incidence of obstructive sleep apnea (OSA) combined with erectile dysfunction; (2) To analyze the correlation between OSA and ED; (3) To explore the treatment response and possible mechanism of uvulopalatopharyngoplasty (UPPP) to patients with OSA and ED. In short, it will provide a theoretical basis for clinical diagnosis and comprehensive treatment of patients with OSA and ED, and improve the prevention and treatment of OSA-related ED diseases. Methods: Clinical data of 135 subjects were collected, including basic clinical data such as age, smoking status, drinking status, BMI, blood pressure, etc. Special data such as polysomnography (PSG), Epworth sleepiness score, Baker anxiety score, Baker depression score, IIEF-5 score, ASEX score, and sex hormones, etc. According to the PSG results, they were divided into an OSA patient group (124 cases) and a non-OSA subject group (11 cases), and then the OSA patient group was divided into a mild-moderate group (61 cases) and a severe group (63 cases). According to the patients' IIEF-5 score, 124 OSA patients were divided into the ED group (80 cases) and the non-ED group (40 cases). Normally distributed measurement data were expressed as mean ± standard deviation, and non-normally distributed measurement data were expressed as median (quartile)

[M(Q25~ Q75)]. Normally distributed measurement data, independent-sample t-test or Pearson's chi-square test was used for comparison between two groups, single-sample ANOVA test was used among three groups. Mann-Whitney U test was used for non-normally distributed measurement data between two groups, three groups Kruskal-Wallis H test was used for comparison between the two groups. Spearman correlation analysis was used to test the correlation between non-normally distributed measurement data. In univariate analysis, significant variables were included in multivariate analysis, and binary logistic regression analysis was performed. ROC curve was used to evaluate the AUC (area under the curve) of the relevant factor, and then evaluate the performance of the factor as a criterion. Result:Among the three groups of non-OSA subjects, patients with mild to moderate OSA, and patients with severe OSA, the BMI (p = 0.001), neck circumference (p = 0.005), waist circumference (p = 0.001), hip circumference (p = 0.006), Epworth score (p= 0.003), Baker anxiety score (p <0.001), and ASEX score (p <0.001) were significantly increased in turn, while IIEF-5 score (p <0.001) decreased significantly. Among the three groups of non-OSA subjects, patients with mild to moderate OSA, and patients with severe OSA, there was a significant difference in prolactin (p = 0.728), follicle-stimulating hormone (p = 0.062), luteinizing hormone (p = 0.294), Six serum sex hormone secretion levels of progesterone (p= 0.821), estradiol (p= 0.686) and testosterone (p= 0.056) were not found to be statistically different. The incidence of OSA combined with ED was 64.52% (80/124), and the incidence of severe OSA combined with ED was 73.02% (46/63). Among them, every time the AHI value of patients with mild to moderate OSA increased by 1 time/h, the incidence of combined ED increased by 2.259 times. The incidence of combined ED increased by 3.706 times for every increase in the AHI value of patients with severe OSA. The incidence of OSA patients with ED increased with age. The incidence of combined ED increased by 2.444 times for every 1 year of OSA patients in the 18-30-year-old group. The incidence of ED increased by 2.800 times for every 1 year of OSA patients in the 31-40-year-old group. The incidence of combined ED increased by 3.400 times for every 1 year of OSA patients in the 41 to 50-year-old group. The incidence of combined ED increased by 2.400 times for every 1 year of OSA patients in the 51 to 60-year-old group. With the increase of BMI value, the incidence of ED in OSA patients increases. For each increase of 1 kg/m2 in BMI of OSA patients in the normal group, the incidence of combined ED increased by 2.000 times. For each 1 kg/m2 increase in BMI value of over-recombinant OSA patients, the incidence of combined ED increased by 2.471 times. For each increase of 1 kg/m2 in BMI of OSA patients in the obesity group, the incidence of combined ED increased by 3.474 times. Comparing OSA patients with ED and OSA patients without ED, it was found that the BMI (p = 0.039), neck circumference (p = 0.046), waist circumference (p = 0.011), hip circumference (p = 0.046), Epworth score (p = 0.040), Baker depression score (p = 0.011) and ASEX score (p <0.001) in the combined ED group were higher than those of the non-ED group. Comparing OSA patients with ED and OSA patients without ED, it was found that sleep efficiency (p = 0.036), mean oxygen saturation (p = 0.018) and minimum oxygen saturation (p = 0.027) was significantly lower. Compared with the combined ED group, the total number of respiratory events (p = 0.026), the number of obstruction and hypoventilation events (p = 0.024), the total proportion of awake periods (p = 0.030), and the total proportion of light sleep periods (p =0.034) was significantly higher. The ROC curve analysis showed

that the AUC (area under the curve) from high to low was: average oxygen saturation (0.691), minimum oxygen saturation (0.636), the total proportion of light sleep period (0.631), sleep efficiency (0.612). It showed that compared with the IIEF-5 scoring standard, the five related factors of average oxygen saturation, minimum oxygen saturation, the total proportion of light sleep period, and sleep efficiency were of lower diagnostic value. Comparing OSA patients with ED and OSA patients without ED, it was found that the secretion of prolactin (p=0.793), follicle-stimulating hormone (p=0.599) and luteinizing hormone (p= 0.676), progesterone (p=0.533), estradiol (p=0.682), and testosterone (p=0.431) in the combined ED group was not significantly different than that in the non-ED group. The ROC curve analysis showed that the AUC (area under the curve) from high to low was: testosterone (0.554), estradiol (0.535), luteinizing hormone (0.529), prolactin (0.518) and progesterone (0.496), follicle-stimulating hormone (0.464). It showed that compared with the IIEF-5 scoring standard, the diagnostic value of the four related factors of testosterone, estradiol, luteinizing hormone, and prolactin was low, and the remaining two related factors had no diagnostic value. Fifteen patients with mild-moderate OSA combined with ED and fifteen patients with severe OSA combined with ED were followed up. After 6 months of UPPP surgery, the AHI of mild-moderate OSA decreased from 16.55 ± 5.60 times/h to 4.33 ± 1.23 times/h, and the IIEF-5 score increased from 17.94 ± 3.70 to 24.61 ± 4.76 (p<0.05); the AHI of severe OSA decreased from 58.27 ± 14.10 times/h to 13.56 ± 7.25 times/h, and the IIEF-5 score increased from 17.11 ± 3.97 increased to 22.51 ± 5.37 (p<0.05). Conclusion: ED is a common symptom of OSA patients, and mild ED is the main symptom. The incidence of OSA combined with ED is 64.52%, and the incidence of severe OSA combined with ED is 73.02%. The incidence of OSA combined with ED increases with age, BMI, and AHI. Epworth score, sleep efficiency, the total number of respiratory events, number of obstruction, and hypopnea events, the total proportion of waking period, the total proportion of light sleep period, minimum blood oxygen saturation, and average blood oxygen saturation may be the reasons for OSA patients combined with ED. Improving the patient's anxiety and depression is very important for the treatment of OSA combined with ED. OSA patients combined with ED may not be caused by abnormal levels of sex hormones. UPPP surgical treatment is an effective treatment for OSA combined with ED, and its possible mechanism is to improve the patients' nocturnal hypoxia and repeated awakening.

Keywords

Development and validation of the pediatric narcolepsy severity scale

Chenyang Li1,Shaomei Shang1,Chi Zhang2,Fang Han2
1.Peking University School of Nursing
2.Peking University People's Hospital

Objective: To develop and psychometrically test the pediatric narcolepsy severity scale (PNSS) for pediatrics with narcolepsy type 1 (NT1). Methods: The PNSS was developed based on a literature review, clinical judgment of the expert panel, and input of the narcoleptic patients and their parents. Psychometric properties are assessed after applying the PNSS in a sample of 191 patients (younger than 18 years) with NT1 from sleep centers. Analyses included descriptive statistics, item analysis, validity, and reliability. Results: Principal component analysis revealed four distinct and theoretically coherent factors (excessive daytime sleepiness and disrupted nocturnal sleep, cataplexy, hallucination and sleep paralysis and hyperkinetic behavior), explaining 61.101% of the total variance. The final 17-item questionnaire demonstrated good internal consistency (Cronbach's α = 0.736–0.911). PNSS is closely correlated with other measures assessing similar construct Pediatric Daytime Sleepiness Scale (PDSS), the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD), and the Center for Epidemiological Studies Depression Scale (CES-DC) (r = 0.25–0.39, p < 0.01). The intraclass correlation efficient (ICC) for test-retest reliability was 0.74 (p<0.01). Conclusion: PNSS is a valid measure of symptom severity for pediatric patients with NT1. It may serve as a valuable and easily accessible outcome measure for use in narcolepsy trials, the clinic with improved responsiveness, and the long-term follow-up.
Keywords Narcolepsy, validity, reliability

Can daytime Transcranial direct current stimulation treatment change the quality of sleep for depression patients: EEG perspective ?

Zhe Li1,2, Zhuang Yue3,Xue Li Zhao1,4, Wen Pan1,Ming Yin1,Shigeng Gao1,Yingying Shen1,Ying Liu1,Xiang Dong Du1,Guo Rui Liu1,Yu Zhao1,Rui Chen2
1.The Affiliated Guangji Hospital of Soochow University
2.The Second Affiliated Hospital of Soochow University
3.Peking University
4.Xuzhou Medical University

Background: Transcranial direct current stimulation(tDCS) is a non-invasive brain stimulation technique for the treatment of depression. tDCS stimulation during sleep increases slow oscillations, but it is difficult

to treat patients after they fall asleep in clinical, so can daytime tDCS treatment change the EEG of patients during night sleep? To acquire the overall information on the complexity from nonstationary and nonlinear EEG signals, intrinsic MSE was used to analyze EEG signals of depression patients before and after tDCS. Method: In this study, 31 patients with depression were recruited with 18 patients receiving tDCS active stimulation and 13 patients receiving sham stimulation. Ten sessions of tDCS were administered with the anode over F3 and cathode over F4. Each session delivered a current of 2 mA for 30 min per ten working days. Hamilton-24 and Montgomery scales were used to assess the severity of depression, and polysomnography was used to assess the sleep structure and EEG complexity. Eight intrinsic mode functions (IMFs) were computed from per EEG signal in a channel. The sample entropy of the cumulative sum of the IMFs was computed to acquire high-dimensional multi-scale complexity information of EEG signals. Result: After tDCS active stimulation, the complexity of EEG signals decreased significantly. Meanwhile, no significant change in complexity was observed in the sham group. Comparing with sleeping stage N1 and N2, there are more channels and dimensions existing significant change after tDCS active stimulation during sleeping stage Rem, Wake, and N3. There were no significant differences in Hamilton-24(P=0.988), Montgomery scale score(P=0.726), and sleep structure (N1%P=0.383; N2%P=0.716; N3%P=0.772) between the two groups after treatment. Conclusion: Intrinsic MSE of EEG signals is able to characterize the intervention effect of tDCS stimulation in depression patients, with higher sensitivity than sleep structure from PSG and clinical scale rating. Daytime tDCS can change the quality of sleep for patients with depression.

Keywords

Map2k5 deficient mice manifest phenotypes and pathological changes of dopamine deficiency in central nervous system

Yumeng Huang1,Jianfang Ma1,Wang Pei1,Rodrigo Morales2,Qi Luo1
1.Ruijin Hospital，Shanghai Jiao Tong University，School of Medicine
2.University of Texas Health Science Center at Houston

Map2k5, a member of the MAPK family, is associated with central nervous system disorders. However, neural functional of Map2k5 from animal models were not well examined so far. Here, we established a Map2k5 targeted knockout mouse model to investigate the behavioral phenotypes and their underlying molecular mechanism. Our results showed that the Map2k5 mutant mice manifested decreased circadian-dependent ambulatory locomotion, coordination, and the female Map2k5 mutant mice were prone to fatigue. There existed impairment of open field exploration and prepulse inhibition of acoustic startle response in male Map2k5 mutant mice, compared to wild type controls. Furthermore, the Map2k5 mutant mice showed decreased dopaminergic cell survival and tyrosine hydroxylase levels in the nigrostriatal pathway, indicating a crucial role of Map2k5 in regulating the dopamine system of the central nervous

system. In conclusion, this is the first study demonstrating that Map2k5 mutant mice displayed phenotypes by disturbing the dopamine system in the central nervous system, implicating Map2k5 mutant mice as a promising model for many dopamine-related disorders.

Keywords

Butyrate improves cognitive impairment caused by circadian rhythm disorder through regulating JAK2–STAT3 pathway

Lin Xu1,Zhu Ai1,Linlin Wang1,Xiaoning Wang3,Xuan Liu2,Rong Xue1

1.General Hospital of Tianjin Medical University

2.Airport Hospital，General Hospital of Tianjin Medical University

3.The First Affiliated Hospital of Hebei North University

Objective: The study aims to explore the protective effect of butyrate on cognitive impairment caused by chronic circadian rhythm disorder through regulating the JAK2-STAT3 signal pathway. Methods: Male 6-week-old C57BL/6J mice were randomly divided into three groups, the normal control group (NC, n=6), the chronic circadian rhythm disorder group (CRD, n=6), and the butyrate treatment CRD group (CRD+SCFA, n=6). Morris water maze test was performed on mice after 120 days of intervention. The protein expression levels of JAK2, p-JAK2，STAT3, and IL-6 mRNA in mouse hippocampus were measured. Results: 1. Compared with the NC group, the escape latency of the CRD group mice was prolonged, and the difference was statistically significant (**P<0.01). While the SCFA group mice's escape latency was shorter significantly than the CRD group mice (**P<0.01). Compared with the NC group mice, the time of staying in the target quadrant time and the number of crossing the platforms of the CRD group mice was reduced significantly (**P<0.01, **P<0.01). In comparison with the CRD group mice, SCFA Group mice stayed in the target quadrant for a longer time, the difference was statistically significant (**P<0.01), and the number of crossing platforms increased, although the difference was not significant, there was a certain trend. 2. The expression of JAK2, p-JAK2, and STAT3 protein in the hippocampus of mice in each group was not significantly different. But a tendency towards higher was seen in the CRD group and a downward trend after SCFA treatment. 3. Compared with mice in the NC group, the level of IL-6 mRNA in the hippocampus of the CRD group was increased, and a significantly decrease was observed in the SCFA group compared with the CRD group (*P<0.05, *P<0.05). Conclusion: Butyrate may regulate the JAK2-STAT3 pathway by inhibiting the expression of the IL-6, reducing hippocampus inflammation and improving the cognitive function of mice.

Keywords

Validation of a new single–channel wearable EEG device (UMindSleep Forehead Sleep Recorder, Model S1) against polysomnography

Hanrong Cheng1,Yongli Wei1,Jihui Zhang2

1.Shenzhen People's Hospital

2.Guangdong Provincial People's Hospital

Background: Polysomnography is a gold standard measure for the diagnosis of most sleep disorders, but the cost is high. In addition, it is not feasible under routine health care settings. Wearable sleep electroencephalogram (EEG) devices may provide a feasible and accessible method for assessing sleep, especially under daily routine. The aim of the research was to investigate the validity of a new single-channel EEG device in patients with and without obstructive sleep apnea against standard polysomnography. Methods: A total of 97 adults aged 20 to 62 years (mean age 36.6), 67.0% male participated in a single night sleep recording using both standardized whole-night polysomnography and a single-channel EEG device (UMindSleep Forehead Sleep Recorder, Model S1). Sleep stages of polysomnography were manually scored by an experienced registered polysomnogram technologist, while sleep stages of a single-channel EEG device were automatically scored by the auto-score algorithm. Results: Overall, less than 1% of invalid data were identified. The average agreements for differentiating each sleep stage, REM-NREM-wake, and sleep-wake were 0.82 ± 0.05, 0.88 ± 0.04, 0.93 ± 0.04, respectively. The agreement was minimally affected by age, sex, and diagnosis of OSA. The sensitivity in determining wake, stage N1+N2, stage N3, and REM sleep were 0.76, 0.85, 0.76, 0.80 while the specificity in determining wake, stage N1+N2, stage N3, and REM sleep were 0.96, 0.80, 0.97, 0.96, respectively. Conclusions: The new single-channel EEG wearable device has excellent performance in collecting EEG single for analysis. The overall agreement for differentiation of each sleep stage ranges from satisfactory to excellent, which suggests that this device is feasible in measuring sleep in daily life routine.
Keywords

The effect of caregivers' perception on the short–term compliance of CPAP treatment in children with OSAHS

Liqiang Yang,Dabo Liu,Jianwen Zhong

Shenzhen Hospital of Southern Medical University

Objective: To explore the effect of caregivers' perception on short-term adherence of children with OSAHS treated with CPAP. Methods: Twenty-four children with OSAHS treated with CPAP in our department from

2018 to 2020 were retrospectively recruited. First, according to caregivers' perception on OSAHS and CPAP treatment, the patients were divided into two groups: group Ifor CPAP treatment (n = 9) and group II for operation (n= 15). The following parameters of the two groups were compared: demographic characteristics, parameters of short-term adherence in hospital (days of CPAP treatment, day1(h), day2(h), average time of use(h) , the minimum time of use(h), the percentage of ≥4hours in a day), average pressure of autoCPAP, AHI, OAI and LSaO2. Then, the children in group II were divided into a good adherence group (n = 6) and a poor adherence group (n = 9) based on that the AHI decreased by more than 50% or not two months after treatment. Finally, the trend of group I of day1 and day2, the good and poor adherence groups were analyzed. Results: The average time of use (h) of group I was significantly more than group II (p=0.046). The AHI of good adherence group derived from group II was more severe than the poor adherence group (p=0.046). In the trend chart, the day 1 (h) and day 2 (h) of group I remained ahead, while day 1 (h) of good adherence group fell behind the poor adherence's, which reversed in the day2 (h). Conclusions: The short-term adherence of CPAP treatment can be improved by sufficient education of the caregivers.This finding suggests that the education of preoperative CPAP treatment should be carried out in outpatient department for the children with severe OSAHS. In addition, improving the short-term adherence of CPAP treatment in children with severe OSAHS can promote the implementation of long-term adherence, especially in the first two days of CPAP treatment.

Keywords Caregivers' perception; OSAHS; CPAP; short-term adherence

Relationship between neuropeptide–S receptor gene polymorphism and primary insomnia

Jie Fan,Yuping Xie

Gansu Provincial Sleep Clinical Medical Research Center，Gansu Provincial Hospital

Objective: To investigate the assocation between between neuropeptide-S receptor gene polymorphism and primary insomnia. Methods: The SNPs of some NPSR in 158 primary insomnia patients were collected and sequenced. The same sites in 133 heathy controls matched with age and sex were also sequenced. Specific neuropeptide-S SNP sites included rs323922,rs324377,rs324396,rs740347,rs324957,rs324981,rs324987,rs 323920,rs323917,rs2530547,rs887020,rs1963499 and rs2168890. Meanwhile, standard polysomnography was performed to asess the correlation between gene polymorphism and primary insomnia. Results: The genotype distributions of SNPs of the NPSR gene were in Hardy-Weinberg equilibrium in both patients and controls (P>0.05). The allele and genotype distributions of this variant were comparable between men and women (all P>0.05). The T/C gneotype of NPSRrs323920 between patients and healthy controls had statistical significance(p=0.042), the A/G gneotype of NPSRrs324957 between patients and healthy controls had statistical significance(P=0.023). The 13 sites had a linkage imbalance, and the haplotype C A C G G T C C C A G C was significanty different between the PI group and the control group (P < 0.01). Conclusion: The

neuropeptide S gene polymorphisms rs323920 and 324957 may be a susceptibility loci for primary insomnia. The T＞C variant of gneotype of NPSRrs323920 and the A＞G variant of gneotype of NPSRrs324957 may be related to the primary insomnia.

Keywords

Melatonin ameliorates CIH–induced systemic inflammation via improving intestinal barrier dysfunction

Huajun Xu,Fan Wang ,Xinyi Li,Yupu Liu,Feng Liu,Jian Guan,Hongliang Yi,Shankai Yin
The Sixth People＇s Hospital Affiliated to Shanghai Jiaotong University

Genome–wide association study of standard polysomnography confirmed OSA and its related quantitative traits identifies 17 novel risk loci in Han Chinese

Shankai Yin1,2,4,Feng Liu1,2,4,Huajun Xu1,2,4,Zhiqiang Liu3,2,Xinyi Li1,2,4,Yuenan Liu1,2,4,Xiaoxu Zhang1,2,4,Niannian Li1,2,4,Zhenfei Gao1,2,4,Yupu Liu1,2,4,Jian Guan1,2,4,Hongliang Yi1,2,4,Yongyong Shi3,2

1. Department of Otolaryngology-Head and Neck Surgery，Shanghai JiaoTong University Affiliated Sixth People＇s Hospital
2. Shanghai Key Laboratory of Sleep Disordered Breathing
3. Bio-X Center of Shanghai JiaoTong University
4. Otolaryngology Institute of Shanghai JiaoTong University

Objective To identify novel genetic variants associated with obstructive sleep apnea (OSA) and its related quantitative traits, and to explore their functional roles in OSA pathophysiology. Methods: (1) Design: Genome-wide association study. Follow-up functional validation of possible causal variants of OSA. (2)Setting: The Shanghai Sleep Health Study (SSHS) cohort, providing genotypic and PSG confirmed phenotype of OSA, and the Shanghai Sleep Survey Study (4S) cohort, providing genotypic data of most of the controls without obvious snoring. (3) Participants: SSHS cohort including 5438 cases (mean apnea-hypopnea index (AHI) =46.5 times per hour) and 808 controls (AHI<5 times per hour); 4S cohort including 14344 controls. Results Two genome-wide significant loci [the intronic variant rs6455893 within the PACRG gene in 6q26 (odds ratio (OR)=1.619, 95% confidence interval (CI): 1.389-1.888; p=6.98×10-10), and a missense variant rs3746804 (NP_212134.3: p.Pro267Leu) located in the SLC52A3 gene in 20p13 (OR=0.834, 95%CI: 0.787-0.883; p=7.57×10-10)] were identified for OSA; 15 genome-wide significant loci associated with OSA related quantitative traits were also found: 7 loci (1p34.3,

3q26.32, 5q31.2, 6q15, 8p11.21, 9p13.1 and 13q14.11) for respiratory events; 2 loci (12q24.22 and 4p13) for oxygen traits and 6 loci (2p16.2, 4q32.3, 6p21.2, 7p11.2, 9p24.3 and 17p13.3) for sleep architecture. Follow-up functional study revealed that p.Pro267Leu of riboflavin transporter SLC52A3 altered the 3D conformation of cytosolic segment, associated with higher serum riboflavin level and also affected the mitochondrial respiration activity of neural cells. Luciferase reporter assay revealed that the lead variant of OSA rs6455893(6q26), wake duration associated variant rs11733138(6p25.3) and N3 sleep duration associated variant rs12552288(9p24.3) had allele-specific transcriptional activity. Conclusion We reported 17 novel genome-wide significant loci associated with standard polysomnography (PSG) confirmed OSA and its quantitative traits. These findings provided new insights into the genetic architecture of OSA, and SLC52A3 as a possible therapeutic target, along with riboflavin as potential drug.

Keywords obstructive sleep apnea, Genome-wide association study, AHI, single nucleotide polymorphism

Research on sleep quality evaluation algorithm based on multi–event fusion

Chenyang Li,Guan Jian,Xu Huajun,Li Xinyi,Yi Hongliang,Shi haibo,Yin Shankai

Shanghai Sixth People's Hospital

Sleep quality has great impacts on human's life and study ability.In recent years, more than one-third of population worldwide have suffered from a series of sleep disorders such as insomnia and sleepiness. Sleep experts remind that sleep quality is fundamental to maintain physiological functions of the human body, while persistent sleep disorders for example insomnia can cause a series of physiological diseases. The assessment of sleep quality in most current clinical studies is subjective, and the quantitative indicator of sleep quality is lack. It is urgent to establish an objective and concrete method to evaluate people's sleep quality in clinic. This study calculated REM sleep time (TREMS), NREM sleep time (TNREMS), and respiratory disturbance index (RDI), heart rate variability (HRV) analysis index, wakefulness response index and a series of evaluation indicators through a combined analysis of the patient's sleep structure, sleep disorder breathing events, sleep cardiovascular events, and wakefulness response events. The quantitative indicators obtained by the algorithm are compared with the results of polysomnography (PSG) and patient complaints. This quantative method effectively helps doctors to objectively and comprehensively evaluate the sleep quality of patients with sleep disorders. This study offset the limitations of traditional subjective scale assessment of sleep quality. The findings can provide evidence for diagnosis and treatment of patients with sleep disorders.

Keywords

Insomnia Symptoms are Associated with Metabolic Syndrome in Patients with Severe Psychiatric Disorders

Yun Li1,2,Wenjuan Zhang1,2,Qimeng Sun1,2,Baixin Chen1,2,Maria Basta 3,Chongtao Xu1,2

1.Shantou University Mental Health Center

2.Shantou University Medical College

3.University Hospital of Heraklion，Heraklion，Crete，Greece

Objective: The association between severe psychiatric disorders and metabolic syndrome (MetS) is emerging as a public-health question. Insomnia symptoms are common in patients with severe psychiatric disorders. Emerging evidence suggests that insomnia is associated with increased risk for MetS. However, limited studies have examined the association between insomnia symptoms and MetS in patients with severe psychiatric disorders. We hypothesized that insomnia symptoms are independent risk factors for MetS in patients with severe psychiatric disorders. We therefore aimed to examine the association between insomnia symptoms and MetS in severely mentally ill patients. Methods: We conducted a cross-sectional study including 272 patients with severe psychiatric disorders consecutively admitted to Shantou University Mental Health Center Inpatient Department. All patients underwent a psychiatric evaluation. Insomnia symptoms were assessed by the Pittsburgh Sleep Quality Index (PSQI) and defined if a score of PSQI>7. The diagnosis of MetS was defined using the new International Diabetes Federation definition based on clinical and laboratory evaluation. Results: Of the 272 patients included, the mean age was 34.06 years old (standard deviation, 11.52 years), 67.3% were men, and 34.6% presented with insomnia symptoms. Overall, compared with the patients without insomnia symptoms, those with insomnia symptoms had significantly higher frequency of MetS (23.4% vs. 12.4%, p=0.019), hypertriglyceridemia (30.9% vs. 19.1%, p=0.029), and significantly higher levels of fasting insulin (58.75±37.22 pmol/L vs. 51.72±34.09 pmol/L, p=0.050), homeostasis model assessment of insulin resistance (1.83±1.31 vs. 1.62±1.25, p=0.055) and percentage of insulin resistance (55.3% vs. 44.4%, p=0.086) . Multiple logistic regressions showed that patients with insomnia symptoms had significantly higher risk for MetS [odds ratio (OR)=2.99, 95% confidence interval (CI)=1.25-7.14], central obesity (OR=3.02, 95% CI=1.18-7.76), hypertriglyceridemia (OR=2.46, 95% CI=1.28-4.76) and significantly higher odds for insulin resistance (OR=1.68, 95% CI=0.93-3.02) after controlling the potential confounders. Conclusions: Among severely mentally ill patients, insomnia symptoms are associated with the risk of MetS and insulin resistance. Our findings suggest that insomnia symptoms may be independent clinical indicators of underlying MetS in patients with severe psychiatric disorders.

Keywords

Usefulness of Maintenance of Wakefulness Test in assessment of sleepiness

Yingxin Wu,Qishan Wei,Xiuxuan Xiang,Lu Wang,Bating He,Yan Chen,Simin Liu,Sichang Xiao,Yuanming Luo

The First Affiliated Hospital of Guangzhou Medical University

Objectives: Maintenance of wakefulness test (MWT) is usually used to evaluate the sleepiness in patients with OSA. We aimed to evaluate the usefulness of simplified MWT in quantifying daytime sleepiness. Methods: Seventeen patients with suspected OSA and 4 healthy subjects (43.48 ± 12.36 yrs, BMI 27.02 ± 5.06 kg/m2) were recruited. Simplified MWT repeated twice with a gap of 2 hours, and it was performed next morning immediately after full polysomnography. Correlation between ESS and mean sleep latency of simplified MWT was assessed. Seventeen subjects with sleepiness were confirmed having OSA and 4 healthy subjects were normal by PSG. MWT was repeated in eleven of seventeen patients treated with CPAP. Results: The mean sleep latency of OSA patients was shorter than that of healthy subjects (27.8 ± 12.8 min. vs 40.0 ± 0.0 min; p<0.01). There was negative correlation between sleep latency and ESS （r= -0.78,p<0.01）or sleep latency and AHI（r= -0.52,p<0.01）. CPAP treatment could significantly prolong sleep latency in patients with OSA (24.2 ± 12.8 min vs. 32.8 ± 11.5 min; P<0.01). Conclusions: Simplified MWT is useful to assess daytime sleepiness and to differentiate patients with sleepiness from healthy subjects.

Keywords Maintenance of wakefulness test, sleepiness

Inhibitory effect of yishen formula on hippocampal neuron apoptosis in rats with vascular cognitive dysfunction and its mechanism

Jian Xu,Ou Li,Yixia Li,Jie Zhang,Zhongwei Sha

Shanghai Hospital of Traditional Chinese Medicine

Abstract：Vascular cognitive impairment is a syndrome characterized by cognitive dysfunction caused by a series of cerebrovascular factors (including cerebral ischemia, cerebral hemorrhage, acute and chronic hypoxic cerebrovascular disease, etc.).And Yishen recipe has achieved a lot in the process of clinical treatment for patients with vascular cognitive impairment, Therefore, our research group investigated the mechanism by which Yishen recipe inhibited hippocampal neurons apoptosis in rats with vascular cognitive impairment. The experiment proves Yishen recipe can effectively improve the spatial learning ability and memory space in the VCI model rats. It can effectively improve the cerebral infarction area, reduce the apoptosis of hippocampal neurons and correct the morphology of hippocampal neurons in VCI rats. Yishen recipe can increase the expression of Bcl-2 protein and decrease the expression of Bax, thereby reducing the

expression of apoptosis factors Caspase-3 and Caspase-9, which can inhibit the apoptosis of hippocampal neurons. Yishen recipe can promote the expression of p-TrkB and p-Akt and reduce the expression of proBDNF and p75NTR to protect brain-derived neurotrophic factor. These experiments provided a scientific basis and a new way of thinking for the treatment of vascular cognitive impairment with traditional Chinese medicine.

Keywords Vascular Cognitive Impairment; Hippocampus; Neuron ; BDNF; apoptosis

Epidemiology of sleep disturbances during pregnancy and its association with pregnancy complications and perinatal outcomes: a multi–center retrospective study

Chu 珺 Zhang1,2,3,Yijia Su1,2,3,Huajun Xu1,2,3,Yvpu Liu1,2,3,Hongliang Yi1,2,3,Jian Guan1,2,3,Shankai Yin1,2,3

1.Shanghai Jiao Tong University Affiliated Sixth People's Hospital
2.Shanghai Key Laboratory of Sleep Disordered Breathing
3.Otolaryngology Institute of Shanghai Jiao Tong University

Objective: Sleep disturbances during pregnancy are common diseases that may not only be aggravated by physiological changes throughout gestation but also lead to a variety of maternal and infant complications. This study aimed to investigate the prevalence of sleep disturbances among Chinese pregnant women and to explore the relationship between sleep quality and pregnancy complications, as well as adverse pregnancy outcomes. Methods: Integrated online sleep questionnaire combining Pittsburgh Sleep Questionnaire Index (PSQI), Berlin Questionnaire, Epworth Sleepiness Scale (ESS), and Athens Insomnia Scale (AIS) were used to diagnose various sleep disturbances, such as poor sleep quality, insomnia, and excessive daytime sleepiness. Final perinatal outcomes and antenatal screening results, including routine physical examination, lab tests, and fetal heart monitoring, were collected. Statistical analyses were performed using SPSS version 22 to investigate the associations between main sleep quality indexes and each maternal or fetal outcome and how they vary among different subgroups divided by different trimesters of pregnancy, medical history, and physical abnormalities. Results: 5370 valid questionnaires from 7788 collected ones were included in the final statistical analysis. The prevalence of poor sleep quality (PSQI score＞ 5), clinical insomnia (AIS score＞ 6), and excessive daytime sleepiness (ESS score＞ 10) was 38.72%, 18.75%, and 56.89%, respectively. Higher BMI, advancing age, and gestational weeks significantly increase the prevalence of sleep disturbances in pregnancy, respectively ($p<0.001$). Besides, sleep disturbances were significantly associated with preeclampsia, gestational hypertension, gestational diabetes mellitus, preterm birth, but not low APGAR score or low birth weight. Conclusions: The easily ignored sleep disturbances are prevalent among and harmful to Chinese pregnant women. The findings provide potential evidence for the association between

sleep disturbances and the risk of pregnancy complications. Our study indicates a need for more attention on sleep disorders during pregnancy from prenatal counseling and health care services.
Keywords

Association between sleep duration and subjective cognitive decline

Lihua Lin,Wenqi Xu,Shibin Wang,Fujun Jia
Guangdong Mental Health Center

Objective: To explore the association between sleep duration and subjective cognitive decline (SCD). Methods: A cross-sectional study included 717 participants aged above 60 years was conducted. Participants' sleep duration was self-reported. Subjective cognitive questionary 9 (SCD-Q9) was used to measure the symptoms of SCD, with a higher score indicating more severe SCD. Restricted cubic splines and generalized additive model (GAM) were used to explore the shape of the association between sleep duration and SCD symptoms, including global SCD symptoms score, the function of overall memory and time comparison (FMTC) score and daily activity ability score. Result: There was a significant non-linear association between global SCD symptoms scores and sleep duration (EDF = 3.855, p <0.001), function of overall memory and time comparison score and sleep duration (EDF = 4.616, p <0.001), daily activity ability score and sleep duration (EDF = 2.083, p <0.001) in the age- and sex-adjusted GAM. Both the lowest global SCD symptoms score and the FMTC score were observed in those sleeping 8 hours per night. After adjusting for demographic characteristics, lifestyle behaviors and health status, we found strong U-shaped associations between sleep duration and global SCD symptoms score (EDF = 3.830, p = 0.089), and between sleep duration and the FMTC score (EDF = 4.673, p=0.107) through GAM. Similarly, the lowest global SCD symptoms score and the FMTC score were both observed in people sleeping 8 hours per night. Conclusion: Sleep duration of 8 hours per night was associated with the mildest symptoms of SCD. Both longer sleep duration (＞ 8 h) and shorter sleep duration(＜ 6h) were associated with symptoms of SCD. To prevent dementia, we recommend the general population over 60 years to sleep for 8 hours per night.
Keywords

Subjective cognitive decline and its relationship with demographic characteristics and chronic diseases in Chinese elderly

Lihua Lin,Wenqi Xu,Shibin Wang,Fujun Jia
Guangdong Provincial Mental Health Center

Objective: Subjective cognitive decline (SCD) is the first symptomatic manifestation of Alzheimer's disease, but their correlation was unknown . This study examined whether SCD symptoms was related to

demographic characteristics and chronic diseases among Chinese elderly. Method：Participants aged 60 years or older from 7 communities and 2 nursing homes in Guangzhou were recruited and interviewed with standardized assessment tools. The subjective cognitive decline symptoms were measured by SCD questionnaire 9 (SCD-Q9), with a higher score indicating increased severity of the SCD. Multivariate linear regression analyses were used to explore the correlates of SCD. Result：A total of 717 participants were included in the study with the mean age of 73.72 years old (SD =8.27, range = 60-101), while 37.0% participants were men and 63.0% were women. The mean score of the SCD-Q9 were 3.86 ± 2.43 in the whole sample. Multivariate linear regression analyses revealed that older adults aged over 70 years old, female gender, widowed/separated marital status, primary or lower education level, live in nursing home, current smoking status and lower BMI were independently and positively associated with SCD-Q9 score. After adjusting for the socio-demographic characteristics and lifestyle factors, the SCD-Q9 score was significantly higher in those suffering from chronic low back pain, urolithiasis, chronic gastroenteritis/peptic ulcer, cataract/glaucoma, osteoporosis, insomnia, depression and anxiety. Conclusion: Health professionals and policy makers need to pay special attention to subjective cognitive decline among older Chinese population, in order to implement early intervention for Alzheimer's disease.
Keywords

Factors influencing sleep structure changes in OSA pressure titration

Jinxiang Cheng,Jiafeng Ren,Jian Qiu,Yingcong Jiang,Shuyu Sun,Xianchao Zhao,Changjun Su
Department of Neurology，Second Affiliated Hospital of Air Force Military Medical University

Objective: To explore the influence factors of changes of sleep structure during the first pressure titration of obstructive sleep apnea (OSA). Methods: The study retrospectively included OSA patients who underwent both diagnostic polysomnography (PSG) and pressure titration PSG at the Tangdu Hospital Sleep Medicine Center from 2011 to 2016. Results: A total of 501 OSA patients were included in the paired analysis, of which 225 (44.91%) patients presented with rapid eye movement (REM) sleep rebound, 164 (32.73%) exhibited slow wave sleep (SWS) rebound. Higher oxygen desaturation index, lower REM sleep proportion, higher arousal index, and lower mean oxygen saturation in diagnostic PSG, higher Epworth sleepiness score, younger were prone to REM sleep rebound during pressure titration (adjusted R^2=0.482). Besides, compared with non-REM rebounders, REM rebounders in the diagnostic PSG study had significantly longer total sleep time (TST) (p = 0.03), a shorter sleep latency (SL) (p = 0.009), a higher sleep efficiency (SE) (p = 0.012), less wake after sleep onset (WASO) (p = 0.026), less complaints of insomnia (p = 0.004), anxiety (p <0.001), irritability (p = 0.008), and depression (p = 0.023). Longer total time of apnea and hypopnea, lower duration of N3 sleep, low lowest oxygen saturation, lower REM sleep proportion in diagnostic PSG, younger predicted SWS rebound during pressure titration (adjusted R^2 = 0.286).In addition, compared with non-SWS

rebounders, SWS rebounders had significantly longer TST (p = 0.002), a higher SE (p < 0.001), less %N1 (p = 0.027), less WASO (p < 0.001) in the diagnostic PSG study, less complaints of less insomnia (p = 0.001), anxiety (p = 0.011), and irritability (p = 0.034). Conclusion: OSA patients with less severity in apneas and hypopneas, more subjective and objective insomnia and emotional disorders have poor sleep structure during pressure titration.

Keywords

Circadian regulation of sleep –– Insights from zebrafish

Han Wang

Suzhou university

The zebrafish (Danio rerio) has figured prominently as a vertebrate model for studying circadian clocks and sleep. According to Borbely's "two-process model" for sleep regulation, both the homeostatic process (S) that increases with the duration of wakefulness and the circadian process (C) that determines the timing of sleep and wake, contribute to regulation of sleep homeostasis. While we have a good understanding of circadian regulation, relatively less is known about molecular mechanisms underlying circadian regulation of sleep homeostasis. Here we set to investigate regulatory roles of circadian clock protein Period in zebrafish sleep homeostasis. We reported characterization of zebrafish period3 (per3) null mutants generated by transcription activator-like effector nucleases (TALEN). Locomotor assays showed that per3 mutant fish displayed 0.5-hour shortened period and approximately 3-hour phase advance compared with wild types under constant dark, and were completely arrhythmic under constant light. Intriguingly, per3 mutant fish displayed less sleep time, elevated arousal threshold and difficulty to restore sleep after sleep deprivation. As shown by ELISA, the γ-aminobutyric acid (GABA) level was reduced, indicated that the disturbed sleep pattern of per3 mutant fish may be resulted from altered levels of endogenous GABA. Deep sequencing-based transcriptome analysis leaded us to focus on one candidate gene, GABA A receptor gene rho2a, which is up-regulated in the per3 mutant fish. Luciferase reporter assays showed that rho2a was circadian clock-controlled genes and per3 negatively regulated its expression. Taken together, these results ascertained per3's essential roles in the zebrafish circadian system, demonstrated that per3 acted through GABA signaling to contribute to sleep regulation, and provided an ideal sleep disorder vertebrate model for drug screen and pathogenesis analysis.

Keywords

Translation and validation of Berlin questionnaire in patients with obstructive sleep apnoea syndrome in china

Xuelong Jiang1,Cuiying Wei2,Huiling Wang4,Xiaosong Dong3,Qinglong Zhang1,Min Li1,Juan Shi1,Zhongming He1,Fang Han3

1. Karamay Central Hospital of Xinjiang
2. The First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of Science and Technology
3. Peking University People's Hospital
4. Handan Central Hospital

Objective: Obstructive sleep apnea syndrome (OSAS) is a common disorder with significant morbidity and mortality. We aimed to evaluate the predictive accuracy of Berlin questionnaire in patients with suspected OSAS in China. The aim of our study was to validate a Chinese translation of the Berlin Questionnaire (BQ) for obstructive sleep apnoea syndrome (OSAS) and to explore whether this screening questionnaire could be used to help identify community-based setting at greater risk of having OSAS. Methods: We recruited 1709 patients visiting sleep center in Karamay central hospital from Jan 2016 to Dec 2019 , China. They all completed the Chinese Version of the BQ (CBQ) and Epworth Sleepiness Score (ESS). Patients were then referred to a Sleep Center for evaluation of suspected sleep-disordered breathing by Home Sleep Apnea Testing (HSAT). Results: HSAT study was performed in 1709 subjects. BQ identified 70.3% (n =1201) of the patients as high-risk for OSAS and the remaining 29.7% (n=508) as low-risk. The sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of the questionnaire to predict an AHI $\geq$ 5/hr as diagnosed by HSAT were 75.9%, 46.2%, 39.8%, 60.7%, respectively, 81.9%, 38.5%, 73.8%, 50.2%, for an AHI $\geq$15 per hour, and 89.7% ,35.1% ,92.5%,27.6% for an AHI >30 per hour. Conclusions: The Chinese Version of the BQ is a useful instrument for identifying patients at risk for OSAS in community-based setting in China. The findings of our study suggest that such screening tools of CBQ should be used by primary care clinicians for OSAS prediction.
Keywords Berlin questionnaire, Obstructive sleep apnoea syndrome, sensitivity and specificity,validation

Increased expression of Nrf2 protects against renal injury induced by chronic intermittent hypoxia

Yuanai Li,Yueyuan Wang ,Xiaohong Cai

The Second Affiliated Hospital of Wenzhou Medical University，Yuying Children's Hospital

Objective: Oxidative stress-induced apoptosis may be one of the main mechanisms of renal injury in children with obstructive sleep apnea-hypopnea syndrome (OSAHS), meanwhile the Nuclear factor-erythroid

2-related factor (Nrf2) plays a key role in regulating the REDOX balance of the body and anti-oxidative stress injury. In this study, we tested this hypothesis using a model of chronic intermittent hypoxia (CIH) in mice by activating or inhibiting Nrf2 expression with Sulforaphane(SFN) and All-trans retinoic acid (ATRA) respectively and the molecular mechanism of Nrf2 preventing oxidative stress injury of the kidney might be analyzed. Method: Male C57BL/6 mice were randomly divided into the following 6 groups，blank control group (C), air simulation control group (AC), Chronic intermittent hypoxia group (CIH), solvent control group (DMSO), Nrf2 agonist group (SFN) and Nrf2 antagonist group (ATRA).The C group fed normally，while mice in the AC group were placed in the chamber filled with compressed air over a period of 4 weeks. The CIH, DMSO, SFN and ATRA groups were all put into the same CIH chamber. The level of beta 2-microglobulin in urine was determined before and after modeling. Hematoxylin eosin staining was used to assess the pathological changes of renal tissue, serum creatinine and urea nitrogen levels, and Western blotting was used to detect the expression levels of Nrf2, thioredoxin reductase 2, caspase-3 and cleaved caspase-3. Result: The up-regulation of Nrf2 expression induced by SFN significantly reduced the concentration of β2 micro globulin, alleviated the histological damage of renal tubular epithelial cells, and decreased the contents of serum creatinine and urea nitrogen. Nrf2 agonists also attenuate the effect of apoptosis. Conclusion: 1. CIH can cause oxidative stress and lead to renal injury, mainly renal tubular injury. 2. Activation of Nrf2 can reduce the renal damage caused by chronic intermittent hypoxia through the Nrf2/ TrxR2 signaling pathway.

Keywords

Hypoxic ventilatory response in highlander and lowlander Chinese patients with sleep apnea

Dongmei Chen1,Xuelong Jiang1,Qinglong Zhang1,Xiaosong Dong2,Jianping Li1,Juan Shi1,Min Li1,Shilin Ma1,Zhongming He1,Fang Han2

1.Karamay Central Hospital of Xinjiang

2.Peking University People's Hospital

Objective: The aim of this study was to compare the HVR between Uygur people living at high altitude (both with and without obstructive sleep apnea [OSA]) and Chinese Han people living at sea level, and to explore the related factors. Methods: A total of 276 subjects with or without snoring from the Karamay community were recruited. Of them, 226 subjects were divided into the folooowing groups: Han OSA patients (n=71), Uygur OSA patients (n=75), Uygur control subjects without OSA (n=52), Han control subjects without OSA (n =28). All subjects were assessed with PSG. Hypoxic ventilator response (HVR, △ VE/△ SaO2) and the pulse responses to hypoxia changes (△Pulse/△SaO2) were calculated. Results: Among control subjects without OSA, those living at high altitude (Uygur) had a lower HVR compared with those living at sea level (Han)[-0.35L· min-1 per %SpO2 (-0.49 to-0.20L· min-1 per

%SpO2) vs. -0.44L· min-1 per %SpO2 (-0.55 to-0.21L· min-1 per %SpO2)]. Compared with patients with OSA living at sea level (Han), those with OSA living at high altitude (Uygur)had higher neck circumference [43cm (range 39-45cm) vs. 42cm(41-46) cm], higher abdominal circumference [110cm (102-120 cm) vs. 101cm (98- 111 cm], higher LSaO2 [81% (72-85%) vs. 76% (68-81%)], lower AHI [26 events/h (16-43 events/h) vs. 36 events/h (24-62 events/h)] and lower ODI4 [15/h (7-29/h) vs. 37/h (20-54/h)]. Considering patients with mild OSA, those who lived at high altitude (Uygur) had a weaker HVR compared with Han patients [-0.31L· min-1 per %SpO2(-0.42 to-0.20L· min-1 per %SpO2) vs.-0.47L· min-1 per %SpO2(-0.59 to -0.21L· min-1 per %SpO2)]. However, among patients with moderate-severe OSA, the HVR between people living at high and low altitudes was similar. Conclusions: The patients living at high altitude compared with sea level, HVR is weaker in both control subjects and those with mild OSA, however, similar in those with moderate-severe OSA.

Keywords Hypoxic ventilatory response , obstructive sleep apnea, polysomnography, hypoxic pulse response

Male reproductive damage caused by circadian disruption in population and rodent model

Qing Chen,Jia Cao,Xiaogang Wang,Kun Liu,Mengchao He

Army Medical University

Objective: Circadian disruption introduced by modern lifestyles has been an ubiquitous exposure to people living in the 24h-7d society. However, its impacts on male reproductive health remains unclear. This study aimed to explore the impacts of circadian disruption on male reproductive health. Methods & Results: Based on large scale survey of 54,734 males from 35 European countries, we showed that a 10% higher exposure to rotating shift work correlated with a 0.114 (95%CI: 0.061, 0.167, P<0.001) decrease of fertility rate, indicating 11.4 fewer births per 100 women in these countries. Second, the effects of rotating shift work on male reproductive biomarkers (semen quality, sex hormones) was investigated in 1346 community residents: decrease of sperm count was observed, with a 1.26 (95%CI: 1.05, 1.52, P=0.014) fold risk of failure to meet the Chinese standard. Similar damage was also found in a cohort of 796 young men exposed to non-occupational circadian disruption (OR=1.16, 95%CI: 1.02, 1.31, P=0.021), and the damage can be resumed when the circadian disruption was corrected a year later. The damage effect was also replicated in a mouse model, in which circadian disruption was induced by alteration of light/dark cycle. The damage disappeared when the mice were moved to normal light/dark cycle for 35 days. Apoptosis was increased in the testis. The cell types of later stages during spermatogenesis process (round spermatids and elongated spermatids) were decreased. Transcriptome sequencing and RT-PCR showed that homologous recombination, a key event of meiosis was interrupted. Core circadian genes including Clock and Per2 were also down-regulated. Knock-down of the circadian genes in GC2 germ cell line induced apoptosis. Conclusions:These findings suggest that circadian disruption may damage spermatogenesis and leads to subfecundity, although it seems

recoverable. These findings indicate circadian disruption as a potential target for policy makers and health professionals with respect to prevention and medication of male reproductive damage.

Keywords

Validation of the Nox–T3 portable monitor for diagnosis of obstructive sleep ppnea in Chinese pregnancy

Jingyu WANG,Fang HAN

Peking University People's Hospital

Objective: To evaluate the performance of a portable monitor (Nox-T3, Nox Medical Inc. Reykjavik, Iceland) in diagnosing obstructive sleep apnea in Chinese pregnancy. Methods: Eighteen Chinese pregnant women (aged 33.2 ± 4.4 years, body mass index 27.7 ± 4.2 kg/m2) underwent overnight, unattended home sleep apnea testing (HSAT) with the Nox-T3 portable monitor followed by an overnight in-laboratory polysomnogram (PSG) with simultaneous portable monitor recording. The portable monitor recordings were scored using automated analysis and then manually edited using criteria for scoring hypopneas. Polysomnography was scored based on recommended guidelines. Results: When scoring of hypopneas required a $\geq 3\%$ oxygen desaturation event, the apnea-hypopnea index (AHI) was 4.0 ± 6.0 events/h on HSAT and 3.7 ± 3.9 events/h on in-laboratory portable monitor recording, and 4.4 ± 4.8 events/h on PSG. Bland-Altman analysis of AHI on PSG versus HSAT showed a mean difference (95% confidence interval) of -0.32 (-6.87, 6.03). Closer agreements were present when comparing the simultaneous recordings. Conclusions: Despite known differences between HSAT and PSG, the results showed good agreement between the two diagnostic tests in Chinese pregnancy, especially when controlling for night-to-night variability and changes in sleeping environment.

Keywords pregnancy, apnea-hypopnea index, home sleep apnea testing, polysomnography

Alteration of the expression of serum exosomal circular RNAs in OSA patients with acute myocardial infarction

Jiefeng Huang,Qichang Lin

The First Affiliated Hospital of Fujian Medical University

Objectives: Circular RNAs (circRNAs) are recently identified as a class of non-coding RNAs that participate in the incidence of acute myocardial infarction(AMI). However, circRNAs expression pattern in obstructive sleep apnea (OSA) with AMI remains unknown. The aim of this study was to investigate alteration of the expression of circRNAs in plasma exosomes derived from OSA patients with AMI. Methods: The plasma exosomal circRNAs profile of three healthy subjects, three OSA patients without AMI and three OSA

patients with AMI were analyzed using high-throughput sequencing. Bioinformatic analyses were carried out to assess potential core circRNAs. Functional analyses were conducted to study biological functions. Results: Compared with healthy subjects, there were 5225 upregulated and 5798 downregulated circRNAs in exosomes from OSA patients with AMI. We identified 5210 upregulated and 5813 downregulated circRNAs in OSA patients with AMI compared with those without. The differential expression of 2 circRNAs (hsa_circRNA_101147, hsa_circRNA_101561) between healthy subjects and OSA without AMI, and 4 circRNAs (hsa_circRNA_101328, hsa_circRNA_104172, hsa_circRNA_104640, hsa_circRNA_104642) between healthy subjects and OSA with AMI were confirmed by RT-qPCR. In addition, we demonstrated that miR-29a-3p targeted the_circRNA_104642 directly. Conclusions: This study demonstrated that there were a number of dysregulated circRNAs in exosomes from OSA patients with AMI. These circRNAs might serve as a promising diagnostic biomarker and therapeutic targets.

Keywords circular RNAs; exosomes; obstructive sleep apnea; acute myocardial infarction

Changes of serum myocardial enzymes in children with adenoidal hypertrophy and the risk factors of severe upper airway obstruction

Yingying Han,Juanjuan Zou,Yan Wang,Yanzhong Li

Qilu Hospital of Shandong University

Objective: To explore the levels of creatine kinase (CK) ,creatine kinase isoenzyme (CK-MB) ,lactate dehydrogenase (LDH), ischemia modified albumin(IMA) and troponin I (CTNI) in children with adenoidal hypertrophy, further to explore the risk factors of severe upper airway obstruction. Methods: A total of 4,335 adenoidal hypertrophy cases , diagnosed by Lateral view of the nasopharynx, were included in our study. Twenty healthy chirldren served as the controls. The levels of CK,CK-MB,LDH,CTNI and IMA were measured. The rates of abnormal cardiac enzymes in case group were analyzed and the risk factors were assessed. Results: Compared with the control group,the levels of CK,CK-MB,IMA and CTNI were higher (p$<$ 0.05,or p$<$ 0.01) in the cases, but the level of CK-MB of the two groups was similar (p $>$ 0．05). Correlation analyses showed that there was a positive correlation between IMA ,CK-MB and A/N (p $<$ 0.05 or p $<$ 0.001), while a negative correlation between LDH and A/N , BMI (p $>$ 0.05). The detailed information of 924 cases were obtained and 554 cases with myocardial injury were found. Logistic regression analyses suggested that age and BMI were the independent risk factors for myocardial injury in children with adenoidal hypertrophy. PLR and NLR did not directly predict myocardial injury. Conclusions: Severe Upper Airway Obstruction (especially adenoid hypertrophy) can cause myocardial injury in children. Age and BMI are independent risk factors for myocardial injury. The children with severe upper airway obstruction can be properly treated with nutritional myocardial drugs. The clinical value of blood routine related indexes (PLR and NLR) in predicting myocardial injury in children should be further studied.

Keywords

Tissue expression of inflammatory cytokines and rhythm–related genes in sleepdeprived juvenile model animals

Wei Cheng

Xi'an Children's Hospita

Background: Sleep is regarded as an independent factor which plays a vital role in the growth and development of children, especially in learning ability, memory ability, and sexual development. However, its mechanism is not fully understood, and there are many controversies. Objective: To explore the expression of inflammatory cytokines and biorhythm-related genes in the different tissues of sleepdeprived juvenile model animals. Methods: Sleep-deprived juvenile flies were used assleep deprived juvenile model, , and the untreated flies as control. the brains, gut, skeletal muscles and labeling records were obtained by microdissection. tissue chips were made, and mRNA was extracted from these tissues.. The expression of ROS and IL-6 was analyzed by immunohistochemistry in the tissue chips. mRNA sequence information was obtained by Next-generation sequencing technology. Biological information was used to compare the expression of rhythm-related gene DEC2 and its expression level. Results: The levelof ROS and IL-6 in the sleep deprived flies was 2.13-fold in the brain, 3.16-fold in gastrointestinal tract and 1.89-fold in muscles , and motor system respectively, compared to the controls (all $P< 0.01$). The DEC2 expression was significantly reduced in the sleep-deprived model, only 0.03 of that in controls ($P< 0.05$). Conclusion: Sleep deprivation can cause the accumulation of inflammatory cytokines in the brain, gastrointestinal tract, and motor system, leading to immune damage. And by inhibiting the expression of genes related to biological rhythms, the phenomenon of cell biological rhythm disorders is produced.

Keywords

Anxiety and depression in patients with chronic obstructive pulmonary disease and obstructive sleep apnea (overlap syndrome)

Zhiling Zhao,Dongmei Zhang,Haiyan Sun,Junjing Liu,Xiaotao Wu,Xiheng Guo

Beijing CHAO-YANG Hospital，Capital Medical University

Objective: Psychological symptoms attracts increasing attention in patients with chronic diseases. Currently, there are few data available on the mental health of patients with chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA), which also called overlap syndrome (OVS). The aim of this study was to identify the prevalence of and risk factors of anxiety and depression in patients with OVS. Methods: We recruited patients admitted for COPD from July 2018 to July 2019. These patients also underwent polysomnography tests to screen for or assess OSA. Questionnaires were administered to evaluate depression and anxiety in all subjects. We compared the differences in the scores of the above tests between

patients with and without OSA. Results: Seventy-two patients with COPD and 180 patients with OVS were enrolled. The OVS group had a higher body mass index (BMI, 25.82 vs. 24.21 kg/m2) and higher proportions of hypertension (41.1% vs. 20.8%) and coronary heart disease (14.0% vs. 4.2%). A higher proportion of patients in the OVS group complained with chest pain. We found that patients with OVS presented with more severe anxiety (8.00 (4.00, 10.00) vs. 6.00 (3.00, 9.00), p = 0.018) and depression (8.00 (4.00, 10.00) vs. 5.50 (2.25, 10.00), p = 0.022) than patients with only COPD. Chest pain, COPD Assessment Test (CAT) score, depression and OVS were independent risk factors for depression (P<0.05). Anxiety and depression were positively correlated (r=0.638, p < 0.001). Conclusions: Anxiety and depression were more severe in patients with OVS than those with only COPD. More attention should be paid to the mental health of OVS patients.
Keywords

Peripheral iron metabolism was association with legs movements in polysomnography but not with severity and outcomes of restless legs syndrome

Tiantian Wang,Liuqing Pan,Guodong Lou,Lisan Zhang

Sir Run Run Shaw Hospital

Objective: The findings on the relationship between peripheral iron metabolism and restless legs syndrome (RLS) have been published were inconsistent and paradoxical. The aim of present study was to analyze the association between peripheral iron status (storage and transport indicators) and RLS (severity and outcomes and the legs movements of RLS). Methods: One hundred and eight patients with RLS were assessed using questionnaire designed by the SRRSH Center for Sleep Medicine, as well as polysomnography (PSG). Peripheral iron parameters, including serum ferritin, serum iron, unsaturated iron binding capacity (UIBC), total iron-binding capacity (TIBC), transferrin saturation (TSAT) and serum transferrin, were measured after finishing PSG. The patients were divided into 2 groups, i.e., iron-deficiency group (ferritin < 50 ug/L) and non-iron deficiency group (ferritin > or = 50 ug/L). Results: Crude comparisons showed that the severity and outcomes of RLS and legs movements were similar between the two groups. Higher period legs movements in sleep (PLMS) index (OR = 3.074; CI, 1.266-7.456; P = 0.013), PLMS series index (OR = 3.655; CI, 1.484-9.007; P = 0.005), PLMS series duration (OR = 3.238; CI,1.334-7.870; P = 0.009), legs movements in N2 (OR = 3.579; CI, 1.458-8.785; P = 0.005) and legs movements in N3 (OR = 3.099; CI, 1.256-7.645; P = 0.014) were found using multivariate regression in iron-deficiency group. However, no difference of severity and outcomes of RLS were found between the two groups. In addition, the transport indicators (TIBC, UIBC and transferrin) were also associated with some leg movement parameters. Conclusions: Our study found that peripheral iron status mainly associated with leg movements rather than the severity and outcomes in patients with RLS.
Keywords

The prevalence of sleep problems among primary school students and its relationship with cognitive behaviors

Shiyin Yang1,2, Yupu Liu1,2,Huajun Xu1,2,Jian Guan1,2,Shankai Yin1,2

1.The Sixth People's Hospital Affiliated to Shanghai Jiaotong University

2.Shanghai Key Laboratory of Sleep Respiratory Disorders

Objective: To study the prevalence of sleep problems in primary school children in Xuhui District, Shanghai; and, and to explore its relationship with cognitive behaviors. Method: We distributed online questionnaires to the parents of the students from primary schools in Xuhui District, Shanghai. Pediatric sleep questionnaire (PSQ) and obstructive sleep apnea 18-item quality-of-life questionnaire (OSA-18) were used to assess sleep quality. Children's cognitive behaviors were assessed through the Conners' Parent Rating Scales (CPRS). The correlation between sleeping and cognitive behaviors was analyzed by Mann-Whitney U test. Result: A total of 1,9114 questionnaires were collected. Several sleep problems were found in primary school children including: bedtime not fixed (19.5%), falling asleep slow (22.9%), snoring (24.9%), apnea (3.4%), bed-wetting (3.6%), sleep talking (23.6%) and sleepiness in daytime (17.6%). The scores of each subscale of CPRS (Conduct Problem, learning Problem, psychosomatic, impulsive-Hyperactive, anxiety, hyperactivity index for children whose PSQ scores were abnormal (≥ 8) were found significantly higher (p < 0.001) than those with PSQ scores were normal(< 8). Similar finding was observed in children whose OSA-18 scores were abnormal (≥ 60) as compared with those with normal scores (< 60). Conclusion: The sleep problems among primary students in Xuhui District is common. Children with sleeping problems were more likely to have cognitive behavioral problems.
Keywords

Muscle type of palatopharyngeal muscle in children with severe obstructive sleep apnea

Huaihong Chen,Xiaoxing Huang,Yuanshou Huang,Yanqing Ye

Nanfang Hospital，Southern Medical University

Objective: To investigate the fiber-type distribution in palatopharyngeal muscle by adenosine triphosphatase and quantitative real-time polymerase chain reaction in children with severe obstructive sleep apnea (OSA). Methods: Study participants included 12 children with severe OSA and 15 children with simple snoring as the control group. Both groups were diagnosed by polysomnography and treated with tonsillectomy. The samples of palatopharyngeus muscle were studied under adenosine triphosphatase staining and quantitative real-time polymerase chain reaction to classify the different fiber types. Results: The baseline age, body mass index, tonsil size, or sleep stage constitution between the two groups were similar. Dominance (>60%) of

type I fiber was observed both in children with simple snoring (3/15, 20%) and in those with severe OSA (1/12, 8.3%) with adenosine triphosphatase staining. Predominance of type II fibers was observed in 3/15 (20%) in the control group and 6/12 (50%) in the severe OSA group, respectively. Type grouping was also observed in 8/15 (53.3%) in non-OSA group and 6/12 (50%) in severe OSA group, respectively. There was no difference in distribution of subtype fibers assessed by PCR between the two groups; the mean percentages of type I fibers were 25.8% $\pm$ 19.5% and 20.9% $\pm$ 16.6%, respectively (P > .05), similar results were found considering type IIa fibers (35.2% $\pm$ 23.4% and 40.9% $\pm$ 28.8%) (P > .05). There was a decrease in the percentage of type I fibers between children younger and older than 12 years (P < 0.05), although this was not due to OSA (P > 0.05). Conclusions: There were no specific changes with adenosine triphosphatase staining or difference in distribution of subtype fibers by quantitative real-time polymerase chain reaction between children with severe pediatric OSA and those with simple snoring, whereas the percentage of type I fiber decreased dynamically due to age but not OSA.

Keywords

Obstructive sleep apnea and metabolic cardiovascular risk factors: Joint effect modification by age and sex

Yupu Liu1,2,Huajun Xu1,2,Jian Guan1,2,Hongliang Yi1,2,Shankai Yin1,2

1.The Sixth People's Hospital Affiliated to Shanghai Jiaotong University

2.Shanghai Key Laboratory of Sleep Respiratory Disorders

Objective: The associations between obstructive sleep apnea (OSA) and metabolic cardiovascular risk factors varies individually by age and sex. However, clinically important heterogeneities in these studies may be masked if the physiological interplay between age and sex is not considered. Methods: A cross-sectional study was performed. Participants with suspected-OSA were classified into six subgroups according to both sex and age (<40 years, 40-55 years and >55 years) . Medical history, demographic parameters, polysomnographic variables, and biochemical indicators were collected. OSA severity was assessed by apnea-hypopnea index (AHI). Metabolic cardiovascular risk factors were assessed with atherogenic glycolipid profiles. Multivariable linear regression with tests for interactions were applied to investigate the modification effects by age and sex. Results: A total of 3,368 males and 877 females were enrolled. Age only modified the associations between lg (AHI+1) and atherogenic lipid profiles for females (all lg-transformed; fasting triglycerides, total cholesterol, and low-density lipoprotein cholesterol, P-interaction < 0.05), with stronger positive associations in younger than in older individuals. In addition, age modified the associations between lg(AHI+1) and lgHOMA-IR (homeostasis model assessment of insulin resistance) for both females and males (P-interaction < 0.05), but with distinct patterns. For females, the strongest positive association was observed in older individuals (>55 years old); while for males, the strongest positive association was observed in the middle-aged (40-55 years old). Conclusion: Age modified the associations between OSA

and cardiovascular risk factors in a sex-specific manner. These results may broaden our understanding of the heterogeneities in metabolic pathways linking OSA with cardiovascular diseases, and facilitate risk stratification and tailored management across patient subgroups.

Keywords

Clinical characteristics of Chinese pediatric obstructive sleep apnea hypopnea syndrome

Yanyu He,Yuqing Wang,Xueyun Xu

Children's Hospital of Soochow University

Objective: To analyze the clinical characteristics of obstructive sleep apnea hypopnea syndrome (OSAHS) in children. Methods: Polysomnography (PSG) and nasopharynx lateral film were performed, clinical data were collected in children who were admitted to our sleep centre from December 2016 to April 2019 due to "snoring during sleep with mouth opening breathing, hard breathing or suffocation". Samples of venous blood were collected after overnight fasting. Results: Among the enrolled children, 123 (22.6%) were diagnosed with OSAHS, with 70 were mild and 53 were moderate-severe. Percentage of adenoid hypertrophy was higher in OSAHS patients (p <0.01), instead of tonsil enlargement. The OSAHS children were aged 5 (4, 7). Compared with PS, the percentage of snoring, apnea, dyspnea, increased nocturia, and daytime sleepness were significantly higher in moderate-severe patients (p <0.01). In OSAHS groups, AHI, ODI, Longest time of apnea were increased, while minimum SpO2 and mean SpO2 during sleep were decreased significantly (p <0.01) than PS. Time ratio of NREM1 was elevated in moderate-severe OSAHS patients (p <0.01). Time ratio of REM was elevated in mild patients(p <0.01). Compared with the preschoolers, the percentage of leg movement and sleepness were significantly higher in school-agers (p <0.05). The youngers had higher time ratio of NREM3 and better sleep efficiency (p<0.01). However, AHI(p<0.05) and ODI(p<0.01) were higher in elder OSAHS significantly. Snoring (OR =5.745, p < 0.01), adenoid hypertrophy (OR =4.381, p < 0.01), apnea (OR =2.670, p < 0.001), dyspnea (OR =1.975, p < 0.01), and CRP (OR =1.172, p < 0.001) were independent risk factors for OSAHS. Conclusions: AHI, ODI, Longest time of apnea, minimum SpO2 and mean SpO2 should be considered and analyzed simultaneously in diagnosis. The school-age OSAHS patients seems to more serious than the preschoolers. Snoring, apnea, dyspnea, adenoid hypertrophy, and CRP are risk factors for OSAHS.

Keywords

Chronic intermittent hypoxia and sleep deprivation, two pivotal hallmarks of obstructive sleep apnea, alters the gut microbiome and metabolome

Fan Wang1,Huajun Xu1,Hongliang Yi1,Jian Guan1,Shankai Yin1

1.The Sixth People's Hospital Affiliated to Shanghai Jiaotong University

2.Shanghai Key Laboratory of Sleep Respiratory Disorders

3.Institute of Otorhinolaryngology，Shanghai Jiaotong University

Background：Obstructive sleep apnea-hypoxia syndrome (OSAHS) is a common disorder characterized by episodic obstruction to breathing due to upper airway collapse during sleep. Intermittently chronic hypoxia (CIH) and sleep fragmentation (SF) ensue as a result. Considering the changes of Oxygen concentration and disruption of sleep rhythm can affect the ecology of the gut microbiota and metabolome, we hypothesized gut dysbiosis of OSAHS patients may be mediator of complications. We respectively elucidated the cellular and molecular mechanisms involving gut microbial changes and metabolic consequences resulting from CIH or SF. Methods: C57BL/6J male mice were divided into eight groups: Normoxia (NM) group, CIH group, NM+HFD group, CIH+HFD group, Normal Sleep (NS) group, SF group, NS+HFD group, NF+HFD group. CIH was set to 21%–8% O2, 360 s/cycle, 8 h/day for 10 weeks. NF was programmed by twirling 15s every 120s by a mental pole 24h/day for 10 weeks. Gut microbiome and metabolome were characterized longitudinally (using 16S rRNA and LC-MS/MS). Results: CIH-stimulated mice showed higher abundance of Ekmania and Vibrio butyricum, but decreased abundance of Gastrococcus and Clostridium butyricum than the control group. The diversity and richness of probiotics were decreased in SF mice, especially Akkermansia, Bacteroides and Faecalibacterium. However, the pathogen Aeromonas was markedly increased. Joint analysis of microbiome and metabolome data revealed marked compositional changes in both microbial (>10%, most remarkably in Clostridia) and molecular (>22%) species in the gut. Moreover, molecules that altered in abundance included microbe-dependent bile acids, enterolignans, and fatty acids, highlighting the impact of CIH and SF on host-commensal organism co-metabolism in the gut. Conclusions: Both CIH and SF alters gut microbiota and metabolome in murine OSAHS models. Sharply increasing downstream metabolites may be mediators to induce or develop cardiovascular diseases and metabolic syndrome.

Keywords: Metabolome; microbiome; sleep apnea

Astrocytes involved in improvement of learning and memory of orexin dual receptor antagonist in chronic sleep–deprivation mice model

Na Shao1,Yaran Li2,Weiwei Huang3,Shanshan Lu3,Jiyou Tang1,3

1. Shandong Provincial Qianfoshan Hospital，Cheeloo College of Medicine，Shandong University
2. Shandong First Medical University & Shandong Academy of Medical Sciences.
3. The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital

Objective: Chronic sleep deprivation (CSD) is a significant risk factor for cognition impairment and has become increasingly prevalent in young adults, which disturbances the daily sleep/wake cycle regulated by the orexin system. And clearing the brain metabolic waste produced in wakefulness through the astrocyte-dependent glymphatic pathway may be an effective way to prevent cognition impairment after CSD. The potential advantages for cognition function of treating insomnia by dual orexin receptor antagonist were reported. However, little was known about its mechanism on cognition. Methods: We described a mouse model of CSD that 10-weeks male wide-type mice were sleep-deprived by gentle handling for 6 weeks and treated with dual orexin receptor antagonist almorexant (30mg/kg/6 weeks) simultaneously. The Y‑maze and Morris water maze (MWM) tests were deployed to evaluate short- and long-term spatial learning and memory of the mice, changes in expression of GFAP and tau/phospho-tau proteins were observed by western blot and immunohistochemistry. Results: We observed that CSD impaired short- and long-term learning and memory and increased the activation of astrocyte in the hippocampus. And almorexant treatment significantly increased the average escape latency and decreased the number of platform crossings and forced alternation (%). And less activated astrocyte was also observed in the hippocampus of almorexant-treated mice. A mild increase in tau phosphorylation was observed after CSD. Conclusion: We hypothesized that the protective effect of almorexant on learning and memory might be associated with suppressing astrocyte activation in CSD mice modol.

Keywords

Decreased RET and PHOX2B expression in iPSC–Derived Neurons in a child with sleep–related hypoventilation

Dandi Ma,Yunxiao Wu,Li Zheng,Zhifei Xu

Beijing Children’s Hospital，Capital Medical University，National Center for Children’s Health

Our case is a 3 year and 2 months old boy, who had an influenza A virus pneumonia and right upper atelectasis 4 months ago. After recovering from the pneumonia, his echocardiography showed the diameter

of right atrium increased slightly. On examination, his vital signs were normal. On the night of admission, he showed perioral cyanosis during sleep. His polysomnography, simultaneous transcutaneous oxygen saturation (SpO2) and transcutaneous partial pressure of carbon dioxide (TCPCO2) monitoring showed SpO2 decreased to 82%-85%, TCPCO2 increased to 117.8mmHg during sleep. However, these symptoms went back to normal when he was awake. The boy was clinically diagnosed as sleep hypoventilation based on these findings. Later, he was treated with non-invasive ventilation all night, and the SpO2 increased to 98%, TCPCO2 decreased to 70mmHg during sleep. The boy was suspected as congenital central hypoventilation syndrome (CCHS) for an idiopathic failure of the automatic control of breathing, especially during sleep. Then we detected the boy and his parents' the paired-like homeobox gene 2B (PHOX2B) which was the disease-defining gene of CCHS. However, there is no mutation of PHOX2B but receptor tyrosine kinase proto-oncogene (RET) intron14 (c.2608-125C>T) in the boy. We differentiated the neurons of the boy (as a research group) and his mother (as a control group) who had no mutation of RET and PHOX2B gene. There is no significant difference in neuron morphology, length and discharge ability compared with the control group. However, it shows impaired expression of mRNA and protein of RET and PHOX2B. We hypothesize that RET might has a relationship with PHOX2B which could induce sleep related hypoventilation.
Keywords

A preliminary study on the body mass index of patients with obstructive sleep apnea hypopnea syndrome who have similar clinical features with obesity hypoventilation syndrome

Zhijun Wang,Rui Chen
The Second Affiliated Hospital of Soochow University

Objective: To explore the body mass index (BMI) of patients with obstructive sleep apnea hypopnea syndrome (OSAHS) who have similar clinical features with obesity hypoventilation syndrome (OHS). Methods: This retrospective study included patients with primary complaint of snoring admitted to the sleep center of the Second Affiliated Hospital of Soochow University and examined by polysomnography (PSG) and daytime awake transcutaneous carbon dioxide (PtcCO2) monitoring from November 2019 to February 2021. A total of 181 patients were enrolled into the analyses. Binary logistic regression analysis and ROC curve were used to determine the cut-off value of BMI for predicting daytime hypercapnia. All patients were divided into high-BMI group and low-BMI group according to the cut-off value. The differences in general information, PSG parameters, clinical symptoms, comorbidities and nocturnal carbon dioxide levels between the two groups were compared. Results: The cut-off value of BMI predicting daytime hypercapnia was 27.04kg/m2. Of the 181 enrolled patients, 92 were in high-BMI group and 89 in were low-BMI group according to the cut-off value. The proportion of hypercapnia and the level of daytime PtcCO2 of high-BMI

group were significantly higher than those in the low-BMI group (P< 0.001 or P< 0.01). The proportion of daytime sleepiness and ESS score of the high BMI group were both significantly higher than those of the low BMI group (P< 0.05 or P<0.01). The prevalence of hypertension of the high BMI group was significantly higher than that of the low BMI group (P<0.001). The AHI, the proportion of light sleep, ODI, TS 90%, arousal index and respiratory-related arousal index were significantly higher in the high BMI group than those in the low BMI group, while the proportion of deep sleep, lowest oxygen saturation and Mean oxygen saturation were significantly lower than that in the low BMI group (all P<0.01). Among the enrolled patients, 130 patients received continuous PtcCO2 monitoring during sleep. The proportion of PtcCO2≥60mmHg and the proportion of PtcCO2≥65mmHg in the high-BMI group were significantly higher than those in the low-BMI group (P<0.01 or P<0.05). According to AASM criteria, the proportion of nocturnal hypoventilation in the high-BMI group was significantly higher than that in the low-BMI group (P<0.05). Conclusion: OSAHS patients with BMI ≥27.04 kg/m2 were more likely to develop daytime hypercapnia. Their clinical features were similar with those of OHS patients, namely, the proportion of daytime sleepiness and hypertension is higher, nocturnal hypoxia and sleep structure disorders are more serious, and the incidence of nocturnal hypoventilation is higher.

Keywords

The effect of CPAP on reflux–associated cough in obstructive sleep apnea patients

Jiao Su,Songyun Ouyang,Yang Meng,Yifei Fang
The First Affiliated Hospital of Zhengzhou University

Objective: Chronic cough is common in obstructive sleep apnea (OSA). The etiology of chronic cough in OSA patients could be multifactorial. Several studies have reported high incidence of GERD in OSA patients. GERD may be one of the causes of chronic cough in OSA patients. The aim of this study was to investigate the therapeutic effects of CPAP on reflux-associated cough in OSA patients, and the possible mechanism of the association. Methods: A retrospective observational study was conducted. Of the 86 OSA patients comorbid GERD enrolled, 40 patients treated with medications were included into the medication group (omeprazole + mosapride) and the other 46 patients treated with medications and CPAP were included into the combined treatment group (CPAP + medication). The effects of different treatments on chronic cough were assessed. The correlations between cough, OSA and GERD were assessed by Pearson correlation analyses.   Results: Patients had poor sleep quality, severe daytime sleepiness, sleep structural disorder, decreased sleep efficiency, moderate sleep apnea, significant weak acid reflux, and moderate coughing events. These parameters were similar between the two groups at baseline. Compared wit medication group, PSQI, ESS, AHI, the longest time of apnea, the lowest oxygen saturation, VAS, daytime and night cough symptom score were significantly improved from baseline to the third month in combined treatment group

(P< 0.05). Compared with baseline, VAS, daytime and night cough symptom score were slightly improve at the third month after treatment in medication group (P< 0.05), and the improvement were less that that of the combined treatment group. There was a significant correlation between VAS score and weak acid reflux. Conclusion: CPAP can improve reflux-associated cough in OSA patients. The improvement in reflux-associated cough was due to the resolution of OSA. The possible mechanism of cough resolution with CPAP is via improving in GERD in OSA patients.

Keywords

Causal association between snoring and type 2 diabetes mellitus: a Mendelian Randomization study

Jiajin Zhou1,3,Hongliang Feng2,4,Yue Liu2,4,Lulu Yang2,4,Jihui Zhang2,4

1.The First People's Hospital of Yunnan Province，Yunnan，China.

2.Guangdong Provincial People's Hospital

3.Kunming University of Science and Technology

4.Guangdong Mental Health Center

Objective: Epidemiological studies have shown that snoring is independently associated with a higher risk of type 2 diabetes mellitus (T2DM). However, it is unclear whether snoring is casually associated with the risk of T2DM. Thus, we carried out a two-sample Mendelian randomization (MR) study to investigate the causal relationship between snoring and T2DM. Methods: For the two-sample MR analyses, we used publicly available summary statistics from genome-wide association studies on snoring and T2DM. The inverse-variance weighted (IVW), MR-Egger, weighted-median, and weighted-mode were used to investigate the causal relationship between snoring and T2DM. We also conducted the pleiotropy test and leave-one-out sensitivity analysis to testify the assumptions of two-sample MR. Results: The causal association between snoring and T2DM was absent (IVW: β = -0.078, P = 0.93; MR Egger: β = -5.36, P = 0.24; weighted median: β = -0.79, P = 0.33; simple mode: β = -0.92, P = 0.55; weighted mode: β = -1.28, P = 0.33) in Two-sample MR analyses. In addition, The pleiotropy effects were insignificant. The leave-one-out sensitivity analysis showed that the MR results were not driven by a specific SNP. Conclusions: Our findings suggested that it was lack of causal relationship between snoring and T2DM.

Keywords Snoring; type 2 diabetes mellitus; Mendelian randomization study

Sleep fragmentation and risk of type 2 diabetes mellitus: results from the UK Biobank prospective cohort

Xinru Chen1,2,3,Hongliang Feng2,4,Yue Liu2,4,Lulu Yang Yang2,4,Sizhi Ai Ai2,Jiajin Zhou2,Yuping Ning1,3,Jihui Zhang2,4,5

1. The First School of Clinical Medicine，Southern Medical University，Guangzhou，China
2. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，China.
3. The Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou Huiai Hospital)，Guangzhou，China
4. Guangdong Cardiovascular Institute，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，China
5. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin，Hong Kong SAR，China.

OBJECTIVE: Limited evidence has suggested an association between self-reported sleep fragmentation and impaired glucose regulation. However, it remains unclear whether sleep fragmentation can predict the onset of type 2 diabetes mellitus (T2DM). This study aimed to clarify this longitudinal association between accelerometer-assessed sleep fragmentation and the risk of T2DM. METHODS: The participants were from the UK Biobank. The one-week accelerometer was used to assess the rest-activity pattern. The state-transition analysis was used to yield the metric of sleep fragmentation (i.e., kRA). The incidence of T2DM was assessed after the follow-up period. Besides, the hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated by using the multivariable-adjusted Cox regression. RESULTS: Accelerometer data were available in 92483 UK Biobank participants (male: 43%) aged 43-79 years in this study. For all analyses, subjects were excluded if they had diabetes at baseline. A total of 2060 cases (2.2%) were diagnosed with type 2 diabetes during follow-up (5.3 ± 0.8 years). The Cox regression showed that higher sleep fragmentation was significantly associated with the risk of T2DM- the hazard ratio for diabetes was greatest among participants in the highest quartile of kRA level (HRQ4 = 1.3, [95% CI 1.2–1.5]), the hazard ratio was followed by the quartile of participants with the second highest KRA levels (HRQ3 = 1.2, [95% CI 1.1–1.4])，after adjusting for age, sex, and body mass index. Conclusions: The findings suggest that sleep fragmentation may elevate the risk of T2DM. Sleep improvement could play an important role in preventing diabetes. Future interventional studies or Mendelian randomization studies are warranted to further clarify the causal relationship between sleep fragmentation and T2DM.
Keywords Sleep fragmentation, type 2 diabetes mellitus, accelerometer, prospective cohort, UK Biobank

Analysis of the pressure and related factors in non–invasive ventilation therapy in 109 patients with Obstructive sleep apnea hypopnea syndrome

Shilin Ma1,Dongmei Chen1,Xuelong Jiang1,Juan Shi1,Min Li1,Qinglong Zhang1,Hong Guo1,Meirong Han1,Zhongming He1,Fang Han1

1.Karamay Central Hospital

2.Peking University people's Hospital

Objectives: To analyze the pressure and related factors of nocturnal non-invasive ventilation (NIV) in 109 patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). Methods: All patients at Karamay Central Hospital from April 2019 to Oct 2019, 109 patients with OSAHS who underwent pressure therapy were enrolled in this study. Height, weight, neck circumference (NC), and abdominal circumference (WC) were recorded. PSG and home overnight pulse oximetry (OPO) were performed. Sleep apnea-hypopnea index (AHI), oxygen reduction index (ODI4), mean oxygen saturation (MSaO2), minimum oxygen saturation (LSaO2), time spent with saturation below 90% (SIT90) were collected. Night pressure titration was used to monitor the minimum pressure (Min pressure) and maximum pressure (Max pressure) of patients with NIV. Results Totally, 109 patients with OSAHS were included in this study, including 85 Han patients, whose mean age was (53.1±14) years, and 24 Uygur patients, whose mean age was (52.7±9.9) years. The mean age of 80 males was (51.2±13.6) years and the mean age of 29 females were (58.5±9.0) years. There were significant differences in body mass index BMI (28.4±5.0 kg/m2 VS 32.2±5.7 kg/m2), LSaO2[(77.2±6.9)% vs. 70.8±13.7 %]] and WC ((102±11) cm vs. (110±12) cm)] between Han and Uygur patients with OSAHS (P <0.05). Differences on Pressure titration of Max pressure [(10.9±3.1cmH2O) vs. (12.5±2.9cmH2O)] and Min pressure [(4.1±0.9cmH2O) vs. (4.9±1.2cmH2O)] between mild and severe OSAHS (P<0.05). Ninety Percent of the pressure(P90) is (10.3±2.6) cmH2O, which was related to NC (r=0.26, P=0.01), AC (r=0.28, P=0.01), LSaO2 (r=0.22,P=0.04), and ODI4(r=0.28,P=0.01). Conclusions: The pressure of NIV therapy is related to sleep-disordered breathing, P90 positively related to NC、WC 、LSaO2 and ODI4. the Max pressure and Min pressure are increasing with the severity of OSA.

Keywords Obstructive sleep apnea; CPAP; Non-invasive ventilation , Pressure titration

Transformer Neural Network for Apnea and Hypopnea Events Classification

Liu Cheng,Yuan Zhang

Southwest University

Purpose: Although some AI based studies have been performed for sleep apnea detection,they mostly do not rely on EEG analysis. In order to explore the potential relationship between sleep breathing events and the brain nervous system, we use EEG signals to classify apnea and hypopnea events. Recently some pioneering frameworks based on Transformer have gained leading advantages in natural language processing and computer vision. However, there are few studies using Transformer in EEG signal recognition and judgment of sleep breathing events. Therefore this study aims to update the Transformer architecture for the sleep apnea-hypopnea syndrome (SAHS) diagnosis. Method: We select 6-channel EEG signals for feature extraction and extract the power spectral density (PSD) as the main EEG signal feature. In this work, we propose a novel architecture stacked by temporal attention encoder layers and spatial attention encoder layers, and develop an end-to-end training approach. The main function is to extract the features from sub-frames and aggregate features between different channels. Result: The EEG signals of 15 patients are picked for the training set and 5 patients as the test set. Two experiments are implemented to identify the Apnea or Hypopnea events with the accuracy of the model being 77.5% and 71.1%. Respectively our network is relatively better than the contrast model which were based on GBDT, LSTM and CNN. Conclusion: This work verifies the feasibility of Transformer on Apnea and Hypopnea events classification by EEG, with good performance. However, the idea of Transformer is to aggregate and map features by calculating the similarity between different channel features, therefore the correlation between EEG and SAHS still needs to be explored.

Keywords: Deep learning, EEG, Sleep apnea-hypopnea syndrome, Transformer

AUTOMATIC SLEEP SCORING: A DEEP LEARNING ARCHITECTURE FOR PATIENTS WITH SLEEP DISTURBANCE

Rui Yan1,2,3,Fan Li3,Fengyu Cong3,2,4

1. School of information science and engineering，Hebei University of Science & Technology，050018，Shijiazhuang，China
2. Faculty of Information Technology，University of Jyväskylä，40014，Jyväskylä，Finland
3. School of Biomedical Engineering，Faculty of Electronic Information and Electrical Engineering，Dalian University of Technology，116024，Dalian，China
4. School of Artificial Intelligence，Faculty of Electronic Information and Electrical Engineering，Dalian University of Technology，116024，Dalian，China

Objective: Due to our hectic lifestyle, complaints about sleep problems increase dramatically among people, which burdens sleep scoring. Automatic sleep scoring is a great way to alleviate the growing unmet needs. However, the sleep patterns of patients with sleep disturbance are varied, and there exist huge population difference and individual difference. How to build a generalized model for patients′ sleep scoring is still an open question. This paper aims to develop a versatile deep-learning architecture to automate sleep scoring for patients with diverse sleep disturbances.   Methods: The proposed model applies the 2-dimensional convolutional unit and the long-short time memory unit to explore the spatial and temporal information among three types of sleep signals (namely electroencephalograms, electrooculogram and electromyograms). An improved inception module is used to extract features from input signals in multiple resolutions. Then, the learnt features are fed to the long-short time memory unit to exploit long-range contextual relation among sleep stages. Finally, the decision layer distinguishes features and gives the labels of sleep segments. In this article, model performance is tested on the ISRUC dataset, in which subgroup 1 records 100 sleep recordings from 11 types of patients with sleep disturbance. Result: After 5-fold cross-validation, the proposed model achieves an accuracy of 0.86 with a kappa value of 0.82, and the highest classification accuracy is achieved by a fusion of multiple sleep signals. Compared with state-of-the-art methods that use the same dataset, the proposed model exhibits compact structure and high precision. Conclusion: The proposed model obtains good performance on patients with diverse sleep disturbances, which demonstrates good model generalizability. Due to the proven availability and versatility, the proposed method can be integrated with polysomnography systems, thereby facilitating sleep monitoring in clinical or routine care.

Keywords automatic sleep scoring, deep learning, patients with sleep disturbance, multi-modality analysis.

SNORES N DM2: a study on obstructive sleep apnea high risk prevalence, symptoms and sleepiness among patients with uncontrolled type 2 diabetes mellitus

De Leon,Maria Lowella、Jorge,Manuel
University of the Philippines -Manila

Objectives: This study aimed 1) to determine the prevalence of obstructive sleep apnea - high risk (OSA -HR) among the patients with uncontrolled type 2 diabetes mellitus (T2DM); 2) to describe the clinico-demographic profile of OSA-HR among T2DM patients; and 3) to investigate the correlation between OSA-HR and sleep quality. Methodology: This prospective cross-sectional study recruited participants with uncontrolled T2DM. The Berlin Questionnaire (BQ) and the Epworth Sleepiness Score were used to assess OSA risk and daytime sleepiness symptom. Clinico-demographic profile and laboratory data were also obtained. Chi-square test was used to compare intergroup differences for categorical variables. Results: A

total of 240 participants (male: 36.7%) with uncontrolled T2DM were included. The overall prevalence of OSA-HR among patients with uncontrolled type 2DM is 58.33% (n = 140). 75% of the OSA–HR (n = 105) were 46 years old and above. There were significant associations of OSA-HR with the tonsillar grade, malampati score, BMI, HGBA1C, hypercholesterolonemia, and sleepiness (all P < 0.05). Conclusions: The prevalence of OSA-HR is high among patients with T2DM. Several risk factors are associated with OSA-HR among patients with T2DM.

Efficacy of an app–based cognitive behavioral technique (CBT) intervention for Iranian patients with insomnia

IMANI,VIDA1、 Pakpour,AMIR2,3

1. Pediatric Health Research center of Tabriz，Tabriz University of Medicine，TABRIZ，IRAN
2. Department of Nursing，School of Health and Welfare，Jönköping University，Jönköping，Sweden
3. Social Determinants of Health Research Center，Qazvin University of Medical Sciences，Qazvin，Iran

Objective: Sleep hygiene is important for maintaining good sleep and reducing insomnia. Therefore, the present study examined the long-term treatment efficacy of a theory-based app (including cognitive behavioral theory [CBT], theory of planned behavior [TPB], health action process approach [HAPA], and control theory [CT]) on sleep hygiene among insomnia patients. Methods: The study was a two-arm single-blind parallel-group randomized controlled trial (RCT). Insomnia patients were randomly assigned to a treatment group receiving app through six weeks (i.e., CBT on insomnia; CBT-I; n = 156) or a control group receiving patient education (PE; n = 156). Outcomes were assessed at baseline, post-treatment (1 month, 3 months after intervention, and 6 months after intervention). Primary outcomes were sleep hygiene, insomnia, and sleep quality. Secondary outcomes included attitudes toward sleep hygiene behavior, perceived behavioral control, behavioral intention, action and coping planning, self-monitoring, behavioral automaticity, and anxiety and depression. Linear mixed models were utilized to evaluate the magnitude of changes in outcomes between the two groups and across time. Results: Sleep hygiene was improved in the CBT-I group as compared to the PE group (p = 0.02 at 1 month; 0.04 at 3 months; 0.02 at 6 months), as were sleep quality, the severity of insomnia. Mediation analyses suggested that perceived behavioral control on sleep hygiene as specified by the TPB, along with self-regulatory processes from HAPA and CT, mediated the effect of the intervention on outcomes. Conclusions: Healthcare practitioners might consider the CBT-I app to improve sleep among insomnia patients.

MORPHOLOGIC AND FUNCTIONAL CHANGES IS SLEEP PARAMETERS FOLLOWING BIOMIMETIC ORAL APPLIANCE THERAPY IN AN ADULT

Singh,G. Dave1、Kherani,Shamshudin2

1. Vivos Therapeutics Inc
2. Kherani Dental at Aspen

Purpose: The aim of this study was to investigate the effects of biomimetic oral appliance therapy (BOAT) on upper arch morphology and sleep parameters in an adult. Methods: An overnight sleep study was undertaken in a 50yr old male with excessive daytime sleepiness that revealed an AHI of 32.8hr-1. Since the patient was unable to comply with CPAP, study models of the upper and lower jaws were taken and treatment with a mandibular advancement device was initiated. Approx. 10yrs later, another sleep study was performed with no device in the mouth, which revealed an AHI of 67.9hr-1. In view of the deterioration in sleep quality, the patient sought alternative treatment and elected on BOAT. New study models of the jaws were taken and a biomimetic oral device (mRNA appliance®, Vivos Therapeutics, Inc., USA) was delivered. After 10 months, another sleep study was performed with no device in the patient's mouth as well as study models of the upper and lower jaws. Results: After 10 months of BOAT, the overnight sleep study revealed an AHI of 11.8hr-1, a mean oxygen saturation of 94% and a mean oxygen desaturation index of 5.3% with no device in the patient's mouth while sleeping. Finite-element analysis comparing the pre- and post-BOAT study models of the upper jaw showed localized size increases as follows: 15.6% to 16.9% in the premolar regions and 14.9% to 23.4% in the molar regions. A concentric pattern of size change was demonstrable with transverse widening in the midline localized in the molar region. Conclusion: Biomimetic oral appliance treatment may be able to ameliorate worsening of sleep parameters in adults by remodeling the upper arch, unlike mandibular advancement devices, in patients that are reluctant to accept CPAP treatment. However, long-term follow up and further studies are required to verify these preliminary findings.

Sleep quality and sleep pattern among residents and its relation to anxiety and depression during the pandemic of the COVID–19

Cortez,Gabriel Gerardo、Espiritu-Picar,Rosalina

Makati Medical Center

Objectives: This study aimed 1) to evaluate the sleep quality and sleeping pattern of resident physicians in Makati Medical Center during the COVID-19 pandemic, and 2) to measure the association of sleep quality and sleep pattern with depression and anxiety. Methods: This was a single-center cross-sectional study.

Participants accomplished a structured questionnaire (via Google Forms) with the following components: basic information, the Sleep Hygiene Index tool, the Pittsburgh Sleep Quality Index tool, and the Goldberg Anxiety and Depression Scale. Results: A total of 187 residents were included in the study with a mean age of 29.2 years. Drinking 1 to 2 glasses of alcohol was significantly associated with fair to poor sleep hygiene (OR = 2.0, 95%CI = 1.1 to 3.8, p = 0.034) and poor sleep quality (OR = 2.1, 95%CI = 1.01 to 4.4, p = 0.047). Both fair to poor sleep hygiene (OR = 4.3, 95% CI = 1.9 to 9.9, p = 0.001) and short sleep pattern (OR = 1, 95% CI = 0.1 to 0.4, p < 0.001), were significantly associated with poor sleep quality. 44.4% of the participants had probable anxiety and 47.6% had probable depression. Probable anxiety (OR = 5.1, 95% CI = 2.3 to 11.4, p < 0.001) and probable depression OR = 2.6, 95% CI = 1.3 to 5.2, p = 0.006) were both significantly associated with poor sleep quality. Conclusions: There is a high prevalence of poor sleep quality among resident physicians in Makati Medical Center. Almost half of the residents show notable signs of anxiety and depression. Drinking alcohol is a predictor of having fair to poor sleep hygiene while fair to poor sleep hygiene is a predictor of having poor sleep quality. Both sleep hygiene and sleep quality are significantly associated with risk for anxiety and depression. Given these findings, it is recommended that resident physicians practice good sleep hygiene and be given opportunities for optimal sleep quality to minimize the risk of developing anxiety and depression during this COVID-19 pandemic.

Isolated Rapid Eye Movement Sleep Without Atonia (RSWA): A Precursor Biomarker for Neurodegeneration?

Chau,Steven1、Zhang,Jihui2、Liu,Yaping1、Li,Shirley3、Chan,Joey1、Lam,Joyce1、Wing,Y K1

1. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong
2. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China
3. Department of Psychology，The University of Hong Kong

Objectives: Isolated REM sleep without atonia (RSWA) in the absence of REM sleep behaviour disorder (RBD)'s neurodegenerative implication is disputed. The current study aimed to examine the neurodegenerative implication of isolated RSWA among first-degree relatives (FDRs) of RBD patients, as reflected by their 1. loading of neurodegenerative risk factors and prodromal markers and stratal dopamine transmission function. Methods: This case-control study recruited a total of 50 subjects (Mean age = 58.6±9.1 years. 34% female) into three age and gender-matched arms: FDRs of RBD patients with isolated RSWA (n=16), FDRs of RBD patients without isolated RSWA (n=18) and controls who are not FDRs of RBD patients(n=15). Subjects underwent comprehensive clinical, neurocognitive and polysomnographic assessment. Striatal dopaminergic transmission function of the subjects was assessed by triple-tracer (18F-DOPA, 11C-Raclopride and 18F-FDG) PET/CT scan. Results: The three groups did not have significant

differences in their composite prodromal neurodegenerative markers as measured by the MDS Research Criteria for Prodromal Parkinson's Disease likelihood ratio and striatal dopaminergic transmission function. They were significantly different in their prevalence of Parkinson's disease (PD) or dementia of Lewy bodies (DLB) among their FDRs (Fischer exact test: FDRs with RSWA vs FDRs without RSWA vs non-RBD FDRs controls = 58.8% vs 22.2% vs 0%, p = 0.001). RSWA was a significant predictor of having FDRs suffering from PD or DLB using generalized equation model (B=1.61, Wald 95% CI= 0.14 – 3.08, Wald chi-square = 4.59, d.f. = 1, P = 0.032). Conclusion: Individuals with RSWA likely have a higher genetic predisposition of neurodegeneration. Their lack of increased loading of neurodegenerative markers and dopaminergic dysfunction might suggest that RSWA is a marker of very early stage of neurodegeneration in these individuals. Further longitudinal follow-up study will be needed to ascertain their long-term prognosis.

Effects of home–based aerobic interval training combined with resistance training on subjective sleep disorders in adults with obesity and sleep–disordered breathing

Longlalerng,Khomkrip1、 Watanasiripakdee,Siripan 2、 Jeenduang,Nutjaree3、
Habuddhaa,Valainipha 1、 Piya-amornpan,Nitita 1、 Damchuai,Tipwimol4

1. Department of Physical Therapy，School of Allied Health Sciences，Walailak University，Nakhon Si Thammarat，Thailand
2. Department of Pulmonary Medicine and Critical Care，Maharaj Nakhon Si Thammarat Hospital，Nakhon Si Thammarat，Thailand
3. Department of Medical Technology，School of Allied Health Sciences，Walailak University，Nakhon Si Thammarat，Thailand
4. Department of Physical Therapy，Physical Medicine and Rehabilitation Unit，Maharaj Nakhon Si Thammarat Hospital，Nakhon Si Thammarat，Thailand

Background: There are many barriers to perform the exercise at center-based with close supervision by healthcare providers due to the pandemic of COVID-19 worldwide. Home-based aerobic interval training (AIT) combined resistance training (RT) may be helpful for obese adults with sleep-disordered breathing (SDB) to overcome those barriers and improve their subjective sleep disorders. Objective: To examine the effects of home-based AIT combined with RT on subjective sleep disorders in obese adults with SDB. Methods: This study was a one-group pretest-posttest design. Twenty-one adults with obesity and SDB were assigned to perform 8 weeks of AIT combined with RT. Subjective sleep disorder variables including the Pittsburgh Sleep Quality Index (PSQI), Berlin Questionnaire, and Epworth Sleepiness Scale were defined as primary outcomes. Anthropometric variables, physical fitness components, and blood biomarkers were assigned as secondary outcome. All outcome measurements were examined at baseline and post-8 weeks

of training. Results: Daytime dysfunction of PSQI was significantly improved after 8 weeks of the exercise program ($p < 0.05$). Most of the anthropometric variables had no change after 8 weeks of exercise program except for neck and waist circumference (all $p < 0.01$). Upper and lower chest expansion, and estimated maximum oxygen consumption increased significantly after 8 weeks of the exercise program (all $p < 0.05$). None of the other physical fitness variables and blood biomarkers improved after 8 weeks of training (all $p > 0.05$). Conclusion: Home-based AIT combined with RT was less effective for an improvement in subjective sleep disorders. Further studies with a controlled trial are needed to prove the benefits of the exercise program.

Diagnostic Test of STOP BANG Questionnaire, Berlin Questionnaire, Snoring Score, and Stanford Sleepiness Scale Compared With Apnea/Hypopnea Index in Obstructive Sleep Apnea Patient at dr. Saiful Anwar Malang Hospital

Zamroni Afif、Brisda Oktaviana、Farida Widyastuti、Catur Arisetianto、Rodhiyan Rakhmatiar、Harun Al Rasyid

Medical Faculty Brawijaya University

Background: OSA affects about 2-26% of the general population, with increased morbidity and mortality. The gold standard of OSA is the value of Apnea Hypopnea Index (AHI) on polysomnography (PSG), but polysomnography is not always available in various health centers. Some scoring systems help to predict OSA based on clinical and related comorbidities, including STOP BANG Questionnaire (SBQ), Berlin Questionaire (BQ), Snoring Score (SS), and Stanford Sleepiness Scale (SSS). This study aims to test and compare the diagnostic value between these various scoring using parameters of Apnea/hypopnea index (AHI) from polysomnography as the gold standard. Method: This cross sectional study was conducted at the electrophysiology laboratory of Dr. Saiful Anwar Malang Hospital carried out in 2014-2019. Total subjects were 100 patients. Baseline data was taken, as well as the results of SBQ. BQ, SS, and SSS, then all of them were cross-tabulated with AHI through 2x2 table. Results: The sensitivity of SBQ, BQ, SS, and SSS in any degree of OSA (AHI ≥ 5) were respecively 82%, 67%, 94%, and 18%, while the specificity were respectively 77%, 64%, 64%, and 77%. It was found that sensitivity of SBQ, BQ, SS, and SSS to predict severe OSA (AHI > 30) were 94%, 81%, 94%, and 19%, while their specificity were respectively 43%, 50%, 25%, and 81%. SS had a highest sensitivity to predict any degree of OSA. U Conclusion: In this study, SS and SBQ had very high sensitivity, especially to predict severe OSA. But all of these scoring had poor specificity. SS and SBQ might be the good initial screening method for OSA at the setting of primary health care because of their high sensitivity.

REM sleep behavior disorder combined with obstructive sleep apnea: Response to continuous positive airway pressure treatment and its associated factors

Lee,Woo-Jin1、Sunwoo,Jun-Sang 1、Byun,Jung-Ick 2、Jung,Ki-Young1

1. Seoul National University Hospital

2. Kyung Hee University Hospital at Gangdong

Objective: When rapid eye movement (REM) sleep behavior disorder (RBD) is combined with obstructive sleep apnea (OSA), the pattern of temporal association between the apnea-hypopnea (AH) and REM without atonia (RWA) events might be related with the improvement of RBD after continuous positive airway pressure (CPAP) treatment. We evaluated the temporal association of RWA and AH during REM, and investigated its relation to the improvement of RBD symptoms after continuous positive airway pressure (CPAP). Methods: From an institutional cohort of sleep disorders between January 2016 and October 2020, thirty-one patients (5 [16.1%] female, mean age of 66.6±6.6 years old) with RBD confirmed by overnight video-polysomnography (vPSG) and combined OSA with an apnea-hypopnea index (AHI) of ≥15/h, received CPAP treatment, and followed-up for at least six months were included. Along with gross vPSG parameters, mini-epoch based parameters, AH associated electromyography (EMG) activity ratio and AH associated EMG activity index, were used to evaluate the temporal association between the AH and the RWA events. Results: Twenty-three (74.2%) patients exhibited a clinical improvement of their RBD symptoms after CPAP treatment (improvement group). An AH EMG activity ratio of ≥ 15% (Odd ratio [OR] 10.146, 95% CI 1.302–79.032, P = 0.027) and an AH EMG activity index of ≥ 10% (OR 99.045, 95% CI 3.091–3173.908, P = 0.009) were significantly associated with the clinical improvement after CPAP treatment, in each regression models adjusting age, sex, and dichotomized REM AHI. In eighteen patients who both presented with those factors, the probability of improvement of RBD after CPAP was 17 (94.4%). Conclusion: Treatment of combined OSA can improve the symptoms of RBD. Mini-epoch based analysis for the temporal association between the AH and the RWA events might be useful for predicting the improvement of RBD symptoms after CPAP treatment.

Poster contents

Poster contents

Analysis of clinical characteristics and PSG indicators of OSAHS patients based on sleep perception types

Yishu Liu,Huiwen Tan,Yin Zeng,Li Xiao
Shengjing Hospital of China Medical University

Objective: To explore the clinical characteristics of different sleep perception types of obstructive sleep apnea-hypopnea syndrome (OSAHS), and to analyze the correlation between sleep perception and polysomnography indicators in OSAHS patients. Methods: We retrospectively analyzed data from 355 patients who were diagnosed with OSAHS by polysomnography at the Sleep Medicine Center of Shengjing Hospital of China Medical University. Those patients saw doctors due to snoring and daytime sleepiness from March 2017 to March 2018. We excluded the patients who were less than 18 years old, had a history of OSAHS treatment, had other sleep disorders, and could not provide complete data. According to the patients' explanation, medical history, polysomnography, and morning questionnaire after polysomnography, the patients were divided into three groups: normal sleep perception, positive sleep perception abnormal, and negative sleep perception abnormal. Results: 55.5% of OSAHS patients had sleep perception abnormalities, of which 35.5% were positive-perception abnormalities and 20% were negative-perception abnormalities. From the analysis of polysomnography, the sleep perception abnormality was only significantly related to the frequency of spontaneous arousal of the patient (P = 0.003), and was not related to the slight arousal caused by respiratory events, oxygen desaturations, and limb movement events; the patient with negative-sleep perception had more spontaneous arousal (all P > 0.05). The OSAHS patients with positive-sleep perception had higher oxygen desaturation index (P = 0.046). In terms of sleep structure, the OSAHS patients with abnormal sleep perception had shorter REM latency (P = 0.027) than those with normal sleep perception. Conclusions: Sleep perception abnormality is common in OSAHS patients, with more positive- sleep perceptions being found. Sleep perception is related to spontaneous arousal, which is probably associated with increased periodic EEG activity. The OSAHS patients with positive-sleep perception abnormalities have higher oxygen desaturation index, whose hypoxia levels are more severe at night and they require early treatment.
Keywords OSAHS; Sleep perception; Polysomnography

The relationship between napping and adolescent behavior proble

Jing Han,Rendong Huang,Lei Yue,Naixue Cui
School of Nursing，Shandong University，China

Objective: To explore the relationship between napping and behavior problems in adolescents. Methods: A total of 1551 adolescents were enrolled from a vocational high school in Shandong province. The frequency and duration of napping were measured by questions developed by referring to literature, and behavioral problems were measured by the Youth Self Report (11-18 years, YSR). The relationship between napping and behavioral problems was analyzed by the general linear regression model. Results: 75.82% of the participants reported taking a midday nap at least three days per week during the past month, and 86.33% of our sample reported naps less than 60 minutes. General linear regression analysis showed that nap frequency was negatively associated with adolescent behavior problems after controlling for sociodemographic factors, sleep duration at night, and sleep quality. Compared with adolescents who did not nap or napped less than 1 time/week, adolescents who napped 1-2 times/week or 3-4 times/week had a lower level of both internalizing behavior problems and externalizing behavior problems (all P < 0.05). There was no statistically significant association between nap duration and behavior problems. Conclusions: There is a certain relationship between nap frequency and behavior problems of adolescents. Further research is needed to explore the mechanism of the relationship between napping and behavior problems.

Keywords adolescent; daytime napping; behavioral problems; cross-sectional studies

Sleep duration and risk of cardiovascular events: The SAVE study

Jingwei Li,Craig Anderson
First Hospital Affiliated to the Chinese PLA General Hospital，Beijing，China.

Background and aim: Controversy exists regarding cardiovascular (CV) risk about sleep duration. We aimed to determine the relationship between sleep duration and major recurrent CV events in patients with obstructive sleep apnoea (OSA) and established CV disease. Methods: Secondary analyses of the international, multicenter, Sleep Apnea Cardiovascular Endpoints (SAVE) trial. Sleep duration was estimated from overnight home oximetry (ApneaLink monitor) used for OSA diagnosis. The follow-up was conducted at 1, 3, 6, and 12 months, and every 6 months thereafter through a structured interview. Cox proportional hazards models were used to determine associations of categorized sleep duration (< 6 hrs, 6-8 hrs [reference] and >8 hrs) and major CV outcomes: primary, composite of CV death, non-fatal myocardial infarction (MI), non-fatal stroke, and any hospitalization for unstable angina, heart failure, or transient ischemic attack (TIA); secondaries, composite of cardiac, and cerebral (stroke/TIA), events. Results: Oximetry-derived sleep duration estimates were available in 2, 687 participants (average 61.2 yr old, 80.9% are male) who

experienced a total of 436 CV events over a median follow-up of 3.7 years. Compared to the reference category, sleep duration was not associated with risk of the primary composite CV outcome (adjusted hazard ratio [aHR] 1.00, 95% confidence interval [CI] 0.76–1.33, and aHR 1.22, 95% CI 1.98–1.52, for sleep duration < 6 and >8 hours, respectively). However, long sleep was associated with increased cerebral events (HR 1.67, 95% CI 1.17–2.39; P = 0.005) and stroke alone (HR 1.79, 95% CI 1.22–2.63; P = 0.003). Conclusions: Long sleep duration is associated with an increased risk of stroke but not cardiac events in high-risk OSA patients.

Keywords

Research progress on the effect of Health Qigong on sleep

Meina Zhang,Li Cai

Graduate Department，Guangzhou Sport University，Guangzhou，China.

Objective: This review aimed to better understand and apply Health Qigong to improve sleep, and to provide more information and basis for scientific research and clinical work. Methods: The effects of Qigong on sleep quality were summarized by means of literature review, logical analysis and summary. Results and conclusions: Health Qigong has a positive effect on the improvement of sleep quality. Many empirical studies have obtained relevant data as support, but there are still some questions worth thinking about.

Keywords Health Qigong; Sleep ; Review

Depression, anxiety and sleep problems among primary and middle school students during the epidemic of coronavirus disease 2019 (COVID–19)

Feng Yi

The Affiliated Wuxi Mental Health Center of Nanjing Medical University

Objective: To investigate depression, anxiety and sleep problems among primary and middle school students during the epidemic of the coronavirus disease 2019 (COVID-19). Methods: Participants were students from 18 primary and middle schools in Wuxi, China. From March 17 to 30, 2020, a set of online questionnaires, including Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), and the Pittsburgh Sleep Quality Index (PSQI), were used to measure the depression symptoms, anxiety symptoms, and sleep quality, respectively. Results: A total of 3,931 participants were included in this study. 24.0% of them (n = 942) had depressive symptoms, including 32 with mild depression, 11 with moderate depression, and 2 with severe depression. 21.3% of the participants (n = 839) had anxiety symptoms, including 151 with mild anxiety, 39 with moderate anxiety, and 8 with severe anxiety. In addition, 47% of the participants had poor sleep

quality. The detection rate of anxiety symptoms among middle school students is higher than that of primary school students ($\times 2 = 5.557$, P = 0.018). The SAS scores of primary and middle school students with family members engaged in medical care or anti-epidemic are higher than those without (t = 2.687~4.198, P = 0.000~0.007). Conclusions: During the epidemic of the COVID-19, some elementary and middle school students in Wuxi experienced various degrees of depression, anxiety, and sleep disorders. Primary school students of middle school students are prone to have anxiety symptoms. However, elementary and middle school students with family members engaged in medical and anti-epidemic frontline work have a higher level of anxiety.

Keywords Corona Virus Disease 2019; Primary and middle school student; Depression; Anxiety；Sleep

Continuous positive airway pressure (CPAP) for the management of sympathetic activity and resistant hypertension

Xiayin Zhai

The Yellow River Central Hospital

Background: Patients with obstructive sleep apnea (OSA) have increased sympathetic activity and frequently also have resistant hypertension (HTN). Treatment of OSA with continuous positive airway pressure (CPAP) decreases awake and sleep blood pressure (BP) and sympathetic activity. This study was designed to assess the effect of treatment of OSA with CPAP on sympathetic activity and BP in patients with diabetes mellitus (DM), chronic kidney disease (CKD), and resistant HTN. Methods: This was a randomized, double-blind, sham-controlled trial. Patients with DM, CKD, and resistant HTN were randomized to treatment with a therapeutic or subtherapeutic CPAP for 4 weeks. They underwent 24-hour ambulatory BP monitoring and assessment of muscle sympathetic nerve activity before and after 4 weeks on treatment. Results: Treatment with therapeutic CPAP caused significant decreases in awake systolic and diastolic BP from 150 to 140 mm Hg (P = 0.004) and from 84 to 79 mm Hg (P = 0.004) and in sleep BP from 140 to 115 mm Hg (P = 0.045) and from 80 to 70 mm Hg (P = 0.015) compared with treatment with subtherapeutic CPAP. In contrast, treatment with therapeutic CPAP did not decrease sympathetic activity as assessed from muscle sympathetic nerve activity (P > 0.05). Conclusions: Decrease in BP by treatment with CPAP in patients with DM, CKD, and OSA indicates the contribution of OSA to the severity of HTN in this clinical scenario. Decrease in BP in the absence of changes in sympathetic activity is suggestive that other mechanisms induced by OSA play a larger role in the maintenance of HTN in these patients

Keywords Sympathetic Activity Continuous Positive Airway Pressure (CPAP) Resistant Hypertension

Cluster analysis of evaluation of Photoelectric Plethysmography and clinical phenotypes of obstructive sleep apnea hypopnea syndrome

Guofeng Zhu

The Second Affiliated Hospital of Nanchang University

Objective: We aimed to establish a clinical subgroup of OSAHS based on the Photoelectric Plethysmography (PPG) technology using cluster analysis and assess each subgroup, s characteristics. Methods: Patients were selected according to the OSAHS criteria and the American College of Sleep Medicine (AASM) Sleep and Respiratory Events Interpretation Manual. Our research focuses on the pulse wave signals using multi-channel PPGs. The patients of OSAHS could be divided into two groups of high-risk and low-risk based on the cardiac risk cut-off point of 0.5. A Systemic clustering and K-means clustering analysis were performed using the parameter of CRI to determine the clinical subtype of OSAHS. Result: There were 150 cases (52 mild, 39 moderate, and 59 severe) in the OSAHS group, and 68 cases in control group. There was no significant difference in gender, age, height, SBP, smoking history, snoring history and complication history among the four groups (all $P > 0.05$). Body weight, BMI, neck circumference, waist circumference and DBP were increased in moderate and severe OSAHS group ($P < 0.05$), while LaSO2 was decreased in moderate and severe OSAHS group ($P < 0.001$). In addition, high-risk group (CRI > 0.5 group) showed higher AHI and ODI than low-risk group (CRI < 0.5 group) ($P < 0.05$). A model with four phenotype clusters provided the best fit: the first cluster of young people with high cardiovascular risk; the second cluster without cardiovascular risk; the third cluster of hypertension and high cardiovascular risk; the fourth cluster of old people with high cardiovascular risk. Conclusion: We have established a cardiovascular risk model in which CRI was be incorporated, and four major clinical subtypes of cardiovascular complications of OSAHS were established based on the objective indicators of CRI. Keywords Sleep apnea; Photoplethysmography; Cardiovascular risk；Clinical phenotypes

Polysomnogram–measured sleep architectures of patients with type 1 narcolepsy

Meina Wu,Fang Lin,Xiaoyong Wang,Haihong Chen,Xiaolin Ji,Jinzhu Yan

Fujian Province Governmental Hospital

Objective: To explore polysomnogram-measured sleep architectures of patients with type 1 narcolepsy. Methods: This study enrolled 11 patients with type 1 narcolepsy and 20 controls who complained of daytime sleepiness, but without any sleep disorders. All subjects attended the neurology clinic from January 2007 to December 2017. All subjects underwent overnight (>7 hrs) consecutive video-polysomnography (vPSG) with 16 channel electroencephalograph (EEG) and multiple sleep latency test (MSLT) including five nap

opportunities in the next day. Results: Compared with the controls, patients with type 1 narcolepsy had more wake time after sleep onset (WASO) in percentage of time in bed (WASO; %) [17.6 (13.1) vs. 5.0 (12.8), P < 0.05], increased NREM 1 sleep period (N1; %) [19.9 ± 12.0 vs. 10.1 ± 5.6, P < 0.05]. In addition, compared to controls, patients with type 1 narcolepsy showed shorter sleep latency [5.5 (11.5) vs. 13.5 (22.9) mins, P < 0.05] and REM sleep latency [93.5 ± 106.6 vs. 157.5 ± 65.7 min, P < 0.05], less NREM 3 sleep period (N3; %) [17.5 ± 5.6 vs. 24.5 ± 7.6, P < 0.05]. There was no significant difference in sleep efficiency, NREM 2 sleep period (N2; %) , REM sleep period (%), awakening index, sleep periodic leg movement index, and sleep apnea hypopnea index (AHI) between the two groups (all P > 0.05). Conclusions: There are abnormal changes in sleep structures in patients with type 1 narcolepsy patients.
Keywords

The association between sleep apnea and stroke

Xiayin Zhai

The Yellow River Central Hospital

Background: Sleep apnea is increasingly being recognized as one of the important risk factors of stroke and cardiovascular diseases. Sleep apnea is thought to impair the functional recovery following stroke. Therefore, we evaluated the prevalence of sleep apnea among patients with acute ischemic stroke, and compared the functional outcomes of patients with and without sleep apnea, at 90 days after acute ischemic stroke. Methods: Between June 2018 and November 2019, we included 98 consecutive patients with acute ischemic stroke. Sleep apnea was diagnosed using the Sleep Disorders Questionnaire and the Epworth Sleepiness Scale. Functional outcomes were measured using the Barthel score on day 7 and at 90 days following the onset of stroke. Results: Out of 98 patients, sleep apnea was present in 30 (30.6%) patients, more in males (67.7%) and the elderly. Hypertension was present in 66.6% of patients with sleep apnea. NIHSS score at admission did not differ between the two groups. At 90 days, the Barthel score calculated was better among patients without sleep apnea, although it was statistically insignificant (P = 0.12). However, the repeated measure Analysis of Variance (ANOVA) showed that functional independence was significantly lower in patients with sleep apnea than those without (P < 0.001). Conclusions: Sleep-disordered breathing is an independent risk factor for stroke. Sleep apnea is also associated with other known stroke risk factors like hypertension. In acute ischemic stroke, sleep apnea has a negative impact on functional recovery.
Keywords Barthel score—functional dependency—ischemic stroke—sleep apnea

Reduced cortical arousability to nocturnal apneic episodes in patients with wake–up ischemic stroke

Xiang Fu,Jie Li,Chunfeng Liu

The Second Affiliated Hospital of Soochow University

Objectives: Sleep breathing disorders (SBD) have been linked to wake-up stroke (WUS). Respiratory arousals have an important role in responding to danger during sleep, yet currently no studies have investigated respiratory arousability in WUS. In this study, we used a clinical tool to predict low respiratory arousal threshold (ArTH), and then compared respiratory arousability in patients with WUS and non-WUS. Methods: We enrolled 119 patients with acute ischemic stroke and assigned them into WUS (n = 34) and non-WUS (n = 85) groups. All participants underwent polysomnography (PSG) during the acute phase of stroke. The respiratory ArTH predictive tool assigns one point for each of the following: apnea-hypopnea index (AHI) < 30/h, nadir oxygen saturation (SaO2) > 82.5%, and fraction of hypopneas > 58.3%. An ArTH score of 2 represents low respiratory ArTH. Results: Our results reconfirmed the association between moderate-to-severe sleep apnea syndrome and WUS (OR = 2.879, 95% CI: 1.17e7.089, p = 0.021). Significantly fewer participants with obstructive sleep apnea (AHI 5/h) had low respiratory ArTH in the WUS group than in the non-WUS group (34.8% vs. 68.1%, respectively, p = 0.008). High respiratory ArTH was independently associated with WUS (OR = 5.556, 95% CI: 1.959e15.761, p = 0.001). Conclusions: The correlation between SBD and WUS suggests that sleep apnea may induce acute physiological changes that trigger the onset of stroke. Reduced respiratory arousability is associated with WUS, which indicates that reduced cortical capability to generate respiratory arousal may have a role in triggering stroke during sleep.
Keywords

Characteristics of objective sleep and its related risk factors among Parkinson's disease patients with and without restless legs syndrome

Shuyu Sun1, Jiafeng Ren1,Xianchao Zhao1,Jinxiang Cheng1,Chengji Wu4,Junying Zhou1,2,3,Changjun Su1

1.The second affiliated hospital of Fourth Military Medical University

2.Sleep Medicine Center，West China Hospital，Sichuan University

3.Department of Neurology，West China Hospital，Sichuan University

4.Basic Medical School of Fourth Military Medical University，

Objectives: This study aimed to investigate the objective sleep characteristics and its related risk factors among Parkinson's disease (PD) patients with and without restless legs syndrome (RLS) Methods: A total

of 125 patients with PD who underwent overnight polysomnography (PSG) were consecutively recruited. Eighty-one patients including 27 PD with RLS (PD-RLS) and 54 PD without RLS (PD-NRLS) were included in the final analysis after 1:2 propensity score matching. Demographic, clinical, and polysomnographic data were compared between PD patients with and without RLS. The risk factors of sleep quality were examined using the multiple linear regression model. Results: The prevalence of RLS among PD patients was 28.0% (35/125). PD-RLS group had a higher score of the Unified Parkinson Disease Rating Scale (UPDRS) III than the PD-NRLS group. In addition, PD-RLS patients had significantly shorter total sleep time, poorer sleep quality, decreased stage 3 duration, longer wake after sleep onset, and higher arousal index than those without RLS (all $p < 0.05$). In the multiple linear regressions models, PD duration (β = -0.363, 95% CI: -0.652 to -0.074; p = 0.016), UPDRS-III (β = -0.356, 95% CI: -0.641 to -0.071; p = 0.016) and periodic limb movement index (PLMI) (β = -0.472, 95% CI: -0.757 to -0.187; p = 0.002) were specifically found to be the risk factors influencing sleep quality in PD-RLS patients, and the UPDRS-III (β = -0.347, 95% CI: -0.590 to -0.104; p = 0.006) and HAMD scores (β = -0.343, 95% CI: -0.586 to -0.100; p = 0.007) were significantly associated with sleep quality after adjustment of confounding factors in PD-NRLS patients, respectively. Conclusions: PD-RLS patients have more disturbed and fragmented sleep in objective sleep architecture than PD-NRLS patients. Notably, our findings indicate that PLMI is the risk factor influencing the objective sleep quality in PD patients with RLS.
Keywords Parkinson's Disease, Restless Legs Syndrome, Polysomnography

Dyslipidemia is a risk factor for recurrence and disease course of the coronavirus disease (COVID–19): findings from two independent cohorts

Xiaolong Zhao1,Hui Jin2,Junji He3,Zhiyue Ma1,Bin Li1,iangang Fan1,Chuan Dong1,Gang He1
1.Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital
2.Wuhan Third People's Hospital
3.Chengdu Public Health Center

Background: The coronavirus disease (COVID-19) outbreak has spread around the world. However, the effect of dyslipidemia and lipid-lowering therapy on the clinical endpoint of COVID-19 has not been studied. Methods: In this retrospective, multi-center cohort study, we recruited 430 adult patients with COVID-19 from Chengdu and Wuhan starting in February 2020 and followed up until April 30 2020. We collected the demography, blood glucose, blood lipid and other laboratory indicators, treatment measures and clinical endpoint data for COVID-19. The primary outcome included death during hospitalization and nucleic acid reactivation after discharge. The secondary outcome included invasive ventilator use and admission to the intensive care unit during hospitalization. Results: In the Chengdu cohort, multivariate Cox regression showed that abnormalities in low-density lipoprotein cholesterol (LDL-C) at admission were associated with

COVID-19 recurrence during follow-up (P < 0.05). In the Wuhan cohort, patients with abnormal triglycerides (TG) had an increased risk of in-hospital death (P < 0.05). However, the use of statins during the course of COVID-19 did not affect these clinical endpoints in either cohort. In addition, these dyslipidemia had similar predictive effects on invasive ventilator use during hospitalization and admission to the intensive care unit. Participants in Wuhan cohort tend to be sicker than those in Chengdu, but presented with lower serum lipid level. The multivariate analysis showed that lipid levels were independently correlated with inflammatory markers and indicators representing liver and kidney function (P < 0.05). However, these correlations were inconsistent: 1) Total cholesterol, high-density lipoprotein, and low-density lipoprotein were negatively correlated with CRP; 2) Total cholesterol, triglyceride, high density lipoprotein, and low density lipoprotein were positively correlated with liver transaminase and creatinine. Conclusions: Baseline dyslipidemia may be a risk factor for poor prognosis and recurrence of COVID-19. Lipid levels may be influenced by inflammation and SARS-CoV-2 infection. The role of lipid-lowering therapy in patients with COVID-19 infection needs to be further studied.

Keywords

The correlation between obstructive sleep apnea and coagulation function

Yina Zhu,Wenjing Wang

The Second Affiliated Hospital of Nanjing Medical University

Objective: The purpose of this study was to investigate the abnormal coagulation function of OSA patients with different degrees of severity, and to lay a foundation for further elucidating the relationship between OSA and cardiovascular and cerebrovascular diseases. Methods: According to the presence and severity of OSA, patients were divided into mild OSA group, moderate OSA group, severe OSA group, and control group. All patients were tested by PSG, blood routine, blood coagulation routine, and thromboelastography. Results: There was no significant difference in PLT, PCT, MPV, and APTT between the four groups (P > 0.05). PDW of mild to moderate OSA group was significantly different from that of control group (P < 0.01). There were significant differences in PT and INR between the moderate and severe OSA group and control group (P < 0.01). There were significant differences in R, K, and MA between mild, moderate, and severe OSA group and control group, respectively. R and MA in moderate and severe OSA group were significantly different from those in mild OSA group (P < 0.01). There was a significant difference in K between severe and mild OSA groups (P < 0.01). Conclusions: This study reveals that OSA patients have abnormal coagulation function. With the increase of AHI, the hypercoagulability status is more significant, which may be related to the increased risk of OSA for cardiovascular and cerebrovascular diseases. Compared with routine blood test and routine blood coagulation, thromboelastography is more sensitive and has more comprehensive clinical significance.

Keywords

Chronic intermittent hypoxia promoted lung cancer stem cell–like properties via enhancing Bach1 expression

Shengyu Hao,Pan Jiang,Shanqun Li,Liu Zilong

Zhongshan Hospital，Fudan University

Lung cancer is the leading cause of cancer death. Despite advances in anti-tumor therapies, the five-year survival rate of lung cancer is still low. In the past decade, several population studies have shown that obstructive sleep apnea (OSA) is prevalent among lung cancer patients and increased cancer incidence and mortality. The deterioration in survival is at least partially attributable to limitations in understanding the mechanisms underlying the comorbidity of primary lung cancer and OSA. Cancer stem cells (CSCs) are described as a subpopulation of tumor cells with the capacity to self-renew, differentiate, and promote tumor growth. Besides, CSCs are increasingly recognized as a key factor in tumor progression, metastasis, and drug resistance. However, the relationship between OSA and CSCs has not yet been explored. To the best of our knowledge, this study is the first to uncover the relationship between OSA and the lung CSCs. Besides, we also identified that chronic intermittent hypoxia（CIH）promoted lung CSC-like properties by activating mtROS, which was partially mediated by Bach1.

Keywords obstructive sleep apnea, chronic intermittent hypoxia, cancer stem cells, lung cancer, Bach1

Blockade of cholinergic muscarinic receptor improves sleep depth in a model of light sleep

Jichuan Zhou1,2,Fengfei Ding2,Han Guo2,Weimin Qu2,Zhili Huang1,2

1. Institutes of Brain Science; State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science，Fudan University
2. Department of Pharmacology，School of Basic Medical Sciences，Fudan University

Objective: Insomnia is not only the reduction in sleep quantity, the difficulties in sleep initiation and maintenance, but also the abnormal sleep depth, that is, the increased light sleep along with the reduction in slow wave sleep (SWS). Increased light sleep reduces the clearance of β-amyloid in brain tissues, which increases the risk of β-amyloid aggregation related dementia. Therefore, it is imperative to establish an animal model of light sleep, and to find available strategies to increase sleep depth. Methods: By using the real-time synchronous sleep-wake recording system, EEG/EMG signals of freely moving mice were recorded, and chemogenetics was used in ChAT-Cre mice to specifically regulate the basal forebrain (BF) cholinergic neurons. To explore the effect of BF cholinergic neurons on sleep homeostasis, we activated BF cholinergic neurons in sleep deprivation (SD) model of ChAT-Cre mice. Next, the effects of trihexyphenidyl (0.5, 1 and 2 mg/kg, i.p.) and scopolamine (1 mg/kg, i.p.) on the sleep depth were evaluated.

Finally, Y maze test and novel object recognition test were used to detect the effects of trihexyphenidyl and scopolamine on the spatial learning and memory in mice. Results: Specific activation of BF cholinergic neurons significantly reduced delta power spectrum in NREM sleep. And imbalance of sleep homeostasis was observed after SD. However, activation of BF cholinergic neurons during sleep recovery reduced the delta power spectrum. Trihexyphenidyl increased delta power spectrum and ameliorated the light sleep evoked by activation of BF cholinergic neurons. Behavioral tests showed that scopolamine, not trihexyphenidyl, decreased the spontaneous alteration ratio and the percentage of time spent exploring novel objects in mice. Conclusion: Specific blockade of muscarinic receptors is the potential target to improve sleep quality.

Keywords Slow wave sleep, Delta power, Light sleep, Cognitive function, Trihexyphenidyl

Nightmare distress as a mediator between frequent nightmares and depressive symptoms in Chinese adolescent

Xiao-Fan Yang1,2,Zhenzhen Liu1,2,Shujuan Liu1,2,Cunxian Jia1,2,Xianchen Liu3,2

1.School of Public Health，Cheloo Medical College，Shandong University

2.Shandong University Center for Suicide Prevention Research，Jinan，Shandong，China

3.Center for Public Health Initiatives，University of Pennsylvania，Philadelphia，PA，USA

Objective: Frequent nightmares are related to depression in adolescents. Few studies focus on pathways of how nightmares affect depression. The study aimed to examine the association between frequent nightmares, nightmare distress, and depression in a large sample of Chinese adolescents. Methods: A total of 11,831 adolescents who participated in the baseline survey of Shandong Adolescent Behavior and Health Cohort were included in the analysis. A self-reported questionnaire was used to measure nightmare frequency, nightmare distress, depression, sleep, and demographic characteristics. Linear regressions and mediation analyses were performed to examine the associations between frequent nightmares, nightmare distress, and depression. Results: Of 11831 participates, 50.9% were males and the mean age was 14.9 years. Mean scores of nightmare distress in adolescents with and without frequent nightmares were 30.18 (SD: 11.4) and 21.37 (SD: 7.96), and mean depression scores were 22.69 (SD: 10.94) and 16.37 (SD: 9.38), respectively. Nightmare distress mediated 51.2% and 80.0% of the total effect of frequent nightmares on depression in males and females, respectively. In males, the total effect was 2.99 (95%CI: 2.20-3.78), including 1.46 (95%CI: 0.68-2.24) for direct effect and 1.53 (95%CI: 1.22-1.87) for indirect effect. However, in females, the direct effect was not significant (β = 0.54, 95%CI: -0.27-1.36), and the total and indirect effects were 2.75 (95%CI: 1.92-3.58) and 2.20 (95%CI: 1.83-2.61). Conclusions: The association between frequent nightmares and depression appears to be mediated by nightmare distress. Further research is warranted to examine the psychosocial and biological mechanisms between frequent nightmares and depression in adolescents.

Keywords Frequent nightmares; Nightmare distress; Depression; Adolescents

mGluR1 mediates hypoxia sensory response of carotid body via presynaptic mechanism

Chaohong Li,Lu Huang,Baosheng Zhao,Ya-nan Fan,Yuanyuan Geng,Yuzhen Liu

The First Affiliated Hospital of Xinxiang Medical University

Aim: The carotid body (CB) plays a critical role in oxygen sensing; however, the role of glutamatergic signaling in the CB response to hypoxia remains uncertain. We previously found that multiple glutamate transporters and inotropic glutamate receptors (iGluRs) are expressed in the CB. The aim of this current study is to investigate the expression of group I metabotropic glutamate receptors (mGluRs) (mGluR1 and 5) in the CB and its physiological function in rat CB response to acute hypoxia.Methods: RT-PCR and immunostaining were conducted to examine the mRNA and protein expression of group I mGluRs in the human and rat CB. Immunofluorescence staining was performed to examine the cellular localization of mGluR1 in the rat CB. In vitro carotid sinus nerve (CSN) discharge recording was performed to detect the physiological function of mGluR1 in CB response to acute hypoxia.Results: We found that: 1) mRNA of mGluR1 and 5 were both present in the human and rat CB. 2) mGluR1 instead of mGluR5 protein was detectable in rat CB. 3) mGluR1 was distributed in both type I cells and type II cells of rat CB. 4) Activation of mGluR1 inhibited the hypoxia-induced enhancement of CSN activity (CSNA), as well as prolonged the latency time of CB. 5) The inhibitory effect on the CB response towards hypoxia via mGluR1 activation could be blocked by GABAB receptor antagonist. Conclusion: Taken together, our findings revealed that mGluR1 in CB involves in a presynaptic feedback inhibition mechanism in response to hypoxia.
Keywords

Cognitive deficits caused by lipid droplet accumulation through JNK/SREBP/ACC pathway in obstructive sleep apnea syndrome mice

Dongze Li,Yan Yu,Na Xu,Wanting Li,Yanyan Hou,Xi Wang,Yeying Sun,Wenxue Lu,Guiwu Qu,Changjun Lv,Fang Han

Binzhou Medical University

The mechanisms of chronic intermittent hypoxia (CIH)-induced cognitive deficits remain unclear. Here, our study found that 12 weeks CIH treatment induced lipid droplets (LDs) accumulation in hippocampal neurocytes of C57BL/6 mice, and caused severe neuro damage including neuron lesions, neuroblast (NB) apoptosis and abnormal glial activation. Studies have shown that the neuronal metabolism disorders might contribute to the CIH induced-hippocampal impairment. Mechanistically, the results showed that pyruvate dehydrogenase complex E1α subunit (PDHA1) and the pyruvate dehydrogenase complex (PDC) activator pyruvate dehydrogenase phosphatase 1 (PDP1) did not noticeable change after intermittent hypoxia.

Consistent with those results, the level of Acetyl-CoA in hippocampus did not significantly change after CIH exposure. Interestingly, we found that CIH produced large quantities of ROS, which activated the JNK/ SREBP/ACC pathway in neurocytes. ACC catalyzed the carboxylation of Acetyl-CoA to malonyl-CoA and then more lipid acids were synthesized, which finally caused aberrant LDs accumulation. Therefore, the JNK/SREBP/ACC pathway played a crucial role in the cognitive deficits caused by LDs accumulation after CIH exposure. Additionally, LDs were peroxidized by the high level of ROS under CIH conditions. Together, lipid metabolic disorders contributed to neurocytes damage, which ultimately caused behavioral dysfunction. An active component of Salvia miltiorrhiza, SMND-309, dramatically alleviated these injuries and improved cognitive deficits of CIH mice.

Keywords

The clinical effect of the Modified Suanzaoren Decoction on medication–dependent Insomnia

Guiling Fu

Beijing Changing Hospital of Chinese and Western Medicine

Objective: To observe the effect of using the modified Suanzaoren decoction to treat medication-dependent insomnia. Methods: A total of 96 patients with medication-dependent insomnia were enrolled in the study between March 2017 and May 2018 in the Beijing Changping district Hospital of Combined Chinese and Western Medicine. They were randomly divided into treatment group (n = 48) and control group (n = 48). The study group patients were given the modified Suanzaoren Decoction while the control group patients were given estazolam. The clinical efficacy such as sleep quality was evaluated by the Pittsburgh Sleep Quality Index (PSQI). Results: The total effective rate of the intervention group was higher than that of the control group (89. 6% vs. 64. 6%, P < 0. 05). In addition, the intervention groups had lower PSQI score than the control group (P < 0. 05). Conclusions: Our findings suggest that the modified Suanzaoren Decoction may be effective in the treatment of medication-dependent insomnia.

Keywords Suanzaoren soap; Sleep drug-dependent insomnia; Clinical effect

Clinical experience of Traditional Chinese Medicine (TCM) comprehensive treatment of chronic stubborn insomnia

Guiling Fu

Beijing Changing Hospital of Chinese and Western Medicine

Objective: To explore the clinical efficacy and experience of traditional Chinese medicine in the treatment of chronic stubborn insomnia. Methods: Seventy-two patients with chronic stubborn insomnia admitted to

our hospital from October 2016 to July 2018 were enrolled in this study. They were divided into two groups according to the random even odd number method: control group (n = 36) and treatment group (n = 36). The control group was treated with Western medicine, and the treatment group was treated with Traditional Chinese Medicine (TCM) comprehensive treatment. The sleep improvement effect, clinical efficacy and treatment satisfaction were measured. The clinical efficacy was evaluated by the Pittsburgh Sleep Quality Index (PSQI). Results: The total effective rate of treatment and the satisfaction of treatment in the treatment group were lower than those in the control group. After treatment, both TCM comprehensive treatment and control groups showed decreased PSQI scores ($P < 0. 05$). Conclusions: TCM comprehensive treatment may be effective for the treatment of chronic stubborn insomnia.

Keywords Comprehensive treatment of TCM Chronic obstinate insomnia; Clinical experience

Functional connectivity alteration of the locus coeruleus–norepinephrine system in chronic insomnia disorder

Liang Gong1,Jian Wang1,Bei Zhang1,Chunhua Xi2
1.Chengdu Second People's Hospital
2.Anhui Medical Universtiy

Background: Mental symptoms are a common comorbidity in patients with chronic insomnia disorder (CID). The locus coeruleus noradrenergic (LC-NE) system is considered to be the crucial system in the modulation of emotion and sleep/wake cycle. However, whether the LC-NE system contributes to the underlying mechanism linking insomnia and these comorbidities remain unclear. Methods: Seventy patients with CID and 63 matched good sleep control subjects (GSC) were recruited and underwent resting-state functional MRI scan. LC-NE functional network was constructed by using seed-based functional connectivity (FC) analysis. The alteration of the LC-NE FC network in patients with CID and the clinical significance of these alterations was explored. Results: Compared with the GCS group, the CID group shown decreased FC in left inferior frontal gyrus and left inferior frontal gyrus (IFG), while increased FC in the left supramarginal gyrus and left the middle occipital gyrus (MOG) ($P < 0.05$). The FC between the left LC and left MOG was associated with the duration of disease, while abnormal FC between right LC and dACC was associated with the anxiety scores in patients with CID ($P < 0.05$). Conclusion: The present study substantially extended our understanding of the neuropathological of CID, and provided the potential treatment target for CID comorbid with anxiety.

Keywords

Effect of extracorporeal diaphragm pacing on stroke hemiplegic patients with OSAHS

Yiming Xu

The Fourth Rehabilitation Hospital of Shanghai

Objective: To investigate the effects of extracorporeal diaphragm pacing (EDP) on pulmonary function, diaphragm function, and PSG parameters in stroke patients with obstructive sleep apnea hypopnea syndrome (OSAHS). Methods: From January 2018 to December 2019, 65 stroke patients with OSAHS hemiplegia (31 males and 34 females, age: 73.90 ± 3.81 years) were prospectively selected and divided into aerobic breathing exercise group (n = 34) and aerobic breathing exercise + EDP group (n = 31) according to whether to use extracorporeal diaphragm pacing. All patients completed aerobic breathing exercises and/or EDP for 24 weeks. Pulmonary function, diaphragm ultrasound, and polysomnography (PSG) were measured before and after treatment. The differences of parameters before and after treatment and between groups were compared. Results: The pulmonary function and PSG parameters, diaphragm thickness (0.22 ± 0.01 vs. 0.20 ± 0.02 cm], diaphragmatic quiet activity (1.44 ± 0.13 vs. 1.31 ± 0.96 cm], maximum diaphragmatic activity (3.98 ± 0.49 vs. 3.23 ± 0.35 cm] were significantly improved in EDP group (all P < 0.05). FVC, FEV1 / FVC and diaphragmatic activity were improved in aerobic exercise group after treatment (all P < 0.01)) There were no significant differences in FEV1, diaphragm thickness and PSG parameters (all P > 0.05). The pulmonary function, PSG parameters, and diaphragm function of the aerobic breathing exercise + EDP group were significantly better than those of the aerobic breathing exercise group (all P < 0.05). Conclusions: Aerobic exercise combined with EDP can significantly improve the pulmonary function and diaphragm function of stroke patients with OSAHS.

Keywords

Gut microbiota modulates the inflammatory response and cognitive impairment induced by sleep deprivation

Wenhao Chen1,Zhong Wang1,Suxia Li2,Yanbin Ji3,Zhe Wang1,Ximei Zhu1,Jie Shi2,Lin Lu1,2,4

1. Peking University Sixth Hospital
2. National Institute on Drug Dependence and Beijing Key Laboratory of Drug Dependence，Peking University
3. Qilu Hospital of Shandong University
4. Peking-Tsinghua Center for Life Sciences and PKU-IDG/McGovern Institute for Brain Research，Peking University

Objective: Sleep deprivation (SD) is increasingly common in modern society, which can lead to the dysregulation of inflammatory responses and cognitive impairment, but the mechanisms remain unclear.

Emerging evidence suggests that gut microbiota plays a critical role in the pathogenesis and development of inflammatory and psychiatric diseases, possibly via gut microbiota-brain interactions and neuroinflammation. Methods: The present study investigated the impact of SD on gut microbiota composition and explored whether alterations of the gut microbiota play a causal role in chronic inflammatory states and cognitive impairment that are induced by SD. Results: We found that SD induced gut dysbiosis, inflammatory responses, and cognitive impairment in humans. Moreover, the absence of the gut microbiota suppressed inflammatory response and cognitive impairment induced by SD in germ-free (GF) mice. Transplantation of the "SD microbiota" into GF mice activated the Toll-like receptor 4/nuclear factor- κ B signaling pathway and impaired cognitive function in the recipient mice. Mice that harbored "SD microbiota" also exhibited increases in neuroinflammation and microglial activity in the hippocampus and medial prefrontal cortex. Conclusions: These findings indicate that gut dysbiosis contributes to both peripheral and central inflammatory processes and cognitive deficits that are induced by SD, which may open avenues for potential interventions that can relieve the detrimental consequences of sleep loss.

Keywords

Design and application of an adjustable anti–compression ventilator mask

Xiaoyan Zhang

Xinkunhua Hospital of the First People's Hospital of Yunnan Province

The ventilator continuous positive pressure ventilation is the preferred treatment for patients with moderate and severe obstructive sleep apnea hypopnea syndrome. For continuous positive pressure ventilation, the literature shows that the compliance of continuous positive pressure ventilation is poor, and there are many possible factors affecting the compliance of continuous positive pressure ventilation. In clinical practice, the comfort of nasal masks is the main reason for the low compliance of continuous positive pressure ventilation. For solving the above problems, we designed a new type of adjustable anti-pressure ventilator mask (patent number: ZL 202021401568.1), which includes breathing mask, intake pipe, tearable cloth ring, anti-pressure latex cushion, anti-pressure cloth body, nose cover cloth, aluminum strip, multi-stage adjusting cloth body, mask ear belt, extendable section. The utility model distributes the pressure on the face of the patient with the edge of the breathing mask to a large area around, prevents the compression of the patient's face from producing strangulation marks. In addition, by adjusting the size, it is suitable for different face shapes. This mask can help to improve the compliance of continuous positive pressure ventilation.

Keywords

EEG Power Spectral Analysis of Abnormal Cortical Activations during REM/NREM Sleep in Obstructive Sleep Apnea

Shuling Liu,Rui Chen

The Second Affiliated Hospital of Suzhou University

Objective: To characterize electroencephalogram (EEG) power in different frequency bands during rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep in patients with obstructive sleep apnea (OSA). Methods: Retrospective data from 151 OSA patients were collected and divided into three groups: primary snoring group (AHI < 5/h), mild-moderate OSA group ($6 \leq$ AHI < 30/h), and severe OSA group (AHI $\geq$ 30/h). EEG recordings in the frontal, central and occipital regions were extracted from both REM and NREM sleep, to compute the normalized spectral power densities in the delta, theta, alpha, sigma, beta, and gamma frequency bands, using Fast Fourier Transform. Correlations between the computed EEG power and PSG parameters were analyzed. Results: In NREM sleep, elevated normalized power spectral density (PSD) in the delta band was observed in the severe OSA group compared to the other two groups. In contrast, the PSD of the other frequency bands showed a corresponding decrease in the severe OSA group. In REM sleep, similar changes were observed in the frontal region. Delta band PSD was positively correlated with Apnea Hypopnea Index (AHI) (r = 0.33), longest time of apnea, oxygen desaturation index (ODI) (r = 0.34), percent sleep time below 90% SaO_2 (T90%) (r = 0.30), Arousal Index (ArI) (r = 0.29) and negatively correlated with N3%, minimum oxygen saturation ($minSaO_2$). Conclusion: Our findings provide neurophysiological evidence for pathological cortical activation during REM/NREM sleep, which may be associated with the arousals and cognitive impairments in OSA. The technique of power spectral analysis could prove a potentially useful tool in complementing traditional PSG parameters in assessing disease burden to guide therapeutic decisions. Keywords Obstructive Sleep Apnea, Polysomnography, REM and NREM Sleep, Power Spectral Analysis, normalized EEG power

The Effects of Light and Activity on Insomnia and Drowsiness at an Altitude of 3600 meters: Results of Actigraphy Monitoring

Ren jiafeng,Shuyu Sun,Xianchao Zhao,Jinxiang Cheng,Changjun Su

Sleep Disorders Center，Department of Neurology，Tangdu Hospital，Fourth Military Medical University

Objective: The study aimed to analyze the reason why no-native Chinese youth had insomnia and evaluate the effects of light and activity on insomnia and drowsiness at high altitudes environment. Methods: A total of 26 Chinese youth living at an altitude of 3,600 meters (Tibet) were included in the study. All people were monitored by actigraphy for 7 consecutive days. They also completed questionnaires to determine their subjective sleep characteristics. Results: People with insomnia and insomnia-drowsiness spent more time in

bed (control vs. insomnia, 476.84 ± 14.96 min vs. 510.77 ± 30.66 min, p = 0.031; control vs. insomnia-drowsiness, 476.84 ± 14.96 vs. 515.31 ± 29.24 min, p = 0.015), had a longer wake after sleep onset (WASO) time (control vs. insomnia, 33.25 ± 9.90 vs. 49.08 ± 16.41 min, p = 0.040; control vs. insomnia-drowsiness, 33.25 ± 9.90 vs. 55.60 ± 25.98 min, p = 0.021), and greater light exposure during the active period than the control group. Conclusions: Young, non-native people need more time to adapt to high altitude training, to avoid sleep problems such as insomnia and drowsiness. Bright light after 16:00, and artificial light exposure during the rest period, have deleterious effects on sleep quality.

Keywords

Effect of comorbid insomnia on CPAP in patients with obstructive sleep apnea

Ren jiafeng,Shuyu Sun,Xianchao Zhao,Jinxiang Cheng,Changjun Su

Sleep Disorders Center，Department of Neurology，Tangdu Hospital，Fourth Military Medical University

Objective: Patients with co-morbid insomnia and sleep apnea (COMISA) had suffered from more terrible daytime function and greater impairment of quality of life. Difficulty falling asleep (DFA), difficulty maintaining sleep (DMS) and early morning awakening (EMA) were different symptoms of insomnia. We aimed to analyze the effect of comorbid different number of insomnia symptoms on initial exposure to CPAP. Methods: A total of 501 patients were included in the study from 2011 to 2016. All patients completed both diagnostic polysomnography (PSG) and pressure titration PSG in Tangdu Hospital Sleep Laboratory. Results: The prevalence of COMSIA was 43.31%. Compared to OSA only, COMSIA had significant difference after PAP treatment in AHI (-52.01 ± 23.15 counts/h vs. -44.52 ± 21.61 counts/h, p < 0.001), NREM AHI (-52.26 ± 24.37 counts/h vs. -44.41 ± 22.30 counts/h, p < 0.001), REM AHI (-47.88 ± 23.49 counts/h vs. -44.56 ± 35.06 counts/h, p = 0.014), ODI (-42.33 ± 28.15 counts/h vs. -34.16 ± 26.42 counts/h, p = 0.001). Ordinal multinomial logistic regression analysis showed that patients with zero, one, or two insomnia symptoms had a 3.25 (95% CI 1.55-6.82; p = 0.002), 2.78 (95% CI 1.29-6.03; p = 0.009), or 3.24 (95% CI 1.39-7.55; p = 0.007) times higher rate of REM% between pressure titration study and diagnostic polysomnography than patients with three insomnia symptoms. Conclusions: COMISA patients have suffered from more terrible daytime function and greater impairment of quality of life. More numbers of insomnia symptoms had less therapeutic efficacy after initial CPAP. Therefore, individualized treatment of insomnia combines with PAP treatment may have beneficial to COMSIA patients.

Keywords

Effect of REM Sleep Behavior Disorder Associated with EMG activity

Ren jiafeng,Shuyu Sun,Xianchao Zhao,Jinxiang Cheng,Changjun Su
Department of Neurology，Tangdu Hospital，Fourth Military Medical University

Background: Rapid eye movement sleep behavior disorder (RBD) is a sleep disorder characterized by rapid eye movement (REM) sleep without atonia, the muscle activity of RBD on PSG can be divided into two types: phasic and tonic. The phasic and tonic EMG activities of patients with RBD have different neural mechanisms. The purpose of this study is to explore the effects of different types of EMG activity on sleep. Methods: 70 patients who met the inclusion and exclusion criteria in our hospital from January 2017 to December 2019 were retrospectively analyzed. The EMG activities of all patients were clustered into groups, and the differences of clinical characteristics, subjective and objective results between different EMG activity groups were observed. All data were tested by Shapiro-Wilk for normality test. For normal data, one-way ANOVA was used for comparison between groups, and the Kruskal-Wallis H test was used for comparison between non-normal data groups. The counting data were analyzed by the chi-square test. $P < 0.05$ was considered statistical significance ($P < 0.05$). Results: After clustering grouping, the PSG parameter of the group with a high percentage of tonic EMG activity was lower than that of the group with a similar percentage of phasic and tonic EMG activity, and the instability of the stage of N3 showed the statistical difference. Conclusions: More tonic EMG activity has a greater impact on night sleep. According to the characteristics of the disease and the different effects of EMG activities on sleep, timely and effective symptomatic treatment is very necessary.

Keywords

Effect of comorbid insomnia on continuous positive airway pressure ventilation in patients with obstructive sleep apnea

Ren jiafeng,Shuyu Sun,Jinxiang Cheng,Cheng jinxiang,Changjun Su
Sleep Disorders Center，Department of Neurology，Tangdu Hospital，Fourth Military Medical University

Objective: To explore the therapeutic effects of continuous positive airway pressure (CPAP) on comorbid insomnia symptoms in patients with obstructive sleep apnea (OSA). Methods: A total of 202 patients with CPAP in the Department of Neurology of Tangdu Hospital of Air Force military Medical University from 2011 to 2016 were recruited. Age, sex, height, weight and disease history were collected. The Epworth Sleepiness Scale and polysomnography were used to assess sleepiness and sleep characteristics during the diagnostic night and CPAP titration night. Results: There were 101 patients with comorbid insomnia and sleep apnea (48.95 $\pm$ 11.75 years old), and 101 patients with OSA only (48.39 $\pm$ 11.23 years old).

Compared with other insomnia groups, there were significant differences in the proportion of Non-REM Stage 2 (NREM 2), the proportion of Stage NREM 3, Apnea-hypopnea index (AHI), mean pulse oxygen saturation, and oxygen desaturation index in the group of difficulty maintaining sleep after treatment (all P < 0.05). Conclusions: The therapeutic efficacies of CPAP on comorbid OSA and different insomnia symptoms are different. Individualized therapy for insomnia symptoms combined with OSA therapy is a benefit for the rehabilitation of these patients.

Keywords

Preliminary analysis of intestinal microflora in patients with different severity of obstructive sleep apnea hypopnea syndrome

Lijuan Wang,Bei Wang,Chong Yang,Zhanjun Dou,Peipei Wang,Zixuan Hu

Department of respiratory and critical care medicine，The second hospital of Shanxi Medical University，

China

Objective: To analyze the characteristics of intestinal microflora diversity, abundance and structural composition of patients with different severity of obstructive sleep apnea hypopnea syndrome (OSAHS), and to explore its potential role in the occurrence and development of OSAHS. Methods: A total of 27 healthy volunteers (N) and 100 patients with OSAHS were enrolled, and patient-related sleep monitoring data and medical history data were collected. According to the AHI classification and whether there were complications, OSAHS patients were divided into mild group (L), moderate group (M), severe group (S) and severe complication group (SC). Using 16S rRNA high-throughput sequencing technology to analyze the intestinal flora of all people. Results: There was no significant difference in intestinal flora Alpha and Beta diversity among all groups (P > 0.05). At the phylum level, the relative abundance of Bacteroides in OSAHS group was lower than that in normal group (N: 24.96%, L: 18.31%, M: 12.95%, S: 15.78%, Sc: 16.48%). With the aggravation of OSAHS, the relative abundance of Bacteroides (N: 16.03%, L: 10.82%, M: 9.79%, S: 9.29%, Sc: 8.25%) and Faecalibacterium (N: 11.21%, L: 10.42%, M: 10.21%, S: 8.54%, Sc: 6.27%) showed a decreasing trend, while the relative abundance of Bifidobacterium (N: 3.20%, L: 2.47%, M: 4.10%, S: 4.93%, Sc: 6.27%) and Blautia (N: 2.52%, L: 3.59%, M: 3.81%, S: 4.11%, Sc: 5.86%) showed an increasing trend. Compared with the S group, the relative abundance of Roseburia (S: 10.22%, Sc: 6.65%) in the Sc is lower and the relative abundance of Shigella (S:4.64%, Sc:10.01%) is higher. RDA redundancy analysis showed that AHI, SpO2min, SpO2mean, and Tmax were not significantly correlated with the overall abundance of intestinal flora (P > 0.05), However, there was a significant correlation between the abundance of different flora and sleep monitoring indicators. Conclusions: There is an intestinal microecological imbalance in patients with OSAHS, mainly due to the reduction of the relative abundance of probiotics producing short-chain fatty acids and the increase of pathogenic bacteria, suggesting that the disturbance of intestinal flora may be related to the occurrence and development of OSAHS.

Keywords Obstructive sleep apnea hypopnea syndrome ;Intestinal flora;Hight-throughput sequencing

The role of mitophagy in the mechanism of genioglossal dysfunction caused by chronic intermittent hypoxia and the protective effect of adiponectin

Wenjing Wang1,Yina Zhu1,Xilong Zhang2

1. The Second Affiliated Hospital of Nanjing Medical University (The Second Clinical Medical College of Nanjing Medical University，The Second Red Cross Hospital of Jiangsu Province)
2. Jiangsu Provincial People's Hospital

Purpose: Dysfunction of the genioglossus muscle is important in the pathogenesis of obstructive sleep apnea due to chronic intermittent hypoxia (CIH). Mitochondrial impairment resulting from hypoxia is mitigated by mitophagy to avoid cell apoptosis in cardiomyocytes. This project was designed to explore the effects of CIH on mitophagy in the genioglossus muscle and the impact of adiponectin (Ad).Methods: 180 male SD rats were randomly divided into 3 groups (normal control (NC], CIH, and CIH + Ad groups), with 60 rats in each group observed for 5 weeks. Comparisons of serum Ad levels, mitochondrial structure and function, mitophagy, and cell apoptosis in the genioglossus were made at different time points.Results: (1) The CIH group was significantly different from the NC group as follows: During the first 3 weeks, serum Ad levels, the reactive oxygen species (ROS), relative proteins and mRNA of mitophagy, autophagy biomarker LC3-II, and autophagosomes increased, while during the last 2 weeks, most parameters decreased. (2) There was no difference among the 3 groups in mitochondrial structure and function-associated mRNA during the first 3 weeks, while damaged mitochondrial structures developed during the last 2 weeks. Exacerbation of apoptosis was also detected in the last 2 weeks. (3) All of the damage was partially alleviated in the CIH + Ad group in contrast to CIH group at the end of this study.Conclusion: Disturbances of genioglossal mitophagy could be related to damaged mitochondrial structure and function induced by CIH, which could be alleviated by supplementation of exogenous Ad via increasing mitophagy.
Keywords

The key to reverse the accelerated aging and degeneration of cervical spine

Jun Zhao

Nanning Jingbeibao Sleeping Technology Co.，Ltd.

According to the survey of China International Exchange cervical and lumbar disease prevention and control committee, 82% of people over 60 years old suffer from cervical spondylosis. The prevalence rate of 20-40 years old was 59.1%. Who has ranked cervical spondylosis as the second of the "top ten persistent diseases in the world"？The prevention and treatment of cervical spondylosis in the world as a whole have failed.

So what are the causes of the failure? According to our research and experiments, we have found that it is more comfortable for human beings to replace their arms with earth rock, vegetation, and pillows from the beginning, and then the elders form the habit of using pillows for their descendants from generation to generation. After being beautified and strengthened by craftsmen, it became a closed loop without pillows, so that it was habitually coerced for tens of thousands of years, and it is still common to use pillows to lift the original human body. The back of the baby's head protruding from the back of itself changes the natural physiological structure so that the cervical spine has been displaced and tilted forward in teenagers. At the present stage of change, the increment of bad posture makes the cervical spine hidden danger which used to attack in the name of the senile degenerative disease continue to be injured by the joint force of pillow and cushion fatigue even if preventive measures are taken, it is also due to the adverse effect of all preventive measures and sleep. The injury ratio of physiological pillow is lagging behind and short in timeliness and duration, which is mostly offset by the reaction of pillow. If so Pillow pad can eliminate the injury to cervical vertebra and help it to repair the strain of the day and the night. How can it become a disease? It is generally accepted by the medical profession that the standard height of a pillow for sleeping on one's side should not be against the natural radian of the neck. Similarly, it is the same for sleeping on one's back. Up to now, there is no high standard pillow for sleeping on one's back. Responsible doctors are embarrassed by the media because they don't want the public to follow blindly. They are all against the physiological pillow, but they have to use the vague concept of "moderation" Avoid. It is necessary to tie the bell. The inventor has been engaged in the research of non-drug prevention and treatment of diseases for decades and has tried all kinds of methods to get rid of his cervical disease, and finally, he is in pain. In contrast to the special differential sensitivity of cervical vertebra in the critical state, we found that pillow "culprit" and mattress "accomplice" were generally underestimated, and changed them into two. The pillow and cushion combination with 0 pressure on the cervical vertebra and self-stretching function of the whole cervical vertebra is unique in the world. After three years of trial sleep, all cervical spondylosis disappeared; the scientific principle of the product. It can stand the questioning of any cervical spondylosis experts in the world. And just one step to sleep can far surpass McKenzie's "seven steps to say goodbye to cervical spondylosis" popular in Western Europe and other countries. Defecation therapy (which has been cited as a textbook in our country) has more advantages than it: it can protect the neck forward, rich and noble bag and camel from the baby to the adult when they sleep in a straight posture back, cervical spondylosis "bottom" make it the no longer chronic accumulation of disease conditions. This kind of sleeping appliance with the double breakthrough in killing and gain shows the leading subversive advantage in the world and has the conditions to formulate the international standard for healthy sleep pillow, which can make the sleeping appliance more convenient. From then on, human beings get rid of the chaos caused by the high standard of no supine pillow and also get rid of the disadvantageous situation that our country has been following the trend for a long time in the sleeping appliance industry. It is a great opportunity to drive the healthy sleep industry to overtake on the curve and lead the new trend of the world.

Keywords

Relationship between sleep disorders and acquired weakness of ICU in critically ill patients

Yueting Cui,Aizhi Zhang,Bei Wang

The second Hospital of Shanxi Medical University

Objective: This study aimed to explore the correlation between sleep apnea and acquired weakness of ICU; to identify other risk factors of ICU-AW, and 3) to find better intervention and treatment sites, and to provide new ideas for the pathogenesis, prevention, or treatment of ICU-AW. Methods: A retrospective survey was conducted on 63 critically ill patients who were treated in the Department of Critical Medicine, the Second Hospital of Shanxi Medical University from January 2020 to January 2021. The electronic grip strength meter was used to identify ICU-AW (the cutoff value of ICU-AW was: male < 11kg, female < 7kg). They were divided into two groups according to whether they were diagnosed as ICU-AW (ICU-AW group and non-ICU-AW group). The basic conditions of the patients were recorded. Using SPSS 26.0, t-test and Mann-Whitney test were used for inter-group comparisons. The results were presented by mean ± standard deviation or median (IQR). P < 0.05 was considered statistically significant. Results: The prevalence of ICU-AW was 47.6%. 2. There were significant differences in age, sex, APACHEII score, muscle strength, mechanical ventilation time, sepsis, serum albumin, serum glucose, lactic acid, sedatives, analgesics, neuromuscular blockers, parenteral nutrition, operation after admission, total sleep time, sleep efficiency, deep sleep time and the ratio of deep sleep time to total sleep time between the two groups (p < 0.05). In addition, binary logistics multivariate regression analysis showed that age, serum albumin, time of deep sleep, surgical treatment after admission, and multiple organ dysfunction syndrome were statistically significant (p < 0.05). Conclusion: Acquired weakness is a common complication in critically ill patients in ICU. Age, serum albumin, time of deep sleep, surgical treatment after admission, and multiple organ dysfunction syndrome may be independent risk factors for ICU-AW.

Keywords

The value of orexin–A level in cerebrospinal fluid in the evaluation of clinical sleepiness

ZHAO Meng-ke,Jiyou Tang,Xiao Zhang,Shanshan Lu,Weiwei Huang

The First Affiliated Hospital of Shandong First Medical University

Objectives: To detect the level of orexin-A in cerebrospinal fluid (CSF) of patients with different nervous system diseases, and to analyze the relationship between orexin-A and the severity of daytime sleepiness, and then investigate the changes of the orexin system in different nervous system diseases. Methods: From September 2019 to December 2020, 55 patients with nervous system diseases (such as narcolepsy, acute

cerebral infarction, central nervous system infection, etc.) in the Department of Neurology, the First Affiliated Hospital of Shandong First Medical University, were selected in strict accordance with the inclusion and exclusion criteria. The Epworth Sleepiness Scale (ESS) was used to assess daytime sleepiness. At the same time, the corresponding clinical data, sociodemographic data, health-related variables, social-psychological variables were recorded. CSF samples of all subjects were collected and sub packed and stored in - 80℃ refrigerator. Enzyme-linked immunosorbent assay (ELISA) was used to detect the level of orexin-A. All data were analyzed by SPSS 26.0 software. $P < 0.05$ was statistically significant. Results: 24 females (43.64%) and 31 males (56.36%) with an average age of 42 (20, 61) years were recruited. There was a significant difference in ESS score among different nervous system diseases ($F = 10.062$, $P < 0.001$). There was a difference in the level of orexin-A in different degrees of the ESS group ($P < 0.05$). Orexin-A level was negatively correlated with ESS score ($r = -0.268$, $P = 0.007$). The results of multiple linear regression analysis on the influencing factors of orexin-A level showed that the regression model of orexin-A level had statistical significance ($P = 0.001$), and the most relevant factor with orexin-A level was ESS score ($β = -0.301$, $P = 0.039$). Conclusion: The findings suggest a negative correlation between the level of orexin-A in CSF and the severity of daytime sleepiness.

Keywords

Characteristics of excessive daytime sleepiness in patients with narcolepsy: a case–control study based on multiple sleep latency tests

Baokun Zhang1,2,Shanshan Lu1,Weiwei Huang1,Xiao Zhang1,Jiyou Tang1
1.Qianfoshan Hospital of Shandong Province
2.Qilu Medical College of Shandong University

Objective: Exploring the differences in Narcolepsy type I/II among Excessive daytime sleepiness based on multiple sleep latency test (MSLT) to make precise daytime sleep plan for different types of narcolepsy. Methods: The subjects were collected through the inpatien and outpatient clinics, which include: 11 patients with narcolepsy type I (NT-1); 13 patients with narcolepsy type II (NT-2). Nocturnal polysomnography (n-PSG), as well as the following day's Multiple Sleep Latency Test (MSLT), were conducted for all patients. In these two groups of either n-PSG or each of MSLT, the contents which were compared are the sleep latency, the REM/N2 sleep latencies, the number of SOREMPs, sleep efficiency, and the proportion of sleep stages. Results: There's no difference in the nocturnal sleep between these two groups ($P > 0.05$). The feature of excessive daytime sleepiness based on MSLT in these two types of patients was that the total sleep time and sleep latency correlate negatively, and the sleep latency in naps of forenoon had a shorter time than afternoon's naps but the forenoon has more wake after sleep onset. In addition, the effect of the former

sleep on the latter sleep is obvious, especially reflected in the first/third nap. This effect of sleep's benefit in NT-1 showed an analogous rhythmic waxing-waning pattern. Conclusions: The daytime sleep feature of narcolepsy is heterogeneous between NT-1 and NT-2 both in macrostructure. The NT-1 may represent a rhythmic waxing-waning pattern but the NT-2 have a relatively smooth curve that waxes or wanes. So we recommend that it may be appropriate to take a nap about thirty minutes before work both in the morning and afternoon, especially the patients with NT-1.

Keywords

Depression among nurses: The role of nocturnal and daytime sleep

Fangxiang Mao,Fenglin Cao

School of Nursing and Rehabilitation，Shandong University

Background: Sleep disturbance has negative effects on mental health. However, the association between nocturnal and daytime sleep patterns and depression among nurses remains unknown. Methods: Our study was a prospective nested case-control study. By Multi-stage stratified random sampling, 709 eligible tertiary hospital nurses with first-onset depression were recruited in 2018. Depression was measured by the Patient Health Questionnaire-9 scores (PHQ-9). PHQ-9 score greater than 10 was defined as clinical depression. Nocturnal sleep quality was measured by the Pittsburgh Sleep Quality Index. Sleep disturbance was defined when participants had moderate or severe sleep problems. Regular daytime sleep was defined when participants reported more than one time a week sleep in the daytime. Binary logistic regression was used to investigate the association between different patterns of sleep and depression. Results: Compared to nurses without nocturnal sleep disorders and having daytime sleep, those with nocturnal sleep disorders and not having daytime sleep has a significant risk of developing depression (OR = 10.00, 95%CI: 2.55-39.29), after adjusting age, monthly income, education status and frequency of night shift. Nurses with nocturnal sleep disorders and having daytime sleep (OR = 3.07, 95%CI: 0.72-13.08) as well as those without nocturnal sleep disorders and not having daytime sleep did not have significant risks of developing depression (OR = 0.92, 95%CI: 0.51-1.66), compared to nurses without nocturnal sleep disorders and having daytime sleep. Conclusions: Nocturnal sleep is particularly important for nurses' mental health. While daytime sleep may be an effective way to release the negative effects of nocturnal sleep disturbance.

Keywords

Changes of serum inflammatory factors and oxidative stress indicators in children with OSAHS

Xueyun Xu,Yuqing Wang

Children's Hospital of Soochow University

Objective To investigate the changes of serum inflammatory factors and oxidative stress indicators in children with Obstructive sleep apnoea hypopnea syndrome（OSAHS）, as well as to study their correlation with OSAHS severity.Methods A total of 53 children with OSAHS and a control group of 49 normal subjects were enrolled from December 2016 to November 2019. Full night polysomnography was performed in each patient. C-creative protein (CRP) levels were measured. Serum cytokine levels were detected by ELISA, including TNF-a, IL-6, and IL-10, as well as oxidative stress indicators, including malondialdehyde (MDA), human 5-hydroxosatetraenoic acid (5-HETE), hypoxia inducible factor 1α（HIF-1α）, and Semaphorin 4D (Sema4D).Results The serum levels of CRP, IL-6, IL-10, TNF-a, HIF-1α, Sema4D and 5-HETE in the OSAHS group were significantly higher than those in the PS[y1] group (all P <0.05), while there was no statistically significant difference in MDA between the two groups (t=1.411, P=0.161). CRP was positively correlated with AHI and ODI and negatively correlated with LSaO2 (r = 0.207, 0.292, -0.238, P <0.05). IL-6, IL-10, HIF-1α, and TNF-α levels were positively correlated with AHI, IL-6, IL-10, and TNF-α（r=0.565, 0.528, 0.522, all P <0.05）. IL-6, IL-10, HIF-1α, and TNF-α were positively correlated with ODI, IL-6, and IL-10 (r= 0.380, 0.288, all P<0.05). IL-6 was negatively correlated with LSaO2 (r = -0.345, P <0.001). 5-HETE was positively correlated with AHI and ODI (r = 0.221,0.268, all P <0.05), and there was no correlation with LSaO2 (P = 0.106).Conclusion Our results suggest that CRP, IL-6, IL-10, and TNF-α are inflammatory biomarkers that can be used to evaluate the severity of OSAHS.

Keywords

Comparison of upper airway Sleep–MRI and drug–induced sleep endoscopy in the localization of obstructive sleep apnea

Shuangshuang Tang,Guohui Nie,Jin Tao

Shenzhen Second People's Hospital

Objective To compare the positive rate, advantages and disadvantages of cine MRI and drug-induced sleep endoscopy in the diagnosis of upper airway localization in OSA, and to explore their clinical value. Methods Sleep-MRI and DISE were performed in 43 patients with OSA diagnosed by polysomnography admitted to the Department of Otorhinolaryngology of the Second People's Hospital of Shenzhen from December 2019 to June 2020 to determine the upper airway obstruction in patients with OSA. Results The positive rates of obstruction or stenosis at velum level, oropharynx lateral walls level, tongue base level and epiglottis level in OSA patients were determined by comparing the two methods. The positive rates of DISE

and Sleep-MRI at velum level were the same [all 100% (42 cases)], the positive rate of DISE at oropharynx lateral walls level was higher than Sleep-MRI [95.24% (40 cases) vs. 85.71% (36 cases)], and the positive rate of DISE at tongue base level and epiglottis level was lower than Sleep-MRI [61.90% (26 cases) vs. 69.05% (29 cases), and 50.00% (21 cases) vs. 61.90% (26 cases), respectively]; $P > 0.05$, the difference was not statistically significant. Conclusion At present, there is no significant difference between Sleep-MRI and DISE in locating the plane of obstruction in patients with OSA. Both Sleep-MRI and DISE can be considered as the preoperative examination method for patients with OSA. Both of them can accurately reflect the upper airway collapse of patients. However, we recommend DISE in clinical applicability.

Keywords

The relationships of cytokines with anxiety and depression in patients with chronic insomnia disorder

Lijuan Geng

The First Hospital of Hebei Medical University

Objective: To investigate the relationships of cytokines with anxiety and depression in patients with chronic insomnia disorder. Methods: A total of 199 CID patients admitted to the Second Department of Neurology, the First Hospital of Hebei Medical University from 2018-10 to 2021-01 were selected. All patients were evaluated by the Pittsburgh Sleep Quality Index (PSQI), Hamilton Anxiety Rating Scale (HAMA), and Hamilton Depression Rating Scale (HAMD). The levels of serum cytokines IL-2 and IL-10 were detected by flow cytometry, and correlation analysis and regression analysis were performed. Results: The CID patients with elevated serum IL-2 level had more serious anxiety [18.00 (14.00, 21.75) vs. 14.00 (12.25, 18.00), $P = 0.012$], depression [18.00(14.00, 21.75) vs 14.00 (12.25, 18.00), $P = 0.009$], elevated serum IL-10 had more serious anxiety [19.00(16.50, 23.00) vs 17.00 (11.00, 21.00), $P = 0.003$]. Severe anxiety and depression are also often accompanied by increased levels of IL-2 [1.29(0.48, 2.23) vs 2.24(1.64, 3.30);2.24 (1.53, 3.09) vs 1.18 (0.43, 2.20), $P < 0.05$], IL-10 [2.04(0.94, 3.65)vs1.31(0.73, 2.84);2.10(0.93, 3.76) vs 1.31(0.78, 2.84), $P < 0.05$] and IL-2/IL-10 [1.02(0.69, 1.85) vs 0.688 (0.28, 1.15); 1.00 (0.63, 1.86)vs0.77(0.32, 1.16), $P < 0.05$]. IL-2 was positively correlated with HAMA ($r = 0.420$, $P = 0.000$)and its component mental anxiety ($r = 0.331$, $P = 0.000$), somatization anxiety ($r = 0.410$, $P = 0.000$), HAMD ($r = 0.372$, $P = 0.000$) and its component anxiety/somatization ($r = 0.419$, $P = 0.000$), and retardation ($r = 0.310$, $P = 0.001$). IL-10 was positively correlated with HAMA14 component somatization anxiety ($r = 0.185$, $P = 0.050$), and there was no significant correlation between IL-2/IL-10 and HAMA, HAMD. Multiple linear regression results showed that elevated IL-2 level was a risk factor for anxiety and depression in CID patients ($t = 2.440$, $P = 0.016$; $t = 1.978$, $P = 0.050$). Conclusion: Anxiety and depression are positively related to serum IL-2 and IL-10 in CID patients. Monitoring the level of IL-2 may be an objective and effective examination method for the diagnosis of anxiety and depression in CID patients.

Keywords

The effects of repeated transcranial direct current stimulation on sleep quality and depression symptoms in patients with major depression and insomnia

Qi Zhou,Dongsheng Zhou

Ningbo Kangning Hospital

Importance: Although several strategies using transcranial direct current stimulation (tDCS) have been investigated to treat major depressive disorder (MDD), the efficacy of this treatment for patients with MDD who also have insomnia is unclear. Objective: To observe the effects of tDCS on sleep quality and depressive symptoms in patients with comorbid MDD and insomnia. Methods: We conducted a randomized, double-blinded study involving adults with comorbid major depression and insomnia. We randomly assigned patients to either add tDCS or sham tDCS to their regular treatment. After randomization, we treated a total of 90 patients at the Kangning Hospital, Ningbo, China. We allocated 47 patients to the tDCS group and 43 to the sham tDCS group. The tDCS treatment procedure included 20 sessions of 2-mA stimulation of the dorsolateral prefrontal cortex (DLPFC) for 30 min, which was followed by four weekly treatments. The anode and cathode electrodes were placed on the left and right DLPFC, respectively. We used the Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS), Pittsburgh Sleep Quality Inventory (PSQI), and Polysomnography (PSG) on Day 1 and Day 28. Results: Compared with the sham tDCS group, the active tDCS group showed improved total scores of SAS and SDS (all P < 0.05). PSQI total score and all PSQI sub-divisions, except for sleep duration and sleep efficiency, significantly improved after treatment (all P < 0.05). We also observed that tDCS affected sleep architecture, by increasing total sleep time and improving sleep efficiency through PSG. Conclusions: Our study suggests that the effect of tDCS on sleep quality and depressive symptoms in patients with MDD and insomnia. These results suggested that tDCS stimulation not only improved symptoms of depression and anxiety but also had a positive effect on sleep quality in patients with MDD. For patients with comorbid depression and insomnia, tDCS stimulation could be a good supplement to drugs.

Keywords

Acupuncture treatment relieve insomnia symptoms by modulating hypothalamus functional network: a controlled longitudinal study

Siyi Yu,LeiXiao Zhang,Youping Hu,Jie Yang,Fang Zeng

Chengdu University of Traditional Chinese Medicine

Background: Acupuncture therapy is effective in treating insomnia. However, the brain underlying mechanism of the acupuncture treatment is unclear. We aimed to investigate the acupuncture effect on the

hypothalamus functional network in patients with chronic insomnia disorder (CID). Methods: Forty-two patients with CID and 23 matched good sleep control (GSC) were enrolled in this study. The CID patients were randomized into real acupuncture (RA) and sham acupuncture (SA) treatment groups for 4 weeks. The Pittsburgh Sleep Quality Index (PSQI), self anxiety scale, self depression scale, and resting-state functional connectivity of the hypothalamus (HYP-FC) were measured at the beginning and end of the experiment. Results: We found that the PSQI score was significantly decreased in the RA group, but not in the SA group. The anxiety and depression scales were not significantly changed in both groups. Compared to GSC subjects, the patients with CID shown increased HYP-FC in the left lateral orbital frontal cortex (LOFC) and medial OFC, and decreased HYP-FC in right posterior insular. After RA treatment, the HYP-FC alterations were found in the left superior frontal gyrus (SFG), LOFC, and right fusiform area. The RA and SA treatment showed different HYP-FC alterations in the left dorsolateral prefrontal cortex, dorsal anterior cingulate cortex, and SFG. Importantly, the increased HYP-FC in the left LOFC would be reduced after 4 weeks of treatment in the RA group. In addition, the altered HYP-FC in the left LOFC was significant associated with the PSQI change in the RA group (r = -0.692, p = 0.006). Conclusion: Our findings indicate that the acupuncture treatment modulates the functional connectivity of the hypothalamus and LOFC to treat CID. Keywords

Characteristics of sleep–wake cycle of golden hamsters with circadian rhythm disorder: rhythm disruption and fragmentation

Jinjin Li,Yunfei Chen,Jing Wang,Wenling Xu,Yixing Zheng,Xingyu Chen,Cong Wang
Yueyang Clinical Hospital of Integrated Chinese and Western Medicine

Objective: The sleep/wake are physiological behaviors with obvious circadian rhythm. Circadian rhythm and sleep homeostasis are the main factors affecting the maintenance and transition of sleep-wake state. Light has been proved to have a certain regulatory effect on sleep and circadian rhythm. It has been reported that the disruptive phase-shift (DPS) model can cause circadian rhythm disorders in animals and have a certain impact on cognitive behavior and immune system. However, how the sleep-wake cycles are altered by DPS has not yet been revealed. Methods: We evaluated the sleep-wake structure alterations and wakefulness level changes in the golden hamsters with disturbed circadian rhythm modeled by DPS. Results: The hamsters after modeling were divided into the arrhythmia group (ARR group) and the entrainment group (ENTR group) by cosine analysis. By comparing the 24-hour electroencephalogram (EEG) and electromyography (EMG), thesleep structure were analzyed, and the grip strength test (maximum grip force) was used to evaluate the vigilance state during awakening. According to Pearson correlation analysis, NREM and REM in ARR group showed a negative correlation in the later stage. Conclusion: The current study suggested that the sleep duration and the number of sleep-wake transitions in the ARR group were significantly disturbed after DPS modeling, and the function of the awakeningwas decreased. Pearson's correlation coefficient found that,

compared with ENTR group, persistent abnormal sleep status (NREM, REM) (negatively correlated with baseline) in ARR group may be related with the abnormal activity. This animal model can be used to model circadian rhythm disorders, sleep fragmentation and daytime fatigue in patients with insomnia, inducing the psychiatric and neurodegenerative diseases as consequences.

Keywords

Improvements of e–aid cognitive behavioral therapy on sleep quality and mood of nurses on site during COVID–19 epidemic period

Zhou Kaili1,Xue Rong2

1.Airport Hospital of Tianjin Medical University General Hospital

2.Tianjin Medical University General Hospital

Objective: To investigate the improvements of e-aid cognitive behavioral therapy on sleep quality, anxiety, and depression of nurses on site during the COVID-19 epidemic. Methods: A total of 51 nurses on site with insomnia, anxiety and depression in the Airport Hospital of Tianjin Medical University General Hospital during the COVID-19 prevention and control period from February 2020 to August 2020 were recruited. The subjects were divided into the e-aid cognitive behavioral therapy (eCBT-I) group (n = 24) and the control group (n = 27) by a completely randomized grouping method. The eCBT-I group was given the standard eCBT-I for 6 weeks. The Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI) were used to evaluate the sleep quality of the subjects. The Generalized Anxiety Scale and the Patient Health Questionnaire-9 (PHQ-9) were used to assess the subjects' anxiety and depression, respectively. The changes in sleep quality, anxiety, and depression before and after treatment were compared between the two groups. Results: The scores of PSQI and ISI in the eCBT-I group were significantly lower after treatment than before treatment ($p < 0.05$). Compared with the control group, the scores of PSQI and ISI in the eCBT-I group were lower after treatment ($p < 0.05$). The scores of the generalized Anxiety Scale and PHQ-9 scale in the eCBT-I group were all lower after treatment than before treatment ($p < 0.05$). Compared with the control group, subjects in the eCBT-I group had lower scores on the generalized Anxiety Scale and PHQ-9 scale after treatment ($p < 0.05$). Conclusion: eCBT-I can improve the sleep quality of frontline nurses during COVID-19 prevention and control, and relieve anxiety and depression. Keywords: e-aid cognitive behavioral therapy; COVID-19 epidemic period; nurses on site; sleep quality; anxiety and depression

Malignant arrhythmias associated with obstructive sleep apnea

Jianqing Wang1,Zhao Dan1,Wang Yan1,Liu Suyan1,Chen Baoyuan1,Zhu Lei2

1.Tianjin Medical University General Hospital

2.Tianjin Medical University Cancer Hospital

Growing studies have shown that obstructive sleep apnea (OSA) is an independent risk factor for the morbidity and death of a variety of cardiovascular diseases. OSA can also seriously affect the electrical activity of the heart to produce arrhythmias, which can further cause hemodynamic disturbance in a short time, and finally result in syncope and even sudden death. However, not enough attention has been paid to OSA and malignant arrhythmias in the clinic. This article systematically reviews the relationship between OSA and malignant arrhythmias, possible inducing mechanism, ECG predictors, and the therapeutic effect of non-invasive positive pressure ventilation.

Keywords

The Characteristics of Sleep Apnea in Hospitalized Patients with Coronavirus Disease

Ke Hu1,Miaochan Lao2,3,4,Huaheng Mo1,Dong Zhao1,Zhaofu Zeng1,Weihua Hu1,Peichuan Hong2,3,4,Qiong Ou2,3,4

1.Renmin Hospital of Wuhan University (Hubei General Hospital)

2.Guangdong Provincial People's Hospital

3.Guangdong Academy of Medical Sciences

4.Guangdong Provincial Geriatrics Institute

Purpose: This cross-sectional study investigated the characteristics of sleep apnea in hospitalized patients with coronavirus disease 2019 (COVID-19). Methods: Hospitalized patients with COVID-19 were recruited at the Renmin Hospital of Wuhan University. Obstructive sleep apnea was diagnosed based on assessments with a one-channel type-4 sleep monitor. Clinical features and prognostic data were recorded. Results: Ninety-one patients with COVID-19 (46.2% male, mean age 55.0 $\pm$ 14.3 years) were recruited, and categorized as mild (4.4%), common (63.7%), severe (28.6%), and critical (3.3%). Patients with mild disease were significantly younger than those with other clinical subtypes (P = 0.001). The prevalence of sleep apnea (oxygen desaturation index ≥ 5) was 25.3%; 8.8% of patients were of the moderate to severe type (oxygen desaturation index ≥ 15). Nadir oxygen saturation was significantly lower and daytime sleepiness was more prominent among patients with sleep apnea (P = 0.036). There were no significant differences in gender, BMI, neck circumference, or waist circumference between patients with and without sleep apnea. All four patients with mild coronavirus disease were diagnosed with sleep apnea, and the prevalence of sleep apnea

was not significantly different from the other clinical coronavirus disease subtypes. The time from symptom onset to admission was significantly shorter in patients with sleep apnea (P = 0.038), while there was no significant difference in the length of hospital stay (P = 0.112). Conclusion: The prevalence of obstructive sleep apnea is relatively high in patients with COVID-19. Patients with sleep apnea may have a lower tolerance to COVID-19.
Keywords

Association between obstructive sleep apnea and nonalcoholic fatty liver disease in pediatric patients: a meta–analysis

Lida Chen1,Qi-Chang Lin2
1.Zhangzhou Affiliated Hospital of Fujian Medical University
2.The First Affiliated Hospital of Fujian Medical University

Background: Multiple studies have reported a relationship between obstructive sleep apnea (OSA) and non-alcoholic fatty liver disease (NAFLD) in a pediatric population. However, this issue remains controversial. Objectives: The purpose of the present study was to investigate the association between OSA and NAFLD in the pediatric population.Methods: We systematically searched PubMed, Web of Science, and Embase for eligible studies. The data involving markers of NAFLD including alanine aminotransferase (ALT), aspartate aminotransferase (AST), hepatic inflammation, and hepatic fibrosis of both the OSA group and control group were extracted. Pooled standardized mean difference (SMD) and weighted mean difference (WMD) were appropriately calculated through a fixed or random-effect model.Results: 9 cross-sectional studies with 1133 children and adolescents in total were included. OSA was significantly associated with ALT, AST, and NAFLD fibrosis stage, but not with NAFLD inflammation grade. Subgroup analysis indicated that both mild and severe OSA were significantly associated with elevated ALT and AST. Furthermore, in the studies with all main confounding factors (age, gender, and BMI) matched, the OSA group had higher ALT and AST levels than the control group.Conclusions: This meta-analysis suggested that OSA was associated with NAFLD evidenced by elevated liver enzymes and progressive hepatic fibrosis in pediatric population. Screening and monitoring of NAFLD in pediatric patients with obesity-related OSA are necessary in clinical work.
 Keywords

Differences of Psychological and Sleep Status in College Students at Different Altitudes

Shixu Du1,Shuai Liu1,2,Jia Yu3,Huaihong A2,Xin Shao4,5,Hui Wu2,Shuheng Xiao1,Bin Zhang1

1.Southern Medical University Nanfang Hospital

2.The Third People's Hospital of Qinghai Province

3.The Third People's Hospital of Panzhihua

4.School of Physics Science and Information Technology

5.School of Physics and Electronic Information Engineering

Objective: To investigate the differences in the psychological and sleep status among college students at different altitudes, and to explore the influence of different altitudes on college students' psychological and sleep status. Methods: We surveyed 3287 college students in Chengdu Campus (altitude 500m) and Xining Campus (altitude 2260m) using general information questionnaire，Self-rating Anxiety Scale (SAS), Beck Depression Inventory (BDI), Chinese Big Five Personality Inventory-15 (CBF-PI-15), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Morning and Evening Questionnaire-5 (MEQ-5). Results: In general, a considerable proportion of college students had anxiety (28.2%), depression (55.4%), insomnia (42.8%), and daytime sleepiness symptoms (25.1%). Compared with college students in Xining Campus, the incidence of depression and insomnia symptoms were higher among college students in Chengdu Campus (depression: OR=1.262, 95%CI 1.061-1.502; insomnia: OR=1.270, 95%CI 1.072-1.505, all p<0.01). The incidence of daytime sleepiness symptom was lower (OR=0.601, 95%CI 0.488-0.741, p<0.01), and no difference was found in the incidence of anxiety symptom and circadian rhythm types (anxiety: OR=0.954, 95%CI 0.793-1.148, p=0.620; eveningness: OR=1.091, 95%CI 0.830-1.435, p=0.531; morningness: OR=1.191, 95%CI 0.964-1.472, p=0.105). Conclusions: Compared with high altitude areas (Xining), low altitude areas (Chengdu) may reduce the risk of daytime sleepiness symptoms and increase the risk of depression and insomnia symptoms. Keywords College students; Altitude; Psychological status; Sleep status

The correlation study of hypnotic drugs on the cognitive function of patients with chronic insomnia.

Shasha Li1,Jiyou Tang2,Xiao Zhang2,Shanshan Lu2,Weiwei Huang2

1.Shandong First Medical University

2.Shandong Provincial Qianfoshan Hospital

Objective: To explore the effect of hypnotic drugs on the cognitive function among patients with chronic insomnia.Methods: All the subjects were assessed for sleep quality, anxiety, and depression, and cognitive

function. Based on their previous hypnotic medication history, they were divided into the non-medication group (n=25), benzodiazepines (BZDs) group (n=45)，and non-benzodiazepines (N-BZDs) group (n=26). Results: Compared with the non-medication group, the BZDs group and the N-BZDs group presented increased night's sleep time, and decreased anxiety and depression scores (P<0.05); Compared with the N-BZDs group, the scores of immediate memory and delayed memory were decreased in the non-medication group and the BZDs group, and the difference was statistically significant (P＜ 0.05); Binary logistic regression analysis indicated that compared with BZDS group, patients in N-BZDs group had a lower risk of immediate memory and delayed memory impairment (P < 0.01).Conclusion: The sleep time of patients with chronic insomnia was reduced. Memory function was negatively correlated with the duration of insomnia and the severity of depression. Non-benzodiazepines have been shown to increase sleep duration and may improve memory function in people with insomnia.

Keywords

Status Quo and influencing Factors of Metamemory in Snoring Patients

chenhuaying1,Yamin Li1,Weihong Wang2,Huilin Zhang1,Na Nie1,Qingxiang Liao3,Lezhi Li4
1.the Second Xiangya Hospital，Central South University
2.Nursing Teaching and Research Section，Medical college，Hunan Normal University
3.Neurology department，the First Hospital of Changsha City，Hunan Province
4.Xiangya Nursing School，Central South University

Objective To explore the status of metamemory and its influencing factors among snoring patients. Methods Outpatient and inpatient snorers from department of respiratory and critical care medicine in 3 provincial and municipal hospitals in Changsha, Hunan wererecruited. They were investigated by the general information questionnaire, and the brief version of the questionnaire of metamemory in adulthood (MIA). Results The scores of memory strategy, memory task, memory capacity, memory change, memory anxiety, memory achievement and memory locus were 15.20 ± 3.82, 10.08 ± 2.29, 13.99 ± 3.07, 10.10 ± 3.18, 15.10 ± 3.39, 17.30 ± 3.43 and 15.50 ± 2.61 respectively. The results of logistic regression analysis showed that age, gender, marriage, body mass index, comorbidities, smoking history were the influencing factors of metamemory of snoring patients（P<0.05）. Conclusions The severity of metamemory disorder is different among snoring patients is, which is dominantly severe impairment. Health care workers should pay more attention to the population of elderly, male, single divorced, obese, combined with lung disease and smoking history, and take active measures to help them improve their metamemory levels.

Keywords

Prevalence and Risk Factors Associated with Insomnia Symptoms among the General Population in China during the Remission Period of the Coronavirus Disease 2019 Epidemic

Junlong Guo1,Lulu Yang1,Yan Xu1,Chenxi Zhang1,Xian Luo1,Shuai Liu1,4,Lihua Yao2,Xiaofen Zong2,Hanping Bai1,Jihui Zhang3,Zhongchun Liu2,Bin Zhang1

1.Nanfang Hospital，Southern Medical University

2.Renmin Hospital of Wuhan University

3.Guangdong Mental Health Center

4.Third People's Hospital of Qinghai Province

Introduction The prevalence rate and related factors of insomnia remained unknown during the remission period of the COVID-19 epidemic. Therefore, we conducted this survey to investigate the prevalence rate and related factors of insomnia symptoms in the general population of China during the COVID-19 remission period. Methods An online survey was conducted among Chinese citizens through the JD Health APP. The self-designed questionnaire was used to collect demographic data and other informationrelated to the COVID-19 outbreak. Insomnia Severity Index, Patient Health Questionnaire-9, Somatic Symptom Scale-8 and Impact of Events Scale-Revised were used to measure psychological symptoms. A binary logistic regression was used to examine the associations of sociodemographic and psychological factors with insomnia symptoms. Results In total, 14 894 eligible participants were included, among whom 4 601 (30.9%) participants were found to have insomnia symptoms. The regression model revealed that a higher risk of insomnia symptoms was associated with being over the age of 40 years, having a history of a psychiatric disorder, smoking, having infected friends or colleagues, having depressive or somatic symptoms, experiencing psychological distress and feeling estranged from family members. Whereas a lower risk of insomnia symptoms was associated with being female, having closer family relationships, not feeling alienated from others and being satisfied with the available information. Conclusions In our study, 30.9% of the participants in the general population reported insomnia symptoms during the remission period of the COVID-19 epidemic. When providing precise interventions for insomnia, extra attention should be paid to individuals who are male, elderly, smokers and those with a psychiatric disorder history, infected friends or colleagues, psychological symptoms and poor social support.

Keywords

Orexin dual receptor antagonist almorexant ameliorates learning and memory impairment caused by sleep fragmentation in APP/PS1 mice

Yaran Li,Na Shao,Jiyou Tang,,Yanyan Chang,Shanshan Lu,Xiao Zhang,Weiwei Huang

Qianfoshan Hospital of Shandong Province

Aims: Sleep disturbance is one of the main clinical manifestations of Alzheimer's disease(AD). Previous studies have found that sleep fragmentation not only accelerated the damage of learning-memory, aggravated impairment of glymphatic system and accelerated amyloid-beta (Aβ) protein deposition in the brain, but also enhanced the activity of the orexin system in the hypothalamus. Here we further observed whether almorexant, a dual orexin receptor antagonist, could ameliorate the cognitive decline in APP/ PS1 mice and investigated the possible mechanisms .Methods: The present research was performed on APP/PS1 mice at 6 months of age. They were randomly divided into three groups: APP/ PS1-vehicle (CON), APP/ PS1-sleep disruption and vehicle (SD+vehicle), APP/PS1-sleep disruption and almorexant, (SD+Almorexant). Mice were subjected to chronic sleep disruption (SD) using a modified mouse cage with a motorized rotating bar moving at 2 revolutions/min, from 11 am to 7 am the next day for 8 weeks. 30 mg/kg of almorexant or vehicle was administered by intraperitoneal injection to mice daily at 7 am (the beginning of the sleep disruption) for 8 weeks. After SD, mice received behavioral, neuropathological, and neurochemical analyses.Results: Here, we reported that the chronic sleep disruption exacerbated cognitive deficits of 6-month old APP/PS1 mice, with increased Aβ accumulation, astrocyte activation and loss of perivascular AQP4 polarization in hippocampus and cortex. Whereas almorexant treatment effectively alleviated the cognitive impairments after SD, resulting in less Aβ deposition, astrocyte activation and impairment of AQP4 polarization ,comparing with the SD group.Conclusion: These results indicate that almorexant treatment ameliorates cognitive impairments caused by chronic SD. The neuroprotective effects of almorexin against AD are involved in reduction of astrocyte activation and Aβ plaques, improvement in perivascular AQP4 polarization by improving sleep, suggesting that dual orexin receptor antagonist could be beneficial for sleep improvement and retardation of pathological progression of AD. Keywords

Advances in research on microstates

Wang Ru1,2,Tang Jiyou1,Lu Shanshan1,Zhang Xiao1,Huang Weiwei1

1.Shandong Provincial Qianfoshan hospital

2.Cheeloo College of Medicine，Shandong University

The electroencephalography (EEG) topographic map maintains a relatively stable state within 60 ~ 120ms, and then quickly changes to another state and remains stable. This quasi-stable state is called EEG microstate,

which reflects the transient stable brain topological structure with temporal and spatial characteristics. The microstates simultaneously consider the signals of the entire cerebral cortex region and can be divided into four classical modes A, B, C, and D. These four EEG microstates can each explain a large-scale network of brain resting states. Microstate B reflects the visual resting state network; Microstate C reflects the negative network of tasks and reduction of the activity during the cognitive task execution. Microstate D is associated with dorsal attention network and sleep. The damage of these networks is associated with several neuropsychiatric disorders and to some extent reflects the neurophysiological changes of the disease. In schizophrenia, an increase in microstate C has been shown to be possibly associated with positive symptoms (hallucinations). A decrease in microstates B and D and an increase in microstates C may indicate a disruption of normal network activity that underlies the onset of disease. The microstate C of frontotemporal dementia patients was significantly shorter than that of healthy controls and Alzheimer's disease patients, and the major microstate transition pattern of frontotemporal dementia (D→ C) was also reversed compared with control patients (C→ D). Earlier studies have shown that microstate duration might be inversely correlated with the degree of cognitive impairment in Alzheimer's disease. In patients with narcolepsy, there are unstable EEG microstates and higher terrain variability in early NREM sleep, which may indicate general network instability and lead to macrostructural symptoms of nocturnal sleep fragmentation. There have been no studies on insomnia. EEG microstates is a promising neurophysiological tool for understanding and evaluating the dynamics of brain networks in healthy and diseased populations on a millisecond time scale.

Keywords

Relationships between a range of inflammatory biomarkers and subjective sleep quality in chronic insomnia patients: A clinical study

Ping Zhang,Guihai Chen
Chaohu Hospital of Anhui Medical University

Objective: Insomnia is associated with inflammation. However, previous studies have only explored a few inflammatory factors in insomnia patients, while the associations with other kinds of inflammatory factors remain unclear. The aim of this study was to examine whether associations exist between chronic insomnia disorder (CID) and overlooked inflammatory factors (serum amyloid-A [SAA], tumor necrosis factor [TNF]-α, granulocyte-macrophage colony-stimulating factor [GM-CSF], and regulated on activation and normal T cell expressed and presumably secreted [RANTES]).Methods: A total of 65 CID patients (mean age, 41.37±12.12 years, 58.5% female) and 39 sex- and age-matched good sleeper (GS) controls (mean age, 42.15±14.28 years, 51.3% female) participated in this study. They completed a baseline survey to collect data on demographics, depression, anxiety, and sleep, followed by blood sample.Results: The CID group had higher serum levels of SAA, TNF-α, and GM-CSF and a lower level of RANTES than GS group. In the Spearman's correlation analysis, SAA and GM-CSF positively correlated with the PSQI and AIS scores.

After controlling for sex, HAMD-17 score, and HAMA-14 score, the partial correlation analysis showed that GM-CSF was positively correlated with PSQI score ($P < 0.05$). Further stepwise linear regression analyses showed that GM-CSF was positively associated with the PSQI and AIS scores, while RANTES was negatively associated with them ($P < 0.05$), and SAA was positively associated with just the AIS score. Conclusions: The serum levels of inflammatory mediators (SAA, TNF-α, and GM-CSF) were significantly elevated and the level of RANTES was significantly decreased in CID patients and, to some extent, the changes are related to the severity of insomnia. These findings may help us to improve interventions to prevent the biological consequences of CID by inhibiting inflammation, thereby promoting health.
Keywords

Analysis of risk factors and consequences for concurrent obstructive sleep apnea in chronic obstructive pulmonary disease patients

Xiong Mengqing,Ke Hu

Renmin Hospital of Wuhan University

Objective To compare clinical characteristics between patients with chronic obstructive pulmonary disease (COPD) and COPD - obstructive sleep apnea (OSA)concomitant patients, and to determine the risk factors for OSA in patients with COPD.Methods A total of 431 patients with COPD were divided into COPD-OSA group with AHI>15 events/h or COPD group with AHI $\leq$ 15 events/h according to the results of polysomnography. Their clinical characteristics were summarized. Risk factors for OSA overlap in COPD patients were identified by univariate and multivariate logistic regression analyses.Results There were no significant differences of gender composition, dyspnea scale (mMRC) score, the numbers of acute exacerbations and hospitalizations in the last year, prevalence of coronary heart disease, cor pulmonale or diabetes mellitus between the two groups (all P>0.05). Age, BMI, neck circumference, smoking index, COPD assessment test (CAT) score, the values of FEV1 or FEV1%, FEV1/FVC ratios, and the prevalence of hypertension in COPD-OSA group were significantly higher than those in COPD group, while the duration of COPD and the proportion of severe COPD were lower than those of the COPD group(P<0.05). The scores of Charlson Comorbidity Index, Epworth Sleepiness Scale (ESS) and Sleep Apnea Clinical Score (SACS) in the COPD-OSA group were significantly higher than those in the COPD group, with all P values<0.05. Risk factors for OSA coinciding in patients with COPD included BMI, neck circumference, ESS, SACS and CAT (P<0.05). Furthermore, BMI, ESS and CAT were independent risk factors for OSA in COPD patients (P<0.05). Compared with mild or moderate COPD cases, patients with severe COPD (FEV1%<50%) had a lower risk of having OSA (β =-0.459,OR=0.632,95% CI 0.401-0.997,P=0.048).Conclusions Compared to COPD patients, COPD-OSA patients had a worse quality of life, more daytime sleepiness and higher prevalence of hypertension. BMI, ESS and CAT were independent risk factors for OSA in patients with COPD. The risk of having OSA in severe COPD patients was lower than cases with mild or moderate COPD.
Keywords

Orexin A improves cognitive function impairment in mice exposed to chronic intermittent hypoxia

Jing Zhu,Hu Ke

Renmin Hospital Of Wuhan University

Background: The orexin neuron in lateral hypothalamus(LH) was involved in the regulation of sleep-wake. However, the effect of orexin A (OXA) on cognitive function impairment resulting from diverse diseases remains controversial. In this study, we clarified the effect of OXA on cognitive function impairment in mice exposed to chronic intermittent hypoxia(CIH).Methods: Thirty-two male C57BL/6 mice were randomly divided into the following four groups: normoxia control (NC)+normal saline (NS), NC+OXA, CIH+NS and CIH+OXA group. The CIH mice models were established for 4 weeks. OXA was injected into the right lateral ventricles of mice by a micro-injection system. Water maze test was used to assess spatial memory abilities of mice . The expression of OXA and c-Fos in LH were analyzed by immunofluorescence staining. The change of apoptosis and oxidative stress in hippocampus were measured using TUNEL, western blot and biochemical analysis, respectively.Results: Behavioral tests revealed that the escape latency and time of arriving at platform in CIH+NS group significantly increased comparing with NC+NS group(P<0.05), but the time in CIH+OXA group was markedly less than that of CIH+NS group(P<0.05). Similarly, the CIH+NS group was worse than NC+NS group in terms of the number of platform crossing and time in the target quadrant, which could be improved after OXA treatment (P<0.05). CIH+NS group remarkably increased the expression of c-Fos+/OXA+ in LH compared with NC+NS group (P<0.05). We found that the relative indicators of apoptosis and oxidative stress in the hippocampus of the CIH+NS group significantly changed comparing with the NC+NS group, but the change of apoptosis and oxidative stress could be attenuated by micro-injection of OXA (P<0.05).Conclusion: OXA may improve cognitive function impairment in mice exposed to CIH by inhibiting hippocampal apoptosis and oxidative stress.
Keywords

Effect of lung function on the apnea–hypopnea index in patients with overlap syndrome: a multicenter cross–sectional study

Zhu Jing,Ke Hu

Renmin Hospital of Wuhan University

Objective Patients with chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are referred to as having overlap syndrome (OVS). However, the relationship of lung function with the apnea-hypopnea index (AHI) in patients with OVS has not been evaluated. This multicenter study aimed to evaluate the relationship. Methods COPD patients diagnosed by spirometry were recruited from four

Chinese tertiary hospitals. Those patients were requested to attend an overnight polysomnography (PSG). The relationships between parameters of lung function and sleep respiration in patients with OVS were assessed using multiple regression analyses. Results A total of 520 OVS patients and 246 patients with COPD only finally met inclusion criteria for study. After adjustment for age, sex, bodymass index, neck circumference, economic status, smoking status, alcohol consumption, and hypertension, the forced expiratory volume in the first second (FEV1) had a positive correlation with the AHI in patients with OVS (β, 0.17; 95% CI, 0.06–0.28; P < 0.01). However, when the severity of lung function of patients with OVS was stratified, the correlation of the FEV1 of each grade with the AHI was absent (P > 0.05). Additionally, The FEV1 was positively correlated with the nadir oxygen saturation (SaO2) (β, 0.18; 95%CI, 0.08–0.27; P < 0.01) and was negatively correlated with the percentage of time spent with an SaO2 below 90% (TS90%) (β, − 0.41; 95% CI, − 0.61–0.21; P < 0.01) in patients with OVS using multiple regression analyses. Conclusion Lung function was associated with the AHI in patients with OVS. The lower FEV1 may play some protective role in the severity of AHI in OVS patients.

Keywords

Effect of Body Mass Index on Lung Function in Chinese Patients with Chronic Obstructive Pulmonary Disease: A Multicenter Cross–Sectional Study This

Zhu Jing,Ke Hu

Renmin Hospital of Wuhan University

Objective The aim of this study was to explain "obesity paradox" in chronic obstructive pulmonary disease (COPD) by evaluating the effect of body mass index (BMI) on lung function in Chinese patients with COPD. Methods A total of 1644 patients diagnosed with COPD were recruited from four Chinese tertiary hospitals and were divided into four groups including underweight, normal weight, overweight and obese according to BMI classification standard. The medical data of these patients were collected and used for multiple linear regression analyses. Results After adjustment for age, sex, educational level, economic status, smoking status, alcohol consumption, duration of COPD history, events of acute exacerbation in previous year, hypertension, diabetes mellitus, cardiovascular disease, cerebrovascular disease and osteoporosis, BMI had a curvilinear correlation with the forced expiratory volume in the first second (FEV1) in patients with Global Initiative for Obstructive Lung Disease (GOLD) 1–2 grade (first-order coefficient β, 0.09; 95% CI, 0.03–0.16; second-order coefficient β, −0.002; 95% CI, −0.003–- 0.001; P<0.01). However, BMI had a positive correlation with FEV1 in patients with GOLD 3–4 grade (β, 0.01; 95% CI, 0.008–0.017; P<0.01) when BMI was used as a quantitative variable. When BMI was used as a qualitative variable, only FEV1 in overweight group with GOLD 1–2 grade was significantly higher than that in normal weight group

(P<0.01). Interestingly, both overweight and obese groups had higher FEV1 in GOLD 3–4 grade compared with normal weight group (β, 0.06; 95% CI, 0.02–0.11; β, 0.11; 95% CI, 0.04–0.18; P<0.01). The effect of BMI on predicted percentage of FEV1 (FEV1%) was similar to that of FEV1 in different GOLD grades. Conclusion Obesity had a protective effect on lung function in COPD patients with GOLD 3–4 grade rather than GOLD 1–2 grade.

Keywords

Chronic intermittent hypoxia vs chronic continuous hypoxia: Effects on vascular endothelial function and myocardial contractility

Jing Zhu,Hu Ke

Renmin Hospital Of Wuhan University

Background and aim: Both chronic intermittent hypoxia (CIH) and chronic continuous hypoxia (CCH) are risk factors for cardiovascular disease, which are associated with cardiac systolic function, dysfunction of endothelia and coagulation-fibrinolysis system in the vasculature. However, the different effects of these two hypoxic models are not fully understood. In our study, we systemically compared the effects of CIH and CCH on cardiac function and related factor levels in serum using rat model. Methods: Forty-five male Sprague-Dawley rats were randomly divided into the normoxia control (NC), CIH and CCH groups. The rat CIH and CCH models were established, then the blood and tissue samples were collected to analyze the function of endothelium and the coagulation-fibrinolysis system. Also, the ultrasound cardiogram was performed to directly assess myocardial contractility. Results: Both CIH and CCH significantly decreased the NO, eNOS, P-eNOS and AT-III levels in the rat serum but significantly increased the levels of ET-1, vWF, COX-2, NF-κB, FIB, FVIII and PAI-1 in the rat serum (P < 0.05). The expression of ET-1, VWF and ICAM-1 in CIH group were higher than CCH group (P < 0.05), however, the expression of CD62p was increased in CCH group but not in CIH group. The expression of t-PA in CIH group were lower than CCH group (P < 0.05), but there was no significant difference between CCH group and NC group (P > 0.05). Using transmission electron microscope, we found that the mitochondrial ultrastructure of thoracic aorta endothelial cells in CIH and CCH group were damaged. Moreover, the myocardial contractility in CIH and CCH group were significantly decreased compared with NC group. Conclusion: Our results suggested that CIH and CCH could cause endothelial dysfunction, dysfunction of the coagulation-fibrinolysis system and decreasing of myocardial contractility. Compared with CCH, CIH has greater effect on vasoconstriction and adhesion of vascular endothelial cells, and stronger procoagulant effect.

Keywords

Effect of immunodeficiency on susceptibility of pneumonia with cerebral ischemia–reperfusion

Dong Zhao, Ke Hu

Renmin Hospital of Wuhan University

Objective: To investigate the effects of immunodeficiency on susceptibility of pneumonia in mice with cerebral ischemia-reperfusion. Methods: C57BL/6J male mice weighing 20-25g were purchased for the study. The C57/BL6J mice were divided into control group, pneumonia model group (SP group), cerebral ischemia-reperfusion group (CIR group), pneumonia group after cerebral ischemia-reperfusion (SAP group). The mouse model of cerebral ischemia-reperfusion (CIR) was established by injecting pathogenic bacteria into the trachea of the model animals. At 24h after the operation, the peripheral blood and bronchoalveolar lavage (BAL) of each group were collected to detect the tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), Interleukin-10(IL-10) by ELISA; BAL, peripheral blood and lung homogenate were carried out for bacterial culture by blood plate; The volume of cerebral infarction in CIR group and SAP group was calculated by TTC staining after 72h. And statistical analysis of the above indicators was conducted by SPSS 22.0 software. Results: The levels of TNF- α [(87.20±4.37) ng/L] and IFN- γ [(86.71±11.25) ng/L] in SAP group were lower than those in control group [(112.96±9.91) ng/L, (126.42±14.61) ng/L, (t= 5.32, 4.815, P<0.05)], and IL-10 level [(192.36±20.23) pg/mL] was higher than that in control group [(148.85±22.35) pg/mL, (t= -3.227, P<0.05)].Besides，there was no significant difference in the level of inflammatory factors between SAP group and control group, SP group (P > 0.05). A comparative study of bacterial load in peripheral blood [(6.77±16.79) ×104CFU/mL, 0], BAL [(14.07±7.59) ×105CFU/mL, (7.69±14.74)×104CFU/mL] and lung homogenate [(5.03±2.85) ×106CFU/mL, (9.76±9.24)×104CFU/mL], the mount of bacteria in SAP group increased when compared with SP group. The degree of pulmonary inflammatory reaction in SAP group was stronger than that in control group and lighter than that in SP group, which was consistent with the pathological score of lung tissue; The total score of SAP group was 9.00 ± 2.27, higher than that of the control group (0.53 ± 0.30), lower than that of SP group (15.20 ± 2.52), and the difference was statistically significant (all P<0.05). And the apoptosis of spleen cells in SAP group and MCAO group was observed by calculating spleen index and changing spleen histopathology. There was no significant difference in the volume of cerebral infarction between MCAO group and SAP group (t=-0.435, P=0.677). Conclusions: Stroke-induced immunodeficiency is a risk factor for pneumonia after stroke. Keywords

The Screening Value Of ESS, SACS, BQ, And SBQ On Obstructive Sleep Apnea in Patients with Chronic Obstructive Pulmonary Disease

Mengqing Xiong,Ke Hu

Renmin Hospital of Wuhan University

Objective: To compare the performance of Epworth sleepiness scale (ESS), sleep apnea clinical score (SACS), Berlin questionnaire (BQ), and STOP-BANG questionnaire (SBQ) in screening obstructive sleep apnea (OSA) in patients with chronic obstructive pulmonary disease (COPD). Methods: A total of 431 patients were analyzed. All subjects completed lung function test, ESS, SACS, BQ, and SBQ survey and overnight polysomnography (PSG). According to lung function and PSG results, participants were divided into COPD with OSA group (OVS, AHI ≥5) and without OSA group (AHI <5). The value of ESS, SACS, BQ, and SBQ was compared in predicting OSA in patients with COPD by receiver-operating characteristic (ROC) curve statistics. Results: Of the 431 subjects, there were 96 cases in COPD without OSA group, and 335 cases in OVS group, consisting of COPD patients accompanied with mild (n=183), moderate (n=96) and severe OSA (n=56). The performance of ESS was poor in predicting different degrees of severity of OSA in COPD patients, with all the values of area under the curve (AUC) < 0.7. SACS and BQ had moderate predictive value in screening severe OSA with the AUC of 0.750 and 0.735 respectively. The SBQ performed best in predicting various degrees of OSA. For screening mild OSA (AHI ≥5), the ROC statistics recommended the cut-off score of SBQ >2 as the high risk of OSA. The sensitivity, specificity, AUC and the odds ratio (OR) were 92.8%, 40.6%, 0.723 and 2.161 respectively. AUC for SBQ was 0.737 when AHI ≥15. In predicting severe OSA (AHI ≥30), the ROC curve showed cut-off point >4. The sensitivity, specificity, and AUC for SBQ were 66.1%, 82.1%, and 0.824 respectively. The positive and negative likelihood ratio were 3.70 and 0.41 separately and the OR was 2.977.Conclusion: SBQ performed better than ESS, SACS, and BQ in predicting OSA in patients with COPD.

Keywords

Hydrogen–rich water, but not lactulose, protects against vascular injury induced by chronic intermittent hypoxia

Yingni Lin,Yaru Yan,Shiqi Li,Yi Wang

Ruijin Hospital，Shanghai Jiao Tong University，School of Medicine

Purpose: Chronic intermittent hypoxia, which is a hallmark feature of obstructive sleep apnea (OSA), is possibly associated with cardiovascular sequelae. We aimed to check whether hydrogen attenuates endothelial injury induced by chronic intermittent hypoxia (CIH).Methods: Fifty male C57BL/6 mice were randomly divided into 5 groups: control, CIH, CIH+H2 (administrated with hydrogen-rich water), CIH+lactulose (administrated with 30mg/ml lactulose in tap water), CIH+lactulose+antibiotics (administrated with 30mg/ml lactulose +0.2mg/ml metronidazole+0.1mg/ml ampicillin in tap water). Mice were exposed to CIH or air for 8 hrs/d for 28 days. Histological analyses of abdominal aorta were performed, and ROS levels of abdominal aorta and serum MDA and SOD levels were measured. Results: CIH induced the derangement, enlargement and proliferation of smooth muscle cells, and disrupted endothelium of abdominal aorta, which were attenuated by administration of hydrogen-rich water. Moreover, hydrogen-rich water improved the impaired mitochondrial ultrastructure, and suppressed apoptosis of endothelial cells in CIH group. Compared to CIH group, the ROS levels in abdominal aorta, and the serum MDA and SOD levels were reduced in CIH+H2 group. However, lactulose did not improve the vascular injury nor decrease serum MDA and SOD levels in CIH group. IH exposure upregulated protein levels of Txnip, which was partially attenuated by hydrogen treatment.Conclusions: Hydrogen-rich water, but not lactulose, inhibited endothelial cell apoptosis, and protected against vascular injury induced by CIH.
Keywords

Sleep–disordered breathing and Cheyne–Stokes respiration in heart transplantation patients

Zhaofu Zeng, Ke Hu

Renmin Hospital of Wuhan University

Objective: Sleep-disordered breathing (SDB), especially central sleep apnoea (CSA) which usually manifests as Cheyne-Stoke's respiration, is frequent in patients with chronic heart failure and is strongly associated with the severity of the patient's cardiac dysfunction and worse prognosis. End stage heart failure refers to cardiac decompensation, extremely low cardiac function and heart disease that cannot be cured by traditional medical treatment and conventional surgery, which are caused by various reasons. The most effective therapy is heart transplantation. However, there is still controversy whether heart transplantation can eliminate SDB and Cheyne-Stokes respiration. We conducted this study to explore the characteristic

of SDB in patients waiting for heart transplantation and the changes in SDB after the surgery,.Methods: 34 eligible patients who were hospitalized to receive heart transplantation during the time from September 2018 to December 2019 in the Departments of Cardiovascular Medicine and Cardiovascular Surgery, Renmin Hospital of Wuhan University were included to the study. All of them underwentPolysomnography (PSG). Based on corresponding results, they were divided into three groups: non-SDB group, CSA group and obstructive sleep apnoea (OSA) group. Their clinical characteristics, use of drugs and results of PSG before heart transplantation were compared. Besides, the relation between pretransplant left ventricular ejection fraction (LVEF) and parameters of Cheyne-Stokes respiration was analyzed. After heart transplantation, the results of PSG, echocardiography and so forth of patients from non-SDB group and CSA group before and after the surgery were contrasted.Results: 1. Among the 34 patients waiting for heart transplantation, 31 were males and 3 were females, with an average age of 52.1 ± 11.4 years, and an average body mass index of 22.9 ± 5.0 kg/m2. There were 22 cases of dilated cardiomyopathy, 9 of ischemic heart disease, 1 of congenital heart disease, 1 of valvular heart disease and 1 of hyperthyroid heart disease. 2. About 76% of those patients had SDB, primarily CSA with Cheyen-Stokes respiration. Based on the results of PSG, patients were divided into 3 groups: 22 in CSA group, 4 in OSA group, and 8 in non-SDB group. There were no statistically significant differences in LVEF, PaCO2, NT-proBNP, age, gender, and any kind of heart diseases of patients between the CSA group and the non-SDB group, while the Epworth score, the mean body mass index and PaCO2 among the OSA group were obviously higher than patients from non-SDB group. No significant distinction was found in the use of drugs among the three groups while waiting for heart transplantation. In the meantime, in contrast with SDB group, patients from CSA group and OSA group had a higher percentage of SpO2<90% in their sleeping time and lower minimum nocturnal oxygen saturation. Compared with the CSA group, the AHI of OSA group was significantly higher, and SpO2 much lower.3. The average LVEF of 34 patients in this study was 31.1 ± 7.6 %, and 22 had CSA, of which 21 showed typical patterns of Cheyne-Stokes respiration. LVEF negatively correlated with circle length (CL) (r = - 0.493), but it displayed no obvious correlation with other parameters. The linear regression analysis in patients with Cheyne-Stokes respiration revealed a negative correlation between LVEF and CL (F = 6.087, P < 0.05). The regression equation was CL = 112.5 - (1.31 × LVEF).4. 21 patients successfully underwent heart transplantation, of which only 15 conducted PSG about 2 weeks after surgery. Among the patients of CSA group, one still had CSA, one transformed into OSA. However, the group witnessed a significant decrease in AHI, a complete disappearance of Cheyne-Stokes respiration and a huge increase in PaCO2 and LVEF. As for the non-SDB group, they didn'ｔ develop SDB after the transplantation, with no significant changes in PaCO2. But their LVEF increased conspicuously.Conclusion: Patients waiting for heart transplantation are susceptible to SDB, mainly in the form of Cheyne-Stokes respiration with CSA. However, heart transplantation may eliminate the Cheyne-Stokes respiration in patients with chronic heart failure. Keywords

Long non–coding RNA JPX correlates with poor prognosis and tumor progression in non–small–cell lung cancer by interacting with miR–145–5p and CCND2

Jing Meng,Hu Ke

Renmin Hospital Of Wuhan University

Emerging studies have shown that the aberrant expression and function of long non-coding RNAs (lncRNAs) are involved in carcinogenesis and the development of various cancers. The long noncoding RNA JPX (lncRNA JPX) on the X chromosome is an activator of X-inactive-specific transcript (XIST) and a molecular switch for X-chromosome inactivation. However, the mechanism of JPX in non-small-cell lung cancer (NSCLC) development is not well studied. Here, through integrating clinical data and a series of functional experiments, we found that lncRNA JPX expression is significantly upregulated in NSCLC tissues compared with that in paired adjacent normal tissues from two independent datasets. lncRNA JPX expression was also significantly associated with a poor survival rate and malignant phenotypes (tumor stage, tumor volume) of NSCLC. Furthermore, we elucidated that JPX functions as an oncogene in NSCLC-promoting cell proliferation and cell migration by affecting cell-cycle progression. Mechanistically, JPX upregulates cyclin D2 (CCND2) expression via a competing endogenous RNA mechanism by interacting with miR-145-5p, thus provoking the development and progression of NSCLC. These findings reveal the mechanism of X-chromosome lncRNA JPX and its core regulatory circuitry JPX/miR-145-5p/CCND2 in the development and progression of NSCLC, which bring us closer to understand the molecular drivers of NSCLC.
Keywords

Investigation on the Relationship Between the Occurrence and Progression of Lung Cancer and Nocturnal Intermittent Hypoxia, Apnea and Daytime Sleepiness

Wei Liu, Ke Hu

Renmin Hospital of Wuhan University

Objective: This study investigated nocturnal snoring, apnea, intermittent hypoxemia, and daytime sleepiness in patients with lung cancer, in order to explore the possible relationship among lung cancer and nocturnal intermittent hypoxia and apnea, especially the possible relationship between lung cancer and obstructive sleep apnea syndrome (OSAS). Methods: The patients were recruited from the Third Affiliated Hospital of Kunming Medical University between January 2017 and December 2017. 45 cases (lung cancer group) who were diagnosed with primary lung cancer with surgical indications and 45 healthy cases (control

group) had no significant differences in age, sex and other general data. The general situation, snore score, Epworth sleepiness score (ESS), Pittsburgh sleep quality index score(PSQI) and apnea hypopnea index (AHI), oxygen subtraction index (ODI4), minimum pulse volume oxygen saturation (LSpO2), oxygen minus less than 90% of the time (min) [T90% (min)], blood oxygen saturation <90% of the time as a percentage of total sleep time (TS90%) during sleep were collected, To explore the relationship between lung cancer and OSAS in the above examination results, we followed up the participants in one year, and the endpoint events were defined as recurrence, metastasis or death during the follow-up period. Results: 1. ESS score, AHI, LSpO2 (%), T90% (min), TS90(%), ODI and snore score were considered statistically significant between lung cancer group and control group ($P < 0.05$); 2. Patients in the lung cancer group were divided into with OSAS group (group A) and without OSAS group (group B) according to the international standard for the diagnosis of OSAS. Results of our study revealing BMI, age, staging, hypertension, coronary heart disease, snore score, ESS score, LSpO2 (%), T90% (min), TS90(%), and ODI were statistically significant between the two groups, $P < 0.05$; 3. Correlation analysis revealed highly negative correlation between AHI and LSp02%, moderate positive correlation were found between AHI and age. Low positive correlation were found between AHI and ESS score, snoring score, T90% (min), TS90(%), ODI , BMI, all $P<0.05$;4. As for the follow-up of 45 patients with lung cancer in one year after operation, there was no significant difference in mortality, recurrence rate and metastasis rate between the two groups at the end of follow-up period, $P>0.05$；A total of 9 patients in group A had metastasis or recurrence, and 5 patients in group B had metastasis or recurrence. A total of 10 patients in group A had metastasis, recurrence or death, and 5 patients in group B had metastasis, recurrence or death, the difference of two groups was statistically significant, $P<0.05$. Conclusions: Compared with the normal control group, patients with lung cancer were more likely to have symptoms such as nocturnal hypoxemia, apnea, snoring and daytime sleepiness. Patients with lung cancer had a higher proportion of OSAS. The incidence of death, recurrence, metastasis malignant tumor progression events were increased in lung cancer with OSAS after one year follow-up, suggesting that OSAS may be a contributing factor to the occurrence and progression of lung cancer.

Keywords

Clinical study of traditional Chinese medicine fumigation combined with agomelatin in the treatment of senile depression with insomnia

Yinan Li,Xiaole Yang

Shenyang Mental Health Center

Objective: To observe the clinical efficacy of traditional Chinese medicine fumigation therapy combined with agomelatin in the treatment of senile depression (LLD) with insomnia. Methods: 76 elderly patients with depression and insomnia from May 2019 to October 2020 in Shenyang mental health center were selected and randomly divided into conventional treatment group (38 cases) and observation group (38 cases). The

conventional treatment group was given oral treatment of agomelatin, and the observation group was given traditional Chinese medicine fumigation treatment on the basis of agomelatin treatment for a total of 8 weeks. The changes of Hamilton Depression Scale (HAMD) score, Pittsburgh sleep quality index (PSQI) score and the change trend of serum homocysteine (Hcy) were assessed after 8 weeks of treatment. Results: No significant difference in HAMD, PSQI and Hcy was observed between the two groups at baseline ($P < 0.05$); After 8 weeks of treatment, the HAMD and PSQI scores of both two groups were significantly lower than those of same groups before treatment. The scores of HAMD and PSQI in the observation group were better than those in the conventional treatment group ($P < 0.05$), and the decrease of Hcy was more obvious than that of the conventional treatment group ($P < 0.05$). Conclusion: Traditional Chinese medicine fumigation therapy can effectively improve the clinical efficacy and sleep of elderly patients with depression and insomnia, and shows the advantages of safety, less side effects and comfortable experience of patients, which is worthy of clinical promotion.

Keywords senile depression; herbal fumigation therapy; agomelatin

The association between obstructive sleep apnea and lung nodule, carcinoembryonic antigen

Aiming Zeng,Qichang Lin,Lida Chen
The First Affiliated Hospital of Fujian Medical University

Objective: The association between obstructive sleep apnea (OSA) and cancer risk is gaining more and more attention. Data on the association between OSA and lung cancer risk are limited. This study was to investigate whether a link existed between low-dose computed tomography (LDCT) scanning of the chest findings, carcinoembryonic antigen (CEA) and OSA in suspected OSA patients. Methods: The cross-sectional study included patients aged >18 years who underwent continuous nocturnal polysomnography at our sleep center between February 2019 and November 2020. All subjects underwent chest LDCT and CEA assessement. OSA group was defined as an apnea-hypopnea index (AHI) of ≥15/h，whereas participants withan AHI ＜ 15/h was classified into control group.Results: A total of 277 patients were enrolled in the study. 176 patients were categorized into the OSA group, and 101 patients were categorized into the control group. There is no relationship between any OSA-related parameter and presence of lung nodule or presence of ≥6mm lung nodule in the binary logistic regression analysis. OSA group presented a significant higher value of CEA than control group. Stepwise multiple linear regression analysis showed that LaSO2 (β =-0.256, p＜ 0.001), smoking status (β =0.156, p=0.007) and age (β =0.153, p=0.008) were independent predictors of elevated CEA.Conclusion: In a group of suspected OSA patients, we confirmed an independent correlation between nocturnal hypoxia and elevated CEA levels. OSA was not related with presence of pulmonary nodule or≥6 mm pulmonary nodule in LDCT.

Keywords Obstructive sleep apnea (OSA); lung nodules; carcinoembryonic antigen; lung cancer

Stigma in Patients with Chronic Insomnia disorder: A Clinical Study

Shuo He,Xuejia Ke,Yan Wu,Huiqin Sun,Guihai Chen

The Affiliated Chaohu Hospital of Anhui Medical University

Background: To explore the stigma and related influencing factors in patients with chronic insomnia disorder (CID).Methods: A total of 70 CID patients and 70 healthy subjects were enrolled in the study. The Pittsburgh Sleep Quality Index (PSQI) and Hamilton Depression Rating Scale (HAMD) were used to assess sleep quality and depression severity, respectively. The Chinese-Beijing Version of Montreal Cognitive Assessment scale (MoCA-C) was used to assess cognitive function. The stigma and life quality were measured by the Chronic Stigma Scale and 36-Item Short-Form Health Survey (SF-36).Results: The CID group had increased stigma (U=662.0, P<0.001), PSQI (U=2485.0, P<0.001) and HAMD-17 (U=69.5, P<0.001) scores, as well as lower scores of MoCA-C (U=3997.5, P<0.001) and SF-36 in the items of Physical role (U=1560.5, P<0.001), Body pain (U=1633.5, P<0.001), General health (U=1194.0, P<0.001), Vitality (U=1169.5, P<0.001), Social function (U=1703.0, P=0.001), Emotional role (U=1451.5, P<0.001), Mental health (U=1147.0, P<0.001) and Health transition (U=1341.0, P<0.001) than control subjects. A partial correlation analysis showed that different items of stigma scale were positively correlated with the duration of disease, PSQI and/or HAMD-17 scores, while negatively correlated with one or more items of SF-36. Multivariate regression analysis showed that the duration of disease and Mental health domain of SF-36 were independent risk factors for stigma in CID patients (P<0.001, P=0.008). Conclusion: Patients with CID had a certain degree of stigma, and the duration of disease, quality of life, mood and sleep quality, particularly duration of disease and mental health are the factors affecting patients with CID.

Keywords

Effect of Baduanjin combined with agomelatonin on patients with depression and insomnia

Xiaole Yang

Shenyang Mental Health Center

Objective: To observe the clinical effect of Baduanjin combined with agomelatin in the treatment of depression with insomnia. Methods: 58 inpatients with depression and insomnia were divided into control group (29 cases) and observation group (29 cases) according to the method of random number table. The patients in both groups were given the oral administration of agomelatonin tablets. On this basis, the observation group was treated with Baduanjin health care method every day. The Hamilton Depression Scale (HAMD) score and Pittsburgh sleep quality index (PSQI) score of the two groups were assessed after 8 weeks of treatment Changes. Results: In terms of depression improvement, there was no significant difference

in HAMD score between the two groups (P > 0.05). Conclusion: Baduanjin traditional skill can improve the sleep quality of patients with insomnia accompanied by depression, and has the advantages of simplicity, no side effects, economy, etc., which is worthy of clinical promotion.

Keywords Baduanjin; agomelatonin; depression; insomnia

Etiological analysis of hypotension in insomnia patients

Hongju Hua

Ningxia Chinese Medicine Research Center

Objective: To investigate and test the common causes or risk factors of hypotension in insomnia. Methods: To observe the correlation between symptoms and blood pressure changes of hypotensive patients before and after adjusting hypotension factors. Results: There were 79% women, 11% with a family history of hypotension, 96% ones with a low salt diet and 79% ones with low body mass index in 399 cases of insomnia accompanied with hypotension. In addition, the changes of symptoms and blood pressure in hypotensive patients were related to the following factors: 3% eating in moderation, 85% excessive time in bed is 85%, low level of physical activity is 75%, 8% overdose of antihypertensive drugs, 11% taking antipsychotics. Diabetes with frequent nocturnal hypoglycemia is 2%. The risk factors are different in different patients, with single factor accounting for 3.4% and multi factors accounting for96.3%. Conclusions: There are many causes or risk factors for hypotension. Common causes or risk factors are as follows: family history of hypotension, female，low salt diet, low body mass index. Be moderate in eating, Excessive bed in time, Low level of physical activity, Overdose of antihypertensive drugs, Taking antipsychotics, Diabetes with frequent nocturnal hypoglycemia.There are single factor or multiple factors on Each individual with hypotension probably. Hypotension caused by multiple factors is more common.

Keywords

Prevalence, risk factors, and clinical correlates of insomnia in volunteer and at–home medical staff during the COVID–19

Xingxing Li1,Haihang Yu 1, Guolin Bian1,Zhenyu Hu1,Xiaoli Liu1,Qi Zhou1,Chang Yu1,Xiang Wu2,Ti-Fei Yuan3,Dongsheng Zhou1

1. Ningbo Kangning Hospital
2. The Affiliated Hospital of Medical School，Ningbo University
3. Shanghai Key Laboratory of Psychotic Disorders，Shanghai Mental Health Center，Shanghai Jiao Tong University School of Medicine，China

Objective: The 2019 novel coronavirus disease (COVID-19) has resulted in significant public health

problems. Frontline medical staff suffered from huge psychological stress during this epidemic. The study aimed to compare the sleep quality of volunteer and at-home medical staff. Method: A cross-sectional study of 948 (219 volunteered to Wuhan, 729 stayed at Ningbo) medical staff personnel was conducted online from February 15 to February 22, 2020. Demographic data were collected using questionnaires, and mental health variables were evaluated using the Athens Insomnia Scale (AIS) and Self-Reporting Questionnaire-20 (SRQ-20). Results: There was no significant difference in gender, age, educational background, and marital status between the two groups (p > 0.05). The medical staff in Wuhan had higher insomnia (score > 6) than whom in Ningbo (58.90 vs. 24.97%; p = 0.001) and had more severe physical and psycho-emotional symptoms (13.24 vs. 8.64%; p = 0.044). Multivariate logistic regression analyses showed that among the medical staff in Wuhan, the symptoms of insomnia were related to gender (OR=1.379, P =0.042, 95% CI=0.65–2.17), education (OR=1.54, P=0.0076, 95%CI=0.69–2.52), and physical and psycho-emotional symptoms (OR=2.124, P<0.01, 95%CI=1.69–2.67). Among the medical staff in Ningbo, insomnia was not only related to physical and psycho-emotional symptoms (OR=1.60, P<0.01, 95%CI=1.48–1.74) but also related to marital status (OR=0.57, P=0.046, 95%CI=0.33–0.99). Conclusion: Insomnia is highly prevalent in volunteer medical staff in Wuhan, when compared to stay-at-home population. This warrants clinical attention for mental well-being of these volunteer medical staff.

Keywords

Validation of a Contact–Free Sleep Apnea Monitor in Chinese Adults with Obstructive Sleep Apnea

Jianbo Xue,Rui Zhao,Jing Li,Long Zhao,Bing Zhou,Xiaosong Dong,Fang Han

Peking University People's Hospital

Objective To evaluate the diagnostic value of a contact-free sleep apnea monitor in Chinese adults with obstructive sleep apnea (OSA). Methods 198 participants with snoring were recruited in the study between July 2018 to May 2019 in the sleep center of Peking University People's Hospital, using nocturnal polysomnography and contact-free sleep apnea monitor simultaneously. We evaluated the agreement between AHI generated by contact-free sleep apnea monitor and PSG, calculated the sensitivity and specificity of OSA diagnosis using the contact-free sleep apnea monitor. Then，113 participants agreed to proceed the home sleep apnea test (HSAT) using the contact-free sleep apnea monitor. We also evaluated the agreement of AHI between the PSG and this device and the diagnostic value of OSA. Results PSG and contact-free sleep apnea monitor showed no significant differences in AHI[24.0 ± 23.2 vs 24.0 ± 21.1(in lab), 20.0 ± 21.5 vs 16.0 ± 14.4(HSAT), P> 0.05 respectively], and they were significantly correlated (ICCinlab=0.911, ICCHSAT=0.618, P< 0.05 respectively), with mean differences of -0.06(95% CI：-18.44,18.31) in lab and 4.06（95%CI：-26.69,34.82）at home, respectively. The ROC curve showed that if AHI≥5 events/h was used as diagnostic criteria, the sensitivity and specificity of diagnosing OSA were 91.2% and 58.0%, respectively.

The sensitivity and specificity of the contact-free sleep apnea monitor in diagnosing moderate and severe OSA were 90.1% and 71.1%, respectively with AHI≥13.3 events/h.Conclusion The accuracy of AHI from the contact-free sleep apnea monitor is high, and it can be used for the screening of OSA patients.

Keywords Contact-free sleep apnea monitor, Polysomnography, Obstructive sleep apnea

Investigation and analysis on the situation of anxiety, depression and insomnia in medicos

Fang Wang

The First Affiliated Hospital of Anhui Medical University

Objective: To investigate the status of anxiety, depression and insomnia of medical students, and to analyze their correlations and influencing factors. Methods: 360 undergraduates in Anhui Medical University were randomly selected as the research objects, Self-rating Anxiety Scale (SAS), Self-rating Depression Scale (SDS), Pittsburgh Sleep Quality Index (PSQI) and self-made questionnaire on influencing factors were used to evaluate anxiety, depression and insomnia symptoms.. Results: The standard score of anxiety of medical students was 40.00 (35.0,46.25) and the detection rate of anxiety was 16.5%. The standard score of depression was 43.75 (37.5, 51.25) and the detection rate was 31.5%. The total average score of PSOI was 5.0 (4.0,7.0) and the insomnia rate was 20.3%. There is a significantly positive correlation between anxiety and depression (r=0.771，P<0.01), and the total score of PSQI was positively correlated with anxiety (r=0.396, P<0.01) and depression (r=0.370, P<0.01). Grades and family member support are the main influencing factors of anxiety, depression and insomnia. While relationship with classmates is the main influencing factor of depression and insomnia, and recent diet is the main influencing factor of anxiety and depression. But parents' health status is only related to anxiety, and parents' relationship is only related to insomnia. In addition, the number of good friends, professional satisfaction, the total number of courses in this semester, satisfaction with figure and appearance, and the main solutions when encountering troubles only affect depression.

Keywords

Brain metabolic imbalance in perivascular space during obstructive sleep apnea

Yanlu Jia,Chunling Liu

The Second Affiliated Hospital of Zhengzhou University

Objective: There is increasing evidence of a causal association between obstructive sleep apnea (OSA) and white matter hyperintensity (WMH). While WMH and enlarged perivascular space (EPVS) are neuroimaging

markers of cerebral small vessel disease (CSVD). Thus, the goal of this study was to determine whether a contextual relationship existed between OSA and PVS. Methods: In this study, 107 participants underwent 1-night polysomnography, brain MRI and health screening examinations and were classified as 63 OSA patients (mild, moderate, and severe groups), and 44 healthy controls. We assessed the sleep characteristics in OSA group, quantified the total dilated VRS from magnetic resonance imaging (MRI) and correlated them with the measures of polysomnography-derived sleep parameters. Polysomnography revealed that 63 patients had sleep architecture alteration. A higher proportion of N2 phase sleep(N2%), a lower N3% and REM%, as well as increased arousal index (AI) and lowest arterial oxygen saturation (LSaO2), oxygen desaturation index (ODI) were detected. The results also indicated higher prevalence and larger number of EPVS, and lower Mini Mental State Scale (MMSE) scale score in OSA group. LSaO2, REM% and N3% were negatively correlated with the total EPVS, whereas ODI, AI and N2% were positively correlated. The findings suggested that OSA patients had sleep disturbances with a higher incidence and more severe of EPVS. Furthermore, the EPVS in OSA might be secondary to sleep disturbances, intermittent hypoxemia and the respiratory event-related hemodynamic changes. Thus, our findings highlighted the importance of early recognition and treatment of OSA in reducing the risk of stroke and dementia.

Keywords Obstructive sleep apnea; Polysomnography; Sleep; Mini Mental State Scale; perivascular space

Clinical Study of transcranial substantia nigra ultrasonography in restless legs syndrome

Xiaoxuan Wang,Wei Wu

Tianjin Medical University General Hospital

Objective: To study the pathogenesis of restless legs syndrome (RLS) and its changes in insomnia and mood. Methods: Through the imaging examination of the echo signal of the transcranial substantia nigra ultrasound-related nuclei in the RLS group and the healthy control group, the difference of serum iron markers between the two groups was analyzed, and the effects of RLS on sleep and mood. Results:From September 2020 to January 2020, 26 patients of Tianjin Medical University General Hospital who met the 2014 International Restless Legs Diagnostic Criteria were enrolled.20 healthy volunteers matched with the disease group were assessed for serum iron markers, insomnia and emotional level, the severity of restless leg syndrome should be evaluated in the ill group. In addition, 22 patients with RLSe and 20 healthy controls were selected for transcranial substantia nigra ultrasound imaging. Results: 1. Compared with healthy control group, the presence of hypoechoic substantia nigra in RLS patients was more significant, and the difference was statistically significant ($p < 0.05$). 2. Patients with RLS scored significantly higher in HAMA and HAMD($p < 0.05$) . 3. The scores of ESS and ISI in RLS patients were significantly higher than those in healthy control group ($p < 0.05$) There was no significant difference in the scores of PSQI compared with normal subjects ($P > 0.05$) . 4. There was no significant difference in blood test in RLS ($P > 0.05$) . Conclusion: 1. The iron

deposition in substantia nigra was less and the depression was more significant in RLS than in normal group. 2. People with RLS are more prone to anxiety. 3. RLS patients are more prone to daytime sleepiness and more severe insomnia, but the quality of sleep may not be significantly different from the normal population. 4. Serum iron-related marker levels were not found to change significantly in RLS patients.

Keywords

Intraperitoneal injection of ozone prevents spatial learning and memory deficits following sleep deprivation in rats

Yining Yan1,2,Jianxiong An1

1. Aviation General Hospital of China Medical University & Beijing Institute of Translational Medicine，Chinese Academy of Sciences
2. Chinese Academy of Sciences

Abstract: Sleep deprivation (SD) is a frequent health problem in modern society and negatively associated with spatial learning and memory deficits. In this study, we investigated the effect of the intraperitoneal injection of ozone on learning and memory function following sleep deprivation in rats. The rats received SD and an intraperitoneal injection of ozone for 28 days; we then performed a morris water maze (MWM) test to evaluate spatial learning and memory ability. Morphological changes in the brain were evaluated using hematoxylin and eosin (HE) staining and transcriptome sequencing was performed to seek a common mechanism. The expression of targeted proteins was examined by western blot. Results showed that ozone injection prevented behavioral and morphology deficits in SD rats that were associated with downregulation in the expression of sema3A in the hippocampus.

Keywords sleep deprivation, ozone therapy, midazolam, RNA-sequence, cognitive impairment.

Dexmedetomidine ameliorates sleep deprivation–induced cognitive impairment in mice by activation

Yu Liu1,2,Jianxiong AN1

1.Aviation General Hospital of China Medical University

2.University of Chinese Academy of Sciences

Objective: The experimental study aimed to explore whether dexmedetomidine can improve the cognitive function induced by chronic sleep deprivation, and the mechanism of EphA5 / ephrina5 pathway in improving cognitive impairment in mice after chronic sleep deprivation.Methods: 28 male ICR mice were randomly divided into three groups: large platform group (Control group), sleep deprivation + saline group (SD group), sleep deprivation + dexmedetomidine group (Dex group, intraperitoneal injection of 20 μ g /

kg), and sleep deprivation + midazolam group (Mid group, intraperitoneal injection of 0.5 mg / kg). Sleep deprivation was performed for 21 days (18 hours / day) using the modified multiple platform method, followed by medication for 7 days (once a day). The morris water maze including navigation experiment and space exploration experiment were carried out to test the learning and memory ability of mice. The navigation experiment was carried out for 4 days, and the space exploration experiment was carried out on the fifth day. The brain, spinal cord and hippocampus of the mice were collected. The brain and spinal cord were stained with he to observe the morphology of central nerve cells in cerebral cortex, prefrontal lobe, hippocampus, locus coeruleus, cervical, thoracic and lumbar segments of spinal cord, Western blot and immunohistochemistry were used to detect the expression of eph-a5 and ephrin-A5 in hippocampus. Results: In the navigation navigation experiment, the escape latency and the distance to the target quadrant of the SD group were increased and the distance to the target quadrant was decreased compared with the control group on the fourth day, and the escape latency and the distance to the target quadrant of the SD group were increased, the difference was statistically significant (P < 0.05). In the space exploration experiment,The DEX group were in the target quadrant, the distance was shortened, and the number of crossing platform was reduced, the difference was statistically significant (P < 0.05). The results of He stain showed that the morphology of nerve cells in Ctrl group was regular and the structure was complete. In SD group and Mid group, there were different degrees of cytoplasmic staining decrease, nuclear deep staining, and accompanied by necrotic neurons and glial cell aggregation. Compared with SD group and Mid group, the structure, staining depth and glial cell aggregation of DEX group were improved. Western blot and immunohistochemistry results showed that the expression of eph-a5 and ephrin-A5 in hippocampus of mice treated with dexmedetomidine increased, but there was no significant difference among SD group, Ctrl group and Mid group. Conclusion: Dexmedetomidine can improve the cognitive impairment induced by chronic sleep deprivation in mice and protect the neurons of nervous system; Dexmedetomidine may improve the cognitive impairment of mice after chronic sleep deprivation by activating EphA5 / ephrina5 pathway. Keywords

The relationship between the upper airway length indexes and severe OSA

Liu Zhang,Yaru Yan,Qingyun Li

Ruijin Hospital，Shanghai Jiaotong University School of Medicine

Objectives: Obstructive sleep apnea (OSA) is characterized by repeated airway collapse, which is more related to upper airway structure in Asian populations. This article intends to explore the abilities of upper airway structure indexes in OSA and the gender differences.Method: In 573 participants, basic information [age, sex, height, weight, neck circumference (NC) and waist circumference (WC)] were collected. All subjects underwent airway structure indexes measurements, including maximum interincisal distance (MID),

TMD (thyromental distance), TSD (thyro-sternum distance), which are usually used for airway management. OSA was diagnosed by overnight polysomnography. Logistic regression analysis was used to screen OSA risk.Results: 524 patients were enrolled in the study. H/TMD (OR=1.152, p<0.001), and H/TSD (OR=1.211, p<0.001) were indicators for OSA. And both of them had stronger degree of correlation with apnea-hypopnea index (AHI) in female subjects. Conclusion: Measure of the upper airway length was associated with increased OSA risk and severity. Of which, H/TMD and H/TSD may be new indicators of OSA.

Keywords

Preliminary study on the relationship between sleep periodic limb movement index and imaging features of cerebral small vessel disease

Fubing Ouyang,Mengshi Liao, Linfang Lan,Hao Li,Xiaolu Liu,Yuhua Fan

The First Affiliated Hospital of Sun Yat-sen University

Objectives: In recent years, studies have suggested that sleep periodic limb movements (PLMs) can increase the risk of cardiovascular and cerebrovascular disease. We intended to explore the relationship between PLMs index and the imaging features in patients with cerebral small vessel disease (CSVD). Methods: From September 2018 to June 2020, we enrolled patients with CSVD in the department of neurology, First Affiliated Hospital of Sun Yat-sen University. Data of Pittsburgh Sleep Quality Index Scale, Epworth Sleepiness Scale, polysomnography and brain MRI were collected. Fazekas score was used to assess the severity of white matter lesions. The Accubrain software was used to calculate the white matter hyperintensity volume, the number of lacunar infarctions, the number of cerebral microhemorrhages, and the number of perivascular spaces in basal ganglia. The total CSVD score combined the above imaging features was also calculated. Patients were divided into two groups (PLMs index ≥ 15 and PLMs index <15).Results: A total of 37 patients were included in the preliminary study. We found that CSVD patients with PLMs index ≥15 had lower sleep efficiency, reduced slow-wave sleep duration, increased apnea hypopnea index compared with the control group. Moreover, PLMs index was positively associated with an increase in perivascular spaces in basal ganglia and the total CSVD score.Conclusions: This study initially found that the PLMs index ≥ 15 may be a predictor of the perivascular spaces in the basal ganglia in CSVD. PLMs index can be used as one of the new markers of disease burden of CSVD.

Keywords

Dexmedetomidine reverses postoperative spatial memory deficit by targeting surf1 and cytochrome c

Kun Niu,Jianxiong An

Aviation General Hospital of China Medical University

Objectives: Anesthesia and surgery are associated with postoperative neurocognitive disorders (PND). Dexmedetomidine is known to improve PND in rats; however, little is known about the mechanisms. We design this animal study to explore the mechanisms of dexmedetomidine for preventing PND.Methods: Male Sprague-Dawley rats were subjected to resection of the hepatic apex under propofol anesthesia to mimic the clinical human abdominal surgery. The rats were divided into four groups: control group (C), sham group (S), model group (M), and model+dex group (D). Cognitive function was evaluated with the Morris water maze (MWM). Neuronal morphology was observed with H&E staining, Nissl's staining and immunohistochemistry. Transcriptome analysis and quantitative real-time PCR were performed to investigate functional mitochondrial mRNA changes in the hippocampus. Protein levels were measured by Western blotting at 1, 3, and 7 days after surgery.Results: Surgery-induced cognitive decline lasted for three days, but not seven days after surgery in the M group; however, rats in the D group were significantly improved by dexmedetomidine. No significant differences in the number of neurons were observed between the groups after surgery. Rats from the M group showed significantly greater expression levels of Iba-1 and GFAP compared with the C group and the M group. Rats in the M group demonstrated increased Surf1 and Cytochrome c expression on days 1 and 3, but not day 7; similar changes were not induced in rats in the D group.Conclusion: Dexmedetomidine appears to reverse surgery-induced behavior, mitigate the higher density of Iba-1 and GFAP, and downregulate the expression of Surf1 and Cytochrome c protein in the hippocampus of rats PND model.
Keywords

The protective effect of dexmedetomidine against spatial learning and memory impairment induced by sleep deprivation in rats and its mechanism

Wenhao Zhang1,2,Jianxiong An1,2

1.Aviation General Hospital of China Medical University

2.University of Chinese Academy of Sciences

Objective: Sleep is an essential to retain biofunction of life and sleep loss can lead to cognitive impairment. Hippocampus is related to spatial learning and memory in rodents. Sleep deprivation could impair

hippocampal neurons and inhibit synaptic formation, subsequently reduce the ability of spatial learning and memory. Dexmedetomidine could attenuates postoperative cognitive dysfunction, however, the efficacy of cognitive dysfunction caused by sleep deprivation is still unclear. In this study, we aimed to investigate the effect and mechanism of dexmedetomidine on learning and memory impairment in rats with chronic sleep deprivation.Methods: A total of 50 male Sprague Dawley rats were randomly divided into normal control group (Con group), wide platform control group (WPF group), sleep deprivation group (SD group), sleep deprivation with dexmedetomidine supplement group (SD+DEX group), and sleep deprivation with midazolam supplement group (SD+MID group) (n=10). Modified multiple platform method (MMPM) was conducted to cause the sleep deprivation of rats. Dexmedetomidine and midazolam were administered by intraperitoneal injection. Learning and memory ability was assessed through Morris water maze. Morphological changes of rat hippocampal neurons and synaptic were detected by HE staining and Golgi staining. The gene expression in hippocampus of each group was detected by RNA-seq and verified by RT-PCR and Western Blot.Results: Compared with SD group, the escape latency of rats in SD+DEX group tends to be shortened (P< 0.05), the number of crossing platforms and the target quadrant time of the SD+DEX group were significantly both higher (P< 0.05, respectively), while SD+MID group were no different from those in SD group. Compared with SD group, the neurons was more closely aligned and more regularly in the CA1 areas of rat hippocampal in SD+DEX group. The RNA-sequence showed that sleep deprivation mainly affected the gene expression related to metabolism. Among them, the significantly different gene was Alox15, which is associated with the progression of Alzheimer's disease. Dexmedetomidine reversed the expression of this gene, thereby enhance the plasticity of synapses in the hippocampus, and protect cognition. Conclusion: Sleep deprivation could cause memory acquisition deficit, while dexmedetomidine but not midazolam alleviates learning and memory dysfunction induced by chronic sleep deprivation in rats, and this protective effect may be related to the enhanced synaptic plasticity in the hippocampus CA1 areas of rats. Keywords

Application of sleep ward management in the treatment of insomnia patients

Ying Liu

Aviation General Hospital of Medical University

Objective: To summarize the application of sleep ward management concept for insomnia admitted to our department.Methods: Insomnia is characterized by continuous light sleep and difficulty in deepening sleep, easy to wake up after falling asleep due to sound, light and other factors, difficulty in falling asleep again. In order to improve the sleep quality of insomnia patients, our department puts forward eight sleep ward management concepts: 1. Anew concept of "snore free ward" dividing insomnia patients into snores and non-snores for separate admission; 2. Humidifiers and music aromatherapy are provided in the wards of

insomnia patients for mood management through music therapy. 3. Insomnia patients performed functional exercise twice a day in the morning and afternoon. 4. Insomnia patients performed outdoor activities twice a day in the morning and afternoon. 5. Equipped with a set of sleeping position adjustment pillow for insomnia patients. 6. Psychological assessment of insomnia patients to judge the degree of anxiety and depression. 7. Intervention for patients with severe snoring. 8. The last and most critical step is to monitor the patients' sleep and follow up the medication use according to the monitoring results.Results: The management concept of snore free sleep ward has been well received by patients and has improved the sleep quality of patients. Conclusion: Most outcomes depend on the patients' trust in the hospital and the doctor after admission and the patients' confidence in the treatment effect. Therefore, excellent sleep ward management is as important as medical intervention and snore free ward management is the most critical step for patients in the ward. It is a new cognition for us to treat insomnia to use the concept of sleep ward management to manage insomnia patients in an all-around way.

Keywords

Effect of electro–acupuncture on postoperative memory dysfunction under low–dose propofol anesthesia in rats

Jian Guo,Jianxiong An

Aviation General Hospital

Postoperative neurocognitive dysfunction is one of the most common postoperative complications in elderly patients over 65 years old. The main manifestations are delirium that occurs within a few hours to several days after surgery and impaired execution and memory that lasted for a longer time. Our previous studies have found that learning and memory impairment incidence is higher after surgery under low-dose propofol anesthesia. Data from several studies suggest that electro-acupuncture can improve postoperative learning and memory impairment. The purpose of this study was to investigate the effect of electro-acupuncture on memory after surgery under low-dose propofol anesthesia in rats. A rat model of postoperative neurocognitive dysfunction was established under low-dose propofol anesthesia with left lateral hepatic lobectomy. Six electro-acupuncture treatments were performed 1, 2, 3 days before the operation and 1, 2, 3 days after the operation. The water maze test was performed before the operation and on the 3rd, 7th, and 13th day after the operation to test rats' memory ability. The results showed that the number crossing the platform and time in the target quadrant on the third day after the operation was increased in the electro-acupuncture group compared with the model group. The finding to emerge from this study is that perioperative electro-acupuncture can improve memory impairment after surgery in rats under low-dose propofol anesthesia.

Keywords

Assessment Model for Carotid Body Chemosensitivity in Patients with Obstructive Sleep Apnea

Hongpeng Li1,2,Ning Li1,2,Liu Zhang1,2,Shiqi Li1,2,Yaru Yan1,2,Huanhuan Lu1,2,Qingyun Li1,2
1.Ruijin Hospital，Shanghai Jiaotong University School of Medicine
2.Respiratory Research Institute，Shanghai Jiaotong University School of Medicine

Objective:The carotid body (CB) is a major peripheral respiratory chemoreceptor. In patients with obstructive sleep apnea (OSA), high CB chemosensitivity (CBC) is associated with refractory hypertension and insulin resistance and known to further aggravate OSA. Thus, the identification of high CB (hCBC) among OSA patients is of clinical significance, but detection methods are still limited. Therefore, this study aimed to explore the association of CBC with OSA severity and to develop a simplified model that can identify patients with hCBC. Methods: In this cross-sectional study of subjects who underwent polysomnography (PSG), CBC was measured using the Dejours test. We defined hCBC as a decrease of >12% in respiratory rate (RR) after breathing of pure O2. The association of CBC with OSA severity was explored by logistic regression, and a model for identifying hCBC was constructed and confirmed using receiver operating characteristic analysis. Results: Patients with OSA (n=142) and individuals without OSA (n=38) were enrolled. CBC was higher in patients with OSA than in those without OSA (% decrease in RR, 15.2%±13.3% vs. 9.1%±7.5%, P<0.05). Apnea-hypopnea index (AHI), fraction of apnea-hypopnea events in rapid-eye-movement sleep (Fevents-in-REM), and longest time of apnea (LTA) were associated with hCBC independently (odds ratio [OR]=1.048, OR=1.082, and OR=1.024 respectively; all P<0.05). The model for identifying hCBC allocated a score to each criterion according to its OR values, i.e., 1 (LTA >48.4 s), 2 (AHI >15.7 events/hour), and 3 (Fevents-in-REM >12.7%). A score of 3 or greater indicated hCBC with a sensitivity of 79.4% and specificity of 88.2%. Conclusions: High CBC is associated with the severity of OSA. A simplified scoring system based on clinical variables from PSG can be used to identify hCBC.
Keywords

Hydrogen sulfide involved in the cih–induced carotid body hyperactivity through upregulating AT1 Expression

Hongpeng Li1,2,Ning Li1,2,Liu Zhang1,Shiqi Li1,2, Yaru Yan 1,2,Qingyun Li1,2
1.Ruijin Hospital，School of Medicine，Shanghai Jiao Tong University
2.Institute of Respiratory Diseases，School of Medicine，Shanghai Jiao Tong University

Objective: To explore the mechanism of Hydrogen Sulfide (H2S) involving the increased Carotid Body (CB) activity caused by chronic intermittent hypoxia (CIH).Methods: In animal study, the rats were divided into three groups: normoxia group (Con group), CIH group and CIH + L-PAG group (enzyme inhibitor of

H2S production). The following parameters were measured: hypoxic ventilation response, hydrogen sulfide production in carotid body tissue level ex vivo, expression of AT1. In cells study, PC12 cells were divided into: normoxia group, AOAA group, DTT group, Losartan group, IH group, IH + AOAA group, IH + DTT group and IH + losartan group. The following indicators were determined, (1) the intracellular calcium concentration; (2) the expression of AT1; (3) the S-sulfhydrylation level of Sp1; (4) the binding of Sp1 to the promoter region of AT1 gene.Results: The basal ventilation volume (64.5 ± 9.9 ml/min vs. 40.5 ± 5.6 ml/min, P < 0.001) and hypoxic ventilation (79.6 ± 13.1 ml/min vs. 60.3 ± 10.5 ml/min, P < 0.001) in CIH group were significantly higher than in Con group, while there was no significant increase in CIH +L-PAG group (P = 0.478). The H2S produced by CB tissue between groups had the same pattern as ventilation. The expression of AT1 in CIH group was significantly higher than in Con group (3.79 ± 0.43 vs. 1.58 ± 0.17, P < 0.001), while L-PAG inhibited upregulation of AT1 expression caused by CIH. In cells study, IH significantly upregulated the expression of AT1 and increased the intracellular calcium concentration ([Ca2+]i) of PC12, which could be inhibited by AOAA, DTT and Losartan. IH resulted in S-sulfhydrylation of Sp1 and promoted the binding of Sp1 to AT1 gene promoter.Conclusions: IH upregulated the expression of AT1 through S-sulfhydration of Sp1 and increases the activity of carotid body.

Keywords

The pathological changes and the expression of VEGF and occludin in lung of rat under chronic intermittent hypoxia

Ningning Zhe,yuqi Yuan,chao Si,Na Liu,yitong Zhang,Haiqin Liu,xiaoyong Ren

The Second Affiliated Hospital of Xi'an Jiaotong University

Objective: To investigate the pathological changes and the expression of VEGF and occludin in lung of rat under chronic intermittent hypoxia. Methods: Twenty male SD rats were randomly divided into a normal control group (10 rats) and an intermittent hypoxia group (10 rats). After culturing for six weeks, the lungs were taken for hematoxylin-eosin staining and Van Gieson staining to preliminarily evaluate the pathological changes. Further immunohistochemical localization and semi-quantitative analysis of VEGF, occludin protein expression to explore the causes of pathological changes in lung tissue. Results: Compared with the control group, HE staining of the lungs of rats in the chronic intermittent hypoxia group showed pulmonary vascular congestion, a large number of inflammatory cell infiltrations and rupture of alveolar cavity. After 6 weeks of chronic intermittent hypoxia, VG staining showed the deposition of collagen fibers and fibrosis in the lung tissues increased significantly. Immunohistochemical results showed that VEGF was expressed in lung inflammatory cells, bronchial epithelial cell cytoplasm and nucleus, and compared with the control group, the expression of VEGF was significantly increased in the chronic intermittent hypoxia group; Occludin was mainly distributed in alveolar epithelial cells and some endothelial cells, and there was no statistically significant difference compared with two group. Conclusion: Chronic intermittent hypoxia induced pathological changes in the lung tissue of rats, included inflammatory infiltration and fibrosis related

to the increased expression of VEGF. But it did not affect the expression of tight junction occludin protein, besides the lung gas and blood barrier.

Keywords

Aquaporin–4, connexin–30, and connexin–43 arebiomarkers for decline of object sleep quality and/or cognition

Shuai Yang,Guihai Chen

Department of Sleep Disorders. The Affilated Chaohu Hospital of Anhui Medical University

Objectives: The aim was to examine the serum concentration changes of aquaporin-4, connexin-30, connexin-43 and their correlations with cognitive function in patients with chronic insomnia disorder (CID). Methods: Seventy-six CID patients and thirty-two healthy controls (HC) were enrolled. Serum levels of aquaporin-4, connexin-30, and connexin-43 were measured using an enzyme-linked immunosorbent assay. Sleep and neuropsychological function were measured by questionnaires, polysomnography, Chinese-Beijing Version of Montreal Cognitive Assessment (MoCA-C), and Nine Box Maze Test (NBMT). Results: Compared to the HC group, the levels of aquaporin-4, connexin-43, and connexin-30 significantly reduced in the CID group (Z = -3.690; Z = -4.451; Z = -5.292, $P < 0.001$). The partial correlation analysis in the CID showed that aquaporin-4 was positively linked with MoCA-C (r = 0.332, $P < 0.01$) and negatively correlated with errors in spatial working memory (SWM) (r = -0.422, $P < 0.01$). Concomitantly, aquaporin-4 was positively with N3% (r = 0.235, $P < 0.05$). However, the levels of connexin-43 and connexin-30 were only positively linked with N3% (r = 0.287, $P < 0.05$; r = 0.338, $P < 0.01$).Conclusion: Serum aquaporin-4, connexin-30, and connexin-43 levels were decreased in the CID group, indicating astrocyte-neuron networks dysfunction, and were linked with object sleep quality and/or cognition function. In addition, aquaporin-4, connexin-30, and connexin-43 may be a marker for object sleep quality rather than subject sleep quality of insomnia.

Keywords

Cardiac imageology changes in patients with mild obstructive sleep apnea without cardiovascular disease

Zuogeng Hong1,2,Qiong Ou1,Yilu Cheng1,Yanxia Xu1,Hongwen Fei1,Hui Liu1

1.Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences)
2.Medical College of Shantou University

Objective: To assess changes in cardiac imageology of patients with mild obstructive sleep apnea (OSA) without cardiovascular disease.Methods: All enrolled participants underwent polysomnography (PSG). Some participants underwent transthoracic echocardiography, speckle tracking echocardiography, and

cardiac enhanced magnetic resonance imaging (MRI)voluntarily. Participants were divided into three groups according to PSG results: non-OSA, mild OSA, and moderate-to-severe OSA. Imageology parameters were compared and the relationship between OSA severity and imageology indices was analyzed by correlation analysis and multiple linear regression.Results: Of the 352 enrolled participants, 274 participants with OSA had an apnea-hypopnea index (AHI) ≥5 (86 mild OSA and 188 moderate-to-severe OSA cases), and 78 participants with non-OSA had an AHI <5. Transthoracic echocardiography showed that E/A and E'/A' values were lower in the mild OSA group than those in the non-OSA group (1.12±0.37 vs 1.27±0.45 and 0.83±0.33 vs 0.99±0.42, respectively, P<0.05). Aorta and ascending aorta widths were smaller in the mild OSA group than those in the moderate-to-severe OSA groups (27.36±2.87 mm vs 28.87±2.95 mm and 30.27±3.79 mm vs 31.63±3.74 mm, respectively, P<0.05). A regression analysis showed that cardiac function changes in patients with OSA may be related to age, obesity, and OSA severity.Conclusion: Patients with mild OSA without cardiovascular disease displayed changes in cardiac structure and function on transthoracic echocardiography.

Keywords

The Poor Sleep Quality Mediates Increased the Risk of Stroke: A Study on The Levels of CD62E+ and Angiotensin II in Insomnia Patients

Juntao Chen,Guihai Chen

Chaohu Hospital of Anhui Medical University

Background: Insomnia may affect vascular factors and increase the risk of stroke. The specific mechanisms are still poorly understood. A pro-inflammatory state and other vascular risk factors have been proposed as mechanisms that may underlie this association. Few studies have been concerned with the CD62E+ and angiotensin II (Ang II) levels in patients with sleep disorder. We investigated whether CD62E+ microparticles and Ang II levels were changed in patients with insomnia.Methods: Patients with insomnia (CID group, N =75) and healthy controls (HC) without sleep problems (N =32) were enrolled. PSQI, HAMD, MoCA-C and polysomnography were used to assess their sleep and neuropsychological function. A quantitative sandwich enzyme-linked immunosorbent assay was used to quantify serum levels of CD62E+ and Ang II .Results: The CID group had higher levels of CD62E+ and Ang II than the HC group. Spearman correlation analysis revealed that neither CD62E+ nor Ang II level had significant correlation with the PSQI scores (P >0.05). Serum concentration of CD62E+ negatively correlated with TST (r = -0.265, P=0.022), SE (r = -0.285, P=0.013) and WASO (r= -0.251, P=0.03). Serum Ang II level negatively correlated with SOL (r = -0.248, P=0.032) and Arl (r = -0.329, P<0.01) (arousal index). After controlling for sex, age and course, the partial correlation analysis indicated that correlation still existed.

Keywords

Serum NFL and tau levels in children diagnosed of Adenotonsillar Hypertrophy with Obstructive Sleep Apnea and their associations with cognitive impairment

Yewen Shi1,Yani Feng1,Haiqin Liu1,Lei Shang2,Zhijun Tan2,Yitong Zhang1,Bingjie Zhao1,Junjie Zhao1,Xiaoyong Ren1

1.The Second Affiliated Hospital of Xi'an Jiaotong University

2.The Fourth Military Medical University

Background: Obstructive sleep apnea (OSA) in children has attracted broad interest in recent years because of its complicated complications, such as cognitive impairment. There is no research about neurofilament light (NFL), a marker of neuro-axonal damage, reported in children with OSA and its relationship with cognitive impairment caused by OSA.Method: We determined serum concentrations of NFL and tau in children diagnosed of adenotonsillar hypertrophy (ATH) by commercially ELISA assay and single-molecule array.Results: Concentrations of NFL and tau in serum were higher in the OSA group (29.10 (22.46-40.16) pg/ml, 3.35 (2.17-5.77) pg/ml) than the non-OSA group (19.40 (15.34-25.68) pg/ml, 2.77 (1.56-3.85) pg/ml) ($p < 0.001$, $p = 0.028$) in children diagnosed of ATH. Moreover, NFL concentration is correlated with AHI, OAI, OAHI, SaO2, RAI and cognitive impairment evaluated by Chinese Wechsler Intelligence Scale for Children (WISC) with Spearman's correlation analysis ($p < 0.05$). The area under ROC (AUC) of NFL was 0.81 (0.718-0.901).Conclusion: Concentrations of NFL and tau in serum in OSA children were increased compared with non-OSA children diagnosed of ATH. NFL concentration in serum might be accessible diagnostic and screening markers of OSA in children, especially in those with cognitive dysfunction. Keywords

Observation on the changes of intestinal barrier in OSAS model mice

zhanjun Dou,Bei Wang,Peipei Wang,Zixuan Hu

The Second Hospital of Shanxi Medical University

Sleep apnea syndrome (OSAS) can be defined as complete or partial closure of the upper respiratory tract during sleep leading to periodic cessation of breathing or significant reduction of respiratory amplitude (hypopnea), which can lead to cardio-cerebrovascular, blood, kidney and other multiple system damage. In recent years, it has been found that OSAS may increase intestinal permeability by changing the intestinal barrier, and then lead to the occurrence and development of metabolic complications.Objective: Observe the changes of intestinal barrier in OSAS model mice.Methods: A total of 24 male 6-week-old C57BL/6 mice

weighing 20-25 g were selected in this study. The mice were randomly divided into 4 groups: normal control 4 weeks group (N4 group), OSAS4 week group (O4 group), normal control 6 weeks group (N6 group) and OSAS6 week group (O6 group), with 6 mice in each group. The OSAS model was made with American-made BiospherixA84 equipment, and the normal control group was fed under normoxic condition. The mice in the corresponding group were killed at 4 weeks and 6 weeks respectively, and the colon tissue was taken for HE staining to observe the morphological changes of colon tissue.Results: Compared with the normal control group, the colonic tissue of OSAS group showed obvious mucosal swelling, connective tissue porosity and lymphocyte infiltration, and it was more obvious in the 6-week group than in the 4-week group. Conclusion: 1.OSAS could cause intestinal barrier damage, and this damage was positively correlated with the condition. 2.The injury of intestinal barrier caused by OSAS was related to inflammatory reaction. Keywords Obstructive sleep apnea syndrome; Intestinal barrier; Inflammatory response

Study on the changes of school–age children's emotional and behavioral problems during the COVID–19 quarantine

Xiaoyan Chou1,2,Chenjin jin2,1
1.Shanghai Children's Hospital，Shanghai Jiao Tong University，
2.shanghai children's hospital

Objective: To explore the status of emotional and behavioral disorder in school-age children during COVID-19 outbreak. Method: Four primary schools in a district of Shanghai were selected using simple random sampling, then cluster sampling was performed based on class. The general questionnaire, strength and difficulty scale were applied to the parents of students. Information on the basic situation of children and families quarantined at home during COVID-19 was collected. Results: Children from single-parent families had increased emotional symptoms (3.07 ± 2.50), conduct problems (2.00 ± 1.54) and prosocial behavior scores (7.88 ± 1.77). Emotional and behavioral problems changed in school-age children during the quarantine period, and increased scores for behavioral problems were found in girls aged 7-9 years compared with the Shanghai norm (P&L;0.05), while the hyperactivity inactivity score was decreased in boys aged 6 to 9 years (P&L;0.05);Compared with SH2018, scores for behavioral problems increased for children of all ages ($P<0.05$), and the prosocial behavior scores of children aged 7-9 years were decreased. Conclusion: The study found that the emotional problems of children in single-parent families and lineal families, and the conduct of children in single-child families and lineal families should be paid more attention to. When similar public health events occur in the future, stratified and classified interventions should be carried out for children with different emotional and behavioral problems. Keywords

SR9009 protects nigrostriatal dopaminergic neurons in the MPTP mouse model of PD

Liang Kou,Tao Wang

Union Hospital of Tongji Medical College of Huazhong University of Science and Technology

OBJECTIVE:In this study, we investigated the effects of SR9009 dopaminergic neurons in the MPTP mouse model of PD. BACKGROUND:Accumulating evidences demonstrated that Rev-Erb α , a nuclear receptor and circadian clock component, is involved in regulating neuroinflammation and determining the fate of neurons. Therefore, we studied the effect of treatment with the Rev-Erb α specific agonist SR9009 in the MPTP mouse model of PD. METHODS:PD models were induced by MPTP (30 mg kg−1 in saline intraperitoneally) once a day for 7 consecutive days. SR9009 was administered to mice via intraperitoneal injection once daily for 7 days prior to MPTP treatment, and continued along with MPTP treatment. The effects of SR9009 on neuronal loss were assessed by immunohistochemistry and western blot.RESULTS:Our further findings revealed that treatment with SR9009 inhibited the loss of dopaminergic neurons in the striatum of MPTP mouse model. CONCLUSIONS:Taken together, these results suggested that the clock gene Rev-Erb α may contribute to the pathological process of PD and the activation of Rev-Erb α may have neuroprotective effects.

Keywords

Preliminary study on clinical characteristics of Chinese patients with positional obstructive sleep apnea

Xiaona Wang,Rong Huang

Chinese Academy of Medical Sciences & Peking Union Medical College Hospital

Objective: The objective of this study was to evaluate the prevalence, the clinical characteristics, and the possible predictors of Chinese patients with positional obstructive sleep apnea (POSA) according to the Amsterdam Positional Obstructive Sleep Apnea Classification (APOC).Methods: A retrospective study in the sleep unit of Peking Union Medical College Hospital was conducted to analyze the clinical and polysomnography data of Chinese patients with obstructive sleep apnea (OSA).Results: This study included 372 patients with OSA, and 53.76% of the participants met the APOC criteria for POSA. In this study, the prevalence of POSA was significantly higher in female OSA patients than that in males. Chinese patients with POSA had a lower apnea–hypopnea index, oxygen desaturation index, and the percentage of time spent at oxygen saturation below 90% in total sleep time; and a higher mean oxygen saturation (SaO2) and minimum SaO2 during sleep, which were remarkable in the APOC Ⅰ group. By multivariate logistic regression analyses, the higher mean SaO2 (≥95%) during sleep and mild and moderate OSA were positive predictors

of POSA. Mild and moderate OSA was the independent predictor of POSA in females. Higher mean SaO2 (≥95%) during sleep was the independent predictor of POSA in males.Conclusion: According to the APOC, the prevalence of POSA is high in Chinese patients with OSA, especially in females. Chinese patients with POSA had less severe OSA and lower degree of nocturnal hypoxia, which was remarkable in the APOC Ⅰ group.

Keywords

The influence of craniofacial width on nasal respiratory function and morphology of upper airway

Xu Gong,Xuemei Gao

Peking University School and Hospital of Stomatology

Objective：To observe the influence of craniofacial width on nasal respiratory function and morphology of upper airway.Method: Subjects were selected from patients who visited the Orthodontics Department at Peking University School and Hospital of Stomatology. A total of 14 males, 33 females, aged 25.17 ± 5.25 years, were included. These 47 healthy subjects were divided into three groups according to their mandibular position. Cone beam computed tomography (CBCT) was performed, and nasal airflow and nasal resistance were measured. Differences in nasal respiratory functions and upper airway morphology were compared. A correlation analysis was conducted for nasal respiratory function, upper airway morphology, and craniofacial width.Results: The nasal inspiratory and expiratory capacity was positively correlated with the skeletal transverse dimension [100mL/s NCi vs Or-W：r=0.336（P=0.021）, vs Zy-W：r=0.392（P=0.006）, vs Go-W：r=0.311（P=0.033）]. The nasal resistance was negatively correlated with the skeletal transverse dimension [150mL/s NRe vs Naso-W：r=-0.317（P=0.032）]. And the volume and cross-sectional area of upper airway were mainly positively correlated with the skeletal transverse dimension [Glosso-V vs Zy-W：r=0.432（P=0.002）；Glosso-Amin vs Zy-W：r=0.460（P=0.001）].Conclusions: Craniofacial width may affect nasal respiratory function and the upper airway.

Keywords

The mechanism of caffeine activate the neurons of medial parabrachial nucleus to reduce the apnea neonatorum

Xiaohong Cai,Shi Hua

The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University

Objective：Apnea neonatorum is a common condition of newborns especially in prematurity. Caffeine has been used as a first-line drug treating apnea neonatorum for decades as it's safe and effective.

However, the mechanism of caffeine in central nervous system reducing apnea neonatorum is still unclear. Medial parabrachial nucleus (MPB) is part of the respiratory center of pons. Explosure to caffeine in utero can cause an increase of adenosine 1 receptors (A1Rs) in MPB suggesting that caffeine may activate the neurons of MPB by blocking the A1Rs. In this study, patch-clamp technique was performed and the antagonist of A1Rs and A2Rs, 8-cyclopentyl-1,3-dimethyl-xanthine (CPT) and Istradefylline (KW6002), were used to mimic the effects of caffeine. The spontaneous firing rate and the membrane potential and the spontaneous excitatory/inhibitory postsynaptic currents (sEPSC/ sIPSC) were recorded to investigate the effect and mechanism of caffeine in MPB of mice in different ages, may provide a new drugs on specific target.Materials: Healthy C57BL/6 mice in 4 age groups, caffeine, CPT and KW6002, DMSO,TTX, PTX, NBQX and APV, MPB and locusceruleus(LC). Methods: Different drugs were applied to investigate the mechanism of caffeine, records sEPSC and sIPSC. Results:1.Electrophysiological property and the differences of MPB neurons among groups. 2.Caffeine could excite MPB neurons.3.CPT can be used to mimic the effect of caffeine in MPB 4.TTX could complete lyeliminate the spontaneous action potiential. 5.Caffeine could increase the frequency and the amplitude of sEPSC in the existant of PTX.Conclusions: 1. Caffeine could excite the MPB neurons. The excitable rate had no significant difference between different ages. 2. Caffeine could barely excite the LC neurons. 3. Caffeine excited the MPB neurons by blocking A1 receptors. 4. Caffeine could increase the efficiency of synaptic transmission to excite the MPB neurons.

High serum nerve growth factor concentrations are associated with good functional outcome at 3 months following acute ischemic stroke

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Objective: Previous studies in animal model have demonstrated that neurotrophins were associated with functional outcome following stroke. However, the relationship between serum nerve growth factor (NGF) and functional outcome in stroke patients has not been explored. Our objective was to investigate the association between serum NGF concentrations at admission and functional outcome of patients at 3 month after stroke. Methods: One-hundred eight-five patients with acute ischaemic stroke were recruited in our study. Serum NGF concentrations were measured by ELISA at admission. The stroke severity at admission was assessed by the National Institute of Health Stroke Scale (NIHSS). The modified Rankin Scale (mRS) was used to assess the functional outcome of patients at 3 month after stroke. In addition, 100 healthy controls were recruited. Results: Serum NGF concentrations were higher in good functional outcome group (mRS score of 0–2) than that in poor functional outcome group (mRS score of 3–6) (9.51 $\pm$ 2.33 vs. 8.12

$\pm$ 1.61, P < 0.001). Meanwhile, the serum NGF concentrations in healthy group were lower than that in acute ischemic stroke patients (7.17 $\pm$ 1.49 vs. 9.15 $\pm$ 2.24, P < 0.001). Moreover, our results demonstrated that high serum NGF concentrations (> 9.21 ng/l) were independently associated with the better functional prognosis at 3 months following the occurrence of stroke (OR 0.048, 95% CI 0.012–0.185, P < 0.001). Conclusions: High concentrations of serum NGF at admission may predict good functional outcome of patients at 3 months after acute cerebral ischemia stroke.

Keywords

High levels of plasma fibrinogen and Prothrombin time are related to post

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Introduction: Studies have shown that high levels of the fibrinogen (FIB) are related to anxiety and depression. However, the relationship between FIB and post-stroke emotional impairment (PSEI)remains unclear, which includes post-stroke anxiety (PSA) and post-stroke depression (PSD). Methods: A total of 555 patients with acute ischemic stroke (AIS) were enrolled in this study. Ultimately, 443 patients completed 1‑month follow‑up. Blood samples were collected at hospital admission. Clinical depression and anxiety were evaluated 1 month after stroke.Results: High levels of FIB were observed in patients with PSEI compared with the non‑EI group (p = 0.003). Levels of FIB were divided into three tertiles, and the prevalence of PSEI was significantly higher in the third FIB tertile (p = 0.016). After adjusting potential confounders, the third FIB tertile was independently associated with the prevalence of PSEI (OR = 1.785, 95%CI = 1.049-3.039, p = 0.033), taking the first tertile as a reference. In this model, prothrombin time (PT) was also independently associated with the prevalence of PSEI (OR = 1.602, 95%CI = 1.181-2.173, p = 0.002).Conclusion: High levels of plasma FIB and PT are associated with the prevalence of PSEI.

Keywords

Increased BDNF may not be associated with cognitive impairment in heroin–dependent patients

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

A growing number of evidence suggests that brain-derived neurotrophic factor (BDNF) plays an important part in modulating the activities on the basis of hippocampus neural plasticity, such as learning and memory. Heroin addiction has a series of cognitive impairments that may be associated with BDNF. In this study,

we explored the association of BDNF with cognitive function in heroin dependent patients. We enrolled 86 heroin-dependent patients and 238 normal control subjects and examined their cognition by the repeatable battery for the assessment of neuropsychological status (RBANS) and serum BDNF levels in 2 groups. BDNF levels were significantly higher in patients than controls (P<.001). Cognitive scores of the RBANS showed that attention and language index (P<.05) were significantly lower in heroin-dependent patients than control groups. Unfortunately, we found no positive association between BDNF and cognitive function in patients, except that BDNF was positively associated with visuospatial/constructional index in control groups. Our findings suggest that BDNF may not be involved in the pathophysiology of heroin dependence, but more studies about cognitive impairment in heroin addiction are needed.

Keywords

Association between serum malondialdehyde levels and depression during early methamphetamine withdrawal

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Some evidence suggested that malondialdehyde (MDA) as a marker of oxidative stress played an important part in modulating the activities of depression. Methamphetamine (METH) dependence often lead to depression that may associate with MDA. In this study, our purpose was to explore the association between serum MDA levels and depression during METH withdrawal. 179 METH-dependent patients were recruited in this study and 144 (80.4%) finished the assessment. We measured serum MDA at 532nm spectrophotometrically at admission. The short form of the Beck Depression Inventory (BDI-13) was used to evaluate depression symptoms. Patients were identified to have depression symptoms with the BDI score $\geq$ 8. As a result, 89 (61.8%) of the remaining 144 METH-dependent patients were identified to have depression symptoms. Patients with depression symptoms showed significantly higher serum MDA levels than non-depression patients (3.42$\pm$1.60 nmol/ml vs. 2.43$\pm$1.25 nmol/ml; p< 0.001). After controlling for potential confounding variables in our logistic model, serum MDA levels were independently associated with the development of depression during early METH withdrawal (OR =1.952, 95% CI, 1.414-2.694, p<0.001). Furthermore, our study found a positive association between Beck Depression Inventor (BDI) score in early METH abstinence and serum MDA levels (r =0.185 ; p= 0.026). Our results indicated that higher serum MDA levels were related to higher risk of depression symptoms during early METH withdrawal.

Keywords

Low serum 25–hydroxyvitamin D concentrations in chronic insomnia patients and the association with poor treatment outcome at 2months

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Background: The association between low 25-hydroxyvitamin D [25(OH)D] and sleep disorder has been reported. We investigated whether serum concentrations of 25(OH)D are altered in chronic insomnia patients. The relationship between serum concentrations of 25(OH)D and the treatment outcome in patients at 2 months was also investigated.Methods: In total, 181 chronic insomnia patients were consecutively recruited. All patients received pharmacotherapy for the treatment of chronic insomnia. Serum 25(OH)D concentrations were quantified by a competitive electrochemiluminescence protein binding assay. Treatment outcomes were defined as "response" versus "non-response", according to the change of the Pittsburgh Sleep Quality Index (PSQI). We also recruited 100 healthy subjects as a control group.Results: Fifty-four out of 181 (29.8%) patients met the criteria for non-response. Chronic insomnia patients had significantly lower 25(OH) D concentrations compared with healthy controls (23.01 ± 9.18 vs 27.17 ± 6.41 ng/ml, $P < 0.001$). Non-response patients also had significantly lower 25(OH)D concentrations than those with response. Vitamin D deficiency(25(OH)D concentrations < 20 ng/ml) was independently associated with a higher probability of treatment non-response at 2 months (odds ratio 11.636, 95% confidence interval 3.966-34.142, $P < 0.001$). Conclusions: Measurement of serum 25(OH)D concentrations are probably useful for judging treatment outcomes of pharmacotherapy in chronic insomnia patients.
Keywords

Low serum uric acid levels in chronic insomnia patients: A case–control study

Xiaoqian Luan,Jincai He

The First Affiliated Hospital of Wenzhou Medical University

Recent studies have demonstrated the presence of oxidative stress in insomnia patients. Uric acid (UA) is regarded as one of the most important antioxidants that may attenuate oxidative stress. The aim of our study was to investigate whether there is an alteration of serum UA levels in chronic insomnia patients. The association between sleep quality and serum UA in chronic insomnia patients was also investigated. We recruited 300 chronic insomnia patients and 300 age- and gender-matched normal controls. The uricase-PAP method was used to measure the concentration of UA both in patient and normal control subjects. The

Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality of chronic insomniac participants. As a result, significantly lower serum UA levels were observed in patients with chronic insomnia when compared with normal control subjects (279.56 ± 65.80 vs. 299.10 ± 61.17 mol/L, $t = -3.991$, $p < 0.001$). Low serum UA levels were correlated with high PSQI scores in multiple linear regression models ($= -0.322$, $p < 0.001$). Our results suggested that low serum UA levels were associated with the presence and severity of chronic insomnia.

Keywords

Significance of Determining Plasma Orexin Levels and Analysis of Related Factors for the Diagnosis of Patients with Narcolepsy

Yanmei Zhu1,Jiaqi Shi1,2,Jingyuan Wu1, Jia He1,Haiyan Gou1,Yan Chen1,Yulan Zhu1
1.The Second Affiliated Hospital of Harbin Medical University
2.Harbin Children's Hospital

Objectives: Decreased cerebrospinal fluid (CSF) orexin levels are one of the diagnostic and classification criteria for narcolepsy. Because of the difficulty in obtaining CSF, its clinical application is limited. Here, we aimed to determine the significance of plasma orexin levels in the diagnosis and treatment of narcolepsy by comparing these levels between narcolepsy patients and healthy controls and analyzing related factors. Methods: Twenty-four patients with type I narcolepsy who visited our hospital from October 2017 to January 2020 and who met the relevant inclusion and exclusion criteria were selected. Simultaneously, healthy controls with matched basic characteristics were selected at a 1:1 proportion. Patient basic information was collected and the Epworth Sleepiness Scale was recorded. The nocturnal polysomnogram and multiple sleep latency test were performed, and the patients' electrophysiological characteristics were analyzed. The blood samples of the patient and control groups were collected and stored at -80°C after centrifugation. Plasma orexin levels were assessed by ELISA, following which the results of the two groups were compared,and the relevant factors were analyzed.Results: Our results revealed significantly lower plasma orexin levels in the narcolepsy patients compared to those in healthy subjects. There were no correlations between plasma orexin levels and sex, age, body mass index, disease duration, and the severity of sleepiness, and between plasma orexin levels and electrophysiological indicators, including mean sleep latency and sleep-onset rapid eye movement periods.Conclusions: Determining plasma orexin levels has the potential to replace the detection of CSF orexin levels.

Keywords

Effect of Low Resistance Thought Induction Psychotherapy(TIP) on perioperative insomnia in patients with newly diagnosed breast cancer

Min Zhang,Weidong Wang ,Dejian Huang,Li Sun

Department of Breast Cancer Surgery，Affiliated Hospital of Nanjing University of Traditional Chinese Medicine，Nanjing 210029，China

Objective: To observe the clinical efficacy of Low Resistance Thought Induction Psychotherapy(TIP) on perioperative insomnia patients with newly diagnosed breast cancer. Methods: Forty hospitalized insomnia patients with breast cancer before surgery were divided into TIP group (n=20) and control group (n=20). Patients in control group received conventional treatment and nursing, while those in TIP group received TIP intervention besides conventional treatment and nursing. The clinical efficiency of each group after treatment was compared using Pittsburgh sleep quality index, PSQI). Results: After the intervention, the PSQI index was significantly decreased in both groups($P < 0.05$). However, the scores of sleep quality, time to fall asleep, sleep efficiency, sleep disturbance and daytime dysfunction were significantly lower than that of the control group($P < 0.05$). The overall effect of TIP intervention was significantly better than that of control group ($P<0.05$). Conclusion: TIP is effective for improving the sleep quality of newly diagnosed breast cancer patients with perioperative insomnia.
Keywords Breast cancer; Sleep Disorders; Insomnia

The Prevalence of Insomnia and Its Risk Factors among Mongolian and Han Chinese adults in Inner Mongolia：A Cross-sectional study

Yanchao Chen1, Lixia Chen1,Ruiqi Wang1, Jie Yan3,Xiaojie Sui1,Zhiguo Guo1,Hua Ding3,Xiaoe Zhang1,Tingting Zhang2, Zhiqiang Zhang1, Zhijian Bai1,Ping Lv3,Li Zhang1,Yueqin Huang1,Dongsheng Lv1

1. The Third Hospital of Inner Mongolia Autonomous Region(Mental Health Center of Inner Mongolia Autonomous Region)
2. Peking University Sixth Hospital，Peking University Institute of Mental Health，NHC key Laboratory of Mental Health(Peking University)，National Clinical Research Center of Mental Disorder (Peking University Sixth Hospital)
3. Peking University Institute of Social Science Survey

Objective: To determine the prevalence of insomnia and its risk factors among Mongolian and Han Chinese adults in Inner Mongolia. Methods: From July 2019 to December 2019, a total of 14164 Respondents aged 18 and over who have resided locally for 6 months or more were selected from 246 communities among 41 districts or counties in Inner Mongolia. Respondents were selected from a provincial representative multi-stage disproportionate stratified sampling procedure. Insomnia was diagnosed with the Diagnostic criteria for non-organic insomnia of International Classification of Diseases-10.Socio-demographic information and the diagnose of other mental disorders were obtained by using the Composite International Diagnostic Interview-3.0. Finally, Mongolian and Han Chinese respondents were divided into two groups, Pearson correlation Analysis and logistic regression were adopted for statistical analysis. Results: Totally 12315 respondents finished the survey, and 11938 respondents were Mongolian (n= 2089) or Han Chinese(n=9849). The prevalence of Mongolian and Han Chinese adults were 4.63%（95%CI：2.58 %-6.68%）and 4.95%（95%CI：3.40 %-5.92%）respectively，and there was no significant difference between them（$x2$=0.127，P=0.953）. Mongolians and Han Chinese shared certain risk factors for insomnia：low economic status, living in the northeast region, suffering from alcohol use disorders, depression, chronic pain, heart disease, diabetes (or hyperglycemia), stomach ulcers or intestinal ulcers. However, there were still differences between them: 55 to 64 years old, no job and suffering from anxiety disorder were unique risk factors for insomnia to the Han Chinese, and the unique protective factors were higher education level (high school) and married marital status；whereas the unique risk factor for insomnia to Mongolian was a diet heavy on dairy products and red meat. Conclusions: There was no statistical difference in the prevalence of insomnia between Mongolian and Han Chinese adults, but the risk factors of insomnia were different among the two races, which might be caused by their different production and living habits.

Keywords

Survey of Perioperative Anxiety and Sleep Quality in China: A Multicenter Observational Study

Li Xirong1,2,Wen-Hao Zhang1, John P. Williams3,Tong Li4, Jian-Hu Yuan5,Yun Du6,Jin-De Liu7,Zhe Wu1,Zhao-Yang Xiao8,Rui Zhang2,Guo-Kai Liu9,Dong-Ya Zhang11,Hong Ma12,Qu-Lian Guo13,Jian-Xiong An1,2

1. Aviation General Hospital of China Medical University and Beijing Institute of Translational Medicine，Chinese Academy of Sciences
2. School of Anesthesiology，Weifang Medical University
3. Department of Anesthesiology，University of Pittsburgh School of Medicine
4. Department of Pain，Lanzhou Maternity and Child Healthcare Hospital
5. Department of Anesthesiology，Beijing Anorectal Hospital
6. Department of Anesthesiology，University of Chinese Academy of Sciences Affiliated Chongqing Hospital

7. Department of Anesthesiology，University of Chinese Academy of Sciences Affiliated North China Hospital

8. Department of Anesthesiology，Second Affiliated Hospital of Dalian Medical University

9. Department of Anesthesiology，Beijing University of Chinese Medicine Affiliated Dongzhimen Hospital

10. Department of Anesthesiology，Shengli Oilfield Central Hospital

11. Department of Anesthesiology，First Affiliated Hospital of Tsinghua University

12. Department of Anesthesiology，First Affiliated Hospital of China Medical University

13. Department of Anesthesiology，Xiangya Hospital of Central South University

Objectives: Anxiety and insomnia are common problems during perioperative period. The objectives of our study were to describe patient characteristics associated with preoperative anxiety and sleep quality and subsequently assess the relationship between preoperative anxiety and postoperative anxiety, pain, sleep quality, nausea and vomiting. Methods: This was an observational study conducted at Aviation General Hospital of China Medical University and 11 other tertiary hospitals in China from March to December 2019. Patients scheduled for selective operation from different clinical disciplines participated in this survey. Of surgical types, craniotomy, thoracotomy and laparotomy were categorized as highly invasive surgery. The State-Trait Anxiety Inventory (STAI) and the Athens Insomnia Scale (AIS) were used to assess anxiety and sleep quality respectively before surgery. Evaluations of anxiety, pain, sleep quality, nausea and vomiting were quantified using the visual analog scale on postoperative days 1 and 2. Results: Data from 997 patients were analyzed. Preoperatively, 258 (25.9%) patients had high anxiety (STAI-State＞ 44) and 345 (34.6%) patients showed insomnia (AIS≥6). Multivariate analyses showed a significant relationship between high anxiety and female gender (OR: 1.66, 95% CI: 1.08-2.57, p=0.02), highly invasive surgery (OR: 2.29, 95% CI: 1.29-4.06, p=0.005), higher trait anxiety (OR: 1.24, 95% CI: 1.20-1.28, p<0.001) and insomnia (AIS≥6, OR: 1.79, 95% CI: 1.17-2.76, p=0.008). Preoperative anxiety demonstrated a negative correlation (p<0.05) with postoperative anxiety following highly invasive surgery. However, this became a positive relationship following less invasive surgery (p<0.05). Besides, preoperative anxiety was also positively related to postoperative pain and poor sleep quality (p<0.05). However, the correlation between preoperative anxiety and postoperative nausea and vomiting was not statistically significant (p>0.05). Conclusion: Female gender, highly invasive surgery, higher trait anxiety and insomnia constituted independent risk factors for high preoperative anxiety. Postoperative anxiety, pain and sleep quality were significantly correlated with preoperative anxiety.

Keywords

Toll‑like receptor‑4‑mediated inflammation is involved in intermittent hypoxia‑induced lung injury

Fangfang Zou1,Xiaoli Su2

1.Hunan Chest HospitalXiangya Hospital

2.Central South University

Purpose: Intermittent hypoxia (IH) is a recognized risk factor for multiple organs damage, resulting in lung injury. Its pathophysiology is still poorly understood. Toll-like receptor 4 (TLR4) signaling plays a critical role in host immune response to invading pathogen and non-infectious tissue injury. The role of TLR4-mediated inflammation in IH-induced lung injury was investigated in this study.Methods: Lean adult male TLR4-deficient (TLR4-/-) mice and their controls (C57BL/6 mice) were exposed to either IH(FiO2 6–8% for 25 s, 150 s/cycle, 8 h/day) or air (normoxic mice) for 6 weeks. Animals were sacrificed after six weeks exposure, and the lung tissues were harvested for morphological and inflammatory analyses. The expression of TLR4 and nuclear factor kappa-B (NF-κB) P65 were examined by real-time quantitative polymerase chain reaction and immunohistochemical method. Serum cytokine levels of interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-α) were analyzed by enzyme- linked immunosorbent assay. Results: IH induced morphological and inflammation changes in the lung. IH for 6 weeks induced higher expression of TLR4 (C57BL/6-N vs C57BL/6-IH, $P < 0.05$) and resulted in higher release of TNF-α , IL-6 ($P < 0.05$), and NF-κB P65 ($P < 0.05$). These alterations were remitted by TLR4 deletion. Conclusions: TLR4-mediated inflammation plays an important role in the development of IH-induced lung injury in mice, possibly through mechanisms involving nuclear factor-κB. Targeting TLR4/NF-κB pathway could represent a further therapeutic option for sleep apnea patients.

Keywords

The impacts of obesity and craniofacial disharmony on obstructive sleep apnea (OSA) patients

Liping Huang,Xuemei Gao

Peking University School and Hospital of Stomatology

Objective: The purpose of this study is to explore the contribution of obesity and craniofacial disharmony to OSA severity，which often lead to sleep apnea together. Methods: All the OSA patients from January 2014 to December 2017 entered the study. Among 169 males and 38 females, they were divided into normal weight (BMI < 24kg /m2,55males and 22 females), overweight (24≤BMI< 28kg /m2,91 males and 14 females) and obese (BMI≥28kg/m2,23 males and 3 females). Multiple linear regression analysis was then used to identify BMI and the cephalometric measurement variables that had significant effects on AHI values in overall OSA

patients after controlling the age and gender. Subsequent pairwise comparisons were performed to define inter-group differences by Bonferroni post hoc analysis. Results: After controlling for gender and age, AHI were affected by BMI increasing, posterior airway narrowing, tongue elongation and inferiorly positioned hyoid bone. Among different groups, shorter maxillary and mandible, and steeper mandibular plane (P < 0.0167) appeared more in the normal body weight group, while the most severe skeletal restriction and the most obvious soft tissue enlargement (P < 0.0167) both contributed to the severity of sleep apnea in the obese group. Conclusions: Though obesity and skeletal malformations were both etiological factors of OSA, obesity seemed to have a greater influence in all BMI groups. Only in normal-weight group, it was affected by both cephalometric variables and BMI.

Keywords

The role of epigenetic abnormalities and intervention in OSA target organs

Yanru Ou,Dandan Zong,Ruoyun Ouyang

The Second Xiangya Hospital，Central South University

Obstructive sleep apnea (OSA) is a common condition that has considerable impacts on human health. Epigenetics has become a rapidly developing and exciting area in biology, and it is defined as heritable alterations in gene expression and has regulatory effects on disease progression. However, the published literature integrating both of them is not sufficient. The purpose of this thesis is to explore the relationship between OSA and epigenetics and offer better diagnosis and treatment options. Epigenetic modifications mainly manifest as posttranslational modifications in DNA and histone proteins and regulation of non-coding RNAs (ncRNAs). Chronic intermittent hypoxia (CIH)-mediated epigenetic alterations are involved in the progression of OSA and diverse multiorgan injuries, including cardiovascular disease, metabolic disorders, pulmonary hypertension, neural dysfunction and even tumors. This study provides deeper insights into the disease mechanism of OSA and potential applications of targeted diagnosis, treatment and prognosis in OSA complications.

Keywords

Application of Tower of Hanoi (TOH) in the Evaluation of Cognitive Impairment Caused by Chronic Insomnia

Yuan Wang1,Zucheng Han2,Jie Yuan2,Jie Chen2,Yaling Lei2,Fan Luo1,Wenting Liu1,Dongling Liu2,Pei Wang2,Cui Wang2,Ling Lin1

1.Shaanxi University of traditional Chinese Medicine

2.Shaanxi Provincial Hospital of Traditional Chinese Medicine

Objective: To study the application of Tower of Hanoi (TOH) in evaluating the severity and diagnostic value of cognitive impairment in patients with Chronic Insomnia Disease (CID). Methods: Tower of Hanoi (TOH) and Montreal Cognitive Assessment (MoCA) were performed on 65 patients with chronic insomnia and 35 normal people, and the differences between the two groups in key indicators were compared.Results: The mean value of number of TOH moving steps, the number of TOH wrong moving steps, the total time of TOH and the MOCA score were 30.29 ± 10.94, 5.17 ± 7.89, 231.46 ± 132.02 and 25.98 ± 3.02 respectively in the chronic insomnia patient group, and 31.37 ± 15.73, 4.00 ± 7.59, 114.17 ± 80.48 and 27.82 ± 1.64 respectively in the normal group. There was no significant difference in the number of moving steps and wrong steps of TOH between two groups (r=1.08, r=0.47, P>0.05); The total time of TOH had better sensitivity and specificity for identifying cognitive impairment (P<0.01). The MoCA score of insomnia group was significantly lower than that of normal group (P<0.01). Conclusion: (1)Tower of Hanoi has diagnostic significance in evaluating the cognitive impairment of chronic insomnia;(2)The cognitive impairment of chronic insomnia is reflected in the prolongation of the total time of TOH, which may be related to the decline of overall planning coordination ability and spatial short-term memory ability.

Keywords

Application of Rey–Osterriche Complex Figure Test in Cognitive Assessment of Chronic Insomnia Patients

Jie Yuan1,CHEN jie1,Yaling Lei1,Wenting Liu2,LIU wenting2,Zucheng Han1,Dongling Liu1,Pei Wang1,Ruolan Wang2,Yuan Wang1

1.Shaanxi Provincial Hospital of Traditional Chinese Medicine

2.Shaanxi University of Traditional Chinese Medicine

Objective: The Rey-Osterrieth Complex Figure Test (CFT) is commonly used to evaluate visuospatial constructional ability and visual memory in Alzheimer's disease and mild cognitive impairment. The purpose of this study was to evaluate the cognitive function of patients with chronic insomnia disease (CID) by CFT. Methods: People aged between 18 and 45 years with more than 12 years of education who came for physical examination between May and December 2020 were selected to participate in the insomnia

and cognitive assessment. According to the severity index of insomnia (ISI)≥7, they were divided into CID group and healthy control group. Patients with insomnia symptoms lasting less than 3 months were excluded. Subjects in both groups were examined by CFT. Results: ① In the CID group (N=65), the average ISI score was 15 ± 4.67, and the average course of disease was 42.2 ± 48.34 months. In the healthy group (N=35), the average ISI score was 2.77 ± 2.22; ② There were statistical differences in CFT copying score $(34.48\pm2.17, 35.59\pm0.88, P < 0.01)$, delayed recall score $(16.23\pm7.62, 23.94\pm5.05, P < 0.01)$, copying time(minutes) $(4.09\pm1.61, 3.34\pm1.51, P < 0.05)$ and delayed recall time (minutes) $(2.28\pm1.15, 3.03\pm1.29, P < 0.01)$ between the CID group and the healthy group. Conclusion: CID is inferior to healthy people in terms of visuospatial constructional ability and visual memory, and it takes longer time to copy images and less time to delay recall. It is suggested that CFT is sensitive to the recognition of cognitive impairment in CID and can be used to detect cognitive impairment in CID.

Keywords Rey-Osterrieth Complex Figure Test; Chronic insomnia disease; Cognitive impairment;

PPARγ regulates mitochondrial function and cell injury in intermittent hypoxia treated human umbilical vein endothelial cells

Ningfang Lian,Qichang Lin

The First Affiliated Hospital of Fujian Medical University

Purpose: Vascular endothelial injury is a common complication of obstructive sleep apnea (OSA). Chronic intermittent hypoxia (CIH) is the core pathophysiological feature of OSA. The study aimed to clarify the mechanism of CIH-related vascular endothelial injury. Methods: Human umbilical vein endothelial cells (HUVECs) were treated in IH condition; the expression levels of PPARγ were detected by western blot and qRT-PCR. Cell viability, the expressions of apoptosis-associated proteins and mitochondrial division fusion protein, the levels of mitochondrial membrane potential (MMP) and reactive oxygen species (ROS) were assessed via Cell Counting Kit-8 (CCK-8), western blot, and flow cytometry, commercial kit of ROS and JC-1 respectively. The PPARγ agonist rosiglitazone, the mitochondrial specific antioxidant tempo and PPARγ interfering RNA treated the cells respectively. Results: IH reduced cell viability, enhanced cell apoptosis, accumulated ROS, decreased MMP. The expression levels of PPARγ decreased in IH treated HUVECs. Both Rosiglitazone and tempo pretreatment improved cell viability and relived cell apoptosis. And Tempo pretreatment improved mitochondrial function. While PPARγ interfering reversed the protective effect of tempo on mitochondrial function and cell injury.Conclusions: PPARγ regulated cell viability and cell apoptosis of IH treated HUVECs by alter mitochondrial function, which enhanced the understanding of the pathogenesis of CIH-related vascular endothelial injury.

Keywords

Study on the changes of state anxiety and its awakening–sleep time and sleep phase in mice caused by the Triple test

Yue Yang,Tingli Li

School of Pharmacy，Heilongjiang University of Chinese Medicine

Objective: To observe the changes of state anxiety and its awakening-sleep time and sleep phase in mice induced by the Triple test. Method: Eighteen ICR male mice were used in this experiment and reared adaptively for 7 days. Under the conditions of anesthesia and stereotactic brain positioning, the electroencephalogram (EEG) and electromyogram(EMG) electrodes were embedded in the cortex and neck muscles of the mice. After the recovery period, the EEG and EMG signals of 24h were continuously traced as the sleep baseline before model replication. On the second day, each mouse was free to explore for 15 min in the Triple test at 12:00 am. After the completion of the daily test, continuous 24h EEG and EMG recordings were performed, The behavioral test and the EEG monitoring after the test occurred for 7 consecutive days. Result: The results showed that compared with the first day, it revealed a significant decrease in the inner time and % time of 3-6 days in OF ,and the number of entries and % time of 4-7 days in the open arms of EPM increased significantly, in LDB, time spent in the dark compartment of 2-4 days increased significantly ($p<0.05$ or 0.01). Compared to baseline, the awakening time and its proportion were significantly prolonged, NREM sleep and its proportion were significantly decreased on the 1-5 and 7 days, and a significant increase occurred in REM sleep and its proportion on the 1, 2, and 4 days ($p <0.05$ or 0.01). Conclusion: The triple test can replicate the state anxiety model of mice. It presented more anxiety-like behaviors in the first 4 days, and can induce sleep disorders in mice with state anxiety.

Keywords : Anxiety; Sleep; Electroencephalogram; Triple test

Effects of endurance exercise on sleep and activity status in aging Drosophila

Qiufang Li,Lan Zheng,Xiaoyi Jian,Jinglin Liu,Ting Huang

Hunan Normal University

Objective The intact expression of core clock genes is essential for organism homeostatic regulation and Clock (Clk) as one of drivers in core circadian gene plays a crucial role to maintain the circadian rhythm. Concurrently, the aging decline of sleep pattern and sleep structure has become the main cause of insomnia in the elderly. In this study, we investigate the effects of endurance exercise on sleep and activity status in aging Drosophila. Methods:GAL4 / UAS system was used to down-regulate the expression of Clk specifically in pigment-dispersing factor (PDF), a neuropeptide rhythmically released from sLNvs in the brain, and

combined with regular climbing exercise from the 3rd week to the 6th week of age. Drosophila activity monitor system (DAMS)was used to collect the activity data. and the sleep and activity status, including total sleep time, sleep fragments, sleep latency, number of deep sleep, activities per hourwere analyzedResults The results showed that the morning and evening activity peaks and day and night activities of 6-week-old flies (Pdf-Gal4/+) decreased significantly and ineffective sleep during the day increased , compared with those of 3-week-old flies with the same genetic background (Pdf-Gal4/+). The 3-week Drosophila with Clk RNAi (Pdf > Clk RNAi) showed similar characteristics with the 6-week normal flies (Pdf-Gal4/+) in the weakened bimodal pattern activities, meanwhile they have worse sleep quality during the day, and the 6-week Clk RNAi flies existed a reduced nighttime sleep volume and prolonged sleep latency. After 3 weeks of endurance exercise, the daytime sleep time and deep sleep frequency of normal aged Drosophila (Pdf-Gal4/+) increased. Conclusion Although the regular endurance exercise could not enhance the sleep quality of aged Clk RNAi Drosophila, but it can significantly improve the daytime sleep intensity by ameliorating age-related sleep inefficiency of the normal group.

Keywords

Neuropeptide S mainly from Kölliker–Fuse nucleus promotes wakefulness through activation of cognate receptor–neurons in the paraventricular thalamus

Yufeng Shao, Chenchen Cai,Yunong Chen,Yanli Ren,Guijuan Lu,Junfan Xie,Yiping Hou

Lanzhou University

Abstract: Objective Neuropeptide S (NPS) is a neuromodulator that concentratively expressed in the Kölliker-Fuse nucleus (KF) and pericoerulear area (Peri-LC) in mice. NPS and its receptor (NPSR) system participates multiple biological effects, such as enhancing locomotor and exploratory activities, evoking anxiolytic-like effects, promoting wakefulness, and facilitating olfactory function and memory. The paraventricular thalamus (PVT), a newly identified area that critical for wakefulness, highly expressed NPSR suggesting that NPS-NPSR system may be involved in the regulation of sleep-waking states through PVT. The present study was undertaken to investigate effects of NPS on the sleep-waking states. Methods Microinjection, immunohistochemistry, retrograde tracing and fluorescence in situ hybridization (FISH) in mice were used in this study. Results We found that PVT microinjection of 0.05 and 0.5 nmol NPS significantly increased the waking time (32.49 $\pm$ 5.08 min and 59.06 $\pm$ 7.95 min respectively, vs. 11.44 $\pm$ 3.24 min seen with saline injections, $p < 0.05$ and $p < 0.001$) by delaying episode duration. The promoting effect of NPS was blocked by the selective NPSR antagonist [D-Val5]NPS. Ex vivo c-Fos and NPSR immunohistochemistry revealed that NPS markedly enhanced Fos expression in the NPSR-immunoreactive neurons in the PVT. In addition, we combined retrograde tracing and fluorescence in situ hybridization to map the origin of NPS neurons. The

results shown that 22.46 ± 4.44% and 21.10 ± 3.66% NPS neurons in the KF and Peri-LC input to PVT respectively. In total NPS neurons that input to PVT, 83.19 ± 4.08% neurons were from KF and 16.44 ± 4.44% neurons were from Peri-LC respectively. Conclusion The primary results show that NPS mainly from KF nucleus promotes wakefulness through activation of cognate receptor-neurons in the PVT.

Keywords neuropeptide S; neuropeptide S receptor; paraventricular thalamus; antagonist; Kölliker-Fuse nucleus

Preliminary exploration of rhinomanometer in oral treatment of OSA patients

Xuehui Chen,Xuemei Gao
Peking University School and Hospital of Stomatology

Objective: Patients with obstructive sleep apnea (OSA) are known to have increased nasal resistance. Oral appliance is one of the commonly used appliances for the treatment of OSA, the main function of which is to advance the mandible and reduce the collapsibility of the upper respiratory tract. However, there are few studies on the effect of oral appliance on nasal function. The purpose of this study was to investigate the effect of oral appliance on nasal resistance in patients with OSA.Methods: Exclusion criteria were rhinitis, asthma and other respiratory diseases, 7 males and 6 females with OSA were recruited in the study. Before and after wearing oral appliance, all participants used NR6 nasal manometer to measure nasal resistance, and SPSS 22.0 statistical software was used for non-parametric test of paired samples for statistical analysis. $P \leq 0.05$ means the difference is statistically significant. Meanwhile this study was approved by the ethics committee. Results: Oral appliance significantly improved the nasal expiratory resistance (p=0.016), the average inspiratory resistance (p=0.023) and the average expiratory resistance (p=0.023) on the dominant side. At the same time, the nasal inspiratory resistance and expiratory resistance of the non-dominant side decreased, but there was no significant difference. Conclusions: Oral appliance can improve the dominant nasal expiratory resistance, average inspiratory resistance and average expiratory resistance in patients with OSA, but a large sample study is still needed.

Keywords

Analysis of the relationship between anxiety, depression and sleep efficiency in patients with insomnia

Haiyan Gou,Yulan Zhu,Yanmei Zhu,Wei Sun,Jia He,Yan Chen
The 2nd Affiliated Hospital of Harbin Medical University

Methods: Outpatients and inpatients diagnosed as insomnia in the sleep monitoring center of in our hospital during March 2019-September 2019 were enrolled in the study. , SAS, SDS, ESS, PSQI, PSG were

applied to evaluate patients' sleep efficiency, and to maintain sleep efficiency. Results: 1. Demographic characteristics: A total of 21 patients with insomnia were enrolled, including 8 males and 13 females, aged 21-70 years old. It suggested that female patients had a higher proportion in the insomnia population. 2. The average SAS score was 63.7 ± 5.80 points. It suggested that insomnia patients with different degrees of anxiety, moderate anxiety accounted for the highest proportion. 3. The average SDS score was 66.5 ± 5.9, suggesting that insomnia patients were complicated with different degrees of depression, and the proportion of moderate depression was the highest. 4. The average score of ESS was 6.5 ± 4.9. It suggested that insomnia patients were less prone to daytime drowsiness. 5. The PSG monitoring SE of severe anxiety group was $30.90\pm7.21\%$, moderate anxiety group $57.4\pm12.4\%$, mild anxiety group $80.3\pm9.8\%$, suggesting that SE is related to anxiety level. The PSG monitoring SME of severe anxiety group was $33.4\pm5.9\%$, moderate anxiety group was $62.7\pm11.2\%$, mild anxiety group was $88.1000\pm4.0792\%$, suggesting that SME is related to anxiety level. 6. The PSG monitoring SE of the mild depression group was $88.5\pm1.6\%$, the moderate depression group was $68.1\pm11.9\%$, and the severe depression group was $38.8\pm9.7\%$.The PSG monitoring SME of the mild depression group was $91.8\pm1.65\%$, the moderate depression group was $71.4\pm11.3\%$, and the severe depression group was $43.7\pm11.6\%$, suggesting that SME was related to depression degree. Conclusions: In insomnia patients with comorbid anxiety and depression state of high occurrence, we should not onlpay attention to clinical diagnosis and treatment for insomnia, butalso pay attention to the state of anxiety and depression, and in a timely manner to psychological counseling of patients with insomnia, cognitive behavioral therapy, anti-anxiety and antidepressant treatment.

Keywords

Research Development in Paediatric Sleeping Disorders and Correlates

Jie Zhang1,Bette Zhang2
1.Hunan Children's Hospital
2.School of Education，The University of Queensland，Australia.

Sleep disorders are the most frequently encountered problems in paediatric clinics. About 25-50% of pre-schoolers and 40% of adolescents have various degrees of sleeping problems. It has been well-documented that inadequate sleeping and sleeping disorders are often accompanied by abnormal behaviour, hyperactivity, lack of concentration, poor memory, which has been termed as neurocognitive dysfunction. Therefore, it is paramount to have early detection and appropriate therapeutic measures and treatment. Currently, most paediatric sleeping studies at home are concerned with epidemiology of certain medical conditions. There have been scarce publications on common clinical sleeping problems and associations. This paper intended to shed some light on the developments of sleeping disorders in children and the correlates.

Keywords

Effects of obstructive sleep apnea on brain electrical activity

Panting Wu1,Yunxiao Wu1,Li Zheng1,Qiaoli Zhang2,Zhifei Xu1

1.Beijing Children's Hospital

2.Ordos Central Hospital

Objective: To compare electroencephalogram (EEG) activities among children with different degrees of OSAS, and to explore the influence of OSAS on EEG.Methods: Children aged 6-12 years old who came to the Sleep Center of Beijing Children's Hospital Affiliated to Capital Medical University for snoring or mouth breathing complaints were recruited from July 2019 to December 2019. Medical history collection, routine physical examination, overnight PSG recording and 6-minute resting state EEG collection were completed in the enrolled children. The differences in the relative EEG power between the groups were compared. Based on the complexity and synchronicity of EEG signals, the brain injury index obtained by multiple brain functional state indexes was automatically calculated to objectively and quantitatively reflect the changes of EEG activitiesResults: Based on the power spectrum analysis, the relative power of α, θ, β and δ waves among the primary snoring group and the mild OSAS group, moderate OSAS group and severe OSAS group had no statistical significance. The brain injury index of the primary snoring group to the severe OSAS group showed a gradually increasing trend.The brain injury index was significantly correlated with OAHI, mean oxygen saturation, and the percentage of REM sleep period in total sleep time. Conclusion: 1. There was no significant difference in the relative power of α, θ, β and δ waves between the primary snoring group and the OSAS group at all levels. 2. The analysis of brain injury index showed that with the increase of OAHI, the brain injury index also increased gradually, and the EEG activity was more abnormal. 3. The brain injury index was independently correlated with OAHI, mean blood oxygen saturation and the percentage of REM sleep in total sleep time.

Keywords

Study on Brain State in Patients with Narcolepsy

Yu JieYang,Qi Tang,Yaru Wang,Huimin Li,Zan Wang

The first hospital of Jilin University

Objective: To study the characteristics of the brain state in narcolepsy patients. Methods: A total of 27 patients with narcolepsy were recruited from out-patients of the Neurology Department, First Hospital of Jilin University from January 2020 to January 2021, and 27 sex- and age-matched healthy controls were recruited. We evaluated the brain state examination, General Hospital Anxiety/Depression Scale (HAD), Patient Health Questionnaire-9 (PHQ-9) and Epworth sleepiness scale (ESS) before, one month and three

months after taking medicine. The control group was given only once brain state examination. The brain waves in 6 minutes' resting state were collected and processed by wavelet analysis. Sixteen related indexes including brain energy consumption, brain inertia, brain chaos, sleepiness, alertness, brain fatigue, anxiety tendency, left and right brain lateralization, brain introversion, brain stability, brain inhibition, memory processing, external focus, internal focus, excitation density and reaction speed were obtained. Then we compared the characteristics of brain state between the two groups and analyzed the correlation between the brain state of narcolepsy patients and polysomnography (PSG) + multiple sleep latency test (MSLT) results, HAD, PHQ-9, ESS scores. Besides, we compared the changes of brain state and scales before and after treatment in the study group. Results: The brain chaos index, brain inertia index, sleepiness index, anxiety tendency index, brain stability index, internal focus index and excitation density index in patients with narcolepsy were higher than these of healthy controls (P < 0.05). The alertness index and reaction speed index in patients with narcolepsy were lower than these of healthy controls (P < 0.05). The brain fatigue index was negatively correlated with mean sleep latency in MSLT in narcolepsy group (r = - 0.454, P < 0.05). The anxiety tendency index was positively correlated with apnea-hypopnea index (AHI) in narcolepsy group (r = 0.420, P < 0.05). There was a positive correlation between sleepiness index and PHQ-9 score in narcolepsy group (r = 0.324, P < 0.05), a positive correlation between sleepiness index and HAD anxiety score (r = 0.353, P < 0.05), and a negative correlation between alertness index and HAD depression score (r = - 0.253, P < 0.05). The brain state indexes and ESS score in narcolepsy group didn't change significantly after one-month treatment; the brain fatigue index and ESS score of narcolepsy group decreased after three-month treatment (P < 0.05). Conclusion: The brain chaos, brain inertia, sleepiness, internal focus, anxiety tendency, brain stability, excitement density index increased, reaction speed and alertness index decreased in patients with narcolepsy. The brain fatigue index in patients with narcolepsy was negatively correlated with the average sleep latency in MSLT, the anxiety tendency index was positively correlated with AHI, the sleepiness index was positively correlated with PHQ-9 and HAD anxiety scores, and the alertness index was negatively correlated with HAD depression score. After three-month treatment, the brain fatigue index and ESS score in patients with narcolepsy decreased.

Keywords narcolepsy, excessive daytime sleepiness, brain state

Study on sleep quality and brain functional state of focal epilepsy

Guo Xiao,dong Wang ,Mingyang Tang ,Ying Wang, Zan Wang

the first hospital of Jilin university

Objective:In this study, the brain functional state quantitative monitoring system was used to evaluate sleep quality and other cerebral advanced functions of patients with focal epilepsy to explore the clinical significance of the brain functional state quantitative monitoring system parameters. And to explore the influencing factors of sleep quality in epileptics. Methods: In this study, we selected 102 focal epilepsy

patients from the outpatient department of neurology from July 2020 to December 2020 in the First Hospital of Jilin University and 102 healthy controls who were matched with the sex and age of the epilepsy patients. General and clinical data of epilepsy patients and healthy controls was collected. Pittsburgh sleep quality index (PSQI) was used to evaluate the sleep quality of patients. Hospital Anxiety/Depression Scale (HAD) was used to evaluate the anxiety and depression of patients. Fatigue Severity Scale (FSS) was used to evaluate the fatigue degree of patients. Each patient underwent the brain functional state quantitative monitoring system. After filtering, wavelet analysis and a series of EEG analysis, 20 quantitative parameters of brain functional state were extracted: brain energy consumption, brain chaos, hypoxia index, sleep index, sleep breathing index, emotional conflict, anxiety tendency index, depression tendency index, reaction speed, left and right lateral brain, brain convergence, brain inhibition, brain stability, brain coordination, memory processing, external focus, internal focus, excitation density, brain inertia, brain fatigue. Then discuss the characteristics and clinical significance of quantitative parameters of brain functional state in epilepsy patients according to the above results and explore the influencing factors of sleep quality in epilepsy patients. Result: 1. Brain energy consumption, brain chaos, brain inertia, emotional conflict, brain fatigue, attention, respiratory index, hypoxia index and anxiety tendency in epilepsy patients were higher than those in control group(P<0.05). Brain introversion, memory processing, reaction speed and brain coordination were lower than those in control group(P<0.05). 2. PSQI total score was negatively correlated with sleep index (r=-0.321, P=0.001); FSS total score was positively correlated with brain fatigue (r=0.387, P<0.001). FSS total score was positively correlated with brain inertia (r=0.276, P=0.001). 3. The excitation density of epilepsy patients with interictal discharge not limited to the frontal/temporal lobe was higher than that of epilepsy patients with interictal discharge only limited to the frontal/temporal lobe (P<0.05). 4.Comparison of quantitative parameters of brain functional state in patients with epilepsy: the brain inertia, brain fatigue and external focus of the obvious fatigue group were higher than those of the no obvious fatigue group(P<0.05). Patients with anxiety had higher brain energy consumption and emotional conflict than those without anxiety, and lower brain introversion and memory processing than those without anxiety(P<0.05). 5.The linear regression analysis of PSQI showed that age, seizure frequency, seizure in sleep, anxiety, depression, and fatigue were the related risk factors for poor sleep quality in epilepsy patients. Among them, fatigue, age, seizure in sleep, and seizure frequency were independent risk factors for poor sleep quality in epilepsy patients. 5. The linear regression analysis of FSS showed that age, seizure frequency, anxiety, depression and sleep quality are the related risk factors of fatigue in epilepsy patients. Among them, anxiety, sleep quality and age are the independent risk factors of fatigue in patients with epilepsy. Conclusion: 1. Brain energy consumption, brain chaos, brain inertia, emotional conflict, brain fatigue, attention, respiratory index, hypoxia index and anxiety tendency in epilepsy patients were higher than those in control group. Brain introversion, memory processing, reaction speed and brain coordination were lower than those in control group. 2. Sleep index can be used to evaluate sleep quality in patients with epilepsy. Brain inertia, brain fatigue, external focus can be used to assess the degree of fatigue in patients with epilepsy. Brain energy consumption, emotional conflict, brain convergence, memory processing can reflect

the anxiety of epilepsy patients. 3. Age, seizure frequency, seizure in sleep, anxiety, depression, and fatigue were the related risk factors for poor sleep quality in epilepsy patients. Among them, fatigue, age, seizure in sleep, and seizure frequency were independent risk factors for poor sleep quality in epilepsy patients. 4. Age, seizure frequency, anxiety, depression and sleep quality are the related risk factors of fatigue in epilepsy patients. Among them, anxiety, sleep quality and age are the independent risk factors of fatigue in patients with epilepsy. 5. Excitatory density is expected to be an indicator for evaluating interictal discharge in epileptic patients.

Keywords epilepsy, sleep quality, brain functional state, fatigue

Sporadic Creutzfeldt–Jakob disease that appears to be Sporadic fatal insomnia：A case report and review of the literature

Qingqing Sun,Pingping Shen,HongmeiMeng,Zan Wang,Li Cui
the first hospital of Jilin University

The aim of this review was to assist in characterizing further clinicopathological subtypes of sporadic Creutzfeldt–Jakob disease (sCJD) based on clinical symptoms and ancillary tests. This article provides an overview of the latest development in the diagnosis of clinicopathological subtypes of sCJD，particularly the thalamic form of sCJDMM2 (Also known as sporadic fatal insomnia). Identification of sCJD subtypes can predict the prognosis. Currently, the diagnosis of sCJD subtypes is mainly based on brain tissue biopsy or autopsy. We describe the clinical characteristics, electroencephalogram, polysomnography, positron emission tomography-computed tomography and other neuroimaging, skin tissue biopsy, and whole blood PRNP gene sequencing of the case, which was eventually diagnosed as sCJDMM. We presented this case as a reminder to consider sporadic fatal insomnia (sFI) in the differential diagnoses of sCJD.

Keywords sCJD, sFI, sCJDMM, PSG, PET, clinical diagnostic criteria

MiR–130a–3p targets PPARγ to regulate Intermittent hypoxia related vascular endothelial cell injury

Ningfang Lian, Qichang Lin
The First Affiliated Hospital of Fujian Medical University

Objective 1. To identify the target proteins in CIH-related vascular dysfunction by proteomics analysis. 2. To explore the potential mechanism of miR-130a-3p in IH-induced vascular endothelial injury. Methods 1. A comparative proteomics analysis was conducted in aortic samples of rats treated with CIH and those with normoxia. Bioinformatics analyses were performed to determine the potential roles of major proteins. The expressions of target proteins were measured by western blotting. 2. The target miRNA of PPARγ were

predicted and verified by bioinformatics analysis and luciferase assays. The effect and potential mechanism of miR-130a-3p in IH-treated vascular endothelial injury were detected by rescue experiment. Results 1. 3593 proteins in aortic tissues of rats were quantified. 92 upregulated proteins and 468 downregulated proteins were identified when the cutoff of fold change was set at 1.5 (CIH vs. normoxia). The results of bioinformatics analysis revealed that the differentially expressed proteins were enriched in the processes of energy metabolism and lipid metabolism. Reduced expression level of PPARγ protein was identified in thoracic aortic tissues of rats with CIH by proteomics analysis and western blotting (p<0.05). 2. Bioinformatics revealed that the seed sequence of miR-130a-3p is complementary to the 3'UTR site of PPARγ, which suggested that PPARγ may be a target gene of miR-130a-3p. Dual-luciferase reporter also confirmed that PPARγ was the direct downstream target of miR-130-3p. In rescue experiment, HUVECs were transfected with Si-PPARγ, miR-130-3p inhibitor, the effects of miR-130-3p silence on cell viability, cell proliferation, the levels of apoptosis-related proteins and the cell apoptotic rate were all reversed by PPARγ knockdown (all p<0.05). Conclusions 1. PPARγ is critical in endothelial dysfunction of rats with CIH. Additionally, further studies on these differentially expressed proteins associated with IH-related endothelial dysfunction are necessary. 2. miR-130-3p mediates IH-induced vascular cell injury by target the protein of PPARγ.
Keywords

Epigallocatechin–3–gallate inhibits self–renewal ability of lung cancer stem–like cells through inhibition of CLOCK

Pan Jiang,Shanqun Li
Zhongshan Hospital，Fudan University

Circadian rhythm plays an important role in diverse physiological processes. Abnormal expression of circadian rhythm genes is associated with increased risk of disease, including different types of cancer. The cancer stem cell (CSC) hypothesis suggests that there is a small subset of stem-like cells within tumors that are responsible for tumor initiation. However, the biological effect of circadian rhythm on CSCs remains largely unknown. Studies have highlighted that the circadian rhythm protein CLOCK controls key aspects of various diseases. In the present study, lung cancer stem-like cells were successfully enriched using a sphere formation assay. Next, it was observed that CLOCK mRNA and protein expression levels in the A549 and H1299 sphere cells were notably increased compared with those in the corresponding parental cells. In addition, flow cytometry was performed to isolate CD133+ cells and, consistently, CLOCK expression was also found to be markedly upregulated in CD133+ lung cancer cells. Subsequently, to determine the effect of CLOCK on lung cancer stem cells in detail, CLOCK was knocked down using targeted short inhibiting RNA and the results demonstrated that the sphere-forming ability of the A549 and H1299 cell lines was reduced.

In addition, CSC-like properties, including the expression of CD133, CD44, sex determining region Y-box 2, Nanog and octamer-binding transcription factor 4, were markedly decreased in the A549 and H1299 sphere cells following knockdown of CLOCK. Epigallocatechin-3-gallate (EGCG), a green tea polyphenol, has been reported to be a potential anticancer phytochemical. EGCG was found to repress CLOCK expression in A549 and H1299 sphere cells. In addition, EGCG also decreased the ratio of CD133+ cells. The Wnt/ β -catenin pathway was notably inactivated by the knockdown of CLOCK in A549 and H1299 sphere cells. Subsequently, using a xenograft model, it was demonstrated that EGCG suppressed the CSC-like characteristics of lung cancer cells by targeting CLOCK. In conclusion, the present study demonstrated that EGCG inhibited the self-renewal ability of lung cancer stem-like cells by targeting CLOCK.

Keywords

Dissociation of subjective and objective alertness during prolonged wakefulness

Chao Hao,Mingzhu Li,Ning Ma

South China Normal University，Center for Sleep Research，School of Psychology

Background: Although the deterioration of subjective and objective alertness during prolonged wakefulness has been investigated rigorously, whether perceived sleepiness and fatigue are consistent with actual decrements in behavior performance in the time course is still disputed. The present study examined the dissociation between decrements of subjective alertness and performance deficits during prolonged wakefulness of one night and explored the relationship between body temperature and the impairments of subjective and objective alertness. Participants and Methods: Thirty-eight participants (27 females; age: 21.76 ± 2.37 years old) underwent prolonged wakefulness for one night in habitual bedtime. Participants completed a 10-min PVT to assess objective alertness. Fatigue and sleepiness ratings to assess subjective alertness every 2 h, and body temperature was measured every hour during scheduled wakefulness. Results: Subjective alertness showed a linear decline across time, but the magnitudes of objective performance deterioration increased significantly between 4:00 and 6:00 am. The increasing magnitudes of performance deficits were associated with the change of body temperature between 4:00 and 6:00 am. Conclusion: These results indicate that the perceived degree of decline in alertness is temporally dissociated with the actual decline in objective vigilance with increased duration of wakefulness. The dissociation of magnitudes of subjective and objective alertness decrements mainly occurs between 4:00 and 6:00 am and the changes of performance deficits have a relationship with body temperature.

Keywords

Isolation of Vigilance and Sleepiness during Sleep Deprivation: a resting–state fMRI study

Yun Tian1,2,Chao Xie3,4,Xu Lei1,2

1. Southwest University
2. Key Laboratory of Cognition and Personality (Ministry of Education)
3. Institute of Science and Technology for Brain-Inspired Intelligence，Fudan University
4. Key Laboratory of Computational Neuroscience and Brain-Inspired Intelligence (Fudan University)，Ministry of Education

Subjectively reported sleepiness and objectively measured vigilance are often used to assess and monitor operating performance. However, some shreds of evidence have shown that the response patterns of the two measures of sleep loss are independent of each other. The neural mechanism behind this phenomenon remains unclear. The current study aimed to investigate whether subjective sleepiness and objective vigilance were associated with each other and further located the neural mechanism of isolation of object and subject parameters. A total of 33 participants were enrolled in the study, and sleepiness, vigilance, and resting-state fMRI data were collected through acute sleep deprivation lasting 34 hours. Firstly, the correlation analysis showed that there was no statistically significant correlation between the changes of vigilance and sleepiness during the sleep deprivation period. Then, through whole-brain functional connectivity analysis combined with machine learning, we found that the different functional connectivity patterns underline the isolation of these two factors during sleep deprivation. The functional connectivities involved in characterizing the vulnerability of objective vigilance are more extensive, involving the collaboration of multiple functional brain networks, such as the default network and frontal-parietal network. The functional connectivity involved in characterizing the vulnerability of subjective sleepiness is limited to the communication between the subcortical thalamus and the somatosensory cortex. This work could help us understand how sleep deprivation affects an individual's cognition and behaviors, and evaluate and predict the performance during sleep loss.

Keywords

Study on the role and mechanism of microglial P2X7/NLRP3 inflammasome pathway in cognitive impairment induced by chronic sleep deprivation in mice

Jie Wu

General Hospital of Tianjin Medical University

Objective: To observe the effects of P2X7/ NLRP3 inflammasome pathway on cognitive function, inflammatory cytokines, microglia morphology and polarization function in the hippocampus of chronic sleep deprivation mice, and to make a preliminary exploration on the role and mechanism of P2X7 in cognitive impairment caused by chronic sleep deprivation. Methods: MMPM was used to establish sleep deprivation model for 5 days.C57BL/6J mice were randomly divided into 5 groups with 6 mice in each group, which were CC group, SD group, SD+BBG (P2X7 antagonist) group, SD+ BzATP (P2X7 agonist) group and SD+PBS group. Morris water maze was used to detect the cognitive function of mice, microglia cell morphology was observed by immunofluorescence staining, protein was detected by Western Blot, and mRNA was detected by RT-qPCR. Results: 1. After sleep deprivation, the molecular expression of P2X7/ NLRP3 pathway in mouse hippocampus increased ($P<0.05$).2. After sleep deprivation, the hippocampal microglia were enlarged, the surface markers of M1-type microglia and pro-inflammatory cytokines were increased, the surface markers of M2-type microglia and anti-inflammatory cytokines were decreased($P<0.05$).3. After intraperitoneal injection of BBG and BzATP, the expression of P2X7/ NLRP3 pathway molecule was decreased or increased, the cognitive function of mice was improved or impaired, the microglia cell body became smaller or larger, the M1-type microglia and pro-inflammatory cytokines were decreased or increased, and the M2-type microglia and ani-inflammatory cytokines were increased or decreased ($P<0.05$). Conclusion: The P2X7/NLRP3 inflammasome pathway may aggravate the cognitive impairment after sleep deprivation by influencing the polarization of microglia and promoting neuroinflammatory damage in mice. P2X7R may be an ideal drug target for cognitive impairment after chronic sleep deprivation, providing new theoretical support and treatment directions for clinical cognitive impairment after sleep deprivation.
Keywords

The impact of screen time changes on anxiety during the COVID–19 pandemic: Sleep and physical activity as mediators

Qiyu Chen,Ning Ma

Center for Sleep Research，School of Psychology，South China Normal University

Under the burden caused by COVID-19 and rapid lifestyle changes, the prevalence of anxiety has been observed in several studies. Many people increased their screen time due to psychological needs and

social requirements. The negative impact of excessive screen time on mental health has been confirmed in previous studies. The current study investigated the relationship between screen time changes and anxiety symptoms during the pandemic. Furthermore, we examined whether sleep and physical activity would mediate the association between screen time changes and anxiety. This study was conducted from March 2020 to April 2020 in a sample of 970 participants via an online questionnaire. Findings from the ordinal logistic regression analyses revealed the adverse effect of increased screen time on anxiety. After adjusting irrelevant variables, people who reduced their screen time significantly were more likely to report higher levels of anxiety than those who kept their screen time unchanged. In multiple mediation analyses, sleep quality directly mediated the association between screen time changes and anxiety, while sleep latency did not. Furthermore, the longer sleep latency caused by increased screen time would amplify anxiety by affecting sleep quality. In addition, the relationship between screen time changes and anxiety was also mediated by physical activity. We concluded that the appropriate time of using electronic devices might help reduce the anxiety symptoms. Besides, sleep and physical activity can alleviate the negative effects of increased screen time as important mediators.

Keywords

Utility of Type IV Portable Sleep Apnea Monitors for Diagnosing Obstructive Sleep Apnea

Yanxia Xu,Qiong Ou

Guangdong Provincial People's Hospital/Guangdong Academy of Medical Sciences/Guangdong Provincial Geriatrics Institute

Objective: To evaluate the accuracy and reliability of type IV portable monitor (PM) devices in the diagnosis of obstructive sleep apnea (OSA). Methods: A total of 182 patients aged 18 years or older were included in the research. All night laboratory polysomnography (PSG) and PM monitoring were performed simultaneously. PSG data were scored according to recommended guidelines of the American Academy of Sleep Medicine (AASM) while PM data were analyzed automatically. Results: There was a strong correlation ($r=0.858$, $p < 0.001$) between the apnea-hypopnea index (AHI) values from PSG testing (20.6 ± 18.9/h) and the oxygen desaturation index (ODI) from the type IV devices (32.2 ± 25.4/h). The mean difference (AHI from PSG, ODI from PM) was positive at 11.6 (-14.6, 37.8)/h. Compared to PSG for detecting AHI≥5/h, the PM demonstrated sensitivity of 86%, specificity of 67%, the area under the ROC curve of 0.90 and the weighted kappa of 0.42. Compared to PSG for detecting AHI ≥15/h, the PM demonstrated sensitivity of 73%, specificity of 97%, the area under the ROC curve of 0.94 and the weighted kappa of 0.62. Conclusion: These results showed that IV PM devices had good accuracy and precision in evaluating the moderate to severe OSA.

Keywords

Efficacy of online versus face–to–face cognitive behavior therapy for Insomnia: a randomized controlled trial

Junjun Chen1,Yishan Xu2,Fiona Barwick2,Wenrui Zhao3,Jie Gao1,Juan Li1,Chenyu Li1

1.Chongqing Traditional Chinese Medicine Hospital

2.Stanford Sleep Medicine Center

3.Southwest University

Objective: Cognitive behavioral therapy for insomnia (CBT-I) is used to treat insomnia, but the propagation and implementation of face-to-face CBT-I are limited. Online CBT-I costs less time and energy. Based on the above reasons, our study aimed to compare the effect of online and face-to-face CBT-I for improving the symptoms of insomnia and emotional symptoms.Methods: A total of 60 participants with chronic insomnia were randomized to 5 sessions of CBT-I delivered via online (n=43) or face-to-face (n=17) communications. Generalized anxiety disorder-7 (GAD-7), patient health questionnaire-9 (PHQ-9) were conducted to evaluate participants' emotional states. Pittsburgh sleep quality index (PSQI), insomnia severity index (ISI), and dysfunctional beliefs and attitudes about sleep-16 (DBAS-16) were used to evaluate their sleep quality, insomnia symptoms, and beliefs and attitudes about sleep.Results: Compared to before-treatment, large treatment effects were found both in online group and face-to-face group for insomnia symptoms, sleep quality, and sleep related beliefs and attitudes (online group: tISI=5.93, p＜ 0.05; tPSQI=3.23, p＜ 0.05; tDBAS=6.90, p＜ 0.05; face-to-face group: tISI=9.08, p＜ 0.05; tPSQI=5.30, p＜ 0.05; tDBAS=8.06, p ＜ 0.05). Similar significant results were also yielded in emotional status (online group: tGAD-7=2.28, p ＜ 0.05; tPHQ-9=4.79, p＜ 0.05; face-to-face group: tGAD-7=3.96, p＜ 0.05; tPHQ-9=2.89, p＜ 0.05). The changes of sleep quality, sleep related beliefs and attitudes, and emotional status between the two groups revealed no significant difference(p＞ 0.05), while one of insomnia symptoms assessed by ISI were statistically significant (t [58]△ISI=-2.43, p＜ 0.05).Conclusions: Our results indicated that online CBT-I is not obviously inferior to face-to-face delivery for improving insomnia symptoms and emotional status. Moreover, online CBT-I could be more efficient and cost-saving, and more available for individuals suffering from insomnia.

Keywords

The level of plasma neurofilament light chain and its correlation with motor and cognition function in idiopathic rapid eye movement sleep disorder

BingXin Song1,Xuan Zhang2,XiaoZhe Wang1,Li Ma1,JingShan Chen1,Rong Xue1

1.Tianjin Medical University General Hospital

2.Tianjin Medical University General Hospital Airport Site

Idiopathic rapid eye movement sleep behavior disorder（iRBD）is characterised by an increase of unpleasant dreams and decreased muscle tone. It has the risk of transforming into α-synuclein disease including parkinson＇s disease(PD). It was found that the increase of plasma neurofilament light chain（Nfl）was related to the decrease of motor and cognitive function of PD. iRBD patients also existed motor and cognition decline with changes of matter microstructure.We aim to compare the level of plasma Nfl between patients with iRBD and healthy controls, and to analyze the correlation of plasma Nfl with motor and cognitive function in the case group. Patients were collected from the Department of Neurology and Sleep specialist Clinic of Tianjin Medical University General Hospital from October 2014 to February 2021.22 iRBD patients who met the diagnostic criteria of ICSD-3 were included as iRBD group.18 healthy controls who had no complaints of abnormal sleep behavior at night were included in the HC group and their age, sex were matched with those of the iRBD group. All subjects were collected the basic information and motor and cognition function scores including the MDS-UPDRS III, the alternate tapping test,3-Metre Timed-Up-and-Go test,Flamingo balance test,MMSE, VFT,AVLT, ROCF, SDMT, and Stroop Color Word Test.The blood of all the subjects was collected and the level of Nfl in plasma was measured by single molecular array (SIMOA).Compared with HC group, the level of plasma Nfl in iRBD group was higher(P<0.05).In iRBD group, the level of plasma Nfl was negatively correlated with the immediate score of digital symbol conversion test (SDMT) (r=-0.477,P=0.033 < 0.05). There was no significant correlation with other cognitive test scores and motor function test (P>0.05). Plasma Nfl is an expectical blood biochemical marker for monitoring the changes of cognitive function in patients with iRBD.

Keywords idiopathic rapid eye movement sleep disorder, neurofilament light chain

Obstructive sleep apnea, short sleep duration, and their joint effect on cardiovascular diseases in adults: The Sleep Heart Health Study

Xiaoyu Wang1,Binbin Han1,Shanshan Wang1,Yilin Zhao1,Zhengzheng Chang1,Guohua Li1,Yujing Sun1,Zhigang Chen1,Yan Li1,Min Zhang2,Sizhi Ai1,Guoan Zhao1

1.The First Affiliated Hospital of Xinxiang Medical University

2.King's College London British Heart Foundation Centre of Excellence

Background: Previous studies have suggested that short sleep duration (SSD) and obstructive sleep apnea (OSA) are risk factors for cardiovascular diseases (CVD). However, the joint effect of these risk factors on CVD risk remains unclear.Methods: Data were derived from the Sleep Heart Health Study (SHHS). Sleep duration and OSA status were determined by one cycle of overnight polysomnography (PSG) monitoring. SSD was defined as a total sleep duration of <6 hours/night. Moderate/severe OSA was defined as an apnea–hypopnea index (AHI) of ≥15. The endpoint event was defined as the first occurrence of CVD events. Cox proportional-hazards models were used to examine the joint effect of SSD and OSA on the risk of CVDs. Results: A total of 4115 participants without prevalent CVD were included in this prospective analysis. Multivariate adjustment for age, gender, BMI, smoking status, hypertension, and diabetes was carried out. Compared with non/mild OSA, the hazard ratios (HRs) (95% confidence intervals [CIs]) of total CVD, CHD, HF, and stroke in participants with moderate to severe OSA were 1.06 (0.92, 1.23), 1.04 (0.87, 1.25), 1.01 (0.82, 1.26), and 1.13 (0.84, 1.52), respectively. Compared with participants with normal sleep duration, the HRs (95% CIs) of CVD, CHD, HF, and stroke in participants with SSD were 0.99 (0.86, 1.13), 0.97 (0.81, 1.15), 0.93 (0.76, 1.15), and 1.02 (0.76, 1.35), respectively. Compared with the normal control group (non/mild OSA and normal sleep duration), the HR (95% CIs) of CVD in the moderate/severe OSA and SSD group was 1.05 (0.86, 1.29). No statistically significant joint effect of OSA and SSD on CVD risk (RERI: −0.03, 95% CI: −0.38, 0.32; P interaction > 0.05) was found. Conclusions: According to the SHHS database, having both moderate/severe OSA and SSD is not associated with an increased risk of CVD events.

Keywords

A case–control study of sleep structure and subjective sleep quality in male alcohol–dependent patients during chronic withdrawal period

Peiru Xu,Xu Chen

Shandong Mental Health Center

Objective: This study aimed to explore the sleep structure, subjective sleep quality, and related factors in patients with alcohol dependence (AD) during the chronic withdrawal period and health volunteers. Method: This study included 23 alcohol-dependent patients in chronic withdrawal period with Clinical Institute Withdrawal Assessment for Alcohol (CIWA)CIWA < 9 (study group) and 14 age-matched male health volunteers as healthy controls (control group). Polysomnography (PSG) and Pittsburgh Sleep Quality Index (PSQI) were used to evaluate the sleep structure and subjective sleep quality. The withdrawal symptoms and psychological craving of the study group were assessed by the CIWA and the Visual Analogue Scale (VAS). Results: The sleep latency of the study group was longer than that of the control group ($t' = 4.77$, $p < 0.05$), and the sleep duration of N2 was significantly longer ($t' = 6.59$, $p < 0.01$). The duration of N3 was less than that of the control group ($t' = 7.24$, $p < 0.01$). The awakening number in the study group was higher($Z = 11.02$, $p < 0.05$). The duration of REM sleep among the study group was longer than that of the control group($t' = 3.20$, $p < 0.05$). The results of Spearman correlation analysis showed that the subjective sleep quality in the study group was positively correlated with anxiety factor scores, headache factor scores, tremor factor scores, and total scores of CIWA($r = 0.61, 0.35, 0.44, 0.31$, $p < 0.05$). The sleep latency was positively correlated with anxiety factor scores and VAS total scores ($r = 0.33, 0.40$, $p < 0.05$). N2 was positively correlated with CIWA total scores, anxiety factor scores, and VAS total scores ($r = 0.40, 0.49, 0.29$, $p < 0.05$). N3 was negatively correlated with the total scores of CIWA($r = -0.33, 0.40$, $p < 0.05$). Conclusion: Male patients with AD during the chronic withdrawal period have abnormal sleep structures and lower sleep quality, which are related to withdrawal symptoms and craving levels.
Keywords

The role of Sesn2/AMPK/mTOR signaling pathway in the abnormal glucose metabolism caused by intermittent hypoxia and reoxygenation

Xinjie Chen1,Hongfei Liu1,Jiahui Tian1,Huanhuan Jin1,Ruiting Ma1,Yan Liu1,Jing Du1,Lijue Ren1,Yunhui Lu2,Cuiying Wei1

1. the First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of Science and Technology
2. Yunnan Provincial People＇s Hospital

Objective Observe the effects of intermittent hypoxia-reoxygenation on fasting blood glucose (FBG) and fasting insulin (FINS) in rats, and explore the possible role of Sesn2/AMPK/mTOR signaling pathway. Methods 36 rats were randomly divided into a control group (NC) and an experimental group, each with 18 rats. The experimental group was placed in an intermittent hypoxic chamber for 8 hours/d for 8 weeks, and then fed under normoxia for 4 weeks; The NC group was always fed under normoxia. The levels of FBG, FINS, liver Sesn2, AMPK, p-AMPK protein, mTOR and LC3mRNA in two groups were measured at baseline, at the 8th weekend and at the 12th weekend. Results Compared between groups, there was no statistically significant difference in various indicators at baseline (P>0.05); after 8 weeks of intermittent hypoxia, the levels of FBG, FINS, HOMA-IR, and mTOR in the experimental group increased, while Sesn2, p-AMPK/AMPK as well as the level of LC3 decreased, and the difference was statistically significant (P<0.05); after 4 weeks of reoxygenation, the standard indicators of the experimental group returned to the baseline level, and there was no statistically significant difference compared with the control group (P<0.05); Pearson correlation analysis showed that HOMA-IR was negatively correlated with Sesn2, p-AMPK/AMPK, and LC3 levels (r=-0.871, -0.974, -837, -0.828, P<0.05), but positively correlated with mTOR levels (r=0.851, P <0.05). Conclusion Chronic intermittent hypoxia can increase the levels of FBG and FINS in rats, which may induce down-regulation of autophagy by inhibiting the Sesn2/AMPK/mTOR signaling pathway in the liver, thereby mediating abnormal glucose metabolism.
Keywords chronic intermittent hypoxia; blood sugar; Sesn2; AMP-activated protein kinase; autophagy

The ontogenetic development of ponto–geniculo–occipital (PGO) waves during REM sleep in kitten

Jinxian Gao1,Xiaobo Wang2,Qinlei Huang1,Hailin Chen1,Yunong Chen1,Yanli Ren1,Xingwen Yang1, Junfan Xie1,Yufeng Shao1,Yiping Hou1

1.Lanzhou University

2.Gansu Provincial People's Hospital

Ponto-geniculo-occipital (PGO) waves occur just before and during rapid eye movement sleep (REM) sleep. PGO waves are involved in multiple central functions such as sensorimotor integration, learning, cognition, dreaming, development of the visual system, visual hallucination, and startle response. Revealing the early developmental characteristics and underlying mechanisms of PGO helps understand the development of its related brain structures and functions during life processes. Magnetic resonance imaging (MRI) was used to assess the stereotaxic locations of lateral geniculate nuclei (LGN) in a kitten for PGO waves recordings. The electrodes of cortical electroencephalogram (EEG), electrooculogram (EOG), and electromyography (EMG) were implanted for analyzing ontogenetic development of sleep-wake states in a kitten from postnatal day (P) 20 to P50. Results: (1) PGO waves were seen during REM sleep at P20 of age. The developmental profile of PGO waves in amplitude and frequency from P20 to P50 kitten displayed progressively increased with age.The PGO amplitude increased from 160 to 400 μV, and its density (waves per min, WPM) during REM sleep increased from 13.55 ± 0.15 to 20.32 ± 1.04 WPM. The density of PGO waves during REM sleep dramatically increased between P20 and P24 (from 13.55 ± 0.15 to 17.53 ± 0.23 WPM), which was similar to that in adult cats at P50. (2) The ontogenetic development of sleep-wake states from P20 to P50 kitten showed that the percentages of REM sleep in sleep-wake states decreased from 41.2 ± 1.23 to 20.1 ± 1.16, and meanwhile NREM sleep increased from 39.7 ± 1.54 to 49.3 ± 3.46, and wakefulness increased from 19.1 ± 2.0 to 30.7 ± 1.74. At P24 of age, the proportion of NREM sleep was higher than REM sleep (42.3 ± 0.14 vs.40.3 ± 2.1). The architectural evolution of vigilance states showed that episode number progressively decreased with age, while the mean duration of episode increased. (3) The brain histologic staining confirmed that MRI was a noninvasive and dynamic approach for locating the LGN in early developmental kitten.

Keywords

A Case of Congenital Central Hypoventilation Syndrome with Nasal BiPAP Treatment, and Literature Review

Maohuan Peng,Rui Zhao,Kai Zhang,Jing Li,Xiaosong Dong, Fang Han

Peking University Peoples Hospital

BACKGROUND: Congenital central hypoventilation syndrome (CCHS) is a rare disorder characterized by alveolar hypoventilation in sleep due to the reduced or absent response to hypoxia and hypercapnia. Current treatments mainly include several types of ventilatory supports. Here we report a Chinese CCHS case treated with nasal BiPAP.CASE PRESENTATION: A 15-month child with recurrent pneumonia and respiratory failure was admitted to our hospital. Since he was 23 days old, he had developed fevers, coughs, and other respiratory symptoms occasionally. He was diagnosed with severe pneumonia and intubated three times. The gas-blood analyses showed hypercapnic respiratory failure repeatedly, strongly suggesting the existence of alveolar hypoventilation. Polysomnography (PSG) and transcutaneous monitoring of CO_2 partial pressure were conducted during sleep, and the result validified the status of hypoventilation during sleep, as PSG showed AHI was 15.6, and mean SpO_2 during sleep was 73%, and mean $TcpCO_2$ was 63.2mmHg. Meanwhile, a genetic test presented the mutation of the paired-like homeobox 2B (PHOX2B) gene, which has been proven to be the causative gene of CCHS. Then nasal BiPAP was applied to reverse hypoventilation, and initiated with S/T mode and backup rate of 16/min at the IPAP/EPAP level of 19/8cmH2O. After adjustment of ventilator settings, the IPAP/EPAP level was set to 16/5cmH2O, and still S/T mode with the backup rate of 16/min. As a result, the mean $TcpO_2$ during sleep was increased from 49.8 mmHg to 73.1 mmHg, and mean $TcpCO_2$ was decreased from 63.2mmHg to 43.2mmHg, which suggested hypoxia and hypercapnia were improved greatly. CONCLUSION: According to our clinical experience in this case, along with other reported cases, reviews, and guidelines, nasal BiPAP can effectively treat hypoventilation in patients with CCHS. In order to prevent hypoxia and hypercapnia as well as related complications, non-invasive ventilation can serve as a good option for regular start-up management of this rare disorder.
Keywords

Functional connectivity between dorsal attentional network and sensorimotor network moderated the effect of sleep reactivity to insomnia: evidence from resting–state fMRI

Teng Li,Rui Wen,Xu Lei Zhao

Southwest University

Objective: Sleep reactivity refers to a trait vulnerability to stress-related insomnia response. The increasing evidence suggests that high sleep reactivity is a critical risk factor in the development of insomnia. However, the neural substrates of sleep reactivity and its predictive ability to insomnia are unknown. The purpose of this study was to investigate whether brain functional connectivity (FC) moderates the relationship between sleep reactivity and insomnia symptoms. Methods: A total of 720 participants with resting-state fMRI were selected from our ongoing project (Behavioral-Brain Research Project of Chinese Personality, BBP) at Southwest University. Sleep reactivity was assessed with the Ford Insomnia Response to Stress Test (FIRST). Insomnia complaints were assessed with Insomnia Severity Index (ISI). Depressive symptoms, anxiety symptoms, and daytime sleepiness were assessed with Self-rating Depression Scale (SDS), Trait Anxiety Inventory (TAI), and Epworth Sleeping Scale (ESS), respectively. The group independent component analysis (ICA) was performed to retrieve large-scale networks and the optimal number of ICA components was set to 25 according to previous studies. Finally, two components of interest for subsequent analysis including DAN (dorsal attentional network) and SMN (sensorimotor network) were determined. Results: The Pearson correlation analysis revealed a significant positive correlation between sleep reactivity and insomnia complaints ($r=0.377$, $p=0.001$). We additionally found a negative correlation between insomnia and the strength of the FC between DAN and SMN ($r= -0.098$, $p=0.009$). The sequential regression analysis results showed that the explanatory degree of the equation increased when independent variables and regulatory variables are added in the second layer when stratified regression was conducted ($R2 = 0.28$, $\Delta R2=0.07$, $p<0.001$). These results indicated the relationship between sleep reactivity and insomnia depends on the strength of the functional network connection between SMN and DAN. Conclusion: These findings suggest that the FC of DAN-SMN moderates sleep reactivity and insomnia symptoms. Our study may help to explain the neural substrates of the strong link between sleep reactivity and insomnia severity.

Keywords sleep reactivity, insomnia severity, dorsal attentional network, sensorimotor network, functional connectivity

A Cross–sectional and Longitudinal Network Analysis Approach to Understanding Connections among Depression and Sleep Components in infertile women undergoing IVF–ET

Liuliu Wu1,Lijing Sun2,Fenglin Cao1

1.School of Nursing and Rehabilitation，Shandong University

2.Reproductive Hospital Affiliated to Shandong University

Objective: To investigate (a) how depression and sleep components are interconnected within a network, and (b) the consistency of the network (symptom connections and network centralities) over time among infertile women undergoing In Vitro Fertilization and Embryo Transfer (IVF-ET). Method: Data from 3 waves of a longitudinal study were used. At baseline (T1), this study included 343 participants who completed the Pittsburgh Sleep Quality Index Questionnaire (sleep) and The Patient Health Questionnaire (depression); on the day of IVF-ET cycle start (T2) 269 were followed; on the day of oocyte retrieval (T3) 261 were followed. Data analysis including network estimation and comparison and change trajectory network for 15 symptoms were performed in R software. Results: The Network Comparison Test showed that no global differences were found between network structures and global strengths from T1 to T3. The strongest edges were found between items across the two disorders as "Daytime Dysfunction" with "Energy" , and from the same disorder like "Guilty" with "Sadness" at 3 waves. A similar pattern of component connections was found in the longitudinal network incorporating node change trajectories. Noticeably, sleep symptom "Daytime Dysfunction" exhibited fairly high centrality during the course of IVF-ET treatment (in terms of strength, bridge strength, and bridge betweenness). Meanwhile, depression symptoms "Sadness" and "Guilty" (strength), "Energy" (bridge strength) played crucial roles in the network. Depression symptom "Concentration" (strength), and sleep symptom "Sleep Quality" (bridge betweenness) showed high centrality at T3 but showed substantial remission at the other waves. Conclusions: This study provides novel insights into examining depression and sleep symptoms as dynamic systems in a network over time and highlights "Daytime Dysfunction" symptoms as central and bridge symptom, which could activate the connection between depression and sleep. The results revealed that daytime dysfunction was consistently associated with worsen depression symptoms, indicating that future psychological interventions should target "Daytime Dysfunction" -related symptoms as a priority.

Keywords

The relationship between depression and insomnia in Qinghai Province university students: Mediating effect of rumination

Shuheng Xiao,Shuai Liu,Shixu Du,Bin Zhang

Nanfang Hospital，Southern Medical University

Objective: To investigate whether rumination is a mediator between depressed mood and insomnia and the extent to which a tendency to ruminate accounts for the associations between depressed mood and insomnia. Methods: It was a cross-sectional survey. A total of 12178 university students in Qinghai Province completed the Insomnia Severity Index (ISI), Ruminative Responses Scale (RRS), and Beck Depression Inventory (BDI) through the questionnaire network platform. Results: The detection rate of insomnia was 32.9%. Insomnia (6.77 ± 4.43), depression (6.59 ± 5.79), and rumination (22.95 ± 5.26) were positively correlated (r=0.25~0.46, P＜ 0.05). Mediation effect analysis showed that depressed mood could directly affect insomnia and indirectly affect insomnia through the mediating effects of ruminant thinking. The fitting of structural equation modeling was ×2/df=72.164, RMSEA=0.076, GFI=0.908. Conclusion: Rumination mediates the association between depressed mood and insomnia, and the direct effect is greater than the indirect effect. Keywords university students; depression; insomnia; rumination; mediating effect

Effects of different designs of nasal masks of the same type on CPAP treatment effect and compliance in patients with OSA

Yuqing Wei,Hanqiao Wang

The Third Hospital of Hebei Medical University

Objective: Noninvasive continuous positive pressure ventilation (CPAP) is the first choice for patients with moderate to severe obstructive sleep apnea hypopnea syndrome. It is widely concerned whether different kinds of masks can affect the therapeutic effect or compliance of CPAP. However, there is no report on the effect and compliance of the same type of nasal mask system with different designs in China. The purpose of this study is to comprehensively evaluate the effect of nasal mask design selection on CPAP treatment compliance by comparing the subjective evaluation of sealing, comfort, stability, air leakage and compliance, overall performance of different nasal mask systems and the objective evaluation of apnea hypopnea disturbance index (AHI).Methods: 22 male patients with OSA were selected from the sleep center of our hospital and received CPAP treatment. They also signed informed consent. Participants randomly started using either of two different designs of the same type of nasal mask system for seven days, and then used the other nasal mask system for seven days. After using the nasal mask, participants filled in a questionnaire to evaluate the applicability of the two nasal mask systems (including comfort, tightness, stability, facial marking and overall performance). Wilcoxon signed rank method was used to compare the scores of the two nasal mask systems. Researcher downloaded the objective data about the use time (hours), air leakage,

air pressure and apnea hypopnea index from the participants' positive pressure devices. The paired t-test method was used for statistical test to compare the treatment effect and compliance of the two nasal mask systems.Results: Compared with different designs of nasal mask, there are significant differences in comfort, airtightness, facial imprint, noise and quiet, stability, facial interference and overall performance ($P \leq 0.01$) in the treatment of CPAP. There were significant differences in air leakage, middle pressure and 95% pressure ($P \leq 0.01$); There were significant differences in daily average use time, AI and AHI between the two nasal masks ($P \leq 0.05$), but there were no significant differences in maximum pressure and HI between the two nasal masks ($P \geq 0.05$).There were statistical differences in the degree of difficulty in adjusting and wearing mask ($P \leq 0.05$), and there was no statistical difference in the difficulty degree of removing mask ($P \geq 0.05$) Conclusion: The choice of nasal mask with the same type and different design plays an important role in the treatment compliance of CPAP, which can ultimately affect the treatment effect and compliance of CPAP. So, it's clinically important to select the nasal mask in the application of CPAP.

Keywords

Changes in insular cortex metabolites in patients with obstructive sleep apnea syndrome

Jing Kang,Mingxian Li
The First Bethune Hospital of Jilin University

Objective: The aim of this study was to investigate the changes in insular cortex metabolites and the correlation with clinical manifestations in patients with obstructive sleep apnea syndrome (OSA). Methods: Lateral insular metabolite levels were measured and relevant ratios were calculated in OSA patients and healthy individuals, including N-acetyl aspartate/creatine (NAA/Cr), choline/creatine (Cho/Cr), inositol/ creatine (Ins/Cr), glutamate compound/creatine (Glx/Cr), N-acetyl aspartate/choline (NAA/Cho), and lactic acid (Lac). Participants' scores on the Hamilton Anxiety Scale (HAMA), the Hamilton Depression Scale (HAMD), the Pittsburgh Sleep Quality Index (PSQI), and the Epworth Sleepiness Scale (ESS) were also evaluated. Apnea-Hypopnea Index, the lowest arterial oxygen saturation, and the mean arterial oxygen saturation (MSaO2) values were monitored by polysomnography. Results: NAA/Cr, Glx/Cr, and NAA/ Cho values in the insular cortex were significantly decreased, whereas HAMA, HAMD, PSQI, and ESS scores were significantly higher in OSA patients compared with the control participants. HAMA and HAMD scores showed a significant negative correlation with the NAA/Cho value in the insular cortex and a positive correlation with PSQI and ESS scores. PSQI scores were correlated positively with the Cho/Cr and Ins/Cr ratios in the left insular cortex, but correlated negatively with the NAA/Cho ratio. Conclusion: The symptoms of anxiety and depression in OSA patients may be associated with insular neuron damage or dysfunction; proton magnetic resonance spectroscopy can provide an objective imaging basis for the early diagnosis and treatment of OSA in clinical practice.

Keywords

Nonalcoholic fatty liver disease is triggered by obstructive sleep apnea: A prospective observational study in China

Jing Kang,Mingxian Li

The first hospital of Jilin University

Introduction: Obstructive sleep apnea (OSA) syndrome and nonalcoholic fatty liver disease (NAFLD) are frequently common among the obese population. However, it remains unknown whether OSA is a trigger factor for NAFLD and the association between severity of OSA and NAFLD is still unclear. Methods: A prospective study was conducted to investigate the prevalence of fatty liver and liver function variables. Patients with different courses or severities of OSA and healthy control individuals were recruited. Improvement of NAFLD with continuous positive airway pressure therapy was also evaluated using the liver FibroTouch (image-guided liver fibrosis and fatty liver degree of integration detection system). Results: The prevalence of fatty liver in the OSA groups was significantly greater than in the healthy control group and escalated with increasing severity of OSA ($p<0.05$ for the severe OSA vs. mild OSA groups). The prevalence of fatty liver also increased with a longer duration of OSA, and significant differences were observed between the 5-10 years group and the <5 years group, and between the >10 years group and <5 years group ($p<0.05$). The Alanine aminotransferase (ALT) was higher in OSA groups than the healthy control group ($p<0.05$) and escalated with increasing duration and severity of OSA ($p<0.05$ for the severe OSA vs. mild OSA groups). No significant differences in the AST, GGT, TBIL, and TBA were found among the patients with different OSA durations and severities.Introduction: Obstructive sleep apnea (OSA) syndrome and nonalcoholic fatty liver disease (NAFLD) are frequently common among the obese population. However, it remains unknown whether OSA is a trigger factor for NAFLD and the association between severity of OSA and NAFLD is still unclear. Methods: A prospective study was conducted to investigate the prevalence of fatty liver and liver function variables. Patients with different courses or severities of OSA and healthy control individuals were recruited. Improvement of NAFLD with continuous positive airway pressure therapy was also evaluated using the liver FibroTouch (image-guided liver fibrosis and fatty liver degree of integration detection system). Results: The prevalence of fatty liver in the OSA groups was significantly greater than in the healthy control group and escalated with increasing severity of OSA ($p<0.05$ for the severe OSA vs. mild OSA groups). The prevalence of fatty liver also increased with a longer duration of OSA, and significant differences were observed between the 5-10 years group and the <5 years group, and between the >10 years group and <5 years group ($p<0.05$). The Alanine aminotransferase (ALT) was higher in OSA groups than the healthy control group ($p<0.05$) and escalated with increasing duration and severity of OSA ($p<0.05$ for the severe OSA vs. mild OSA groups). No significant differences in the AST, GGT, TBIL, and TBA were found among the patients with different OSA durations and severities.

Keywords

Influencing factors of mixed apnea in patients with obstructive sleep apnea

Pengfei Liu,Hanqiao Wang
The Third Hospital of Hebei Medical University

Objective: To investigate the clinical significance of mixed apnea (MA). Methods: A total of 583 patients meeting the diagnostic criteria of obstructive sleep apnea(OSA) based on overnight polysomnography(PSG) in The Third Hospital of Hebei Medical University from July 2011 to June 2015 were enrolled in the study. According to the occurrence of MA, all patients were divided into pure-OSA group (238 cases) and MA-OSA group (345 cases). Results: The occurrence of MA was associated with apnea (r = 2.073, P = 0.000), ESS (r = 1.046, P = 0.007), gender (r = 0.413, P = 0.002), stage I sleep (r = 1.019, P = 0.031), REM sleep (r = 1.080, P = 0.000), and mean oxygen saturation (r = 0.501, P = 0.045). The mean oxygen saturation and gender were protective factors. Conclusion: The severity of OSA, female, excessive daytime sleepiness, the increased proportion of stage I, and REM sleep are independent risk factors for MA in OSA patients. The higher the mean oxygen saturation is, the less likely there is to be MA in OSA patients.
Keywords sleep apnea, mixed apnea, daytime sleepiness, blood oxygen saturation

Three–dimensional evaluation of hyoid bone position changes after orthoganthic surgery in mandibular protrusion patients

Haizhen Li,Yanlong Chen,Xuemei Gao
Peking University School and Hospital of Stomatology

Background: Patients with severe Class III malocclusion are treated with orthognathic surgery which charactered by maxilla advancement and mandible setback. Concerning the possible side effects of mandible setback including the narrowing and obstruction of airways and related sleep disorders, the position of hyoid bone is a good predictor reflecting the status of both tongue and upper airway. The study aimed to investigate the changes of hyoid bone position after orthognathic surgery in Class III patients. Methods: From January 2016 to January 2019, a total of twenty-eight patients (11 males, 17 females, aged 21.8 ± 3.2 years) with severe class III malocclusion in Peking University School and Hospital of Stomatology were enrolled in this study. All participants underwent orthognathic surgery with same surgical procedures including maxilla advancement, mandible setback and genioplasty. CBCT（Come Beam Computed Tomography） were performed two weeks before and one year after the surgery for each patient. We used the image analyzing software (Dolphin ImagingÒ 11.0, Dolphin Inc., Chatsworth, CA, USA) to set up a 3-dimensional Coordinate system for the CBCT images. And the position of hyoid bone was reconstructed in the coordinate system by the 3D Voxel superimposition technology. The changes of the hyoid bone were identified by means of

coordinates in vertical, sagittal and horizontal directions. Paired T-test was practiced on all coordinates we collected and a two-sided p-value of <0.05 was considered to be statistically significant. Results: The hyoid bone showed an average of 1.9mm downward movement in the vertical dimension (P=0.037) and an average of 2.8mm backward movement in the sagittal dimension (P=0.007). There is no significant difference of the hyoid bone movement in the horizontal direction (P=0.892). Conclusions: The position of hyoid bone in patients with severe Class III malocclusion after orthognathic surgery might move downward and backward, which could cause the narrowing and obstruction of the upper airway. Those changes may be risk factors contributed to sleep-disordered breathing (SDB), to which great importance should be attached so as to reduce the incidence of SDB induced by orthognathic surgery.

Keywords Key words: Orthoganthic surgery; Hyoid bone; 3D superimposition technology; Class III malocclusion.

Rostromedial tegmental nucleus–substantia nigra pars compacta circuit mediates aversive and despair behavior in mice

Yanfei Sun,Jing Cao,Chunpeng Xu,Xiaofeng Liu,Zhicheng Wang,Hua Zhao
Jilin university

GABAergic neurons in the rostromedial tegmental nucleus (RMTg) receive major input from the lateral habenula (LHb) conveying negative reward and motivation related information. At the same time, GABAergic neurons in the rostromedial tegmental nucleus (RMTg) project intensively to midbrain dopamine neurons in the ventral tegmental area (VTA) and substantia nigra pars compacta (SNc). The RMTg-VTA circuit has been shown regulating the affective behavior, but the role of the RMTg-SNc circuit in aversion and depression has not been well understood. This study demonstrated that activation or inhibition of VgatRMTg-SNc neurons sufficiently increased or decreased immobility time in the forced swim test (FST), respectively. Furthermore, activation of VgatRMTg-SNc pathway caused aversive behavior. Ninety percent of the SNc putative dopamine neurons were inhibited in extracellular recordings. Furthermore, inhibition of the VgatRMTg-SNc pathway reversed behavioral despair in chronic restraint stress (CRS) depression model mice. Manipulations of the pathway did not affect the hedonic value of the reward in the sucrose-preference test (SPT) or general motor function. In conclusion, these results indicated that the VgatRMTg-SNc pathway involved in regulating aversive and despair behavior, which suggested that the RMTg may mediate the role of LHb in negative behaviors through regulating the activity of SNc neurons.

Keywords

The convergence of aversion and reward signals in individual neurons of the mice lateral habenula.

Jicheng Li,Renfei Fan,Xiaofeng Liu,Xiangfeng Shen,Xin Liu,Hua Zhao
Jilin university

The lateral habenula (LHb) closely connects to ventral tegmental area (VTA) , and they serve as aversion and reward junction of the brain, respectively. This study investigated whether single neurons in the LHb/VTA respond to both aversion and reward stimuli and how these neurons regulate aversion and reward processing. Using optogenetic combined with multi-channel recording of neuronal discharge for LHb / VTA neurons, we found most single neurons in the LHb/ VTA respond to both aversion and reward stimuli. Interestingly, majority of neurons in LHb are aversion-activated and reward-inhibited neurons, consisting mainly of glutamatergic neurons, while most neurons in VTA are reward-activated and aversion-inhibited neurons, which inhibited by glutamatergic neurons in the LHb. Furthermore, optogenetic activation or inhibition of glutamatergic neurons in LHb and their terminals in VTA could induce aversive or reward behaviors. These results indicate that identical neurons in the LHb and VTA have different responses to reward and aversion stimuli. The aversion behaviors induce by activating LHb glutamatergic neurons may be due to its inhibition on reward-activated neurons in VTA. This study suggests that interplay between the LHb and VTA neurons may play a key role in regulating reward and aversion behaviors.
Keywords

Incidence and characteristics of arrhythmia in sleep apnea patients

Yakun Wang, Hanqiao Wang
The Third Hospital of Hebei Medical University

Objective: To investigate the incidence and characteristics of arrhythmia in patients with sleep apnea, and to identify predictors of arrhythmia in those patients.Methods: A total of 529 patients with sleep apnea were recruited in our study. All patients underwent an overnight polysomnography recording and electrocardiogram examination. According to polysomnography, sleep apnea was defined as the apnea hypopnea index (AHI) >5 times/hour. Obstructive sleep apnea (OSA) was diagnosed when obstructive respiratory events predominated. On the condition that central apnea accounted for more than 50% of the total, central sleep apnea syndrome (CSAS) was considered. Meanwhile, sleep apnea was categorized into mild (5 < AHI≤15, times/h), moderate(15 < AHI≤30, times/h), or severe(AHI < 30, times/h) to detect the incidence and characteristics of arrhythmias in patients with different types and severities of sleep apnea. Results: Among 529 sleep apnea patients (32 CSA and 497 OSA), 165 patients were complicated with arrhythmia, and the total incidence of arrhythmia was 31.2%. Premature atrial contraction and premature ventricular contraction had higher

percentages than other types of arrhythmia (47.27% and 30.91%, separately, P < 0.01). Furthermore, sleep apnea with more than one type of arrhythmia was also elevated (54.2%, P < 0.01). However, there were no significant differences in the incidence of arrhythmias between CSAS and OSA patients (37.5% vs. 30%, P =0.37). The occurrence of arrhythmia in severe OSA had a significant increase compared with mild-moderate OSA (32.4% vs. 22.6%, P < 0.05). Logistic regression illustrated that age (P =0.006, OR=1.035), AHI≥40 times/hour (P =0.034, OR=2.178), and proportion of sleep stage (P < 0.01) were significantly associated with the occurrence of arrhythmia in patients with OSA. Conclusion: Our study illuminated that the incidence of arrhythmia in sleep apnea patients was 31.2%, and premature atrial contraction and premature ventricular contraction are the most common among all kinds of arrhythmia. Furthermore, elder, AHI≥40 times/hour, and sleep structure turbulence are predictors of arrhythmia in patients with OSA.

Keywords

Study on the correlation between finger oxygen saturation and intestinal flora metabolites in sleeping OSAHS patients

Tingzhen Xu,Yao qin

Zhejiang Provincial Hospital of Chinese Medicine

Objective: To investigate the oxygenation changes of the lung-intestinal axis in patients with OSAHS and the association between hypoxia during sleep and lung-intestinal axis related diseases by analyzing the changing trend of oxygen saturation and measuring the content of trimethylamine oxide (TMAO) in serum of patients with OSAHS during sleep. Methods: Forty-eight patients with suspected sleep disordered breathing due to snoring at night with or without arousal were selected for sleep monitoring. The subjects received polysomnography monitoring and the data of nocturnal finger oxygen saturation were recorded. The subjects were divided into 4 groups according to the Apnea–hypopnea index (AHI). The data of mean blood oxygen saturation, minimum blood oxygen saturation, and times of oxygen reduction were analyzed. Serum samples of 7 subjects in each group were collected according to the informed consent principle. Using enzyme-linked immunosorbent assay TMAO content in serum, and to analyze its correlation. Results: With the increase of AHI in patients with OSAHS, the hypoxia during sleep showed a gradual aggravation trend. Compared with the data of serum TMAO content in the 4 groups, there were no significant differences, while the serum TMAO concentrations in subjects without apnea or with mild apnea were significantly lower than ones in patients with moderate and severe apnea. Conclusions: With the development of the disease, the indicators of sleep status in patients with OSAHS showed an increasing trend of hypoxia, and the serum TMAO level in OSAHS patients may be related to the disease stages.

Keywords

Aerobic Combined with Resistance Exercise Improves Sleep Quality and C–reactive Protein Levels in Female with Opioid Addicts

Jinglin Liu,Guo Yin,Zheng Lan

Hunan Normal University

Objective: Sleep problems have become an important public health issue and the sleep problems of opioid addiction merit the researchers' attention. As an effective intervention, exercise is acceptable to the public. Meanwhile, a sleep disorder may affect the expression of C-reactive protein(CRP). However, there are few sleep studies on opioid addicts. Therefore, this study intends to carry out an 8-week prescription exercise that explores the effects of appropriate exercise on sleep and CRP of opioid addiction. Methods: In the Compulsory Detoxification Detention Center of Changsha, forty-two females with opioid addiction were recruited based on the graded exercise test. They were randomly divided into the intervention group (NE, 24 subjects) who received conventional rehabilitation and 8-week exercise, and the control group (NC, 18 subjects) which only received conventional rehabilitation. Aerobic exercise intensity should be controlled at 40%-60% of heart rate reserve; The strength of resistance movement is 12-15 repetition maximum; Exercise performed 5 times every week with 90 minutes per session. The Pittsburgh Sleep Quality Index (PSQI) scale and serum CRP were tested before and after the intervention.Results: The PSQI global scores of the NE group and the NC group were greater than 5 before the intervention. After 8 weeks, in the NE group, the PSQI global score and the expression of CRP decreased, and the subjective sleep quality and habitual sleep efficiency were improved. Besides, Sleep latency in the NE group was shorter and sleep duration was longer. The results showed that there were significant differences in sleep latency, sleep duration, PSQI global score, and CRP between groups. In addition, the correlation results indicated that PSQI global score was significantly positively correlated with CRP level. Conclusion: Sleep problems are common among individuals with opioid addiction. Sleep quality is positively correlated with CRP level. By reducing the expression of CRP through exercise, sleep quality may be further improved.
Keywords

Changes of Sleep Parameters in Patients with Different Severity of OSA after Oral Appliance Treatment

Mingcong Rao1,2,Minfang Huang 1,Shenghuan Tan 1,2,Rongbin Zhong1,2

1.The People's Hospital of Guangxi Zhuang Autonomous Region

2.Youjiang Medical University for Nationalities

Objective: To compare the changes of sleep parameters and respiratory parameters in patients with obstructive sleep apnea (OSA) of different severity before and after treatment with mandibular advancement

appliance. Methods: 85 patients with OSA (61 males and 24 females) were selected according to the criteria of inclusion. According to the severity of the disease, 85 patients were divided into three groups, including 20 mild, 25 moderate and 40 severe group. The changes of sleep parameters and respiratory parameters were monitored by multi-channel sleep map before and after the mandible anterior oral appliance, and were compared in each group. Results: The results of sleep parameters comparison between OSA patients with different severity showed that the percentage of S3 phase increased from (5.16 ± 6.30) to (8.21 ± 7.75)%. The number of wakefulness in the moderate group was decreased from (7.28 ± 5.56) to (5.08 ± 3.91), and the difference was statistically significant ($P < 0.05$), and the sleep parameters of the severe group were not statistically significant ($P > 0.05$). The results of comparison of respiratory parameters before and after treatment showed that the minimum oxygen saturation of OSA patients with different severity increased, AI, HI, AHI and the longest pause time were decreased compared with those before treatment, and the difference was statistically significant ($P<0.05$). However, there was no significant difference between the two groups ($P > 0.05$). Conclusion: After the treatment of oral appliance, the times of apnea, time of hypoventilation decreased, the lowest oxygen saturation increased, the proportion of deep sleep increased in mild patients and the number of sleep wakes in moderate patients decreased.
Keywords

The effect of hypoxia and hypercapnia on respiratory drive

Luguang Wu1,2,Shanfeng Liang1,2,Xiuxuan Xiang1,2,Yongyi Chen1,2,Yuanming Luo1,2,Subaan Qasim3,Nadia Zaman3,Uzayr Rajaratnam3

1.State Key Laboratory of Respiratory Disease，Guangzhou Medical University，China

2.The First Affiliated Hospital of Guangzhou Medical University，China

3.Imperial College London，England

Background: Sleep apnea is associated with hypoxia and hypercapnia, which in turn affect the respiratory drive. The neural respiratory drive is usually assessed by hypoxia or hypercapnia but barely assessed by the combination of hypoxia and hypercapnia. Methods: Forty healthy subjects (15 females, 25 males, age 27.2 ± 7.6 years) were recruited in this single-blind study. Each subject rebreathed different kinds of gas to generate hypoxia, hypercapnia, and hypoxic-hypercapnia. Subjects rebreathed from a bag filled with room air and added soda lime in the breathing circuit for absorbing CO_2 to induce pure hypoxia. Hypercapnia was induced by rebreathing from a bag contained gas mixture (8%CO_2 and 92%O_2). Hypoxic-hypercapnia was induced by rebreathing from a bag filled with room air. Tests were conducted with a gap of more than 15 minutes between tests. ET-CO2, SaO2, ventilation, and diaphragm EMG (EMGdi) recorded from the esophageal electrode were recorded continuously during the study. Tests were stopped when SaO2 reached 70% or ETCO2 reached 70 mmHg. Results: EMGdi and VE increased with increasing ETCO2 or decreasing SaO2 ($P < 0.01$). The slop between EMGdi and ETCO2 (r=0.61) was higher than that between EMGdi and SaO2 (r=1.75). However, the slop between EMGdi and Hypoxic-hypercapnia was highest. Conclusion:

Neural respiratory drive is more sensitive to hypercapnia than hypoxia. The combination of hypoxia and hypercapnia can maximally stimulate neural respiratory drive.

Keywords Respiratory drive, hypoxia, and hypercapnia, diaphragmatic electromyogram, ventilation

A survey of co–morbidity of type 2 diabetes and sleep apnea among community residents with different body mass indexes

Tingting Sun1,Zhongming He2,Cuiying Wei1

1. The First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of science and technology
2. Karamay Central Hospital

Objective：The prevalence of abnormal glucose metabolism in the population is increasing year by year, and obstructive sleep apnea (OSA) is closely related to cardiovascular and metabolic diseases. Previous studies suggest that abnormal glucose metabolism and OSA often co-exist. The co-morbidity of OSA and abnormal glucose metabolism increases the risk of stroke. However, the risk factors associated with the disease have not been well studied. The prevalence of OSA with glucose metabolism abnormalities with different body mass indexes (BMI) is poorly reported. The purpose of this study was to investigate the co-morbidity prevalence of OSA and abnormal glucose metabolism in community residents with different body mass indexes. Methods：The study collected questionnaires from 1270 residents aged 35-75 years in the Tianshan community of the city of Karamay. Socio-demographics were collected and body mass index was further calculated based on height and weight. Glucose metabolic status was assessed by medical history and fasting serum glucose. Sleep apnea was defined as oxygen descent index (ODI) $\geqq$ 5 times/hour based on data recorded by portable polysomnography. Data were analyzed using SPSS20.0. Results：Among 1270 respondents, 1178 completed all the questionnaires, with a total response rate of 92.76%. Among all participants, a BMI of 18.5 or lower (low body weight) accounted for 1.26%, and a BMI of 18.5- 24 (normal body weight) accounted for 26.8%, and a BMI of 24-28 (pre-obesity) accounted for 41.42%, and a BMI of 28 or higher (obesity) accounted for 30.51%. There were no patients with the comorbidity of type 2 diabetes and OSA among those with low body weight, but 2.45% of patients with normal BMI had the comorbidity of type 2 diabetes and OSA. The comorbidity of type 2 diabetes and OSA were 5.06% in those with pre-obesity and 5.93% in those with obesity. The chi-square test showed that there were significant differences among the four groups in the rate of comorbidity (P<0.05). Conclusion：As body mass index increases, the prevalence of type 2 diabetes and OSA increases, and the co-morbidity of them also increase. BMI is an important risk factor for abnormal glucose metabolism and OSA. A large number of people in this community were pre-obese and obese. Health education on diabetes and sleep apnea should be provided for patients with diabetes and OSA. Appropriate prevention and treatment strategies should be set to prevent cardiovascular diseases and metabolic diseases. Keywords

Effects of chronic intermittent hypoxia/reoxygenation on body weight and glucose metabolism in rats

Huanhuan Jin,Hongfei Liu,Jiahui Tian,Jiayu Hu,Wei Yang,Tingting Sun,Cuiying Wei

The First Affiliated Hospital of Inner Mongolia University of Science and Technology (former: The First Affiliated Hospital of Baotou Medical College)

Objective: to establish a rat model of intermittent hypoxia and observe the changes in body weight and glucose metabolism of rats under chronic intermittent hypoxia/reoxygenation environment. Methods :according to the random number table method, 24 healthy male SD rats, weighing about 200 ± 10 g, were divided into control group (NC group) and intermittent hypoxia group (CIH group), suitable for environmental feeding, free diet. The CIH group rats were placed in an intermittent hypoxic chamber, and nitrogen was first circulated into the oxygen chamber for 25 seconds to gradually reduce the oxygen concentration in the chamber from 21% to the minimum oxygen concentration of 7%-8%, maintaining for 10 seconds, and then filling air for 55 seconds to gradually restore the concentration in the oxygen chamber to 21% and then maintain it for another 30 seconds. Each cycle maintained for 120 seconds. The rats experienced intermittent hypoxia events at 30 times/hour. The exposure time was from 9:00 am to 5:00 pm daily (8 hours in total), a total of 12 weeks. The rats were not given food during the intermittent hypoxia, and the rats were placed in a breeding cage during the rest of the time. They were kept normally and maintained at room temperature and air. From the 13th week to the 16th week, it was placed in a normal air environment for reoxygenation intervention. During the experiment, in order to remove the excess water and carbon dioxide in the oxygen chamber, an appropriate amount of quicklime was added to make it absorbed. The rats in the NC group were not exposed to hypoxia and were kept in normal air to maintain a suitable living environment. The rest of the conditions were the same as those in the CIH group. Before being placed in the oxygen chamber (0 weeks) and every 2 weeks after being placed in the oxygen chamber, the rats in the two groups were fasted with water for 8 hours and their body weight were measured. After the end of the 12weeks intermittent hypoxia, the rats in the CIH group were kept in normal air for 4 weeks, and their body weight was measured in the same way every week. The intracanthal venous blood of rats was drawn every 2 weeks to detect FBG and FINS, and HOMA-IR was evaluated according to the steady-state model. Results: At week 0, there was no difference in body weight between the two groups of rats (NC group vs. CIH group: 226.25 ± 28.55 vs. 224.58 ± 33.93, P>0.05). After 2 weeks of intermittent hypoxia, the weight of the CIH group was significantly lower than that of the NC group (Compared with the CIH group in the NC group: 300.13 ± 30.94 vs. 254.58 ± 35.82, P<0.05). By the end of the 6th week, the body weight of the CIH group was still lower than the NC group. At the 10th and 12th weeks, the weight of the two groups tended to balance. After reoxygenation, the rats in CIH group showed increased weight compared to the NC group. At 2 to 4 weeks of reoxygenation, the body weight of the CIH group was significantly higher than the NC group (2 weeks of reoxygenation in the NC group compared to the CIH group: 458.75 ± 52.01 vs. 497.50 ± 21.93,

P<0.05; 3 weeks of reoxygenation in NC group compared with CIH group: 449.00 ± 50.09 vs. 497.25 ± 25.18, P<0.05; 4 weeks of reoxygenation in NC group compared with CIH group: 450.25 ± 50.99 vs. 502.75 ± 23.21, P<0.05.) Under intermittent hypoxia, the FBG level of the CIH group was significantly higher than that of the NC group at the 8th weekend, and the difference was statistically significant (P<0.05); FINS and HOMA-IR levels were significantly higher at the 4th, 6th and 8th weekend in the CIH group compared to the NC group, the difference was statistically significant (P<0.05); after reoxygenation intervention, the FBG level of the CIH group was higher at the first weekend of reoxygenation than the NC group, and the difference was statistically significant (P<0.05); At the end of the 4th week, the FBG levels of CIH group and NC group were similar, and the difference was not statistically significant (P>0.05); the FINS levels of CIH group and NC group were similar, and the difference was not statistically significant (P>0.05); the HOMA-IR level of CIH group at reoxygenation was higher in the first and second weekends than in the NC group, and the difference was statistically significant (P<0.05); the levels of HOMA-IR at the third and fourth weekends were similar, and the difference was not statistically significant (P>0.05). Conclusion: at the initial stage of intermittent hypoxia, the weight of rats in the CIH group is lower than the NC group. Chronic intermittent hypoxia may inhibit the weight gain of rats; after the rats are adapted to hypoxia, the weight of the rats gradually returns to normal growth, and the rats reachhypoxia tolerance. Status: After reoxygenation, the inhibitory effect on the weight gain of rats was lifted. The weight of the rats in the CIH group was much higher than that in the NC group, and the weight showed retaliatory growth. Intermittent hypoxia may affect the metabolism and growth of the rats. CIH increased the levels of FBG, FINS and HOMA-IR in rats and developed insulin resistance, indicating that CIH involved in the development of insulin resistance in rats. After reoxygenation, insulin resistance in rats was reduced and the glucose metabolism disorder caused by OSAHS was improved.

Keywords

The Effects of Sleep Apnea on Cognitive Function in Patients with Abnormal Glucose Metabolism

Jiayu Hu1,Xinmei Zhao2,Yan Liu2,Ruiting Ma2,Cuiying Wei2

1. The First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of Science and Technology
2. The First Affiliated Hospital of InnerInner Mongolia University of Science and Technology

Objective: Both type 2 diabetes mellitus and sleep apnea are common chronic diseases, which have a serious impact on health. Cognitive impairment occurs among patients with type 2 diabetes mellitus and sleep apnea. However, its underlying mechanism is not clear. A few studies reported that sleep apnea is an important cause of cognitive impairment in patients with type 2 diabetes. Hypoxia inducible factor -1 alpha (HIF-1 alpha) is a key transcription factor of adaptive regulation of hypoxia. Whether it is one of the mechanisms of cognitive impairment in those patients remains unknown. Therefore, the aim of this study was to investigate the effect

of sleep apnea on cognitive function in patients with impaired glucose tolerance and type 2 diabetes, and to explore the mechanism of HIF-1 alpha in cognitive function.   Methods: A total of 178 subjects were included in the study. They were divided into normal group (N group), OSAHS group (O group), impaired glucose tolerance group (I group), type 2 diabetes mellitus group (D group), OSAHS with impaired glucose tolerance group (group IO), OSAHS group with type 2 diabetes mellitus group (OD group). The cognitive function was evaluated by the Montreal Cognitive Assessment scale (MOCA). The level of HIF-1 alpha was measured by ELISA. Data was analyzed using SPSS 17.0, and statistical significance was defined as $P < 0.05$.   Results: Multiple linear regression found that HbAlc (stb=-0.155, P=0.030), TG (stb=-0.249, P=0.001), HIF-1 α (stb=-0.169, P=0.010), and OSAHS (stb=-0.412，P＜ 0.001）have significant different effect on abnormal glucose metabolism in patients with MoCA score. The MoCA score of group D was significantly different from that in N group and I group, while there was no significant difference between N group and I group. The differences between N group and O group were statistically significant, and the differences between IO group and I group were statistically significant. The differences were statistically significant between DO group and D group. With regard to HIF-1 alpha level, there were significant differences among D group, N group, and I group. No significant differences were observed between N group and I group, while the differences between N group and O group were statistically significant. There were significant differences between IO group and I group, and significant differences were also found between DO group and D group.   Conclusions: Type 2 diabetes mellitus and sleep apnea might have adverse effects on cognition. HbAlc, TG, HIF-1 α , and OSAHS are independent risk factors of cognition impairment in patients with abnormal glucose metabolism. HIF-1 α plays an important role in cognitive impairment and the upregulation of HIF-1 α might contribute to cognitive impairment.

Keywords Abnormal glucose metabolism, cognitive function, sleep apnea, hypoxia inducible factor -1 alpha (HIF-1 alpha)

Self–reported Sleep Characteristics Associated with Dementia Among Rural–dwelling Chinese Older Adults

Rui Liu1,Shi Tang1,2,Chengxuan Qiu1,2,3,Yifeng Du1,2
1.Shandong Provincial Hospital，Cheeloo College of Medicine，Shandong University
2.Shandong Provincial Hospital Affiliated to Shandong First Medical University
3.Karolinska Institutet-Stockholm University

Background: Sleep characteristics associated with dementia are poorly defined and their associations stratified by demographic factors and APOE genotype among older adults in rural China are unclear. Objective: To examine the associations of self-reported sleep characteristics with dementia and global cognitive function among rural-dwelling Chinese older adults, and to explore whether the associations were different when being stratified by demographic factors and APOE genotype. Methods: This population-based cross-sectional study included 4641 participants (age ≥65 years, female 57.0%) living in rural China. Sleep

parameters were measured using the Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale. Dementia and Alzheimer's disease (AD) were diagnosed based on international criteria. Data were analyzed using multiple logistic and general linear regression models.Results: A total of 172 participants were diagnosed with dementia (115 with AD). The multivariable-adjusted odds ratios (OR) of dementia were 1.85 (95% CI, 1.20-2.85) for sleep duration ≤4 hours/night and 1.71 (95% CI, 1.12-2.62) for sleep duration >8 hours/night, compared with sleep duration of 4-8 hours/night. The multivariable-adjusted odds ratios (OR) of dementia were 1.60 (95% CI, 1.14-2.26) for low sleep efficiency and 1.64 (95% CI, 1.04-2.59) for excessive daytime sleepiness (EDS). Short sleep duration, low sleep efficiency, and EDS were significantly associated with AD (multi-adjusted OR range: 1.70-1.99; p<0.05). The associations of sleep duration with dementia and AD were evident mainly among young-old adults (65-74 years) and APOE e4 allele carriers. Among dementia-free participants, these sleep characteristics were significantly associated with a lower MMSE score (p<0.05). Conclusion: Self-reported sleep disturbances in dementia are characterized by short or long sleep duration, low sleep efficiency, and EDS, especially among young-old people and APOE e4 carriers.
Keywords

Effect of interaction between slow wave sleep and obstructive sleep apnea on insulin resistance: A large–scale study

Weijun Huang1,2,3,Yuenan Liu1,2,3,Xiaoting Wang1,2,3,Xinyi Li1,2,3,Yupu Liu1,2,3,Jianyin Zou1,2,3,Huajun Xu1,2,3,Huaming Zhu1,2,3,Hongliang Yi1,2,3,Jian Guan1,2,3,Shankai Yin1,2,3
1.Shanghai Jiao Tong University Affiliated Sixth People's Hospital
2.Otolaryngology Institute of Shanghai Jiao Tong University
3.Shanghai Key Laboratory of Sleep Disordered Breathing

Objectives: Slow wave sleep (SWS) and obstructive sleep apnea (OSA) have attracted more and more attention. Their joint effect on insulin resistance (IR) remains to be further studied. This study explored whether less SWS influences the relationship between OSA and IR. Methods: Participants were enrolled in our sleep center from 2007 to 2019. We collected demographic and clinical characteristics and gauged the IR status. SWS was derived from polysomnography data. Logistic regression analyses were used to reveal the associations between SWS and IR. Results: In all, 6966 participants (5709 OSA and 1257 primary snoring [PS] subjects) were enrolled. Less SWS increases the risk of IR in OSA patients but not in PS patients. OSA patients with SWS < 6.5% were more likely to have IR than those with SWS > 21.3%. OSA was an independent risk factor for IR after adjusting for all potential confounding factors. In stratified analyses, according to the percentage of SWS, patients with OSA with SWS < 6.5% had 38.2% higher odds of IR than the PS group after adjusting for all potential confounders. Conclusions: Less SWS is associated with higher odds for IR in OSA patients but not in PS patients. OSA is independently correlated with IR. In addition, OSA combined with an extreme lack of SWS has a more adverse effect on the status of IR than OSA itself.
Keywords: Obstructive sleep apnea, slow wave sleep, insulin resistance

Effects of dead space on sleep structure in healthy subjects

Shanfeng Liang1,2,Luguang Wu1,2,XiuXuan Xiang1,2,Yongyi Chen1,2,Yuanming Luo1,2
1.State Key Laboratory of Respiratory Disease，Guangzhou Medical University，China
2.The First Affiliated Hospital of Guangzhou Medical University，Guangzhou，China

Background: Adding dead space (DS) to increase inspiratory CO2 has been shown to eliminate central sleep apnea (CSA). The effects of DS on sleep quality and structure have not been well studied. The aim of this study was to assess the effect of DS on sleep in healthy subjects. Methods: Eight healthy subjects (5 females, 3 males, age 35 ± 16 years, AHI<5) were recruited to study on two separate nights with or without dead space. A customized face mask with 450 ml of dead space was developed. ETCO2 and diaphragm electromyography (EMG-di) recorded from surface electrodes were made during overnight polysomnography. A questionnaire on sleep comfort was conducted in the morning. Result: ETCO2 with dead space increased significantly (35.67 ± 4.84mmHg vs. 38.44 ± 5.94mmHg, P<0.05). Whereas, the sleep structure including sleep stages and arousal were not markedly different between breathing with and without DS (P>0.05). There is no change in total sleep time (422.6 ± 37.9 min vs. 412.8 ± 37.9min, P>0.05), sleep efficiency ($90.8\%\pm7.0\%$ vs. $90.9\%\pm6.0\%$, P>0.05), and latency (16.2 ± 5.4 min vs. 17.1 ± 10.8min, P>0.05) between two nights. No difference was found in diaphragm EMG strength at stage 2 during breathing with and without DS. However, six of eight subjects complained dead space impaired their sleep quality although the sleep structure recorded from polysomnography with DS was the same as that without DS. Conclusion: Dead space may damage sleep quality based on the questionnaire but it is not confirmed by polysomnography.
Keywords added dead space, CO2, sleep efficiency, sleep structure, diaphragm electromyography

Metabolomics Study of Roux–en–Y Gastric Bypass Surgery (RYGB) to Treat Patients with Obese Obstructive Sleep Apnea and Type 2 Diabetes

Huajun Xu1,2,3,Weijun Huang1,2,3,Xinyi Li1,2,3,Yupu Liu1,2,3,Jianyin Zou1,2,3,Huaming Zhu1,2,3,Hongliang Yi1,2,3,Jian Guan1,2,3,Shankai Yin1,2,3
1.Shanghai Jiao Tong University Affiliated Sixth People’s Hospital
2.Otolaryngology Institute of Shanghai Jiao Tong University
3.Shanghai Key Laboratory of Sleep Disordered Breathing

Background: Roux-en-Y gastric bypass (RYGB) surgery is an effective treatment for obstructive sleep apnea (OSA). However, no previous study had explored the metabolomic changes of RYGB on OSA. Methods: Clinical data, serum and polysomnography (PSG) measurements were collected at baseline and

6 months after RYGB surgery. A metabolomics analysis was performed based on ultra-performance liquid chromatography-mass spectrometry. Results: 37 patients with obese OSA and Type 2 Diabetes (T2DM) were enrolled in this study. After RYGB surgery, metabolic outcomes and sleep parameters were all significantly improved. Metabolomics analysis revealed that HIF1 pathway activation, PI3K/Akt signaling pathway, hypothalamic–pituitary–adrenocortical (HPA) axis and Adenosine 5'-monophosphate -activated protein kinase (AMPK) pathway take part in the mechanism of OSA. In subgroup analysis, OSA remission group presented lower valine, isoleucine and C24:1(cis-15) level, and higher TMAO, hippurate and indole-3-propionic acid level after RYGB surgery when compared with non-remission group. A combination of age, preoperative AHI, C peptide and hippurate might be served as independent predictor for evaluating efficacy of RYGB for patients with obese OSA and T2DM (AUC [Area Under Curve] of ROC [Receiver Operating Characteristic] curve 0.964). Conclusion: RYGB surgery could significantly improve metabolic status (characterized as mitochondrial function improvement and gut microbiota variation) of obese OSA and T2DM. A combination of age, preoperative AHI, C peptide and hippurate might be helpful in individualized treatment for obese OSA and T2DM by RYGB surgery.

Keywords obstructive sleep apnea; metabolomics; Roux-en-Y gastric bypass We do not accept abstracts published online.

Effects of Regular Climbing Exercise on Nocturnal Sleep Quality of Aged Female Drosophila

Yi Xiao,Zheng Lan,Li Qiufang

Hunan Normal University

OBJECTIVE: One of the effects of aging is loss of sleep stability, which is measured by increased number of nocturnal awakenings and shortened nocturnal sleep duration, i.e. increased ineffectual nocturnal sleep. Exercise as an effective and safe intervention can provide sleep efficiency and improve sleep quality. Therefore, in this study, we used Drosophila melanogaster model to further study the effects of exercise on nighttime sleep quality. METHODS: Ninety wild-type virgin flies W1118 were collected and randomly divided into 3-week-old control group, 6-week-old elderly group, and 6-week-old exercise intervention group. They were given normal diet medium and raised under standard environmental conditions (25° C, 50% relative humidity, 12-hour light/dark cycle). The flies in the 6-week-old exercise group exercised from 3 weeks to 6 weeks of age. The independent activities of each fly in 1-min bins were continuously monitored and recorded using the Drosophila Activity Monitoring System (DAMS) and Data Acquisition System. RESULTS: Compared with 3-week-old Drosophila, the number of night sleep fragments in 6-week-old Drosophila group significantly increased, and the total sleep time of 6-week-old Drosophila prolonged while the night sleep duration remained unchanged. After 3 weeks of exercise intervention, the number of sleep fragments at night significantly reduced in the elderly flies, and the nocturnal sleep duration increased, but

the total amount of sleep at night remained the same. CONCLUSION: Regular exercise for 3 weeks can effectively improve the nocturnal sleep quality of aged female Drosophila.

Keywords

Experience of Hai style of traditional Chinese medicine in treatment from liver

Liang Xu,Guohua Wang

Shanghai Hospital of Traditional Chinese Medicine

In today's mental cultivation methods of traditional Chinese medicine in Shanghai style,"treating insomnia from the liver" has become mainstream. Doctors in the past dynasties believed that their disease was in the heart and followed the "rule from the heart", but their prescriptions were mostly selected from the liver meridian. On the basis of the predecessors of the Sleep Research Institute of Shanghai Hospital of Traditional Chinese Medicine, we put forward the academic views of "the brain dominating spirits, the heart dominating blood circulation and vessels and the liver dominating emotions". We also advocated the theory of "correspondence between man and nature" and "the treatment of the liver", combined with the clinical characteristics of contemporary insomnia. Previous studies showed that more than 71.74% of insomnia was caused by mental factors. The middle-aged and elderly patients with insomnia as the main symptom, liver hyperactivity, and kidney deficiency are common. The method of invigorating the liver and tonifying the kidney is the most suitable for them, which can better improve insomnia, liver hyperactivity, and kidney deficiency as well as sleep and memory in patients with memory impairment.

Keywords

Association between serum micronutrient and macroelement level with obstructive sleep apnea among children

Kaimeng Kong,Ying Ding

Shanghai Children's Hospital，Shanghai Jiao Tong University

Objective: This study aimed to identify the association between serum micronutrients (copper, iron, lead, cadmium, zinc) and macroelement level (calcium, magnesium) with obstructive sleep apnea (OSA) among children. Methods: An observational cross-sectional study was carried out. All children underwent overnight polysomnographic evaluation and then were classified into OSA group and non-OSA group. Fasting blood was drawn in the morning, then tested the serum micronutrient and macroelement level by adopting atomic absorption spectrophotometry. Results: A total of 140 children were included in the study, and thirty-eight were diagnosed with OSA. There existed no differences between the two groups in the aspects of age, gender, and body mass index (p=0.391, 0.251, and 0.654, respectively). The serum cadmium level in

the OSA group significantly higher than that for the non-OSA group (1.18 ± 0.89 ug/l vs. 0.70 ± 0.76 ug/l; p=0.002). Moreover, we found the serum cadmium level was negatively associated with stage N2 (p=0.024), but positively associated with the proportion of stage N3 during non-rapid eye movement sleep (p=0.012). Children with OSA had a tendency for higher serum lead levels comparing with non-OSA group, but it did not reach statistical significance (33.11 ± 17.28 ug/l vs. 31.73 ± 19.42 ug/l; p=0.643). The serum copper, zinc, calcium. and magnesium levels in OSA group were similar in children of non-OSA group (p=0.507, 0.987, 0.505, and 0.998, respectively). However, among the 87 male children younger than 7 years old, the serum iron and magnesium level were 7.44 ± 0.5 mmol/l and 1.43 ± 0.16 mmol/l in OSA group, significantly lower than those in non-OSA group (7.79 ± 0.57 mmol/l, p=0.033; 1.53 ± 0.11 mmol/l，p=0.015). Conclusion: The serum cadmium level in the OSA group is significantly higher than that in non-OSA group. Moreover, the serum iron and magnesium level inclined to lower in the OSA group than those in non-OSA group among the male group less than 7 years old.

Keywords

The relationship between Parkinson's disease, rapid eye movement sleep behavior disorder, TNF–α, and orexin levels.

Yuan Yuan1,2,Yimeng Zhang1,2,Yueyang Cheng1,2,Yue Hou1,2,Ning Li1,2,Shuqin Zhan1,2

1.Xuanwu Hospital Capital Medical University

2.Beijing Key Laboratory of Neuromodulation

Objective: To investigate the relationship between tumor necrosis factor α (TNF-α), orexin levels, and the occurrence of rapid eye movement sleep behavior disorder in patients with Parkinson's Disease (PD), which may provide a theoretical basis to find biological indicators for early diagnosis and early intervention in PD patients. Methods: All subjects were divided into PD with RBD (PD+RBD) group, PD without RBD (PD-RBD) group, and idiopathic RBD (iRBD) group. The blood and cerebrospinal fluid of all patients were collected. Serum TNF-α level, cerebrospinal fluid TNF-α, and orexin levels were tested. Results: There were no significant differences in serum TNF-α levels among the three groups (5.52 ± 0.81 vs. 5.90 ± 1.17 vs. 6.32 ± 1.80, P=0.466). The differences were not statistically significant in cerebrospinal fluid TNF-α level of the PD+RBD group, PD-RBD group, and the iRBD group (4.25 ± 0.37 vs. 4.43 ± 0.51 vs. 4.47 ± 0.42, P=0.588). The orexin level of PD+RBD group was not significantly lower than that of PD-RBD group and iRBD group (182.27 ± 47.44 vs. 157.17 ± 35.73 vs. 164.57 ± 32.37, P=0.822). Conclusions: The serum and cerebrospinal fluid levels of TNF-α in PD with RBD patients are not significantly higher than those in PD patients without RBD and iRBD patients, and the level of orexin in cerebrospinal fluid does not decrease significantly in PD+RBD group. Some studies reported the reduction of TNF-α and orexin levels in PD patients and suggested the levels of TNF-α and orexin may be related to the stages of disease in PD patients and the extent of brain damage. Therefore, it is necessary to study the changes of TNF-α and orexin levels

in different stages of the disease and expand the sample size to explore whether TNF-α affects the function of the orexin system that may relate to the occurrence of RBD and disease progression in PD.
 Keywords

Prediction of OSAHS diagnosis based on plasma biomarkers: a proteomics study

Jian Guan1,2,3,Huajun Xu1,2,3,Weijun Huang1,2,3,Xinyi Li1,2,3,Yupu Liu1,2,3,Jianyin Zou1,2,3,Hongliang Yi1,2,3,Shankai Yin1,2,3
1.Shanghai Jiao Tong University Affiliated Sixth People's Hospital
2.Otolaryngology Institute of Shanghai Jiao Tong University
3.Shanghai Key Laboratory of Sleep Disordered Breathing

Background: Full-night polysomnography (PSG) is the gold standard for diagnosing obstructive sleep apnea hypopnea syndrome (OSAHS), but its discomfort, costs, and equipment limit the development of screening and diagnosis. In recent years, the application of proteomics and metabolomics techniques to study OSAHS biomarkers has attracted the attention of scholars at home and abroad. We aimed to explore potential OSAHS biomarkers to diagnose, classify the severity, and evaluate the efficacy. Methods: We enrolled 30 OSAHS patients and treated them with continuous positive airway pressure (CPAP). A total of 90 cases were divided into three groups as those patients before treatment (Group 1), three months after CPAP treatment (Group 2), and 30 non-OSAHS subjects (Group 3). Proteomics analysis of serum samples, including differential protein screening, differential protein clustering, differential protein enrichment analysis, and pairwise comparisons between groups were performed. Results: Through the preliminary analysis of proteomics, we found 172 (Group 1 vs. Group 2), 155 (Group 1 vs. Group 3), and 17 (Group 2 vs. Group 3) different proteins between the three groups respectively. Of the 122 identical metabolites detected among the 3 groups, 24 were consistently higher and 98 were consistently lower. There were also significant differences in the primary component analysis. Through enrichment analysis of differential genes, we had a preliminary understanding of the possible potential pathways, including PI3k-Akt signaling pathway, MAPK signaling pathway, and cytokine receptor interaction, which provided us with significant hints for further research. Conclusions: Further studies are needed to clarify the correlation of the differential proteins. We will establish stage-specific risk factors and serum markers, and analyze the functions of the discovered protein factors to explore the biological mechanisms underlying the differential factors.
Keywords Obstructive sleep apnea hypopnea syndrome; biomarkers; proteomics

Objective sleep characteristics and associated risk factors in heart failure patients with reduced, mid–range, and preserved ejection fraction

Binbin Han1,Shanshan wang1,guohua li1,xuehui wang1,zhigang chen1,guoan zhao1,yingen chen1,meng li1,yan li1,min zhang2,sizhi ai1

1. the First Affiliated Hospital of Xinxiang Medical University
2. King's College London British Heart Foundation Centre of Excellence，School of Cardiovascular Medicine & Sciences

Objective: To investigate the objective sleep characteristics and associated risk factors in heart failure (HF) patients with different ejection fraction. Methods: A total of 107 patients with chronic HF hospitalized in the Department of Cardiology of the First Affiliated Hospital of Xinxiang Medical University from April 2019 to October 2020 were included in this study. They were divided into heart failure with reduced ejection fraction (HFrEF) (n = 35), heart failure with mid-range ejection fraction (HFmrEF) (n = 21), and heart failure with preserved ejection fraction (HFpEF) (n = 51) groups according to the left ventricular ejection fraction (LVEF) measured by echocardiography. The baseline demographic and clinical characteristics of those patients were recorded. To assess the objective sleep characteristics, all patients were scheduled for total night polysomnography (PSG). Spearman correlation and multinomial logistic regression analyses were used to explore the risk factors associated with objective sleep characteristics. Results: Compared with patients in the HFrEF group, the age, LVEF, high density lipoprotein-cholesterol levels, the prevalence of hypertension, and proportion of calcium channel blockers uses were significantly higher in the HFpEF group, while the NT-proBNP levels, and proportion of diuretics, RASS inhibitors, and β-blockers uses were significantly lower (all P < 0.05). For the objective sleep parameters, the proportion of non-rapid eye movement sleep stage 1 (N1), apnea hypopnea index (AHI), and central sleep apnea (CSA) in patients of the HFpEF group were significantly lower than those of the HFrEF group (all P < 0.05). There were no significant differences in baseline demographic data or sleep parameters between the HFmrEF group and the other two groups. Spearman correlation analyses revealed a significant correlation for the male sex, diuretics use, NT-proBNP, LVEF, and total cholesterol levels with the severity of AHI (all P < 0.05). After adjusting for the potential confounders, multiple logistics regression analysis showed that age, drinking, and LVEF levels were independently associated with the severity of AHI (all P < 0.05). Conclusions: Sleep apnea (SA) is prevalent in patients with HF, but the proportions of SA and CSA are relatively lower in patients with HFpEF than those of the HFrEF. Age, drinking, and LVEF levels are the independent risk factors for the occurrence and severity of SA.

Keywords

Effectiveness of One–Week Self–Guided Internet Cognitive Behavioral Treatments for Insomnia Prevent the Development of Chronic Insomnia from Situational Insomnia During the COVID–19 Outbreak

Fei Feng1,Bin Zhang2

1.Shenzhen Kangning Hospital

2.Nanfang Hospital，Southern Medical University

Introduction: The COVID-19 pandemic and the imposed social confinement have caused significant stress which can induce situational insomnia. Without timely and effective intervention, situational insomnia is likely to develop into chronic insomnia, which brings greater negative impacts on individuals and society. Objective: To examine 1)whether one-week self-guided Internet cognitive behavioral treatments for insomnia（CBTI）could reduce the transformation from situational insomnia to chronic insomnia (ISI≥8) during the COVID-2019 pandemic; 2) whether this intervention could reduce insomnia severity, improve pre-sleep arousal, anxiety, and depressive symptoms at short-term (post-intervention) and long-term (three months post-intervention) follow-up. Methods: Participants were recruited through the activity of the "Prevention and Protection Handbook Against epidemic" from March to April 2020 in Guangzhou, China. A one-week Internet CBTI program was performed for all individuals with situational insomnia. All the participants were assessed for the Pre-Sleep Arousal Scale (PSAS), Insomnia Severity Index (ISI), and Hospital Anxiety and Depression Scale (HADS) at baseline, after the intervention, and three months after the intervention. Remission of insomnia symptoms was defined as ISI < 8, and chronic insomnia was defined as ISI ≥ 8. Conversion rates of chronic insomnia were compared between individuals who completed the one-week Internet CBTI intervention and those who didn't. Results: There were a total of 194 participants in our study, and 130 participants completed the assessments after one-week internet CBTI intervention, and 117 participants completed the assessments three months after the intervention. The conversion rates of chronic insomnia were respectively 36.0% (completers' group) and 63.0% (non-completers' group), there were statistically significant differences between the two groups (P< 0.001). For ISI, there were significant group effect(p = 0.009)，time effect (p < 0.001) and group×time effect (p = 0.002). For PSAS, significant group effects were found on total score (p = 0.008) and cognitive score (p = 0.007). with regard to PSAS, there were significant time effects for the total score, somatic score, and cognitive score (all p < 0.001). Group×time effect was significant on the total score(P=0.033) and somatic score(P=0.019). For the HADS, significant time effects were found on the total score, anxiety score, and depression score (all p < 0.001). Conclusion: Our study suggested that one-week self-guided Internet CBTI could reduce the conversion of situational insomnia to chronic insomnia. There were good effects of one-week internet CBTI on situational insomnia during COVID-19 for adults in the community, as well as on pre-sleep somatic hyperarousal symptoms. It has no obvious effects on pre-sleep cognitive hyperarousal, depression, and anxiety symptoms.

Keywords

Cognitive assessment and changes of serum markers in patients with obstructive sleep apnea

Ningning Zhe,Liu Na,Zhang yitong,Yuan yuqi,Si chao,Liu haiqin,Ren xiaoyong
The Second Affiliated Hospital of Xi'an Jiaotong University

Objective: To explore the association between OSA and cognitive impairment and the changes of serum markers. Methods: This study collected 121 OSA patients who were admitted to the Second Affiliated Hospital of Xi'an Jiaotong University from July 2019 to June 2020. Basic patient information, PSG, and MoCA, plasma samples were collected. ELISA was used to detect the expression of Aβ40, Aβ42, VEGF, and TGF-β1, and the results of MoCA were used for grouping. Then we carried out statistical analysis. Results: There were no statistically significant differences in age, gender, BMI, waist circumference, neck circumference, serological indicators Aβ40, Aβ42, and TGF-β1 between patients with and without cognitive impairment. The differences between AHI and VEGF were statistically significant, and were increased in patients with cognitive impairment. In order to find the risk factors of hematology and OSA related to cognitive independence, we constructed two binary logistic regression models. In Model 1, we adjusted the variables including gender, age, BMI, waist, and neck circumference and observed the independent relationship between hematological indicators and cognition. In order to further observe whether the relevant indicators were independent of OSA, we further adjusted AHI≥5 events/hour in Model 2. The analysis of the results found that in Model 1, age, VEGF, and Aβ40 were independent risk factors for cognitive impairment. But it was found in Model 2 that age and AHI were independent risk factors for cognitive impairment. Conclusion: OSA can cause central nervous system damage and manifests as cognitive impairment. Moreover, age and AHI are independent risk factors for cognitive impairment. The influence of VEGF and Aβ40 on cognitive impairment depends on AHI. Therefore, early intervention and treatment for patients with OSA can effectively improve central nervous system damage and relieve cognitive impairment. Keywords

Research status and Prospect of TCM non–Drug Therapy for Insomnia

Yanan Zhao, Peijing Rong,Yue Jiao,Shaoyuan Li,Yu Wang, Shuai Zhang,Jiakai He,Yu Chen
Institute of Acupuncture and Moxibustion，CACMS

Sleep is the most basic life process of the organism. With the change of times, the incidence of insomnia is increasing day by day, which is an important medical and health public problem. Long-term insomnia affects the human neuroendocrine-immune network, causing multiple organ dysfunction and the decline of immune function, and resulting in anxiety, depression, daytime fatigue, cognitive dysfunction, and other damages.

Therefore, "maintenance of healthy sleep, effective prevention and treatment of insomnia" should arouse public attention. The therapy of traditional Chinese medicine (TCM) has made a beneficial attempt to treat insomnia, which shows the unique advantage and is promising. The commonly used non-drug therapies of TCM mainly include acupuncture, moxibustion, massage, acupoint application, psychological therapy, five elements music, and so on. A large number of clinical studies and literature records have shown that non-drug therapy of TCM has great advantages in improving sleep quality and daytime function of patients with insomnia. It is effective, safe, easy to operate with high patient compliance, which has been widely used in the clinic. However, most clinical studies still focused on efficacy observation, the low-level repetitive work still exists and it is not easy to carry out scientific verification and summarization of rules. At the same time, there is a lack of standardized and unified criteria for diagnosis and efficacy. Therefore, a series of high-level evidence-based researches in line with clinical requirements and TCM non-drug therapy related mechanism researches in treating insomnia is the direction that TCM workers should strive for.

Keywords

Expression of BACE1 in rat superior cervical ganglion tissues

Zhen Zhao

The First Affiliated Hospital of Xinxiang Medical College

Object To observe the expression and localization of β-site amyloid precursor protein cleaving enzyme 1 (BACE1) in rat superior cervical ganglion and the effect of chronic intermittent hypoxia (CIH) on BACE1 level. Methods (1) The expression and distribution of BACE1 in superior cervical ganglion were detected by RT-PCR, Western blotting and immunohistochemistry. (2) 16 male SD rats were randomly divided into control group and CIH group, 8 rats of each group. After 2 weeks of modeling, the effect of CIH on BACE1 and PGC-1α mRNA levels were detected by RT-PCR. Results (1) BACE1 was expressed in rat superior cervical ganglion, and mainly distributed in satellite glial cells and nerve fibers, but not in blood vessels, neurons and SIF cells. (2) CIH down-regulated BACE1 mRNA level, but up-regulated PGC-1α mRNA level ($P<0.01$). Conclusion BACE1 is located in satellite glial cells and nerve fibers in the superior cervical ganglion of rats. The decreased level of BACE1 may be involved in the regulation of CIH-induced synaptic plasticity of superior cervical ganglion.

Keywords

Abnormal Gray Matter Volume and Functional Connectivity in Parkinson's Disease with Rapid Eye Movement Sleep Behavior Disorder

Xu Jiang,Li Zhang

Nanjing Brain Hospital

Objective: Rapid eye movement (REM) sleep behavior disorder (RBD) is a common symptom in Parkinson's disease (PD), and patients with PD-RBD tend to have cognitive decline and be akinetic/ rigidity predominant. At the same time, the mechanisms of RBD in patients with PD remain unclear. Therefore, this study aimed to detect the structural and functional differences in patients with PD-RBD and PD without RBD (PD-nRBD). Methods: Twenty-four polysomnography-confirmed patients with PD-RBD, 26 patients with PD-nRBD, and 26 healthy controls were enrolled. Structural and functional patterns were analyzed based on voxel-based morphometry and seed-based functional connectivity (FC). Correlations between altered gray matter volume (GMV)/FC values and cognitive scores and motor impairment scores in PD subgroups were assessed. Results: Compared with patients with PD-nRBD, patients with PD-RBD showed relatively high GMV in the cerebellar vermis IV/V and low GMV in the right superior occipital gyrus (SOG). For the FC, patients with PD-RBD displayed lower FC between the right SOG and the posterior regions (left fusiform gyrus, left calcarine sulcus, and left superior parietal gyrus) compared with the patients with PD-nRBD. The GMV values in the right SOG were negatively correlated with the Unified PD Rating Scale-III scores in patients with PD-RBD but positively correlated with delayed memory scores. The GMV values in the cerebellar vermis IV/V were positively correlated with the tonic chin EMG density scores. there were positive correlations between the FC values in the right SOG-left superior parietal gyrus and MoCA and visuospatial skills/executive function scores and in the right SOG-left calcarine sulcus and delayed memory scores. Conclusion: Higher GMV in the cerebellum may be linked with the abnormal motor behaviors during REM sleep in patients with PD-RBD, and lower GMV and FC in the posterior regions may indicate that PD-RBD corresponds to more serious neurodegeneration, especially the visuospatial– executive function impairment and delayed memory impairment. These findings provide new insights into the complicated characteristics in patients with PD-RBD.
Keywords

Impaired vigilant attention partly accounts for inhibition control deficits after partial sleep restriction

Tianxin Mao1,Hengyi Rao1,2

1.Laboratory of Applied Brain and Cognitive Sciences，Shanghai International Studies University

2. Center for Functional Neuroimaging，Department of Neurology，University of Pennsylvania

Objective: Sleep loss impairs a range of neurobehavioral functions, particularly vigilant attention and arousal. However, the detrimental effects of sleep deprivation on inhibition control and its relationship to vigilant attention impairments remain unclear. This study aimed to examine the extent to which vigilant attention deficits contribute to inhibition control performance after two nights of partial sleep restriction. Methods: We analyzed data from 16 participants in a two-nights of partial sleep restriction experiment (time in bed, TIB = 6 h for each night). During waking periods, participants completed the psychomotor vigilance test (PVT) to measure vigilant attention, and the Go/No-Go task to measure inhibition control. Results: After partial sleep restriction, participants displayed significantly slower reaction times (RT) and more lapses in PVT performance, as well as slower Go RT and more errors of omission during the Go/No-Go task. PVT deficits accounted for 23.7% of the change in Go RT and 20.3% of the change in errors of omission in the partial sleep restriction study. Conclusions: Partial sleep restriction impairs inhibition control during the Go/No-Go task, which can be partly accounted for by vigilant attention deficits during the PVT. These findings support the key role of vigilant attention in maintaining overall neurobehavioral function after sleep loss.

Keywords partial sleep restriction, vigilant attention, inhibition control

The Chronotype and Its Related Factors of College Students

Jiajia Wang,Bin Zhang

Nanfang Hospital，Southern Medical University

Objective: This study aimed to investigate the chronotype and its relationship with social rhythm among college students.Methods: Students from a university in Guangzhou were recruited using the stratified cluster random sampling method. The survey collected sociodemographic data and assessed chronotype, daytime functioning, psychoactive substances, emotion, and mobile phone use. A multivariate logistic regression analysis was performed to determine factors affecting chronotype. Results: A total of 1607 questionnaires were distributed, among which 1569 (97.6%) were valid for further analysis. According to the total score of MEQ-5, 14.9% of the participants were morning types (M-types), while 71.5% were neutral types (N-types) and 13.6% were evening types (E-types). Multivariate logistic regression analysis revealed that high interest in study (OR=1.65, 95% CI 1.21-2.26) and anxiety(OR=1.03, 95% CI 1.01-1.06) were positive predictors of M-types, while procrastination (OR=0.98, 95% CI 0.96-0.99), sleep compensation (OR=0.66, 95% CI 0.55-

0.78), insomnia (OR=0.94, 95% CI 0.90-0.99) were negative predictors of M-types. Regarding E-types, male (OR=1.54, 95% CI 1.11-2.15), procrastination (OR=1.03, 95% CI 1.02-1.05), depression (OR=1.06, 95% CI 1.01-1.10), sleep compensation (OR=1.57, 95% CI 1.36-1.82), urban residence (OR=1.825, 95% CI 1.189-2.801) were positive predictors, while low family income (OR=0.565, 95% CI 0.348-0.916) was a negative predictor. Conclusion: Our study found that the chronotype of college students was mainly N-types. All types of chronotypes were characterized by shorter sleep duration on weekdays, longer sleep duration on weekends, and delayed bedtimes and waketimes on weekends. Our findings emphasize the importance of chronotype and help identify N-type individuals, which may further help improve their physical and mental health.

Keywords

Meta–analysis of seven randomized controlled trials and five observation studies on CPAP in patients with Obstructive sleep apnea and type 2 Diabetes Mellitus

Liqing Zhang, Jiyang Pan,Fangyi Deng,Rui Tang

The First Affiliated Hospital of Jinan University

Obstructive sleep apnea (OSA) is strongly associated with type 2 Diabetes Mellitus (T2DM), and the CPAP is a common treatment method for patients with OSA and T2DM. Because OSA is an independent risk factor for T2DM, we conducted a meta-analysis to investigate the overall effects of CPAP treatment on HbA1c. PubMed, EMBASE, Medline, and the Cochrane Library were systematically searched for articles published until February 2021. Meta-analysis was performed on the included articles by using Review Manager 5.3. A total of twelve studies were included, with seven randomized controlled trials and five observational studies, including a total of 878 participants. The fixed effects model was conducted for the change in HbA1c of seven RCTs (784 patients), and the mean differences revealed no significant effect of CPAP (−0.03, 95% confidence interval (CI) = − 0.16, 0.09; P = 0.61). Among the five observational studies (94 patients), the treatment with CPAP also showed no effectiveness (−0.03, 95% CI = −0.33, 0.26 ; P = 0.82). In conclusion, the meta-analysis suggests that CPAP does not decrease HbA1c levels in patients with OSA and T2DM. Keywords

The psychopharmacological activities of Oplopanax elatus Nakai: characterization of its sedative–hypnotic, antistress, antianxiety, and cognitive effects

Yanyan Wang,Haini Li,Huihui Zeng

Heilongjiang University of Chinese Medicine

Objective: Oplopanax elatus Nakai is an ancient angiosperm plant member. It belongs to the Araliaceae family and has biological activities similar to those of Panax ginseng. It is used to treat different disorders in the medical systems of China, Russia, and Korea. The root of Oplopanax elatus Nakai has a well-known history of use to treat diseases such as neurasthenia, cardiovascular disorders, and cancer. The chemical components of this plant have been widely investigated. Earlier work has indicated that this plant contains volatile oils, aliphatic acids, saponins, flavonoids, and anthraquinones. However, the psychopharmacological effects of Oplopanax elatus Nakai have not been characterized. Thus, in the present study, we screened the psychopharmacological activities of O. elatus Nakai extract (ONE). Methods: The open field and elevated plus-maze were used to evaluate the antianxiety effect, and the cold swimming test was chosen to explore the anti-stress effect. Besides, drosophila was conducted to study the sedative-hypnotic, anti-aging, and antioxidant effects of ONE. Results: Treatment with ONE extended cold swimming endurance time, reduced anxiety-like behavior, decreased spontaneous locomotor activity, prolonged sleep duration, and ameliorated the sleep-wake rhythm. Conclusions: ONE produces biological activities like anti-fatigue, anti-stress, anti-anxiety, sedative-hypnotic, and anti-antioxidant. Meanwhile, due to the limitations of the present study, the specific constituents involved in the pharmacodynamic material basis of ONE are still unknown. This can be a worthwhile focus in future studies. Nevertheless, the results of the present study demonstrate that ONE, like other ginseng species, can potentially be used as an alternative natural remedy for various diseases. Keywords Oplopanax elatus Nakai, Sedative-hypnotic, Anti-antioxidant, Anti-anxiety

Activaion of Nrf2 prevents chronic intermittent hypoxia associated cognitive dysfunction.

Yunjia Tu,Yichun Zhang,Xiaohong Cai

The Second Affiliated Hospital of Wenzhou Medical University，Yuying Children＇s Hospital

Objective:Childhood obstructive sleep apnea-hypopnea syndrome (OSAHS) has become a major public health problem, which can cause damage to brain nerves and cause cognitive dysfunction. The nuclear factor E2 related factor 2 (Nrf2) plays a key role in regulating the oxidation-reduction balance and anti-ERS damage. Therefore, this study established a CIH mouse model and observed changes in

neurocognitive function in mice of each model, and observed neuronal damage in the hippocampus. Methods:The male C56BL/6 mice were divided into 6 groups: air group (C), air control group (AC), CIH control group (CIH), Nrf2 agonist group (SFN), Nrf2 antagonist group (ATRA), and solvent group (DMSO). Using the 8-Arm maze test to observe the performance of spatial memory, and separating the hippocampus to determine the expression levels of ERS-related protein. Using Tunel to observe the neurons' apotosis. Results:(1) 8-Arm maze test: There is a statistically significant difference between the groups (P<0.01), compared with the C group, errors of the CIH group was significantly increased (P<0.01); the ATRA group had more errors than the IH group (P<0.05), errors of the SFN group was significantly decreased than the IH group (P<0.05). (2)TUNEL staining: Compared with the C group, the apoptotic cells in the hippocampal CA1 region of the CIH group were significantly increased; compared with the CIH group, the apoptotic cells in the ATRA group increased, while the SFN group decreased. (3) Western blot: the expression levels of Bip、PERK、Nrf2、HO-1、NQO-1、Chop、Caspase-12 showed statistically significant differences between the groups (P<0.01), they were all UP-regulated significantly in the IH group than the A group (P<0.01). Conclusion:（1）Chronic intermittent hypoxia can cause apoptosis in mouse hippocampal neurons, damages spatial learning and memory function. Activation of Nrf2 reduces cognitive impairment and plays a protective role.（2）Nrf2 may attenuate CIH-induced cognitive impairment by activating the Nrf2 / HO-1 pathway and the Nrf2 / NQO pathway.（3）Nrf2 can attenuate CIH-induced apoptosis through the endoplasmic reticulum and improve cognitive impairment through the PERK-CHOP pathway.

Keywords

The association between gene LOC105369165 polymorphism and sleep parameters within OSA patients

Jinhong Shen,Yaxin Zhu,Weijun Huang,Hongliang Yi,Feng Liu,Jian Guan,Shankai Yin

Shanghai Sixth People's Hospital

Obstructive sleep apnea (OSA) is a common chronic disease that causes an abnormal sleep-wake cycle. Previous studies have demonstrated that OSA is heritable and the genetic factors seriously affect the susceptibility to OSA and the complexity of its clinical symptoms. The present study aimed to identify the genetic loci contributing to OSA-associated disorders of sleep and wakefulness by genome-wide association studies (GWAS) in a large-scale, clinic-based consecutive OSA sample. GWAS analysis was conducted among 5,438 OSA patients diagnosed by standardized polysomnography (PSG) and 15,152 control samples in our clinical database of the specific disease. Rs75414365, a single nucleotide polymorphism (SNP) site located on gene LOC105369165, was found to significantly correlate with the increased duration of wakefulness in OSA patients for the first time (p=5.33×10^{-10}). Also, these loci were found to associate with reduced duration of stages I and II of non-rapid eye movement sleep (NREM), but not with AHI

and minimum oxygen saturation that are indicators of OSA severity. Therefore, our study suggested that LOC105369165 is potentially a novel independent genetic factor that affects OSA-associated sleep-wake symptoms.

Keywords

Comparison of serum vitamin D level between obstructive sleep apnea(OSA) and primary snoring(PS) in children

Ying Ding,Kaimeng Kong,Min Lu

Shanghai Children's Hospital，Shanghai Jiao Tong University

Objective: To evaluate the relationship between serum vitamin D3 level and the severity of sleep disorders in children.Methods: A total of 227 children with snoring, aged 2 to 14 years, were enrolled in the respiratory department of Shanghai Children's Hospital. Polysomnography (PSG) was performed on all the children. The gender, age, neck circumference, height, weight, body mass index(BMI), the longest time of apnea(LTA), the longest time of hypoventilation(LTH), lowest oxygen saturation(LSaO2), average oxygen saturation(ASaO2), sleep efficiency(SE), snoring index (SI), arousal index(ARI), obstructive apnea-hypopnea index(OAHI) and other items were recorded. At the same time, serum 25(OH)VitD3 level, triglyceride(TG), and total cholesterol(TC) were detected. According to OAHI, the patients were divided into primary snoring(PS) group and obstructive sleep apnea(OSA) group. The differences in 25 (OH) VitD3 between the two groups were compared.Results: Serum vitamin D3 level in the OSA group was significantly lower than the PS group. There were statistically significant differences in OAHI, OAI, LSaO2, ASaO2, LTA, LTH, and ARI between the OSA group and PS group (P<0.05); There were significant differences in TC between the two groups in blood lipid (P<0.05), and serum cholesterol in OSA group was higher than PS group. Conclusion: Vitamin D is an important biomarker in children with OSA.

Keywords

Preliminary study on the relationships between narcolepsy type 1 and plasma cytokines

Liang Xie,Liying Deng,Yongmin Ding

The Second Affiliated Hospital of Nanchang University

Background: Narcolepsy type 1 (NT1) is an autoimmune disease. We measured the expression levels of 12 plasma cytokines（IL-1b, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12P70, IL-17, TFN-a, IFN-a1, IFN-Y）in NT1 and aimed to find the associations between the pathophysiology of NT1 and cytokines.Methods: 33 NT1 patients (mean age: 15.39±9.79 years old, 23 males, 32 positive HLA DQB1*0602) and 10 healthy

controls (mean age: 26.11±2.41 years old, 3 males, all negative HLA DQB1*0602)) were included. Plasma cytokines were detected by multiple microsphere flow immunofluorescence assay. Statistical methods (independent sample T TEST for normality, Mann-Whitney rank sum test for skewness data) were used to compare the cytokines levels between NT1 and healthy controls, we also compared the differences of cytokines levels between males and females in the NT1 group, and the differences between the patients with less than one year of disease duration and patients with longer duration. Results: First, There were no statistical differences in 11 cytokines between the NT1 group and the normal group (P >0.05, due to be undetectable in the normal group, IL-2 was not involved in statistics). second, plasma IFN-a1, IL-6, IL-1b, IL-10, and IL-17 in female patients with NT1 were significantly higher than those in males (P<0.05). Third, there were no significant differences in cytokine levels between those with disease onset less than 1 year and those with a longer duration than 1 year in the NT1 group (P>0.05).Conclusions: IFN-a1, IL-6, IL-1b, IL-10, and IL-17 may be involved in the pathogenesis of NT1. This trial is a preliminary study, which needs to expand the sample size of patients with NT1, and more healthy controls according to the characteristics of age and gender of the NT1 group should be recruited.

Keywords

Differential response of different chronotypes to sleep homeostasis pressure

Haien Wang,Yun Tian,Xu Lei

Southwest University

Background: Chronotype is an appropriate tool to study sleep homeostasis and circadian rhythm. The functional connectivity (FC) of the default mode network (DMN) and the anticorrelated network decrease with the increase of sleep homeostasis pressure (SHP), of which the insula plays an important role in the anticorrelated network. However, the response of different chronotypes to differences in SHP is unclear. Methods: The reduced version of the Morningness-Eveningness Questionnaire (rMEQ) was used to assess their chronotypes. A total of 64 morningness-chronotypes participants (MCPs, female=44; age: 18.9±0.9) and 128 eveningness-chronotypes participants (ECPs, female=86; age: 18.7±1.1) were screened out by rMEQ. All participants were performed resting-state fMRI scans at a random time during the day. SHP was divided into three levels (Low, Medium, High) based on the length of time from scan to wake-up time. We used independent component analysis and ANOVA to study FC, focusing on the right insula (rI) and the ventral DMN (vDMN).Results: The interaction between chronotype and sleep homeostasis pressure was significant. MCP and ECPs' FC of rI and the right vDMN (rvDMN) changed significantly with the increase of SHP. MCPs' FC of rI and the left ventral DMN (lvDMN) changed significantly with the increase of SHP. FC of rI-rvDMN at three levels was significantly different between MCPs and ECPs. FC of rI-lvDMN at high and medium levels were significantly different between the two chronotypes.Conclusion: Sleep homeostasis

stress affects brain FC, and MCPs decrease brain FC with increased SHP. The significance of SHP to individuals of two chronotypes is different, there are differences in brain FC of different time types under the same SHP. The response of different chronotypes to SHP was different, and the brain FC of ECPs was reversed under high SHP, which could interact with circadian rhythms and social schedules.
Keywords Chronotype, sleep homeostasis pressure, fMRI, insula, vDMN

Efficacy of H–Palatopharyngoplasty (HUPPP) combined with radiofrequency ablation of tongue base or HUPPP with traction of tongue base on moderate to severe patients with obstructive sleep apnea hypopnea syndrome (OSAHS) ：a multicenter randomized controlled trial

Huaming Zhu1,2,3,Wenjun Yu1,2,3,Huajun Xu1,2,3,Jianyin Zou1,2,3,Yupu Liu1,2,3,Lili Meng1,2,3,Suru Liu1,2,3,Jian Guan1,2,3,Hongliang Yi1,2,3,Jiping Li4,Pin Dong5,Shankai Yin1,2,3

1. Shanghai Jiaotong University 6th People's Hospital，Department of Otolaryngology-Head and Neck Surgery
2. Shanghai Jiaotong University Institute of Otolaryngology
3. Shanghai Key Laboratory of Sleep disordered breathing
4. Shanghai Jiaotong University School of Medicine Renji Hospital，Department of Head and Neck Surgery
5. Shanghai General Hospital，ENT- Neck Surgery Center

Objective: To compare the therapeutic efficacy of H-Palatopharyngoplasty (HUPPP) combined with radiofrequency ablation of tongue base or HUPPP with traction of tongue base on moderate to severe patients with obstructive sleep apnea hypopnea syndrome (OSAHS).Method: This is a multicenter randomized controlled trial. From March 2017 to July 2019, moderate to severe OSAHS patients from three clinical centers in Shanghai who were intolerant to continuous positive airway pressure (CPAP) and with velopharyngeal and glossopharyngeal plane obstruction were enrolled in this study. According to the surgical type, they were 1:1 randomized to HUPPP plus radiofrequency ablation of tongue base group (Ablation group) or HUPPP plus traction of tongue base group (Traction group). All patients completed over-night standard Polysomnography (PSG), upper airway assessment (Friedman classification, müller test, CT and cephalometric examination), preoperative routine examination, Epworth Sleepiness Scale (ESS) and Quebec sleep questionnaire (QSQ). 6 to 12 months after operation, all the above-mentioned examinations were repeatedly performed. Changes of aforementioned variables before and after operation were assessed. Result: A total of 43 patients with moderate to severe OSAHS were enrolled in this study. With one patient lost to follow-up, the remaining 21 were allocated to Ablation group and 21 were allocated to Traction group. The total therapeutic efficacy of all patients was 69.05% (61.90% in Ablation group and 76.19% in Traction

group), but there was no statistical significance between the two groups (P = 0.317). The value of sleep scale score (ESS and QSQ), objective sleep variables (apnea-hypopnea index, oxygen saturation, percentage of time with blood oxygen less than 90% in total sleep time, oxygen desaturation index and micro-arousals) and upper airway cross-sectional area (palatopharyngeal and retrolingual area) of the two groups were improved (P < 0.05), but the differences between the two groups were not statistically significant (P > 0.05). Conclusion: For moderate to severe OSAHS who had glossopharyngeal plane obstruction, both HUPPP plus radiofrequency ablation of tongue base or HUPPP plus traction of tongue base are effective treatment for OSAHS, and the curative effect is similar. The choice of surgical type could be selected according to patient's or surgical conditions.

Keywords

Central Sleep Apnea Increase Risk of Atrial Fibrillation in Patients with Rheumatic Valvular Heart Disease

Dongmei Liu1,Ning Ding2,Xilong Zhang2

1.Lianyungang Hospital of Traditional Chinese Medicine

2.Jiangsu Province Hospital

Background: The clinical and sleep characteristics of patients with rheumatic valvular heart disease (RVHD) and atrial fibrillation (AF) remain unknown. In the current study, the frequency of AF and the risk factors for AF in patients with RHVD were explored.Methods and Results: Patients (n=248) with RHVD were divided into AF (n=134) and no AF (control) groups (n=114) according to electrocardiographic results. All of the patients underwent a standard clinical evaluation and whole night polysomnography. The clinical and sleep characteristics between the two groups were compared. Compared with patients without AF, patients with AF were older, had a shorter 6-minute walk test distance, a higher cardiothoracic ratio, and a larger left atrial diameter (LAD). Multivariate logistic regression analysis showed that a LAD ≥ 50 mm (OR=8.805; 95%CI=4.836-16.032), New York Heart Association class = IV (0R=5.177; 95%CI=2.159-8.197), a history of symptomatic heart failure ≥ 5 years (0R=3.842; 95%CI=2.167-6.812), central sleep apnea (CSA; 0R=3.292; 95%CI=1.571-6.898), and a pH ≥ 7.45 (0R=2.026; 95%CI=1.141-3.598) were risk factors of AF.Conclusions: Patients with RVHD and AF have a high prevalence of CSA. AF patients manifest more advanced symptoms and had greater cardiac function impairment. It may be necessary to identify risk factors for AF by assessing cardiac function and performing a sleep study.

Keywords Sleep-disordered breathing, sleep apnea, atrial fibrillation, rheumatic valvular heart disease

Melatonin regulates sleep period length caused by nmda receptor impairment through ventrolateral preoptic nucleus

Jinhao Sun

Department of Anatomy and Neurobiology，Shandong University School of Medicne

Objective: Sleep is an evolutionarily conserved behavior whose mechanism remains to be further investigated. After decades of study, a lot of sleep theories have been raised to clarify the complicated progress. Among them, the Two-process theory is well accepted. It is widely accepted that sleep is manipulated by both the circadian system and homeostatic systems. Although a lot of progress has been gained, a lot of areas are still unclear. Traditional opinions suggest that the behavioral rhythm is mainly controlled by the circadian system. Methods: Using mouse model by melatonin and MK-801 pharmacology treatment, the running wheel experiment was performed. Results: The data showed that homeostatic systems controlled by ventrolateral preoptic nucleus can also affect the circadian rhythm on the behavioral level and molecular level. Melatonin can recover the period length prolonged by MK-801. Moreover, the Ca2+-CaMKII-p-CREB pathway in the ventral lateral anterior nucleus is identified to play an important role in the process. Conclusion: This study indicates that melatonin can regulate sleep through the homeostatic system. Our studies may offer a new sight in sleep regulation.
Keywords

Study on the role of CRP in sleep–disordered breathing and coronary artery disease

Wei Yang1,Wei Yang1

1. The First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of science and technology
2. The First Affiliated Hospital of Baotou Medical College，Inner Mongolia University of science and technology

Objective: This study aimed to analyze the relationship between CRP and fasting blood glucose, OSAHS, and coronary artery disease and its underlying mechanism. Methods: A retrospective analysis of 91 patients with coronary angiography in the Department of Cardiology of the First Affiliated Hospital of Baotou Medical College from April 2017 to May 2018, and 42 patients were diagnosed with sleep apnea (46.1%). The general condition of the patient was recorded, the first fasting blood glucose and CRP were measured on admission, and the portable sleep monitor was used to determine sleep apnea, and the coronary artery lesions were calculated based on the results of coronary angiography. SPSS20.0 software and Spearman correlation analysis were used to analyze the relationship between CRP and fasting blood glucose, OSAHS, and coronary

artery disease. Results: The P-value between CRP and the number of coronary artery lesions was 0.403>0.05, and the R-value was 0.101. The P-value between CRP and fasting blood glucose was 0.220>0.05, and the R-value was 0.140. The P-value between CRP and OSAHS was 0.291>0.05, and the R-value was 0.124. Conclusion: At present, there is no correlation between CRP and fasting blood glucose, OSAHS, and the number of coronary artery diseases. A large amount of data is still needed to study the relationship between CRP and fasting blood glucose, OSAHS, and the number of coronary artery diseases.

Keywords

Analysis on reliability and validity of SF–36 scale during the first trimester of pregnancy

Wei Hao1, Chenchen Fan1, Wei Song1,Shenglong Zhao1,Shengnan Liang1,Ying Fang1,Xiaowei Liu1,Xiaoyi Wang2

1.Beijing Obstetrics and Gynecology Hospital，Capital Medical University

2.Beijing Tongren Hospital，Capital Medical University

Objective pregnancy, delivery, and postpartum periods are associated with fast changes such as hormones, emotions, and social roles, leading to decreased self-confidence, anxiety, stress, or even maternal depression impairing their quality of life (QOL). Although considered important, the QOL of women during pregnancy is poorly understood. The aim of our study was to evaluate the reliability and validity of the SF-36 scale during the first trimester of pregnancy and provide a reference for the selection of suitable health measure tools for pregnant women. Methods From January 2020 to January 2021, pregnant women aged 18-40 years during the first-trimester visit were admitted to the obstetric department of Beijing Obstetrics and Gynecology Hospital, Capital Medical University. SF-36 scale was used for the measurement of the quality of life and Cronbach´s α coefficients were used for the evaluation of split-half reliability and internal consistency reliability. The convergent and discriminative validity was evaluated by using AMOS 24.0 and the criterion-rated validity was evaluated with correlation analysis and non-parameter test. Structural equation modeling was used in the evaluation of contract validity. Results SF-36 scale had good split-half reliability(R=0.901) and internal-consistency reliability(Cronbach´s α coefficients=0.878). The convergent validity, discriminate validity and the criterion-rated validity(r=0.907) were good. Second-order confirmatory factor analysis model was not well-fitted (RMSEA=0.070，c2/df=3.566，GFI=0.813，CFI=0.814，TLI=0.792，IFI=0.816，NFI=0.761), indicating that the construct validity was poor. Conclusion The reliability, consolidation validity, discrimination validity, and criterion-related validity of the SF-36 scale are good, while the construct validity is poor. Improvement is needed when the scale is used for pregnant women.

Keywords

A case of recurrent isolated sleep paralysis

Liang Xie,Liying Deng,Yongming Ding

The Second Affiliated Hospital of Nanchang University

Recurrent isolated sleep paralysis is called sleep paralysis, which is commonly seen in adolescents or young adults. We provided clinical characteristics and auxiliary examinations of a case, aiming to improve the understanding of this disease for clinicians.The patient was a 16 years old female, with a year of disease course. She was nervous and introverted. The patient took the exam on the day of the first onset. The frequency of attacks increased recently, about 3 to 4 times a week, episodes have an obvious correlation with learning pressure. Sleep paralysis mostly happened during the noon break. The patient was conscious but unable to move in the supine position. After approximately 20-30 seconds, the patient started to move fingers, then the whole body slowly got better. Over the past year, the patient had 4 to 5 sleep hallucinations, which also appeared in the noon break and were manifested as the feeling that someone came in while lying in bed. The patient had no daytime sleepiness or cataplexy. The sleep duration was about 6-7 hours every night with little dreams.Auxiliary examination: blood routine, thyroid function was normal. PSG finding: SOL was 25.5 minutes, sleep efficiency was 85.2%. N1:8.9%,N2:35.4% N3:41.7%, REM:14%, AHI and PLM were normal. MSLT indicated that the latency of sleep was 4.6 minutes, and there were no SOREMPs.Epworth scale:5; RBD-HK scale: 9, MEQ scale:57, intermediate type; Self-Rating Anxiety Scale: 56, Mild Anxiety; Self-Rating Depression Scale:29; Pittsburgh Sleep Quality Index (PSQI):5; Insomnia Severity Index:5. The patient refused medication, and there was no improvement of symptoms during a follow-up visit.Recurred isolated sleep paralysis often leads to anxiety in patients, and patients need to be guided to correct poor sleep hygiene habits, if necessary, drugs that inhibit REM sleep should be taken. Attention should be paid to distinguish it from narcolepsy in diagnosis.

Keywords

The value of portable sleep monitoring in children with obstructive sleep apnea hypopnea syndrome

Zhilin Li,Huilin Cai,Xiaohong Cai

Yuying Children's Hospital，The Second Affiliated Hospital of Wenzhou Medical College

Objective: To investigate the value of portable sleep monitoring to diagnosis of OSAS in children, as well as to provide the basis for intervention in improving the quality of life for children with OSAS.Methods: The study design was parallel controlled clinical trial. We compared the sleep monitoring parameters between professional staff again(PSG) and Morpheus Ox portable sleep monitoring in children in different age. Eighty children diagnosed with sleep-disordered breathing were randomly selected from outpatient

department from June 2017 to December 2018. All of study sample underwent overnight PSG and Morpheus Ox at the same time. Morpheus recording AHI, LSaO2, total sleep time, sleep efficiency, pulse, etc was assessed with automatic analysis software. The PSG parameters including AHI, LSaO2, OAI, total sleep time, sleep efficiency, etc were reported by the professional staff. Two kinds of sleep monitoring indexes in each group were compared and analyzed. With PSG as the reference standard, ROC curve was used to analyze the sensitivity and specificity of Morpheus Ox in the diagnosis of OSAS.. Results: The study sample was divided into two groups: 1) the preschool age group ageing from 1 to 6 years old , with an average age of 4.2 years odl (standard deviation, 1.2), including 24 males and 16 females; 2) the school age group ageing from 7 to 14 years old as, with an average age of 8.8 years odl (standard deviation, 2.3), including 28 males and 12 females. The diagnostic and oxygen saturation monitoring parameters of Morpheus Ox portable sleepometer for OSAS in children aged 1-14 years were statistically consistent with PSG and well correlated. Conclusions: Morpheus Ox portable sleep apparatus had clinical practical value in screening and diagnosing OSAS in children.

Keywords

Effects of single nucleotide polymorphisms in ATP binding cassette subfamily C member 4 on the sleep traits of OSA

Li Xu1,2,Xiaoting Wang1,2,Weijun Huang1,2,Wenjun Yu1,2,Zhenfei Gao1,2,Feng Liu1,2,Guan Jian1,2,Hongliang Yi1,2,Shankai Yin1,2

1.Shanghai Jiao Tong University Affiliated Sixth People's Hospital

2.Shanghai Key Laboratory of Sleep Disordered Breathing

Objective: Obstructive sleep apnea (OSA) is characterized by sleep fragmentation. Micro-arousals are one of the causes of sleep fragmentation. Micro-arousals index (MAI) is an important indicator of micro-arousals. The study aimed to explore the genetic mechanism of micro-arousals in OSA.Methods: This study enrolled 5,515 patients from January 2011 to June 2019. We performed Genome-Wide Association Studies (GWAS) for all subjects. SNP loci. (rs871052) genotyping was performed. All subjects underwent overnight polysomnography. The differences of sleep traits among different genotypes were compared with ANOVA. Multiple linear regression analyses with stepwise models were performed to assess the associations between SNP (rs871052) and MAI.Results: MAI was significantly different among groups with different genotypes (rs871052, G>A) (F=3.025, P=0.047), whereas AHI (P=0.205), ODI (P=0.170), S1% (P=0.821), S2% (P=0.515), S3% (P=0.735) didn't show significant differences. Multiple linear regression analysis indicated that the variation of SNP (rs871052) was correlated with MAI (β =-0.939, P=0.022).Conclusions: SNP loci (rs871052) are associated with MAI. Mutations in this site may promote sleep.

Keywords

Obstructive sleep apnea hypopnea syndrome comorbid hypoglycemia: a case report

Kangkang Peng,Lijuan Hao
Qinghai Red Cross Hospital

In recent years, Obstructive sleep apnea hypopnea syndrome (OSAHS) characterized by apnea and hypopnea during sleep has been widely studied. Many studies have shown that OSAHS lead to insulin resistance, abnormal glucose metabolism, and even diabetes. OSAHS is independently associated with insulin resistance and type 2 diabetes. However, it is unkonwn that whether OSAHS is related to the occurrence of hypoglycemia. We aimed to explore the relationship between the OSAHS and hypoglycemia by analyzing a case of OSAHS comorbid hypoglycemia.

Keywords

Review of Alzheimer's disease comorbid sleep disorders with traditional Chinese medicine treatment

Shu Xiao,Li Nana,Sha Zhongwei,Li Ou
Shanghai Hospital of Traditional Chinese Medicine;

Western medicine treatment for Alzheimer's disease comorbid sleep disorders has some side effects, while the traditional Chinese medical treatment for this disease advantage the western treatment in safety, This review summarizes the causes of Alzheimer's disease comorbid sleep disorders, the current advantages and shortcomings of traditional Chinese medicine treatment and the Chinese medicine non-drug treatment, therefore, put forward treating recommendations for Alzheimer's disease comorbid sleep disorders. A standard criteria of clinical diagnosis, treating protocol, and evaluation of this disease should be proposed and made., More large-scale clinical trials and experimental studies to testify the efficacy of Chinese medicine in treating Alzheimer's disease comorbid sleep disorders are warranted.

Keywords

Effects of severe sleep apnea on cerebrovascular disease

Gangyu Ding,Jihong He,Jianhua Xu
iading Central Hospital Shanghai University of Medicine & Health Science

Objective: Several studies have documented that sleep apnea during rapid eye movement sleep is related to risk of cerebrovascular disease(CVD). This study aimed to explore the effects of severe sleep apnea on cerebrovascular disease. Methods: Patients aged ≥18 years admitted with acute ischemic stroke was

randomly recruited between December 2019 and March 2020. We collected the demographic and clinical data including age, sex, admission glucose, NIHSS score, Modified Rankin Scale score, and history of hyptertension, diabetes, atrial fibrillation, and heart failure. The study sample was divided into two groups: group A (acute ischemic stroke with sleep apnea); group B (acute ischemic stroke with sleep apnea without sleep apnea). The severity of sleep apnea measured by apnea-hypopnea index(AHI, events/h) was categorized as mild, moderate, severe degrees. Mann-Whitney non-parametric tests were further used for statistical analysis of the data from group A and 3 subgroups in group B. All analyses were carried out using SPSS, version 25 and the figures was made using R version 3.5.3.Results: No statistical differences were found between group A and B with respect to age, sex, admission glucose, history of hyptertension, diabetes, atrial fibrillation, or heart failure. The NIHSS score and Modified Rankin Scale score were both significantly different between the two groups. The data were statistically different among the 4 groups ($p < 0.05$). The po st hoc pairwise comparisons showed that only severe sleep apnea was significantly different between the two groups. Binary logistic regression revealed that a factor was independently associated with NIHSS score but not the severity of sleep apnea .Conclusion: Severe sleep apnea may have effects on CVD. Further studies with large sample sizes are warranted to further validate this finding.

Keywords

Association between serotonin transporter SLC6A4 gene and primary insomnia

Xubin Wang,Yuping Xie
Gansu Provincial Hospital

Objective: 5-hydroxytryptamine (5-HT or serotonin) promotes arousal and inhibits slow wave sleep (SWS) and rapid-eye-movement sleep (REMS). The solute carrier family 6 member 4 (SLC6A4) gene encodes 5-serotonin transporter (SERT), which uptakes 5-HT from the brain synapses into the presynaptic neuron rapidly. Thus,this study aimed to explore the association between SLC6A4 gene polymorphisms and primary insomnia (PI). Methods: A total of 129 patients with PI and 149 healthy controls completing the sleep scales and polysomnography (PSG) were included. All SNPs were genotyped by Sequenom MassArray system. Results: The association between single-nucleotide polymorphisms (SNPs) in SLC6A4 gene and PI was observed in all the subjects. There were different degrees of linkage disequilibrium among 4 loci on SERT gene. There was a complete linkage disequilibrium between rs140700 and rs6352 (D′=1.000). A strong linkage disequilibrium was observed between rs2020936 and rs3794808 (D′=0.771), rs3794808 and rs6352 (D′=0.993), rs2020936 and rs140700 (D′=0.803), rs2020936 and rs6352 (D′=0.958), and rs140700 and rs3794808 (D′=0.958). The haplotype CGTT showed significant differences between PI and control groups (p=0.027). Conclusions: All SNPs distributed equally in both the groups. However, the probability of PI was higher when the genotypes in the four sites were arranged in a combination of CGTT.

Keywords

Neuroprotective and Memory–Enhancing Effects of Antioxidant Peptide From Walnut (Juglans regia L.) Protein Hydrolysates

Wei Qu1,2,YANG WEN1

1.Hefei University of Technology

2.Sinphar Tian-Li Pharmaceutical Co.，Ltd

Peptides have been reported to possess interesting biological properties. The present study was designed to evaluate neuroprotective and memory-enhancing effects of antioxidant peptide from walnut (Juglans regia L.) protein hydrolysates. The neuroprotective effect of walnut peptide (WP) against oxidative stress on PC12 cells was evaluated. And zebrafish was used as the model to corroborate the effect. Its effect on learning and memory of mice using the Morris water maze and the step-down passive avoidance tests were performed. Moreover, the acute toxicity of WP was carried out to assess its safety profile. It was found that WP was able to suppress H_2O_2-induced cell death in PC12 cells. In the zebrafish model, WP had an obvious neuroprotective effect, and the ratio reached 42% at 222 μg/mL. The mechanism study revealed that WP could inhibit the activity of caspases 3/7 and 8, reduce the mRNA expression levels of Bax and glial cell line-derived neurotrophic factor, and improve the mRNA expression level of brain-derived neurotrophic factor significantly. Besides, the treatment of mice with WP shortened the escape latency and exhibited much longer target time and more crossing times significantly, compared with untreated control groups in the Morris water maze test. Similarly, the step-down passive avoidance test showed that WP could ameliorate memory impairments. The administrated dose (20.1 g/kg body weight [BW]) did not produce mortality or treatment-related adverse effects with regard to BW, general behavior, or relative organ weights of the tested male and female mice. The current results indicated that WP could exert neuroprotective effect, and attenuated learning and memory impairments. These ameliorating effects of WP may be useful for treatment of memory impairment in Alzheimer's and its related diseases.

Keywords

Association of sleep traits and bone mineral density: observational and Mendelian Randomization studies

Jie Chen1,Jihui Zhang1,2,Hon-Cheong So3,Sizhi Ai1,Ningjian Wang4,Tan Xiao5,6,Yun-Kwok Wing1

1. Li Chiu Kong Family Sleep assessment Unit，Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Shatin，Hong Kong SAR，China

2. Guangdong Mental Health Center，Guangdong Provincial People's Hospital，Guangdong Academy of Medical Sciences，Guangzhou，Guangdong，China

3. School of Biomedical Sciences，Department of Psychiatry，KIZ-CUHK Joint Laboratory of Bioresources

and Molecular Research of Common Diseases，Cheung Research Centre for Management of Parkinsonism，Faculty of Medicine，The Chinese University of Hong Kong，Hong Kong SAR，China

4. Institute and Department of Endocrinology and Metabolism，Shanghai Ninth People's Hospital，Shanghai JiaoTong University School of Medicine，Shanghai，China

5. Department of Neuroscience，Uppsala University，Uppsala，Sweden

6. Department of Clinical Neuroscience，Karolinska Institutet，Stockholm，Sweden

Objective: Observational studies have suggested that sleep and circadian disturbances are potentially modifiable risk factors for low bone mineral density (BMD), but the causal relationship is unclear. This study aimed to 1) replicate the findings on the observational association of sleep traits with low BMD; 2) examine whether these associations were causal by using mendelian randomization (MR) analyses, and 3) investigate potential modulation effects of sex and menopause. Methods: Three hundred and ninety-eight thousand one hundred and thirty-seven white British subjects (aged 39-73y) with valid BMD estimated by quantitative ultrasound of the heel (eBMD) at baseline were included. Linear regression analyses and inverse-variance weighted method were used for observational and one-sample MR analyses respectively, to investigate the associations between self-reported sleep traits (sleep duration, chronotype, daytime sleepiness and insomnia) and low BMD. Furthermore, sensitivity analyses were performed in subgroups based on sex and menopause in both observational and MR analyses. Results: In observational analyses, short/long sleep, insomnia and definite eveningness were associated with low eBMD (short sleep: β = -0.045, effect in standard deviation change of rank-based inverse normally transformed eBMD; long sleep: β = -0.028; sometimes insomnia: β = -0.012; usually insomnia: β = -0.021; definite eveningness: β = -0.047), while definite morningness was associated with decreased risk of low eBMD (β = 0.011). Subgroup analyses suggested associations of short/long sleep and definite eveningness with low eBMD among men, short sleep with low eBMD among premenopausal women, and short sleep, eveningness and daytime sleepiness among postmenopausal women. In bidirectional MR analyses, there was no causal relationship between sleep traits and eBMD in either overall sample or subgroup analyses.Conclusions: Although observational analysis showed a robust association of low eBMD with sleep duration, chronotypes and insomnia, there was no evidence of causal relationship as suggested by MR analyses.

Keywords sleep traits, bone mineral density, mendelian randomization, UK Biobank

Review of progress of food and medicinal resources treating insomnia

Wei Qu,Yang Wen
Hefei University of Technology

Insomnia is common and causes a variety of diseases and complications. It seriously affects people's life, and has become a global concern. The treatment of insomnia has attracted much attention. Compared with psychotropic chemical drugs used to treat insomnia, the application of natural food and medicinal resources is safer with less drug resistance and dependence, and is a sustainable slow conditioning mode. Based on a large number of literature reports, this paper systematically summarizes the main types of sleep-improving food and medicinal resources, such as foods, Chinese medicinal materials for medicinal purposes, and also reviewed the underlying mechanisms. The purpose of this review is to pave a way for the utilization of sleep-improving food and medicinal resources to treat insomnia, and the development of functional foods to improve insomnia. Keywords

Establishment of Predictive Model for Children with Obstructive Sleep Apnea with Attention Deficit Hyperactivity Disorder Based on Polysomnography

Yitong Zhang,Ningning She,Haiqin Liu,Xiaoyong Ren
The Second Affiliated Hospital of Xi'an Jiaotong University

Objective To analyze the effects of obstructive sleep apnea (OSA) on children's sleep structure and attention deficit hyperactivity disorder (ADHD), and further establish a risk prediction model for OSA with ADHD in children based on the parameters of polysomnography (PSG). Methods A total of 112 children with OSA admitted to the Department of Otorhinolaryngology Head and Neck Surgery of the Second Affiliated Hospital of Xi'an Jiaotong University from January 2019 to June 2020 were retrospectively included. Their clinical data, data of PSG and cognitive examination were collected. According to the severity of OSA, the patients were divided into three groups: mild, moderate and severe degree. Their demographic characteristics, sleep parameters and occurrence of ADHD were collected. According to the results of ADHD examination, the patients were divided into ADHDand non-ADHD group. Binary Logistic regression model was established to predict the risk of OSA associated ADHD among children with the abovementioned variables as predictor. Results Grouped by OSA severity, the differences in AHI, OAI, OAHI, and lowest oxygen saturation among the three groups were statistically significant (P<0.05); the average oxygen saturation and N1 phase

time ratio between mild OSA and severe OSA groups were significantly different; the comparison of N3 phase time ratio between mild OSA, moderate OSA and severe OSA group was statistically significant; the correlation coefficient of OAHI and N1 phase time ratio was 0.334, and the correlation coefficient with N3 phase time ratio was -0.360, P< 0.01; there were 10 patients with ADHD in the mild OSA group (ADHD incidence rate 17.54%), 7 patients in the moderate OSA group (ADHD incidence rate 23.33%), and 9 patients in the severe OSA group (ADHD incidence rate 36.00%), the difference was not statistically significant. Grouped by ADHD examination, there were statistically significant differences in sleep efficiency, AHI, OAI, OAHI, lowest oxygen saturation, N1 phase time ratio and N3 phase time ratio between the two groups. The established Logistic regression equation was: X=15.670+0.061 × (sleep efficiency-continuous variable)-0.212× (lowest oxygen saturation-continuous variable)-0.144× (N3 period time ratio-continuous variable), the sensitivity and specificity of the model prediction were 84.6% and 79.1% , respectively when the area under the receiver operating characteristic curves was 86.7%. Conclusions: The disturbance of sleep structure is an important risk factor for OSA and ADHD in children. The predictive model equations based on PSG parameters in this study can be used to assess the risk of OSA with ADHD in children.
Keywords

The association between BTBD9 polymorphism and sleep parameters within OSA patients

Zhenfei Gao1,2,3,Feng Liu1,2,3,Fan Wang1,2,3,Niannian Li1,2,3,Jian Guan1,2,3,Hongliang Yi1,2,3,Shankai Yin1,2,3

1. Department of Otolaryngology-Head and Neck Surgery，Shanghai JiaoTong University Affiliated Sixth People's Hospital
2. Otolaryngology Institute of Shanghai JiaoTong University
3. Shanghai Key Laboratory of Sleep Disordered Breathing

Objective: sleep fragmentation is a main pathophysiology feature of obstructive sleep apnea (OSA), but the underlying mechanism is poorly understood. BTBD9 is a risk factor of Restless leg syndrome and plays an important role in sleep-wake regulating. The aim of our work was to investigate the association between a variant in BTBD9(rs117733138) from our GWAS and sleep-related parameters. Methods: We performed GWAS on SSHS (n=20590) consisting of all suspected cases admitted to Shanghai Sixth People's Hospital from January 2011 to June 2019. Both the cases and controls underwent whole night polysomnography and anthropometry profiles. Affymetrix human genome-wide SNP array 6.0 (SNP6.0) and Affymetrix AxiomTM genome-wide CHB array plate were used for genotyping. Results: We found the distribution of rs117733138(G>A) had no significant difference between patients with OSA and the controls, however, several wake-related sleep parameters were significantly associated the genotype of BTBD9 in patients with OSA. Patients with this variant

had lower sleep efficiency and decreased duration of sleep (β =-0.032, 95%CI -2.276--0.147; β =-0.029, 95%CI -3.683--0.022, P=0.047), and more frequent awakening time (β =0.052, 95%CI 0.017-2.258) during sleep period despite this variant had little effect on structure of sleep (P>0.05). Conclusions: Our study results showed that BTBD9 (rs117733138) polymorphisms was associated with the awakening in patients with OSA. It is urgent to explore the mechanism underlying that how this variant contributed to sleep regulation.

Keywords obstructive sleep apnea; abnormal awakening; genetic; BTBD9,

Association of KLF9 Gene Polymorphism with Obstructive Sleep Apnea and its Sleep−related traits in Chinese adults

Niannian Li, Zhenfei Gao,Yuenan Liu,Chenyang Li,Feng Liu,Jian Guan,Hongliang Yi

Shanghai Sixth People's Hospital

Objective: The abnormal sleep structure of patients with obstructive sleep apnea (OSA) damages central nervous system and causes cognitive impairment. However, its molecular regulating mechanism is still unclear. This study aimed to explore the association of KLF9 rs12552288 (G>C) polymorphisms with the presence of OSA and its sleep-related traits in a Chinese Han adult population.Methods: A cross-sectional study was undertaken including 2,120 adult (1,470 OSA cases and 650 non-OSA controls) admitted to the sleep center of Shanghai Sixth People's Hospital from January 2011 to June 2019. Anthropometric measurements, polysomnographic variables, biochemical indicators, medical history and genotypic data were collected. Chi-square tests were used to compare the allelic frequencies and genotypes between cases and controls. Logistic regression and linear regression were used to explore the association between genotypic polymorphisms with the presence of OSA and its phenotypic traits.Results: There was no significance difference in allelic frequencies and genotype distribution of KLF9 rs12552288 (G>C) between patients with OSA and the controls. The dominant genetic model was selected for further association analysis, we found that these SNPs were closely associated with OSA relating sleep traits. Patients with OSA with rs12552288 GC / CC genotype had higher N3 sleep duration (β =8.02, p=9.2×10^-6) during Non-rapid-eye-movement. Conclusions: KLF9 rs12552288 gene polymorphism is not associated with OSA, however with sleep disorder in patients with OSA.

Keywords Obstructive sleep apnea; single nucleotide polymorphism; KLF9.

Impact of Insomnia and Obstructive Sleep Apnea on the Risk of Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Li Shiqi,Qingyun Li

Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine

Objective: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) increases morbidity and mortality. Sleep disorders including insomnia and obstructive sleep apnea (OSA) are independent risk factors for AECOPD. The aim of this review was to explore the impacts of the sleep disorders on the exacerbation risk in patients with COPD.Methods: A web-based systematic search of PubMed and Embase databases was performed to identify studies that investigated the associations between sleep disorders and AECOPD. Studies were eligible if they explored the prevalence of insomnia or OSA among patients with COPD, the impact of insomnia and OSA on AECOPD, or the impact of treatment for the two sleep disorders on COPD. Results: A total of 41 studies were included. The most frequent sleep disorders in patients with COPD included OSA, insomnia, and restless legs syndrome. Either insomnia or OSA increases individuals' susceptibility to AECOPD. Insomnia is linked to AECOPD via increased sympathetic activity, elevated systemic inflammatory responses, immune dysregulation, improper hypnotics use, and comorbid chronic medical disorders. The coexistence of OSA was also associated with an increased risk of AECOPD underlying by a series of physiological dysregulation such as increased inflammatory responses, oxidative stress, increased sympathetic activity, immune dysregulation, and microbiota variation. Conclusions: Insomnia and OSA were associated with increased risk of AECOPD. Interventions such as effective continuous positive airway pressure treatment of OSA, and proper therapy for insomnia may reduce the risk of AECOPD.
Keywords

Long–term PAP adherence in obstructive sleep apnea: a data analysis using real world data

Huijie Yi

Peking University People's Hospital

Objective: Poor adherence to positive airway pressure (PAP) commonly affects therapeutic response in obstructive sleep apnea (OSA). However, the studies on PAP adherence were conducted under monitoring conditions which failed to reflect the usage in real world. Hence, we aimed to define PAP adherence over the first 12 months based on a large cloud database in Resmed and Philips platform reflecting current technology and real-world clinical care in China. Methods: We assessed de-identified data from a large cloud database of PAP users to examine adherence to therapy from 1-May-2019 to 1-Feb-2020. Patients' compliance data were uploaded from the cloud database of the two platforms respectively. The average

PAP adherence (including usage days, the days≥4 hours PAP use per night, proportion of days compliant (usage≥4 h/night), percentage of participants with "good" adherence (defned as ≥4 h per night), and mean daily usage and mean device usage) were determined at 1 week,1,3,6 and 12 months, respectively. Results: During analyzing period, a total of 228 patients were included in this study, consisting of 117 patients from Resmed platform and 111 patients from Philips platform. The patients' compliance significantly differed between the two platforms at the time of 12 months (204.42 ± 134.99 days vs. 150.49 ± 112.85days;174.872 ± 129.6 days vs.120.52 ± 110.05 days; $48.57\pm36.00\%$ vs.$33.47\pm30.57\%$; 38.46% (45) vs.18.0% (20); 214.17 ± 159.03 mins vs.147.32 ± 130.13 mins; 340.18 ± 98.82 mins vs. 306.09 ± 105.02 mins; all $p<0.001$). Notably, the proportion of days compliant (usage≥4 h/night) and percentage of participants with "good" adherence in the Resmed platform reached the lowest value at the timepoint of 3 month and then gradually increased at the timepoints of both 6 and 12 months. However, the above two indicators in the Philips platform gradually decreased over time.Conclusions: Based on the real-world data in China, long-term PAP adherence in obstructive sleep apnea was generally low and varied among technology devices.

Keywords PAP adherence obstructive sleep apnea real world data

Propofol counteracts depression–like behavior and sleep disturbance

Xin Zheng,Yunong Chen,Tao Huang,Yanli Ren,Jinxian Gao,Hailin Chen,Xingwen Yang,Qinlei Huang,Guijuan Lu,Yufeng Shao,Junfan Jie,Yiping Hou

Lan zhou University

Depression is a common, chronic and recurrent condition, marked by persistent suffering, poor overall health, and deleterious effects on psychosocial functioning and life quality. Sleep disorders cause or exacerbate depression, and people who suffer from depression experience insomnia, hypersomnia, and increased rapid eye movement (REM) sleep, indicating that depression and sleep disorder are comorbid conditions. The lateral habenula (LHb) has emerged as an essential brain region in regulatingdepression-like behavior and sleep disorder. Neurons in the lateral habenula express GABA and NMDA receptors. Propofol is a unique anesthetic that engages GABA and NMDA receptors. Clinical researches have shown that propofol trigger rapid and durable antidepressant effect. In the present study, we investigated the effect and mechanism of propofol on reserpine-induced depression-like behavior and sleep disorder. Methods: The behavioral tests of forced swimming (FST), sucrose preference (SPT) and tail suspension test (TST), and the polysomnographic recording and sleep-wake states analysis were employed to evaluate, respectively, the depression-like behavior and sleep-wake cycle pattern following reserpine injection, and the effect of propofol on reserpine-induced depression-like behavior and sleep disorder. Furthermore, immunohistochemistry of c-Fos was performed to reveal the activated neurons induced by propofol. Results: Intraperitoneal injection of reserpine

(6 mg/kg) induced depression-like behavior which was characterized by increasing immobility time in FST and TST test, as well as decreasing sucrose preference in SPT. Reserpine also decreased REM and non-REM (NREM) sleep latency, and increased REM sleep time due to an increase of episode number. Propofol (50 and 75 mg/kg) antagonized reserpine-induced depression-like behavior and altered reserpine-induced sleep-wake pattern through increasing REM sleep latency, and decreasing REM sleep via diminished episode number. Propofol decreased c-Fos immunoreactive(-IR) neurons induced by reserpine in LHb. Conclusions: Propofol antagonizes reserpine-induced depression-like behavior and sleep disorder through acting on neurons in LHb. Keywords Propofol, Depression, Sleep-Wake State, Lateral Habenular Nucleus, Reserpine

A Review of Sleep in Patients with Disorders of Consciousness

Jianhui Wu, Jianhao Zhang, Jiahui Pan

South China Normal University

With the rapid development of intensive care technology, the number of patients with severe brain injury increased dramatically. At present, the diagnosis of patients with disorders of consciousness (DOC) is difficult because their motor responses may be very limited or inconsistent. Electrophysiological criteria such as EEG or event related potentials have also been studied to establish criteria for diagnosis and prognosis based on command following or active paradigm. However, the use of such task-based techniques in DOC is methodologically complicated and calls for careful analysis and interpretation. The present review focuses on the importance of sleep in the evaluation of DOC and their relationships with diagnosis and prognosis. We discussed the concepts of sleep of patients suffering from DOC, identification of this challenging population, and the prognostic value of sleep. The available literature on vegetative state (VS) and minimally conscious state (MCS) following traumatic or non-traumatic severe brain injury was reviewed. Sleep-like activities in EEG, such as spindles, indicate that patients with DOC may have a higher level of consciousness. VS has more abnormalities than MCS in terms of sleep spindles. Most MCS have sleep and wake alternation, sleep spindle and REM sleep, while VS have few EEG changes. A large number of sleep spindles and organized sleep-wake patterns predict better clinical outcomes. We can distinguish patients with different levels of consciousness by studying the sleep in DOC, which is conducive to their clinical rehabilitation. Keywords

The Validity of nocturnal Lowest Oxygen Saturation combine Scales such as OSA–18 in the screening of obstructive sleep apnea in children

Bingjie Zhao,Lina Ma,Xi Chen,Ning She,Yitong Zhang,Yani Feng,Haiqin Liu,Xiaoyong Ren
Second Affiliated Hospital of Xi'an Jiaotong University

Objective To evaluate the accuracy of nocturnal lowest oxygen saturation (LSaO2) at night combined with OSA-18 and Epworth scales (ESS) for primary screening OSA in children, and to explore a more simple and feasible diagnostic method for OSA in children.Methods A total of 139 children who completed overnight polysomnography in the E.N.T. of Second Affiliated Hospital of XJTU were enrolled in this study, including 82 men and 57 women, from August 2020 to February 2021. Their parents completed OSA-18 and ESS scales with the assistance of doctors. According to the obstructive apnea hypopnea index (OAHI), the children were divided into four groups. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and ROC curve of the serial tests were calculated, respectively.Results According to the ROC curve, the optimal cut-off value of nocturnal LSaO2 for predicting OSA in children was 90.5% (P < 0.00, AUC = 0.83). The sensitivity of OSA-18 and ESS for diagnosis were 74.8 % and 22.7 %, respectively; the specificity was 20.0 % and 60.0 %, respectively; the PPV were 84.8 % and 77.1 %, respectively; the NPV were 11.8 % and 11.5 %, respectively. The sensitivity of LSaO2 combined with OSA-18, LSaO2 combined with ESS and OSA-18 combined with ESS for diagnosis were 42.9.1 %, 11.8 %, and 21.0 %, respectively; the specificity was 95.0 %, 100.0 %, and 75.0 %, respectively; the PPV were 98.1 %, 100.0%, and 83.3%, respectively; the NPV were 21.8 %, 16.0 %, and 13.8 %, respectively.Conclusions The nocturnal LSaO2 has clinical value in the diagnosis of OSA in children. OSA-18 has higher sensitivity but lower specificity than ESS. The sensitivity and specificity of LSaO2 combined with OSA-18 in this diagnosis are higher than the remaining serial tests. This method could be used in primary screening OSA in children at grass-root hospitals where sleep monitoring is impossible.
Keywords

The Change of Cerebral Blood Flow based on ASL–MRI in Chronic Insomnia and its Correlation between Neuropsychologicalcharacteristics

Zheng Li,Yahui Wan,Rong Xue

Tianjin General Hospital

Objective: To investigate the change of cerebral blood flow assessed by ASL-MRI in patients with chronic insomnia, and the relationship between cerebral blood flow (CBF) and neuropsychological characteristics. Methods: Patients were recruited from the Department of Neurology Outpatient of Tianjin General Hospital form June 2019 to December 2020. A total of 20 patients who met the ICSD-3 criteria for diagnosing chronic insomnia disorder were selected into the chronic insomnia group. A total of 20 volunteers without insomnia were recruited into the control group. The demographic data, and the neuropsychiatric characteristics assessed by sleep-related scales, emotion-related scale, cognition- related scale were collected for all subjects. Sleep structure was evaluated with portable sleep monitor. The cerebral blood flow were measured by ASL-MRI. Subjects with a score of AHI above 5 were excluded. All subjects were scanned by pASL on 3.0T MRI system at 3:00 p.m- 6:00p.m., the CBF was measured by Cereflow. All subjects were divided into two groups: chronic insomnia group (CI, n=15) and health group (HC, n=11). The change of cerebral blood flow in chronic insomnia patients and the relationship between cerebral blood flow and neuropsychological scales were assessed with correlation analyses.Results: In CI group, the average CBF and the CBF in bilateral superior frontal gyri, bilateral middle frontal gyri, right inferior frontal gyri, right orbital frontal cortex, bilateral anterior central gyri, bilateral cingulate gyri, right amygdaloid nucleus, bilateral caudate nucleus, left lenticular nucleus, bilateral thalamus, bilateral insular lobes, bilateral gyri temporales transversi, bilateral superior temporal gyri, bilateral middle temporal gyri, bilateral inferior temporal gyri, bilateral temporal pole, bilateral parietal lobe, bilateral occipital gyri were decreased compared with the control group. In particular, the CBF in right middle frontal gyri, right posterior orbital frontal cortex, right gyri temporales transversi, left gyri lingualis in the CI group were lower than that in control group (P< 0.05). In CI group, the CBF of right middle frontal gyri was positively correlated with the average cognitive function and attention ability (MMSE:P=0.031,r=0.597; SDMT:P=0.049,r=0.555); the CBF of right gyri temporales transversi was positively correlated with the average cognitive function(MMSE: P=0.043,r=0.647);the cerebral blood flow of right posterior orbital frontal cortex was positively correlated with the execution ability(Stroop A: P=0.001,r=0.834;StroopB: P=0.002,r=0.789; StroopC: P=0.009, r=0.715). The correlation between CBF and HAMA/HAMD is lack.Conclusions: Patients with chronic insomnia had anxiety, depression and cognitive impairment, particularly, their visual space ability, attention ability, execution ability and memory were more damaged. CI patients presented with decreased CBF, especially in right middle frontal gyri,right posterior orbital frontal cortex,right gyri temporales transversi and left gyri lingualis. The decrease of CBF in CI patients might comorbid cognition impairment.

Keywords Chronic insomnia; cerebral blood flow; ASL; cognitive impairment

Melatonin improves cognitive impairment caused by circadian rhythm disorder through regulating jak2–stat3 pathway

Lin Xu1,Zhu Ai1,Linlin Wang1,Xiaoning Wang3,Xuan Liu2,Rong Xue1

1.General Hospital of Tianjin Medical University

2. Airport Hospital，General Hospital of Tianjin Medical University

3.The First Affiliated Hospital of Hebei North University

Objective: The study aims to explore the protective effect of melatonin(MT) on cognitive impairment caused by chronic circadian rhythm disorder through regulating the JAK2-STAT3 signal pathway. Methods: Male 6-week-old C57BL/6J mice were randomly divided into three groups, the normal control group (NC, n=6), the chronic circadian rhythm disorder group (CRD, n=6), and the melatonin treatment CRD group (CRD+MT, n=6). Morris water maze test was performed on mice after 120 days of intervention. The protein expression levels of JAK2, p-JAK2，STAT3, and IL-6 mRNA in mouse hippocampus were measured. Results: 1. Compared with the NC group, the escape latency of the CRD group mice was prolonged, and the difference was statistically significant (**P<0.01). while the MT group mice＇s escape latency was shorter significantly than the CRD group mice (**P<0.01). Compared with the NC group mice, the CRD group mice stayed in the target quadrant time and the number of crossing the platform was reduced significantly (*P<0.05, *P<0.05). In comparison with the CRD group mice, MT Group mice stayed in the target quadrant for a longer time, the difference was statistically significant (*P<0.05), and the number of crossing platforms increased, although the difference was not significant, there was a certain trend. 2. The expression of JAK2, p-JAK2, and STAT3 protein in the hippocampus of mice in each group was not significantly different. But a tendency towards higher was seen in the CRD group and a downward trend after MT treatment. 3. Compared with mice in the NC group, the level of IL-6 mRNA in the hippocampus of the CRD group was increased, and a significantly decrease was observed in the MT group compared with the CRD group (*P<0.05, *P<0.05). Conclusion: Melatonin may regulate the JAK2-STAT3 pathway by inhibiting the expression of the IL-6, reducing hippocampus inflammation and improving the cognitive function of mice.
Keywords

The research of correlation between sleep structure and cognitive function in chronic insomnia comorbid OSAHS

Mengdi Lv,Yahui Wang,Rong Xue

General Hospital of Tianjin Medical University

Objective: 1) To explore the effects of objective sleep structure, cognitive function of chronic insomnia patients with difffient degrees of OSAHS;2) To analyze the correlation between cognitive function ，

and sleep structure in patients with chronic insomnia comorbid OSAHS.Methods: Patients with chronic insomnia in the Department of Neurology, General Hospital and General Hospital Airport Hospital of Tianjin Medical University from June 2019 to February 2021 were recruited. A total of 80 patients corresponding to ICSD-3 chronical insomnia criteria were included into the chronic insomnia group, while those with complicated neurological and psychiatric diseases, cardiopulmonary diseases, other types of sleep disorder were excluded. Twenty healthy volunteers matched ages, sexes and education level were selected into the control group (HC). The demographic data, and the neuropsychiatric characteristics assessed by sleep-related scales, emotion-related scale, cognition-related scale were collected for all subjects. The cognitive function related scales assessed the general cognition function,language memory ability, visual memory ability, working memory ability, visuospatial ability, attention ability, executive ability, and language ability. Evaluated sleep structure during sleep was exaimined by PSM-100A. Eighty patients were divided into 39 cases with chronic insomnia comorbid OSAHS (CIO) and 41 cases with chronic insomnia (INS) by score of AHI. Comparison of sleep structure and cognitive function between groups were carried out. The correlation between sleep structure, and neuropsychological scales in CIO group was also performed. A total of 39 patients with CIO were divided into 26 cases with chronic insomnia comorbid mild OSAHS and 13 cases with chronic insomnia comorbid moderate-severe OSAHS by a score of AHI. Comparison of sleep structure, and neuropsychological scales were done between groups.Results: The sleep efficiency, the proportion of REM sleep and stable sleep, the average blood oxygen saturation decreased successively in CIO group, INS group and HC group. The proportion of unstable sleep and the number of awakening increased successively in CIO group, INS group and HC group. The total sleep time and the lowest oxygen saturation decreased in CIO group compared with that in INS group and HC group. The total sleep time, the proportion of REM sleep and stable sleep, the average and lowest blood oxygen saturation decreased while the proportion of unstable sleep, the number of awakening increased in patients with chronic insomnia comorbid moderate-severe OSAHS compared with mild OSAHS（p＜ 0.05）.The general cognitive function, memory ability (language memory, visual memory, working memory), visuospatial ability, attention ability and executive ability increased successively in CIO group, INS group and HC group. The memory ability (visual memory, working memory), visuospatial ability, attention ability and executive ability decreased in patients with chronic insomnia comorbid moderate-severe OSAHS compared with mild OSAHS（p＜ 0.05). The immediate recall, short delayed recall and long delayed recall of memory ability and Stroop test A＆ B of executive ability showed positive correlation with the proportion of REM sleep in CIO group. The visual memory and working memory showed positive correlation with the average blood oxygen saturation in CIO group. The visual memory and visuospatial ability showed positive correlation with the lowest blood oxygen saturation in CIO group. The visual memory, working memory, visuospatial ability, attention ability and Stroop test A＆ B of executive ability showed negative correlation with AHI in CIO group.Conclusions: The sleep structure appeared more serious in patients with chronic insomnia with the aggravation of OSAHS degree. OSAHS aggravated the impairment of memory ability, visuospatial ability, attention ability, and executive ability in patients with chronic insomnia. The decrease of cognitive function was correlated with

the shortening of REM sleep, the decrease of blood oxygen level and the severity of OSAHS in patients with chronic insomnia comorbid OSAHS.

Keywords

The research of correlation between autonomic nervous and emotional symptoms in chronic insomnia comorbid OSAHS

Mengdi Lv,Yahui Wang,Rong Xue

General Hospital of Tianjin Medical University

Objective: 1) To examine the effects of autonomic nerve function and emotional symptoms in chronic insomnia patients with OSAHS; 2) to explore the correlation between emotional symptoms and autonomic nervous function in patients with chronic insomnia comorbid OSAHS.Methods: Patients with chronic insomnia in the Department of Neurology, General Hospital and General Hospital Airport Hospital of Tianjin Medical University from June 2019 to February 2021 were recruited. A total of 80 patients corresponding to ICSD-3 chronical insomnia criteria were included into the chronic insomnia group, while those with complicated neurological and psychiatric diseases, cardiopulmonary diseases, other types of sleep disorder were excluded. Twenty healthy volunteers matched ages, sexes and education level were selected into the control group (HC). The demographic data, and the neuropsychiatric characteristics assessed by sleep-related scales, emotion-related scale, cognition-related scale were collected for all subjects. The cognitive function related scales assessed the general cognition function,language memory ability, visual memory ability, working memory ability, visuospatial ability, attention ability, executive ability, and language ability. Evaluated sleep structure during sleep was exaimined by PSM-100A. Eighty patients were divided into 39 cases with chronic insomnia comorbid OSAHS (CIO) and 41 cases with chronic insomnia (INS) by the score of AHI. Comparison of sleep structure and cognitive function between groups were carried out. The correlation between sleep structure, and neuropsychological scales in CIO group was also performed. A total of 39 patients with CIO were divided into 26 cases with chronic insomnia comorbid mild OSAHS and 13 cases with chronic insomnia comorbid moderate-severe OSAHS by a score of AHI. Comparison of sleep structure, and neuropsychological scales were done between groups.Results: The LF decreased while HF, Pnn50, SD1, SD2 increased in CIO group, INS group and HC group. The HF decreased while LF, mean HR increased in patients with chronic insomnia comorbid moderate-severe OSAHS compared with mild OSAHS （p＜ 0.05＝ .The scores of HAMA and HAMD decreased in CIO group, INS group and HC group. The scores of HAMA and HAMD increased in patients with chronic insomnia comorbid moderate-severe OSAHS compared with mild OSAHS（p＜ 0.05＝ . The HAMA score showed positive correlation with LF, LF/HF in CIO group. The HAMA score showed negative correlation with HF in CIO group. The HAMD score showed positive correlation with LF, LF/HF in CIO group. The HAMD score showed negative correlation with HF in CIO group. Conclusions: The autonomic nerve function appeared more serious in patient with

chronic insomnia comorbid OSAHS. The degree of anxiety and depression increased in patients with chronic insomnia comorbid OSAHS. The degree of anxiety and depression was correlated with autonomic nervous dysfunction in patients with chronic insomnia comorbid OSAHS.

Keywords

The level of plasma MAP–2 in Chronic Insomnia and its Correlation with Cognition Impairment

Zheng Li,Yahui Wan,Rong Xue

Tianjin General Hospital

Objective: To investigate the change of the level of plasma MAP-2 in patients with chronic insomnia, and the correlation between MAP-2 and cognition.Method: Patients were recruited from the Department of Neurology Outpatient of Tianjin General Hospital form June 2019 to December 2020. A total of 30 patients who met the ICSD-3 criteria for diagnosing chronic insomnia disorder were selected into the chronic insomnia group. A total of 20 volunteers without insomnia were recruited into the control group. The demographic data, and the neuropsychiatric characteristics assessed by sleep-related scales, cognition-related scale were collected for all subjects. Sleep structure was evaluated with portable sleep monitor. All subjects were measured serum levels of MAP-2 at 8:00a.m.-10:00.a.m. All subjects were divided into two groups: chronic insomnia group (CI, n=27) and health group (HC, n=16). The change of cerebral blood flow in chronic insomnia patients and the relationship between MAP-2 and cognitive scales were assessed with correlation analyses.Results: Compared with HC group, CI group presented with higher HAMA scores, HAMD scores, whereas lower scores of MMSE, visual space, attention, execution ability, memory (P< 0.05). The plasma levels of MAP-2 in CI group were lower than that of HC, the level of MAP-2 was positively correlated with attention ability (TMTA: P=0.027,r=-0.426).Conclusion: Patients with chronic insomnia have anxiety, depression and cognitive impairment. The visual space ability, attention ability, execution ability and memory are more significantly damaged. Chronic insomnia patients had lower level of MAP-2 implicating decreased synaptic function. MAP-2 might act as a biomarker for detecting chronic insomnia patients who have a higher risk of cognitive impairment.

Keywords Chronic insomnia; cognitive impairment; MAP-2

Efficacy and safety of pharmacological treatments for insomnia in the adults: a systematic review and network meta–analysis

Jingli Yue1,Chang Xiangwen2,3,Zheng Junwei2,3,Zhou Xinyu4,Hu Sifan1,Teng Teng4,Sun Hongqiang1,Tang Xiangdong5,Bao Yanping2,Lu Lin1,6,Shi Jie2,3

1. Peking University Sixth Hospital，Peking University Institute of Mental Health，NHC Key Laboratory of Mental Health (Peking University)，National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital)，Beijing，China

2. National Institute on Drug Dependence and Beijing Key Laboratory of Drug Dependence，Peking University，Beijing，China

3. Department of Pharmacology，School of Basic Medical Sciences，Peking University Health Science Center，Beijing，China

4. Department of psychiatry，the First Affiliated Hospital of Chongqing Medical University，Chongqing，China

5. Sleep Medicine Center，Department of Respiratory and Critical Care Medicine，Mental Health Center and Translational Neuroscience Center，State Key Laboratory of Biotherapy，West China Hospital，Sichuan University，Chengdu，China

6. Peking-Tsinghua Center for Life Sciences and International Data Group/McGovern Institute for Brain Research，Peking University，Beijing，China

Objective: To compare and rank medications for insomnia in adults according to the efficacy and safety.Methods: Eight databases and seven trial registers were searched. Relevant reports were hand-screened to identify eligible trials. Placebo-controlled or head-to-head double-blind, randomized trials of pharmacological treatments in adults with primary insomnia were included. Mean differences (MD) and odds ratios (OR) were estimated using pairwise and network meta-analysis with random-effects. Primary efficacy outcomes included sleep efficiency (SE) and total sleep time (TST). Secondary efficacy outcomes included self-reported sleep quality (SQ), sleep latency (SL) and waking time after sleep onset (WASO). Safety outcomes were measured by the number of any adverse events and patients who discontinued for treatment-related causes. The PROSPERO registered number is CRD42020182144.Results: A total of 88 trials involving 15,756 patients were included. For SE, all medications were more effective than placebo, with MD ranging from 13.90 (95% CI 2.81 to 24.99) for temazepam to 1.07 (95% CI -4.89 to 7.03) for zopiclone. For TST, most medications were better than placebo, with MD ranging from 71.80 (95% CI 20.64 to 122.96) for temazepam to 9.70 (95% CI -24.65 to 44.05) for melatonin. Eszopiclone, trimipramine and lormetazepam ranked the first three in improving SQ, while melatonin and tiagabine were less effective than placebo. Zaleplon, triazolam, lemborexant and daridorexant, seltorexant, doxepin ranked top three respectively in improving SL and WASO. Only lormetazepam (OR 0.14, 95% CI 0.03 to 0.65) was better than placebo, while brotizolam, zolpidem, zaleplon, suvorexant and eszopiclone had more adverse events than placebo.

There were no significant differences between drugs and placebo as for treatment-related discontinuation. Conclusions: Medications could significantly improve the SE in adults with insomnia. However, the efficacy of different drugs varied in TST, SQ, SL and WASO. Despite of adverse events, insomnia patients presented good tolerance to all drugs.

Keywords

Chimeric opioid peptide DN–9 promotes wakefulness through mu– and kappa– opioid receptors

Junfan Jie,Feng-Qiu DAI,Hai-Lin CHEN,Jin-Xian GAO,Yu-Nong CHEN,Yan-Li Ren,Xing-Wen Yang,Tao Huang,Qin-Lei Huang,Gui-Juan Lu,Yu-Feng Shao,Yi-Ping HOU

Lanzhou University

Opioid peptides are endogenous ligands of opioid receptors. Opioid receptors, including μ, κ, and δ receptors, are class A members of the G protein coupled receptors superfamily. Previous studies demonstrated that opioids and opioid receptor system play important roles in modulating several physiological functions, such as pain, sleep, emotion and addiction. DN-9, a chimeric opioid peptide synthesized with neuropeptide FF and opioid agonist biphalin, was recently presumed as an agonist of opioid receptors. Our study investigated the effects of DN-9 on sleep-wake cycle and power spectrum of cortical EEG in freely moving rats, and the potential neurons in the brain activated by DN-9. The results showed that 0.1 and 1 nmol of DN-9 i.c.v. administration increased wakefulness (W) during the first 2 h section, meanwhile, decreased rapid eye movement (REM) and non-REM (NREM) sleep accompanied by a decrease in EEG theta (4.5-8.5 Hz) and delta (0.5-4 Hz) activity. The increase of W induced by DN-9 was due to the extended episode duration, while the reduction of NREM and REM sleep was due to decreased episode number. The effects of DN-9 (0.1 nmol) on sleep-wake states were significantly attenuated by β-funaltrexamine (10 nmol, i.c.v) or nor-binaltorphimine (10 nmol, i.c.v), selective antagonist of μ or κ opioid receptor, respectively, but not by naltrindole hydrochloride (10 nmol, i.c.v), an antagonist of δ receptor. DN-9 increased c-Fos immunoreactive neurons in the tuberomammillary nucleus (TMN), nucleus accumbens (NAc), and lateral hypothalamus (LH) compared to vehicle. These findings suggest that DN-9 activates neurons in TMN, NAC and LH through μ and κ opioid receptors to promote wakefulness.

Keywords

Analysis of clinical characteristics in patients with obstructive sleep apnea and non–alcoholic fatty liver disease

Qingqing Xu,Jingwei Mao,Haiying Tang
The First Affiliated Hospital of Dalian Medical University

Objective: To explore the clinical characteristics of patients with obstructive sleep apnea and non-alcoholic fatty liver disease. Methods: We retrospectively analyzed the characteristics of clinical features in patients with OSA and NAFLD, respectively demonstrated the risk factors of OSA, NAFLD and OSA combined with NAFLD, and clarified the impact of OSA on NAFLD. From June 2018 to December 2020, 532 inpatients who underwent PSG examination at the Respiratory and Sleep Clinic in the First Affiliated Hospital of Dalian Medical University. SPSS 20.0 statistical software was used for analysis. Binary Logistic regression analysis was performed with OSA outcome as the dependent variable and gender, diabetes, hypertension, NAFLD, SBP, DBP, waist circumference, BFR, FLD, LAP, VAI, BMI, TG, TC, HDL, LDL, AST, ALT, blood glucose as the independent variables. Results: DBP, BFR, FLD, BMI, HDL, AST, ALT, blood glucose were risk factors of OSA. The result showed that BMI, FLD and hypertension was risk factors for OSA combined with NAFLD. Conclusions: We concluded that avoiding obesity, controlling blood sugar and blood pressure, avoiding high density lipoprotein reduction, improving OSA hypoxia could reduce the risk of NAFLD, OSA combined with NAFLD, and prevent the progression of NAFLD.
Keywords

cAMP–PKA–CREB 信号通路与睡眠 – 觉醒相关性研究进展

Wenlin Xu,Cong Wang,Jinjin Li,Jing Wang,Zhen Liu,Yunfei Chen
Yueyang Hospital of Integrated Traditional Chinese and Western Medicine，Shanghai University of
Traditional Chinese Medicine

Sleep-wake disorder is a common clinical disease caused by the interaction of a variety of internal and external factors, usually with chronic insomnia, circadian rhythm sleep awakening disorder, narcolepsy and other clinical manifestations. Many studies have shown that sleep-awakening is jointly regulated by the body＇s neuro-endocrine-immune system, and the involved regulatory substances include immune cells, adenosine, hormones, neurotransmitters, neurotrophic factors, etc. 5-hydroxytryptamine (5-HT), Melatottin (MT), and Brain-Derived Neuotrophyic Factor (BDNF) and other substances are important for regulating sleep-wake normal state. And these substances are upstream and downstream of the cAMP-PKA-CREB signaling pathway, which is regulated by the cAMP-PKA-CREB signaling pathway and can counteract the signaling pathway. Therefore, the exploration of the multi-directional interaction of locus genes on the cAMP-PKA-CREB signaling pathway with 5-HT, MT, and BDNF as targets will become a new direction for studying sleep-wakeness, which can be Diseases provide new ideas and develop new methods.
Keywords

Differential expression profile and bioinformatics analysis of brain exosomal miRNA in mouse under intermittent hypoxia

Jianyin Zou,Fan Wang,Yupu Liu,Huajun Xu,Jian Guan,Hongliang Yi,Shankai Yin

Shanghai Sixth People's Hospital

Objectives: To detect and screen the differential expression of miRNAs in the brain of mice between intermittent hypoxia group and control group, and conduct bioinformatics analysis to explore the effects of intermittent hypoxia on the expression of miRNAs in brain tissue.Methods: Twelve mice were randomly divided into intermittent hypoxia group and control group. After 8 weeks of feeding, brain tissue were taken. Transmission electron microscopy scanning, nanoparticle tracking analysis technology, and Western blotting were used to identify exosomes; and Illumina Hiseq2000/2500 high-throughput sequencing technology was used to isolate and detect the expression of exosomal miRNA in brain tissue, and construct its differential expression profile. Differentially expressed genes are analyzed by bioinformatics to determine the main biological functions of differentially expressed miRNAs and the underlying signal pathways. Results: Compared with the control group, 77 miRNAs were significantly expressed in the brain tissue of mice in the intermittent hypoxia group, of which 19 were up-regulated and 48 were down-regulated. MiRMiR-134-5p and miR-330-5p were significantly up-regulated while miR-433-3p and miR-409-5p were significantly down-regulated in the intermittent hypoxia group compared with the control group. The results of GO enrichment analysis and KEGG analysis showed that target genes were mainly enriched in the RAS signaling pathway and Wnt signaling pathway.Conclusion: Under the condition of intermittent hypoxia, there are abundant miRNAs in exosomes of the mouse brain tissue, and the expression profiles are significantly different. These different miRNAs may be involved in the changes of cerebral nerve function caused by intermittent hypoxia in mice.

Keywords

Research Progress on the Correlation between cAMP–PKA–CREB Signal Pathway and Sleep–Wakefulness

XU Wen-lin,Yunfei Chen

Yueyang Hospital of Integrated Chinese and Western Affiliated to Shanghai University of Traditional Chinese Medicine

Sleep-wake disorder is a common clinical disease caused by the interaction of a variety of internal and external factors, usually with chronic insomnia, circadian rhythm sleep awakening disorder, narcolepsy and other clinical manifestations. Many studies have shown that sleep-awakening is jointly regulated by the body's neuro-endocrine-immune system, and the involved regulatory substances include immune cells, adenosine, hormones, neurotransmitters, neurotrophic factors, etc. 5-hydroxytryptamine (5-HT), Melatottin

(MT), and Brain-Derived Neuotrophyic Factor (BDNF) and other substances are important for regulating sleep-wake normal state. And these substances are upstream and downstream of the cAMP-PKA-CREB signaling pathway, which is regulated by the cAMP-PKA-CREB signaling pathway and can counteract the signaling pathway. Therefore, the exploration of the multi-directional interaction of locus genes on the cAMP-PKA-CREB signaling pathway with 5-HT, MT, and BDNF as targets will become a new direction for studying sleep-wakeness, which can be Diseases provide new ideas and develop new methods.

Keywords

A deep learning–based apnea events classification approach for accuracy of sleep disordered breathing patients screening and grading

Ruhan Liu1,Huajun Xu2,Chenyang Li2,Xinyi Li2,Jian Guan2,Bin Sheng1

1.Shanghai Jiao Tong University

2.Shanghai Sixth People's Hospital

Objective: Misdiagnosis and missed diagnosis in the sleep-disordered breathing (SDB) due to the time-consuming, expensive, and uncomfortable polysomnography (PSG) have been a pretty severe impact. Moreover, an efficient replaceable method based on oxygen saturation (SpO2) signals using wearable devices suffers impracticability and inaccuracy of signal feature extraction and apneic events detection. This paper presents a methodology to detect automatically apneic-based SpO2 signal segments to compute Apnea-Hypopnea Index (AHI). Methods &Results: First, the apneic-based SpO2 signals segments in raw SpO2 signals were detected, and features in the whole night signals were extracted. Afterward, the SpO2 signal segments were fed into a Bi-LSTM-CNN extractor to obtain local features. Furthermore, we fed the whole night feature and local feature into a linear classifier to identify apnea-related and non-apnea-related. All apnea-related segments were used to compute AHI. The classifiers were developed based on 500 subjects of the Sleep Heart Health Study 1 (SHHS1) dataset and tested on three different datasets, containing 8131 subjects in total. In the validation datasets, we achieved an averaged desaturation classification accuracy of 84.3%. Subjects having SDB with an AHI greater than 15 could be detected with an average accuracy of 88.95%. Conclusions: Wearable devices using automatic SDB detection based on SpO2 signals can screen SDB patients at home.

Keywords

The association between MARCH1 polymorphism and sleep parameters within OSA patients

Deng,Jingyu Zhu,Niannian Li,Zhenfei Gao,Feng Liu,Jian Guan,Hongliang Yi,Shankai Yin

The Sixth People's Hospital of Shanghai

Objective: Sleep fragmentation is a main pathophysiology feature of obstructive sleep apnea (OSA), but the underlying mechanism was poorly understood. Membrane-associated ring-CH-type finger 1 (MARCH1) is a member of the MARCH family of membrane-bound E3 ubiquitin ligases. It has not been previously reported to be related to sleep. The aim of our work was to identify the association between a variant in MARCH1 (rs9715475) from our GWAS and sleep-related parameters. Methods: We performed GWAS on SSHS (n=20590) of which consists of all suspected cases who came to Shanghai Sixth People's Hospital rom January 2011 to June 2019. Both the cases and controls had undergone whole night polysomnography and anthropometry profiles. Affymetrix human genome-wide SNP array 6.0 (SNP6.0) and Affymetrix AxiomTM genome-wide CHB array plate were used for genotyping.Results: We found the distribution of rs9715475 (C>T) had no significant difference between OSA patient and controls (p>0.05), but several wake-related sleep parameters were significantly associated the genotype of MARCH1 within patients. The dominant genetic model was selected for further association analysis, we found that these SNPs are closely related to OSA related sleep traits. Patients with this variant had increased wake duration time (β =7.972, P=0.001989) and WK/SPT (β =1.993, P=0.000542).Conclusions: Our study results showed that MARCH1 (rs9715475) polymorphisms was associated with the awakening in OSA patients. There exists necessity to explore the specific molecular mechanism underlying this variant involved in sleep regulation.
Keywords

The dysfunction of microglia–mediated synaptic pruning correlates with cognitive impairment in sleep–deprived mice: involvement of CX3CR1 signaling

Lu Wang,Zili You

School of Life Science and Technology，University of Electronic Science and Technology of China

The impact of sleep deprivation on memory is becoming more and more serious. However, the inner mechanism still not be claimed clearly. Based on the refinement theory that microglia are involved in synaptic circuits during sleep, we verified the mechanism of cognitive impairment caused by sleep deprivation, which is mainly related to the impaired synaptic pruning mediated by microglia. Mice was placed at mild rotary apparatus for 72h, which was used for acute sleep deprivation model. Fist, we detected the body weight

and the memory behavior of mice in this model and our results showed that acute sleep deprivation caused memory impairment. Besides. We used golgi-cox staining and western-blot to detect the changes of synapse. The results indicated increased synapse number in sleep deprivation group. Therefore, we assumed that microglia played vital role in this mechanism. The morphology of microglia and the ability of phagocytizing synapses were detected by immunofluorescence.. Microglia-mediated synaptic pruning was impaired in sleep deprivation group. We further speculated that CX3CR1,a molecule related to microglia recognition and migration, might be involved in this mechanism. The effect of CX3CR1 on microglia was detected in vitro. The results showed that CX3CL1 improved the phagocytosis of microglia. And sleep deprivation decreased the expression of CX3CR1. Therefore, CX3CL1-CX3CR1 played an important role in impaired microglia mediated synaptic pruning that caused by sleep deprivation.In conclusion, this study examined the changes of microglia morphology, expression factors and phagocytic capacity in sleep-deprived mice, and demonstrateed that microglia can regulate synaptic plasticity through CX3Cl1/CX3CR1 axis, and this mechanism was associated with memory impairments caused by sleep deprivation. This study will provide important theoretical basis for the treatment of memory impairment caused by passive sleep deprivation.
Keywords

Functional network alterations related to first night effect in patients with insomnia disorder: a resting–state fMRI study

Yupeng Guo,Sifan Hu,Yan Shao,Yun Chen,Hongqiang Sun

Peking University Sixth Hospital

Sleep is perturbative in a new environment, particularly during the first night. This phenomenon is regarded as the "first night effect" (FNE) which has often been used to study transient insomnia. By using whole-brain data-driven approach based on resting-state functional MRI data in 27 patients with insomnia disorder (ID) and 22 well-matched healthy controls, we show that FNE is a manifestation with specific brain connectivity alterations by calculating the amplitude of low-frequency fluctuation (ALFF) and degree centrality (DC). Increased ALFF values in bilateral inferior parietal cortex (IPL) and increased DC value in dorsal anterior cingulate cortex (dACC) distinguished patients with FNE from patients without FNE and healthy controls. Furthermore, the ALFF value in the right IPL was positively correlated with score on the Fatigue Severity Scale in patients with insomnia. Our findings underscore that the neural substrates of FNE vulnerability are the intrinsic functional alterations within the networks encompassing attention, execution, and emotion functional systems. The findings provide new evidence supporting that ID patients with FNE was a distinct sub-sample experiencing different clinical severity.

Keywords Insomnia disorder; first night effect; resting-state functional MRI; inferior parietal cortex; dorsal anterior cingulate cortex

Mechanism underlying the posterior PPT enhancing the genioglossus muscle activity

Yang Rui,Zhang Guihong

School of Basic Medical Sciences，Zhengzhou University

The pedunculopontine tegmental nucleus (PPT) is located in the reticular formation of brain stem and involved in sleep. But it is not clear that whether PPT regulates genioglossus muscle (GG) activity. Healthy adult male SD rats were used to investigate the mechanism underlying the posterior PPT participating in the regulation of GG activity by neurophysiological and neuropharmacological techniques. Our results showed that different doses of glutamate (0.01 nmol, 0.1 nmol) microinjection in the PPT enhanced GG Electromyography (EMG). And GG EMG was significantly weakened after microinjection of different doses of NMDA receptor-specific antagonist D-AP5 (0.01 nmol, 0.1 nmol) or AMPA-type receptor specific antagonist CNQX (0.01 nmol, 0.1 nmol) in the PPT ($P <0.001$ and $P <0.01$, n=6). And microinjection of D-AP5 (0.1 nmol) or CNQX (0.1 nmol) in the PPT also decreased the enhancement effect of exogenous glutamate on GG EMG in rats. These results indicated that both exogenous and endogenous glutamate can enhance the GG EMG by activating NMDA and AMPA glutamatergic receptors in the posterior PPT of rats. Keywords

Study on the characteristics and correlation of subjective and objective sleep in late–life depressive patients with Electroconvulsive therapy

Chen Wang,Xiaoming Kong

Hefei Fourth People's Hospital

Objective: Most patients with late-life depression comorbid significant sleep disorders. Electroconvulsive therapy is effective, but the treating mechanism remains unclear. This study aimed to explore the effect of electroconvulsive therapy on sleep characteristics of patients with late-life depression.Methods:Twenty-seven cases of patients with late-life depression who met the inclusion criteria were included into the study. Pittsburgh Sleep Quality Index (PSQI), polysomnography (PSG) and HAMD-24 were used to evaluate the subjective and the objective sleep characteristics and clinical symptoms before and after ECT. We analyzed the subjective and objective sleep changes during ECT, and their correlations between HAMD-24 score, factor score, and PSQI at baseline. Results: After ECT treatment, the subjective sleep time increased, while the subjective sleep latency was shortened and the subjective sleep efficiency was improved ($P< 0.05$). On the objective sleep, NREM1 time and NREM2 time decreased, while NREM3 time increased ($P< 0.05$). Correlation analyses showed that the NREM2 time was positively correlated

with PSQI score at baseline (P< 0.05). The subjective sleep time and subjective sleep efficiency were positively correlated with HAMD-24 score, block score, and sleep disturbance score at baseline (P< 0.05). The subjective sleep latency was positively correlated with HAMD-24 score and sleep disturbance score at baseline (P< 0.05). Conclusions: Electroconvulsive therapy can significantly improve the subjective and objective sleep of patients with late-life depression . After electroconvulsive therapy, the improvement of subjective sleep disorder was related to the severity of depression and sleep disturbance factor, while the improvement of the objective sleep was related to the severity of the subjective sleep disorder. Keywords

The Th17/Treg immune function of patients with obstructive sleep apnea before and after continuous positive airway pressure treatment and the preliminary study on its mechanism

Chong Shen,Ruoyun Ouyang

The Second Xiangya Hospital of Central South University

Objective: To explore the Th17/Treg immune function of patients with obstructive sleep apnea (OSA) before and after continuous positive airway pressure treatment and the mechanism. Methods: Comparing the immune function of Th17/Treg and serum IL-6 and HIF-1 α levels in obstructive sleep apnea (OSA) patients and primary snoring group,and comparing the same factors above in moderate to severe OSA before and after continuous positive airway pressur(CPAP) treatment.At the same time to analyze the correlation between Th17/Treg immune function and serum IL-6 and HIF-1 α level in OSA patients.Thus to evaluate whether the Th17/Treg immune function status and serum IL-6 and HIF-1 α levels in OSA patients have changed compared with primary snoring group, the influence of CPAP treatment on the Th17/Treg immune function status and serum IL-6 and HIF-1 α levels in OSA patients,,and the mechanism causing the changes in the Th17/Treg immune function in OSA patients preliminarily. In a cohort study, a total of 40 OSA patients diagnosed as mild to moderate and severe were included, and a total of 20 patients diagnosed as primary snoring were included in the cohort study.The proportions of Th17 and Treg in CD4+T cells and serum IL17, IL-6, TGF- β 1 and HIF-1 α level were detected inpatients with primary snoring and OSA. After using 3 months CPAP treatment the indicator above the were reevaluated in moderate to severe OSA patients. Results: (1) There exists Th17/Treg immune imbalance in OSA patients, and it was positively correlated with the severity of OSA. (2) The levels of IL-6 and HIF-1 α in OSA patients were significantly higher than those in snoring alone group, and were positively correlated with the severity of OSA. (3) The most significant factors affecting Th17/Treg immune imbalance in OSA patients included the lowest level of SpO2, HIF-1 α and IL-6.

Conclusions: CPAP treatment can improve Th17/Treg immune imbalance, reduce HIF-1 α and IL-6 level in OSA patients.

Keywords

Reliability and validity evaluation of the reasons for nap questionnaire in Chinese college students

谌宏玥 ,*Naixue Cui,Fangxiang Mao*

School of Nursing and Rehabilitation，Shandong University

Objective: Daytime napping is prevalent among Chinese but its effects on sleep and health remain inconsistent. Different reasons for napping may play a considerable role, but it still lacks a valid measurement tool to assess the reasons for daytime napping. Methods: We obtained the permission of translating and validating the Reasons for Nap Questionnaire (RNQ) developed by Duggan et al. (2016) and validated the Chinese version among 597 Chinese college students (76.4% female). Using exploratory factor analysis, we determined a 19-item scale depending on Chinese napping characteristics. Results: The global reliability was 0.888. Results: Four-factor model was more suitable instead of Duggan＇s five reasons for napping. Cronbach＇s α coefficients of four dimensions (Dysregulative, Restorative, Emotional, Appetitive) were 0.754, 0.839, 0.836, 0.765, respectively. Conclusions: These findings suggested that the Chinese version of RNQ was reliable and valid among Chinese college students and could be applied in nap studies. Keywords Daytime napping, reasons for napping, Reasons for Nap Questionnaire (RNQ), college students, China

Genetic inactivation of ANGPTL8 regulates lipoprotein metabolism in obstructive sleep apnea syndrome

Yuenan Liu,Xinyi Li,Anzhao Wang,Niannian Li,Zhenfei Gao,Huajun Xu,Hongliang Yi,Jian Guan,Feng Liu,Shankai Yin

The Sixth People＇s Hospital of Shanghai

Objective: Abnormality of lipid metabolism is often associated with obstructed sleep apnea syndrome (OSAS). It contributes to cardiovascular risk of OSAS patients, but the underlying mechanism is still uncertain. Angiopoietin-like proteins 8 (ANGPTL8) is a cytokine secreted by liver and adipose tissue, and its expression level is positively correlated with the severity of OSAS. Using GWAS analysis, a functional SNP of ANGPTL8 was identified to be highly negatively correlated with lipoprotein and cholesterols in OSAS patients. This study aimed to investigate the role of ANGPTL8 in dyslipidemia induced by OSAS, and to determine whether the SNP variants of ANGPTL8 inhibits its function of regulating lipid metabolism. Methods: Angptl8 shRNA and ANGPL8/ ANGPL8R59W recombinant proteins were used in preadipocytes to investigate the effects of ANGPTL8 in lipid metabolism, total RNA and metabolites were collected for RNA-seq and metabolomics. Preadipocytes were treated with intermittent hypoxia (IH: 21%–1% O2, 1800 s/cycle, 64 cycles) during the process of differentiation into white adipocytes.

C57BL/6J male mice were divided into eight groups: Normoxia (NM) group, Angptl8-/- group, NM+ High-Fat Diet (HFD) group, Angptl8-/- +HFD group, CIH group, CIH+ Angptl8-/- group, CIH+HFD group, CIH+ Angptl8-/- +HFD group. CIH treatment was set to 21%–10% O2, 360 s/cycle, 8 h/day for 4 weeks, food was free to access. The levels of TG, TC, HDL-C, LDL-C were tested in serum, the adipose tissue of mice was weighed. Results: The expression level of Angptl8 and the level of TG increased after IH treatment in adipocytes. Compared with the control group, knock-down of Angptl8 suppresses lipid synthesis. RNA-Seq and metabolomics analyses demonstrated that Angptl8 knock-down suppressed Kreb Cycle and glycolysis in adipocytes, upregulated pentose phosphate pathway. Supplementation of ANGPTL8R59Wrecombinant protein reduced the level of TG in adipocytes. Moreover, the body weight, subcutaneous adipose tissue and visceral adipose tissue of Angptl8-/- mice after HFD treatment were significantly decreased compared with the control group. We also observed higher lipid level, body weight and adipose tissue in CIH modeling along with HFD group. Comparatively, Angptl8-/- mitigated the HFD-induced or CIH-induced dyslipidemia. Conclusions: CIH treatment can increase the expression of ANGPTL8. ANGPTL8-/- can prevent HFD-induced or CIH-induced dyslipidemia. The R59W mutation weakens the effect of ANGPTL8 in promoting lipid synthesis in adipocytes.

Keywords Sleep apnea, lipid, ANGPTL8, intermittent hypoxia, SNP, dyslipidemia.

The differences of carotid atherosclerosis among non–OSAHS and OSAHS patients of different severities: a cross–sectionalstudy

Zeliang Hao,Lu Qin,Juanyao Tong,Na Li,Yi Zhai,Ying Zhao
Xuanwu Hospital Capital Medical University

Objective: Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a widely prevalent problem with many complications, such as hypertension and cerebral vascular diseases. atherosclerosis, and ischemic stroke. The objective of this study is to investigate the differences of carotid atherosclerosis in patients with or without OSAHS. Methods: Patients diagnosed with carotid atherosclerosis by ultrasonography were recruited. They were requested to fill the primary screening OSAHS questionnaire. Patients with high tendency of OSAHS underwent polysomnography (PSG) tests into OSAHS group, and patients without OSAHS were into non-OSAHS group. Blood data and medical history were collected. Carotid atherosclerosis severity was analyzed by carotid artery intima-media thickness (IMT), carotid plaque, blood flow velocity, etc. Differences between the two groups and subgroups were analyzed. Results: A total of 242 carotid atherosclerosis patients were enrolled including 118 non-OSAHS patients (38 males and 80 females) and 124 OSAHS patients (40 mild, 32 moderate, and 52 severe). Significant differences were found in PSV-ICA and EDV-ICA on both sides (p < 0.05) but not in IMT and velocity of CCV. CA patients with OSAHS were younger than those without OSAHS. With the severity of OSAHS increasing, the age of CA patients

decreased. The more severity of OSAHS, the younger the patients were. The levels of serum cholesterol, triglyceride, HDL, LDL, and glucose between the two groups were similar. Conclusions: Considering CIMT, carotid plaque, blood flow velocity, and blood lipid are concerned, the severity of CA is not affected by the severity of OSAHS. The relationship between OSAHS and CA may not be dose-dependent. Keywords: Carotid atherosclerosis; OSAHS; CIMT; Blood flow velocity

Relationship between sleep and respiratory characteristics and antibody levels in convalescent COVID–19 patients

Xijuan Zheng1,2,Sizhi Ai3,Tianqi Di1,2,Lu Tan4,Yanping Bao1,Ping Wu1,Le Shi5,Yan Sun1,Shiqiu Meng1,Xiuping Yang6,Yirong Li7,Guofu Huang8,Xiong Chen6,Bin Zhang9,Xiangdong Tang4,Lin Lu5,10,Jie Shi1,2

1. Peking University Health Science Center
2. Department of Pharmacology，School of Basic Medical Sciences，Peking University Health Science Center，Beijing，China
3. Department of Cardiology，Heart Center，The First Affiliated Hospital，Xinxiang Medical University，Weihui，China
4. Sleep Medicine Center，Department of Respiratory and Critical Care Medicine，Mental Health Center and Translational Neuroscience Center，State Key Laboratory of Biotherapy，West China Hospital，Sichuan University，Chengdu，China
5. Peking University Sixth Hospital，Peking University Institute of Mental Health，NHC Key Laboratory of Mental Health (Peking University)，National Clinical Research Center for Mental Disorders (Peking University Sixth Hospital)，Beijing，China
6. Sleep Medicine Center，Zhongnan Hospital，Wuhan University，Wuhan，China
7. Department of Laboratory Medicine，Zhongnan Hospital，Wuhan University，Wuhan，China
8. Wuhan Wuchang Hospital，Wuhan University of Science and Technology，Wuhan，China
9. Department of Psychiatry，Nanfang Hospital，Southern Medical University，Guangzhou，China
10. Peking-Tsinghua Center for Life Sciences and International Data Group/McGovern Institute for Brain Research，Peking University，Beijing，China

Objectives: Obstructive sleep apnea (OSA) related sleep fragmentation and intermittent hypoxia (IH) could induce dysfunction of the immune system. Serum levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) specific antibodies in both acute and convalescent periods may reflect the disease severity of coronavirus disease 2019 (COVID-19). This study intended to explore the correlation between OSA and COVID-19. Methods: A total of 102 COVID-19 convalescent patients（36 males and 66 females）were included. We monitored the sleep and respiratory characteristics by PSG and tested immunoglobulin G (IgG) titers targeting SARS-CoV-2 spike (S) protein, recombinant receptor binding domain (RBD) and

nucleocapsid (N) protein quantitatively. We also followed up the SARS-CoV-2 IgG titers. Results: According to apnea-hypopnea index (AHI), the convalescent COVID-19 patients were divided into non OSA group (AHI < 5 events/h, 34 patients), mild OSA group ($5 \leq AHI < 15$ events/h, 33 patients) and moderate-severe OSA group (AHI $\geq$ 15 events/h, 35 patients). The results showed that 34.3% participants with moderate-severe OSA had higher levels of body mass index (BMI), higher proportion of male, higher levels of anti-N IgG and total IgG titers compared with participants without OSA. Multivariate linear regression model revealed that oxygen desaturation index (ODI) during rapid eye movement (REM) sleep, BMI, microarousal index (MAI) and time since symptom onset were independently associated with anti-N IgG titers. The SARS-CoV-2 IgG titers declined over time. The declines were independently correlated with interval between first and second testing, MAI and ODI during non-REM sleep. Conclusions: The severity of OSA, especially the recurrent IH and sleep fragmentation were particular independently associated with SARS-CoV-2 IgG levels in convalescent COVID-19 patients. This study suggested that IH and sleep fragmentation might increase the risk of COVID-19 infection and contribute to a stronger immune response by affecting the pathophysiological process of SARS-CoV-2 infection.

Keywords Sleep, Obstructive sleep apnea, COVID-19，Antibody，IgG

The relationship between obstructive sleep apnea and insulin resistance and vascular complications in patients with type 2 diabetes mellitus

Zhiling Zhao1,Guoxian Ma2,Xiaotao Wu1,Junjing Liu1,Xiheng Guo1
1.Beijing CHAO-YANG Hospital，Capital Medical University
2.Beijing Luhe Hospital，Capital Medical University

Objective: The aim of this study was to assess the incidence of OSA in patients with type 2 diabetes mellitus and to examine the relationship between the severity of sleep apnea and insulin resistance. Methods: This was a cross-sectional observational study. Patients hospitalized for poorly controlled type 2 diabetes mellitus were enrolled from the Endocrine department of Beijing Chaoyang Hospital. The demographic and clinical data of the patients were entered into an electronic case report form. Polysomnography (PSG), vascular ultrasound, examination of ocular fundus and 8-hour urinary albumin excretion rate(UAER) were performed in all the subjects. Results: A total of 96 patients with type 2 diabetes were included. Of them, 78 patients (81.28%) were diagnosed as OSA: 18 subjects in the control group, 54 subjects in the mild group and 24 subjects in the moderate-severe group. C peptide area under the curve (AUCcp) was significantly higher in those with moderate-severe OSA compared with non-apnoeic patients in the control group. The insulin resistance index determined by homeostasis model assessment (HOMA-IR) was significantly higher in the moderate-severe group and mild group compared with the

control group. Multiple linear regression analysis showed that AHI and AUCcp was positively correlated (R =0.323, p =0.001). Both AHI and BMI were positively correlated to HOMA-IR (p =0.007 and 0.023, respectively).Multiple linear regression analysis showed that both of the ultrasound score of bilateral carotid artery and arteries of both lower extremities were positively correlated to the percentage of sleep apnea and hypopnea time in the total sleep time (r=0.315, p=0.002；r=0.348, p=0.001, respectively). 8-hour UAER, the prevalence of diabetic nephropathy and diabetic retinopathy were higher in the moderate-severe group than that of the other two groups. Conclusion: OSA is positively related to insulin resistance in the patients with type 2 diabetes mellitus. OSA closely related to incident vascular complications in the patients with type 2 DM.

Keywords

Effect of positive airway pressure on continuous nocturnal blood pressure in OSA patients

Haiyan Sun,Zhiling Zhao,Xiheng Guo

Beijing CHAO-YANG Hospital，Capital Medical University

Objective: To investigate the impacts of positive airway pressure on continuous nocturnal blood pressure in OSA patients. Methods: Subjects in the study were recruited in Sleep Center of Beijing Chaoyang Hospital affiliated to Capital Medical University from May 2017 to May 2018. All subjects underwent polysomnography (PSG) and ambulatory blood pressure monitoring by pulse transit time (PTT), following PAP treatment. Results: Seventy-five subjects were included in final analysis. Body mass index (BMI) and apnea hypopnea index (AHI) were found to be higher in the subjects with elevated nocturnal BP compared with those with normal BP. With PAP treatment, the mean systolic blood pressure (SBP) in (rapid eye movement,REM) sleep of the subjects decreased from 124.80 (18.13) to 131.79(22.05) (p=0.003). The peak-BP were also significantly decreased compared with that at baseline (164.76±25.70 vs 188.87±36.56, p＜ 0.01). The frequency of high blood pressure was significantly decreased after PAP treatment. Conclusions: PAP treatment can stabilize the blood pressure of OSA patients. For patients with severe OSA and pure nocturnal hypertension, PAP treatment leads to a reduction in MAP.

Keywords: Obstructive sleep apnea, positive airway pressure, ambulatory blood pressure, PTT

The study of the relationship of insomnia severity, sleep quality and dysfunctional beliefs in patients with chronic insomnia

Minjie Song

Beijing Anding Hospital Capital Medical University

Objective: The purpose of this study is to explore the relationship between sleep quality, insomnia severity and different dimensions of insomnia dysfunction beliefs in patients with chronic insomnia, and to explore which cognitive dimension is more related to insomnia.Methods: Thirty patients who met DSM-IV criteria for chronic insomnia were enrolled. Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) were used to evaluate the indexes of sleep quality and insomnia severity, and the brief version of Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16) was used to evaluate the index of insomnia dysfunctional belief. We collected these three scales scores of 30 patients, analyzed the correlation among dimensions of DBAS-16, factors of PSQI and items of ISI by Pearson correlation analyses.Results:The dimension of "insomnia consequences" in DBAS-16 was negatively correlated with divisors of "sleep time" and "sleep disorder" in PSQI (P < 0.05); the dimension of " expectation about sleep " in DBAS-16 was negatively correlated with divisors of " daytime dysfunction " in PSQI (P < 0.05). At the same time, DBAS-16, the dimension of "consequence of insomnia" and "worry" in DBAS-16 were significantly negatively correlated with ISI and its other six items except "wake up early" (P < 0.05); the dimension of "expectation about sleep" in DBAS-16 was negatively correlated with ISI and its 5 items except "wake up early" and "the possible influence of insomnia in other's eyes" (P < 0.05); the dimension of "medicine" in DBAS-16 was negatively correlated with the item of "difficulty in falling asleep" in ISI (P < 0.05). Conclusions: This study may suggest that cognitive dimension more relevant with patients' symptoms could serve as the main target when we treat different patients.

Keywords

Clinical study of sleep structure, psychological characteristics and HLA*DQB1 0602 in type 1 narcolepsy

wanglinlin,Lin Xu,Zhu Ai,Danqi Liang,Rong Xue

Tianjin Medical University General Hospital

Objective: To understand the sleep structure and psychological characteristics of narcolepsy type 1 (NC) patients. Methods & Results: 1) The onset peak of NC was between 9 and 15 years old. Among the 20 patients, 100% had narcolepsy, 100% had increased daytime sleep, 70% had sleep paralysis at night, 80% had sleep hallucination, 100% had patients with increased daytime sleep onset. Of the whole sample, 55% was observed with self-reported memory loss, 60% with weight gain, 35% with combined sleep apnea,

55% involved in a traffic accident due to drowsiness, and 25% having desire to drive for short distances. 2) All the 20 patients carried allele HLA*DQB1 0602, among which, homozygous DQB1 0602-0602 accounted for 10%, heterozygous DQB1 0602-0301 35%, DQB1 0602-0504 5%, DQB1 0602-0303 5%, DQB1 0602-0401 5%, DQB1 0602-0202 5%, DQB1 0602-0502 5%, DQB1 0602-0201 5%, DQB1 0602-0302 10%,DQB1 0602-0601 5%. 3) Among the 20 patients, the nocturnal sleep efficiency was reduced, the nocturnal sleep latency and REM sleep latency were shortened, the N1% stage was increased, and the arousal index was increased. Fourteen patients had nocturnal REM initial sleep. 4) There was no statistical difference in gender and age between narcolepsy patients and healthy control group, but there were differences in HAMA, HAMD, TMT-B, DST- B scores (P<0.05), there was no difference in TMT-A, HVLT, DST- F score (P>0.05). 5) In patients with type 1 narcolepsy, HAMA and HAMD scores were negatively correlated with the course of disease (P<0.05), while HAMA score was positively correlated with ESS score (P<0.05). 6) In patients with type 1 narcolepsy, REM sleep latency was negatively correlated with TMT-B score; sleep efficiency was negatively correlated with HAMA score (P<0.05); the proportion of stage I sleep was negatively correlated with DST-B score; the proportion of REM sleep was positively correlated with DST-B score (P<0.05).

Keywords

Changes of cerebral blood flow and its correlation with neuropsychological characteristics in type 1 narcolepsy

Linlin Wang,Lin Xu,Rong Xue

Tianjin Medical University General Hospital

Objective: To understand the sleep structure and psychological characteristics of narcolepsy type 1 (NT1) patients, and to explore whether there is abnormal perfusion of local blood flow in patients with NT1 by using ASL technology, and to explore whether there is correlation between abnormal blood flow value in the brain area and patients’ emotion, cognitive function and severity of the disease. Methods: Twenty patients with NT1 from Tianjin Medical University General Hospital were recruited from June 2017 to June 2021. The group standard conformed to the international society for sleep disorder ICSD-3 in the onset of the latest diagnostic criteria for sleeping sickness. We also recruited 20 age- and sex- matched healthy volunteers as the control group. The basic data such as gender, age, height, weight, years of education, driving status, smoking, alcohol consumption, family history of sleep disorders and previous chronic medical history were collected for all subjects. The Narcolepsy Severity Scale (NSS) was used to evaluate the patients’ cataplexy, drowsiness, hallucination, sleep paralysis and other clinical symptoms.All subjects were assessed with the following scales: Severity of Sleepiness with Epworth Sleepiness Scale (ESS); Emotional status with Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD);Cognitive function with Trail-Making Tests A and B,memory with the Hopkins Verbal Learning Test (HVLT, attention with the Digital

Span Test (DST). All subjects were scanned with ASL sequences. The results of polysomnogram and multiple sleep latency test were collected, and the genetic tests were performed. To investigate the sleep structure, psychological characteristics and clinical manifestations of patients with NT1. We explored whether there was abnormal perfusion of local blood flow in the nervous system and its correlation with emotion, cognition and illness. Results: 1) Compared with the healthy group, the local blood flow in NT1 group was relatively reduced in the right superior temporal gyrus, right insular lobe, left middle temporal gyrus, and right superior frontal gyrus, while local blood flow relatively increased in the left orbitofrontal gyrus and left middle frontal gyrus (P<0.001).2) There was no   correlation between the blood flow in the right superior temporal gyrus, the right insular lobe, the left middle temporal gyrus, the right superior frontal gyrus, the left orbitofrontal gyrus, and the left middle frontal gyrus and scores of HAMA, HAMD, TMT-B DST-B in type 1 narcolepsy (P>0.05), left orbitofrontal gyrus and left middle frontal gyrus were positively correlated with sleep paralysis score (P<0.05). Conclusion 1.Patients with type 1 narcolepsy have extensive abnormal blood perfusion in the right superior temporal gyrus, right insular lobe, left middle temporal gyrus, right superior frontal gyrus, left intra-orbital frontal gyrus, and left middle frontal gyrus, which may be patients-specific imaging markers. 3) Abnormal blood perfusion in the left orbitofrontal gyrus and left middle frontal gyrus in patients with type 1 narcolepsy was correlated with the severity of sleep paralysis, suggesting that the left orbitofrontal gyrus and left middle frontal gyrus may be involved in the occurrence of sleep paralysis.
Keywords

MR quantitative magnetic sensitivity map to evaluate the changes of cerebral iron content in type 1 narcolepsy

Linlin Wang,Lin Xu,Rong Xue
Tianjin Medical University General Hospital

Objective: MR Quantitative magnetosensitivity Mapping (QSM) is a new imaging technology for non-invasive measurement of iron concentration in tissues.We used this technique to determine whether there were changes in iron content in the brain of patients with type 1 narcolepsy. Methods: Twenty patients with type 1 narcolepsy who met the latest diagnostic criteria of ICSD-3 were recruited from the Department of Neurology and Sleep Disorders Clinic of Tianjin Medical University General Hospital and Airport Hospital of Tianjin Medical University General Hospital from June 2018 to June 2020. A total of 20 age- and gender-matched healthy volunteers were recruited.The basic data of the subjects such as gender, age, height, weight, years of education, driving status, family history of sleep disorders, etc.Patients' severity of illness (NSS) were collected. Clinical symptoms such as cataplexy, drowsiness, hallucination, and sleep paralysis were assessed. The following neuropsychiatric symptoms were assessed: narcolepsy with the Narcolepsy Scale (ESS); emotional status with the Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMA); cognitive function with the Connectivity tests A and B to assess attention-executive function, and with the

Hopkins Word Learning Test (HVLT) to assess memory. All subjects received MRI scanns including ESWAN sequences. QSM maps were obtained by post-processing of the original unfiltered phase and amplitude maps of ESWAN. Based on voxel level, the brain iron content in the type 1 narcolepsy group and the healthy control group was analyzed. Results: 1) There was no statistical difference in gender and age between the patients with type 1 narcolepsy and the healthy control group, but there were differences in HAMA, HAMD, TMT-B and DST-B scores ($P<0.05$), but not in TMT-A, HVLT and DST-F scores ($P<0.05$).2) Compared with the healthy control group, the iron content in the right hemisphere of patients with type 1 narcolepsy was abnormal: the iron content in the right inferior frontal gyrus, the right orbitofrontal gyrus, the right straight gyrus, and the right insular lobe was significantly reduced, and the difference was statistically significant (FEW>100, $P<0.001$). Conclusions:The results of this study supported the presence of iron metabolism in the cerebral cortex of patients with type 1 narcolepsy, which may affect cellular DNA synthesis and mitochondrial energy production, thus affecting the function of the cortex, which can explain that patients with type 1 narcolepsy are often accompanied by emotional abnormalities and cognitive impairment. There was less iron in the left hemisphere of the brain compared to the left, and this difference in iron content may be related to the lateralization of motor control.

Keywords

MicroRNA-142-3p regulates the viability of Parkinson's disease model cells by targeting BMAL1

Jiawei Wu

Union Hospital of Tongji Medical College of Huazhong University of Science and Technology

Objective: To investigate the role of miR-142-3p and BMAL1 in PD model cells. Methods: 1. SPF 8-week-old C57BL/6J mice were randomly divided into two groups, with 8 mice in each group. MPTP subacute PD model was prepared in the experimental group, and the same amount of normal saline was injected in the control group. Behavioral evaluation was conducted three days after the completion of model preparation. The expression of TH in the substantia nigra was observed by immunohistochemical staining after paraffin-embedded sections of mouse brains. RNA was extracted from the substantia nigra of mice for real-time fluorescence quantitative PCR (RT-PCR) to detect the expression of miR-142-3p, and protein was extracted from the substantia nigra of mice for Western blot to detect the expression of BMAL1. 2. SH-SY5Y cells were cultured and treated with MPP+ stimulation (0, 20, 50, 100 μM) at gradient concentration. The protein was extracted and the expression of BMAL1 was detected by Western blot. The expression of miR-142-3p was detected by RT-PCR after RNA extraction. 3. SH-SY5Y model cells were transfected with miR-142-3p mimics ,mimics NC), miR-142-3p inhibitor and inhibitor NC respectively, and the expression of miR-142-3p was detected by RT-PCR to verify the transfection effect; 4. SH-SY5Y cells were inoculated on 96-well plates, blank control group, MPP+ group, mimics+MPP+ group, mimics NC+MPP+ group, inhibitor+MPP+

group and inhibitor NC+MPP+ group were set, and CCK-8 reagent was added to detect and calculate the cell viability after 24 hours of culture. 5. SH-SY5Y cells were transfected with miR-142-3p mimics, miR-142-3p mimics NC, miR-142-3p inhibitors and miR-142-3p inhibitors NC. After 24 hours of MPP+ stimulation at 100μM, BMAL1 protein expression was detected by Western blot. Results: 1. The expression of miR-142-3p and BMAL1 protein in the substantia nigra of MPTP subacute PD model mice decreased; In the MPP+ treated SH-SY5Y cell model, the expression of miR-142-3p showed a gradient decrease with the increase of MPP+ concentration, while the expression of BMAL1 protein showed no difference. 2. Inhibition of the expression of miR-142-3p reduced the cellviability. 3. Overexpression of miR-142-3p can inhibit the expression of BMAL1 protein.Conclusion: 1. Posttranscriptional regulation of BMAL1 expression by miR-142-3p. 2. Overexpression of miR-142-3p can reduce the damage of dopaminergic neurons induced by MPP+.

Keywords

Effects of obstructive sleep apnea on bone metabolism: a systematic review and meta–analysis

Yunping Mou,Xiaoxue Wei,Sajitanmu Kadier,Bingqian Zhu

School of Medicine，Shanghai Jiao Tong University

Objective: To evaluate the effect of obstructive sleep apnea on bone metabolism. Methods: Databases including Cochrane library, JBI, PubMed, Embase, CINAHL, Web of Science, CNKI, SinoMed, VIP and WanFang were searched from inception Dec.2020 for literatures on the effects of obstructive sleep apnea on bone metabolism. After data were extracted, two researchers read the papers independently with the inclusion and exclusion criteria to screen the them and extract the data. The quality of the included literatures was assessed by JBI evidence-based health center's quality assessment tool for analytical cross-sectional study. A meta-analysis was conducted using Stata15.1 software. Results: A total of 12 studies with 1,022 patients were included,; of them, 745 patients were included in OSA group and the other 277 patients in the control group. There was a weak negative correlation between AHI and BMD: z(95% CI) = -0.27 (- 0.58,0.03); there was a weak positive correlation between AHI and β - CTX, z (95% CI) = 0.41 (0.30, 0.52). Conclusions: AHI index was positively correlated with β - CTX, indicating that OSA patients were in a state of high bone turnover rate, which may increase the risk of osteoporosis or fracture.There was no direct correlation between AHI index and bone mineral density, and the decrease of bone mineral density in OSA patients might be related to other factors.

Keywords: OSA; bone mineral density; bone metabolism; systematic review; meta

The effect of subjective and objective sleep on chronic pain in patients with insomnia

Liu Liu,Min Wu,Xiangdong Tang,Wensheng Zhang,Junying Zhou

West China Hospital，Sichuan University

Objective: To explore the potential risk factors associated with chronic pain in patients with insomnia and the underlying mechanisms. Methods: A total of 358 patients with insomnia (mean age = 48.41 ± 10.93 years) were recruited in this study. The subjective sleep was evaluated by Pittsburgh sleep quality index scale (PSQI), insomnia severity index scale (ISI) and Epworth sleepiness scale (ESS), meanwhile. The objective sleep was assessed by polysomnography (PSG). Binary logistics regression model was used to evaluate potential factors associated with chronic pain in patients with insomnia. The effects of subjective and objective sleep parameters on pain intensity were analyzed by multiple linear regression. Results: There were 48.9% of patients with insomnia comorbid with chronic pain. Insomnia patients with chronic pain had more severe anxiety and depression symptoms compared with those without. There was a significantly decreased duration of N3 in patients with chronic pain, but no significant differences were found in other objective and subjective sleep parameters. After controlling for the potential influencing factors, the anxiety symptoms and the decreased N3 duration were associated with the increased risk for chronic pain. And poor sleep quality and anxiety symptoms were associated with increased pain intensity assessed by Visual Analogue Scale (VAS). No significant associations were found between the objective sleep parameters and VAS. Conclusions: Chronic pain was commonly seen in patients with insomnia. Anxiety symptoms and decreased duration of slow wave sleep were the risk factors of chronic pain. Poor subjective sleep quality and anxiety symptoms increased the pain intensity. These findings provide a reliable basis for the intervention of chronic pain.

Keywords

Characteristics of sleep apnea hypopnea syndrome in high altitude areas and the incidence and influencing factors that concomitant hypercapnia

Yunhui Lv,Siying Li,Daijin Huang,Hewei Li,Jing Ye

The Affiliated Hospital of Kunming University of Science and Technology，The First People＇s Hospital of Yunnan Province

Objective: To compare the polysomnography (PSG) parameters and the incidence of concomitant hypercapnia in patients with sleep apnea hypopnea syndrome (SAHS) in high altitude areas and those in plain

areas, and to study the risk factors of incident hypercapnia.Methods: A retrospective analysis of the data of two groups of patients with SAHS that matched by age, sex ratio and body mass index (BMI). A total of 1,027 cases were recruited from Kunming City (1890 meters above sea level), and 1,035 cases were from Beijing (50 meters above sea level). PaCO2≥45mmHg and PaCO2≥40mmHg were used as the standard for SAHS combined hypercapnia in plain areas (Beijing) and high altitude areas (Kunming), respectively. We compared the PSG parameters and the incidence of combined hypercapnia in the two groups , and further analyzed the factors influencing the incidence of combined hypercapnia.   Results: The patients with SAHS in high altitude areas had increased AHI, of which CAI and HI increased, while OAI decreased. There were higher level of average SpO2 and minimum SpO2, and longer apnea time compared with patients living in plain areas. The incidence of patients with SAHS comorbid hypercapnia was 3.0% in high altitude areas and 22.7% in plain areas. These differences were significant between the two groups (P<0.01). Multivariate regression analyses showed that the main risk factors affecting the incidence of combined hypercapnia were the minimum SpO2, the longest apnea time in high altitude areas, and the arterial blood PaO2 in plain areas. Conclusions: The PSG parameters of the patients with SAHS in high altitude areas were different from those in plain areas. The incidence of combined hypercapnia was also significantly lower than that in plain areas. The longest apnea period and the lowest minimum SpO2 were risk factors for incident combined hypercapnia.

Keywords High altitude, Sleep apnea and hypoventilation syndrome, Polysomnography parameters, Hypercapnia

A randomized controlled study of daytime changes in brain function in infants with sleep problems

Wanli Deng

Chongqing Health Center for Women and Children

Objective: To understand the classification of common sleep problems in infants, and to clarify whether there was any difference in the brain functional state between normal infants and the infants with sleep problems. Methods: Parents filled in the infant sleep questionnaire. According to the results of the questionnaire, the study included 156 infants with sleep problems, and measured the brain function. According to a 1:1 ratio, we randomly selected the - age- and sex- matched infants without sleep problems admitted to the Department of Child Health as the control group; we also measured the brain function. We then compared the brain function between the two groups.. The indicators of brain function included brain energy consumption, hypoxia index, emotional index, anxiety and depression tendency index, external attention, internal attention, introverted brain, brain inhibition, and brain stability. Results: The sleep problems were common in the case group: having trouble in falling asleep occurred in 41 cases (26.3%), simple frequent night awake in 41 cases (26.3%), simple rhythm of sleep disorders in 0 cases (0%), having trouble in falling asleep + frequent night awake in 53 cases (34.0%), sleep rhythm disorders + having trouble in asleep in 5 cases (3.2%), frequent night

waking +sleep rhythm disorders in 4 cases (2.6%), trouble falling asleep + frequent night awake+ sleep rhythm disorders in 12 cases (7.7%). Compared with normal infants,the brain energy consumption, hypoxia index, emotional index, anxiety and depression tendency, external attention in the sleep problem group were higher than those in the control group (all P<0.05). In case group, the cerebral convergence, cerebral inhibition, cerebral stability and internal concentration were lower than those in the control group (all P<0.05). Conclusion: The common sleep problems of infants are having difficulty in falling asleep, frequent nocturnal awakening, and circadian rhythm inversion. The brain function of infants with sleep problems was significantly altered compared with that of normal infants.

Keywords

Exploration on the construction of sleep evaluation system of TCM based on clinic

Zhuxing Wang,Xi Zhou

Chongqing Tranditional Chinese Medicine Hospital

Objectives: Due to the lack and imperfection of efficacy assessment methods for Patient's subjective symptoms in clinical sleep evaluation system of TCM, it's necessary to develop an exploratory TCM sleep evaluation system based on Patient Reported Outcome (PRO). This study aimed to develop a valuable tool for the evaluation of the efficacy of TCM for insomnia. Methods: Using the literature research method, we extracted the literature on TCM treatment of insomnia in the recent 20 years, combined the TCM clinical research cases and clinical experience of dominant diseases in our department--the National Regional TCM Diagnosis and Treatment Center. We took the TCM four diagnostic methods as core element, highlighted systematic inquiry of TCM and extracted patients' subjective symptoms, and collected data on the four dimensions of the related 30 items: sleep quality, physiology, psychology, social behavior. We constructed a TCM sleep evaluation system based on PRO. We applied the evaluation system together with the PSQI and the SRSS to over 160 patients for clinical application, and conducted a questionnaire survey among doctors and patients to evaluate the applicability of the system. Results: The "TCM sleep evaluation system based on PRO" could not only reflect the sleep quality of insomnia patients, but also reflect the overall state change of physiological state, psychological state and social behavior of insomnia patients. It fully reflected the thoughts of diagnosis, treatment of insomnia, and the preliminary opinions of curative effect evaluation of TCM. Conclusion: This evaluation system can objectively reflect the overall state of insomnia patients and reflect the thinking of TCM clinical diagnosis and treatment. It is easy to operate and has good applicability. It is consistent with the clinical practice of treating insomnia by TCM and can be used to evaluate the clinical effect of treating insomnia by TCM.

Keywords: Clinical TCM; Patient report outcome; Insomnia; Evaluation system

Role of brainstem SOCS3 in obesity–related hypoventilation

Shuang Wang1,Yishuo Shi1,Sheng Wang1,2,Fang Yuan1,2

1.Department of Physiology，Hebei Medical University

2.Hebei Key Laboratory of Neurophysiology

Background: Obesity is currently one of the major epidemics of this millennium and affects individuals throughout the world. It causes multiple systemic complications, such as obesity-related hypoventilation. Itss mechanisms involve the changes caused by the accumulation of adipose tissue and neural leptin resistance. However, the central targets and mechanism related to hypoventilation of leptin resistance have not been identified. SOCS3 signaling plays a negative regulatory role in the activation of the LepRb/JAK/ STAT3 pathway. Hence, the SOCS3 may be the pathogenesis and therapeutic target to obesity-related hypoventilation. Objective: The present study aims to explore the role of brainstem SOCS3 in obesity-related hypoventilation. Methods: In diet-induced obesity (DIO) mouse model, the respiratory function was assessed using whole-body plethysmography. Meanwhile, leptin-activated neurons, reflected by pSTAT3+ neurons, in the tractus solitary nucleus (NTS) and the retrotrapezoid nucleus (RTN) were assessed in DIO mice. Quantitative analysis of SOCS3 and pSTAT3 using Western blot and qPCR technology was performed. Results: Our main findings demonstrate that DIO mice exhibit overweight, hyperleptinemia, hypocapnia. During exposure to room air, DIO mice manifest basal hypoventilation with a rapid and shallow breathing pattern. Exposure to CO_2 elicits impaired HCVR in DIO mice. Besides, the number of CO_2-activated and leptin-sensitive neurons in the RTN and NTS was dramatically reduced in DIO mice. The pSTAT3 was downregulated but SOCS3 was upregulated in the NTS and RTN from DIO mice relative to control mice. Genetic deletion of SOCS3 in the NTS and RTN notably rescued the impaired HCVR in DIO mice. Conclusions: The hypoventilation and the impaired HCVR in DIO mice are associated with changes in the production of pSTAT3 and SOCS3. Genetic deletion of SOCS3 in the NTS and RTN can rescue the impaired HCVR in DIO mice.

Keywords: Leptin; hypoventilation; obesity; hypercapnic ventilatory response; SOCS3

Effect of xiangxuanjieyu recipe on NMDA receptor type 1 and AKT expression in hippocampus of anxiety rats

Jian Xu

Shanghai Hospital of Traditional Chinese Medicine

Objective To investigate the effect of Xiangxuan Jieyu Recipe on the expression of NMDAR1 and Akt in the hippocampus of anxiety rats. Methods Male Wistar rats were randomly divided into control group, model group, and traditional Chinese medicine treated model group, with 10 rats in each group. The anxiety

rat model was established by the method of uncertain empty bottle drinking water stimulation, and the behaviour of rats in each group was tested after the intervention of traditional Chinese medicine. The rats were killed immediately after the behavioural tests, and the hippocampus were isolated on the ice platform. Then, the expression of NMDAR1 and Akt was determined by Western blot and immunohistochemistry. Results The results of Open field test showed that compared with the control group, the total distance and central distance of the anxiety model group were significantly increased at the end of 2 weeks (P < 0.01); compared with the model group, the total distance and central distance of traditional Chinese medicine treated model group were significantly decreased (P < 0.01). The results of elevated cross maze experiment showed that the total distance and central distance of anxiety model group were significantly increased at the end of 1 week (P < 0.01). Compared with the control group, the OT% and OE of the model group were significantly lower (P < 0.05), while there was no significant difference between the traditional Chinese medicine treated model group and the model group (P > 0.05). Immunohistochemical staining showed that the expression of NMDAR1 positive cells in the hippocampus of the model group was significantly increased than that of the control group (P < 0.01). And the traditional Chinese medicine treatment decreased the the expression of NMDAR1 in the hippocampus of the anxiety model (P < 0.01). Meanwhile, Western blot showed that Xiangxuan Jieyu Recipe could inhibit the expression of Akt and p-Akt protein in anxiety rats. Conclusion: The anti-anxiety effect of Xiangxuan Jieyu Recipe may be related to the regulation of NMDAR1 and Akt protein expression in the hippocampus.

Keywords

Exploring potential salivary biomarkers in respiratory diseases: still on its way

Chuanxiang Li1,2,Liu Zhang2,Yaru Yan2,Yongjie Ding2,Yingni Lin2,Pingjian Zhou2,Ning Li2,Hongpeng Li2,Shiqi Li2,Xianwen Sun2,Qingyun Li2

1.Wuhan Third Hospital

2.Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine

Saliva, containing over 400 types of proteins, over 3000 unique mRNAs, and 700 bacterial species, has been widely regarded as biomarkers in several diseases, such as periodontitis, caries, cancers, diabetes mellitus, and cardiovascular diseases. Saliva samples can be collected in a simple, minimally-invasive, and repeated manner, which brings the convenience to the special patients, such as infants, children, and anxious patients etc. With the development of hypersensitive techniques, such as microsensor arrays, enzyme-labelled immunosensors, nanoparticle-labelled immunosensors, capacitive or impedimetric immunosensors, magneto immunosensors, field effect transistor immunosensors (FET), and surface enhanced Raman spectroscopy (SERS) , the sensitivity and accuracy have been improved. Nowadays, saliva has been used as a potential

medium for diseases diagnosis and assessment. However, the exploration of saliva biomarkers is still on its way for respiratory diseases, although the first study was reported in 1977. Thus, we reviewed the studies on potential saliva biomarkers in predicting respiratory diseases, and summarized the progress and the obstacles concerning this issue.

Keywords

Predictors of treatment response to a brief parent–based sleep intervention in children with attention deficit hyperactivity disorder

Xiao Li1,Ka Sin Caroline Shea2,Ching Kwong Dino Wong1,Lok Fan Lau1,Waiyan Vivian Chiu1,Wai Man Mandy Yu3,Albert Martin Li5,Yun Kwok Wing3,Yee Ching Kelly Lai3,Shirley Xin Li1,5

1. Sleep Research Clinic and Laboratory，Department of Psychology，The University of Hong Kong，Hong Kong SAR
2. Department of Psychiatry，Alice Ho Miu Ling Nethersole Hospital，Hong Kong SAR
3. Department of Psychiatry，Faculty of Medicine，The Chinese University of Hong Kong，Hong Kong SAR
4. Department of Paediatrics，Faculty of Medicine，The Chinese University of Hong Kong，Hong Kong SAR
5. State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong，Hong Kong SAR

Objective: Previous research has shown the positive effects of behavioral sleep interventions on improving sleep symptoms in children with attention deficit hyperactivity disorder (ADHD), yet the treatment response was highly variable across individuals. In the present study we aimed to explore the potential predictors of treatment response to a brief parent-based sleep intervention in ADHD children with insomnia. Methods: Thirty-five families with a child (aged 6-12) with clinically diagnosed ADHD comorbid insomnia received a brief parent-based sleep intervention provided by the trained clinicians. All the study participants were assessed by parent-report questionnaires on sleep symptoms (Children's Sleep Habit Questionnaire, CSHQ), ADHD symptoms (Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour Scale), and psychosocial functioning (Strengths and Difficulties Questionnaire, SDQ) at baseline and 2-week post intervention. CSHQ insomnia severity was calculated by the sum of CSHQ bedtime resistance, CSHQ sleep onset delay and CSHQ night wakings. Treatment response was defined as a change in CSHQ insomnia severity score ≥ 3 points (as measured by the reliable change index) at post-intervention. Results: Fourteen out of the 35 participants (40%) responded to the intervention. Compared to children without response to the intervention, children with treatment response were scored significantly higher on CSHQ insomnia severity (22.14 ± 3.03 vs. 19.6 ± 3.8, p = 0.031) and sleep onset delay (7.5 ± 1.09 vs. 6.95 ± 1.73, p = 0.046), had a higher score on SDQ internalizing difficulties (8.82 ± 3.66 vs. 5.71 ± 2.92, p = 0.027) at baseline. Conclusions: ADHD children with less severe insomnia symptoms, especially sleep onset delay, and more

internalizing problems may be less likely to respond to a brief parent-based sleep intervention. There is a need for future research to explore ways to enhance the effectiveness of the behavioral sleep interventions for children with ADHD.

Keywords

A clinical prediction model of severe obstructive sleep apnea in children

Yufen Tang,Zhifei Xu

Beijing Children's Hospital Affiliated to Capital Medical University

Objective: To establish a clinical prediction model of severe obstructive sleep apnea syndrome (OSAS) in children and to evaluate its predictive efficacy. Methods: A total of 1,441 children with habitual snoring were selected, including 959 males and 482 females. According to the data of obstructive apnea hypopnea index (OAHI) monitored by PSG all night, severe OSA was defined as OAHI>10 times/h, and non-severe OSA was defined as OAHI≤10 times/h. The children were divided into severe OSA group (289 cases) and non-severe OSA group (1,152 cases). By using unconditional logistic regression adjusting for all confounding variables, the predicative model was established, and the predicting indexes included in the model were further selected to establish the decision-tree model. The effectiveness of the model was evaluated by using accuracy, recall (i.e., sensitivity), accuracy and F1 score.Results: A total of 1441 subjects, 3out of 4 as training set, a total of 1080 subjects,1 out 4 as test set, a total of 361 people. Age, BMI, neck circumference/height, SRBD respiratory dimension standard score, SRBD other dimension standard score and SRBD total score standard score of 1,080 children's as the predictive factors, the decision tree model was constructed. The accuracy rate of this decision-tree model is 82.87% in training set, and 83.38% in test set. Conclusions: The decision-tree model constructed in this study can easily and effectively screen children with severe OSAS. It has high predictive value and can provide reference for clinical screening of children with severe OSA.

Keywords

Enhancement of CPAP in Obstructive Sleep Apnea Patients by Telehealth Technology

Benjamin Ka Seng Thong1,2,Grace Xin Yun Loh1,2,Jia Jan Lim1,2,Christina Jia Liang Lee1,2,Shu Ning Ting1,2,Hong Peng Li1,Qing Yun Li1

1.Ruijin Hospital，Shanghai Jiao Tong University School of Medicine
2.Shanghai Jiao Tong University School of Medicine

Background: Obstructive sleep apnea (OSA) is a significant global health peril. Continuous airway positive pressure (CPAP) is the current gold standard to treat OSA. However, OSA patients had low adherence to CPAP. American Academy of Sleep Medicine proposed the application of telemedicine in 2015. The suggestion expedited the expansion of telehealth in sleep medicine for the past few years. Therefore, we aimed to examine the effect of current telehealth interventions on CPAP adherence of OSA patients.　Methods: A literature search was conducted from 16/1/2021 to 23/1/2021 with PubMed, Scopus, and Web of Science. All original research articles published from the year 2016 onwards were retrieved. Only original research articles written in English with the primary aim to observe the effect of telehealth interventions in CPAP adherence of OSA patients were considered in this review. Results: Current tele-monitoring strategies are able to possess a short-term effect in improving CPAP adherence. The impact of mobile health interventions (telephone, text message, and apps) remain contentious. Tele-education alone was inadequate to enhance CPAP adherence. Psychological motivation enhancement showed promising results. Future efforts should concern with combining strategies, big data and artificial intelligence, and the advancement of a clinical prediction model. The biopsychosocial factor ought to be an essential consideration for coming studies.　Conclusion: The application of telemonitoring system did suggest propitious results in enhancing CPAP adherence in OSA patients. Combining interventions should be required other than a single educational strategy. Integration of big data and artificial intelligence is recommended to be used in the future.

Keywords Sleep Apnea Syndromes, eHealth, Telemedicine, Compliance, CPAP.

A case report of OSAHS patients with high altitude sickness comorbid systemic multivascular injury

Qi Bian

Qinghai Red Cross Hospital

Altitude sickness is a special disease in the altitude environment. It is a clinical syndrome characterized by polycythemia (Hb≥190 g/L in female, Hb≥210 g/L in male) and hypoxemia due to the gradual loss of acclimatization to the altitude hypoxia environment of the global residents or migrants who live at an altitude

of 2500 meters for a long time. Its main clinical manifestations include headache, dizziness, shortness of breath and/or palpitations, sleep disturbances, fatigue, local cyanosis, burning sensation in the palms and soles of the feet, dilated veins, muscle and joint pain, loss of appetite, memory loss, and inconcentration. The plateau environment is a high risk factor for OSAHS, and OSAHS is also a high risk factor for altitude sickness. The interaction between the three factors makes the symptoms and complications of OSAHS patients with altitude sickness in the plateau environment more severe and the prognosis worse.A patient with OSAHS co-associated with altitude sickness with multiple systemic vascular injuries admitted to our deparment in November 2019. The patient's symptoms improved after CPAP treatment. The report is as follows.

Keywords

Spindle–related brain activation in patients with insomnia disorder: an EEG–fMRI study

Yan Shao,Jie Chen ,Xuejiao Gao ,Hongqiang Sun

Peking University Sixth Hospital

Sleep spindles are defined as phasic events involved in sleep-protection mechanisms. Whereas, no neuroimaging research has investigated the hallmark characteristics of spindle-related brain activation in patients with insomnia disorder (ID). To address this issue, we recruited 16 ID patients and 30 well-matched healthy controls to perform a simultaneous electroencephalogram-functional magnetic resonance imaging recording during the first NREM sleep period. Our data suggested significantly decreased bilateral spindle-related brain activation in the cingulate cortex in ID patients compared with the healthy controls. Additionally, the activation in the cingulate cortex was negatively correlated with the scores of the Self-Rating Depression Scale and Self-Rating Anxiety Scale, as well as sleep latency, the second component of the Pittsburgh Sleep Quality Index in the pooled sample. In a nutshell, this study advanced our understanding of sleep-protection mechanisms of ID and imparted novel insights into the neurobiological basis between sleep spindles and insomnia-related clinical severity.

Keywords Sleep spindle; brain activation; insomnia disorder; EEG-fMRI; sleep-protection mechanisms

Effects of obesity on sleep–disordered breathing and nocturnal hypoxia in patients with obstructive sleep apnea–hypopnea syndrome

Feikai Li1,Wenya Feng1,Huiling Wang1,Zhongming He2,Kuili Chen1,Zhezhe Mao1

1.Handan Central Hospital

2.Xinjiang Karamay Central Hospital

Objective: Obesity, as an important risk factor of obstructive sleep apnea-hypopnea syndrome (OSAHS), plays an important role in the pathogenesis and prognosis of OSAHS. The purpose of this study was to investigate the effects of obesity on sleep-disordered breathing and nocturnal hypoxia in patients with obstructive sleep apnea-hypopnea syndrome. Methods: Patients with OSAHS confirmed by polysomnography (PSG) in Handan Central Hospital were recruited from 2016 to 2020. The participants were divided into three groups: normal (BMI < 24kg/m2), overweight($24 \leq$ BMI < 28kg/m2) and obesity groups (BMI $\geq$ 28 kg/m2). The sleep apnea-hypopnea index (AHI), mean SaO2 (MSpO2), lowest SaO2 (LSaO2), and percentage of time spent with SpO 2 below 90% (SIT90) were measured. Results: A total of 1152 participants (male: 82.3%) with OSAHS were recruited, with 119 cases in the normal group, 418 cases in the overweight group, and 615 cases in the obesity group. There were significant differences in AHI and hypoxia indicators between different groups (p<0.001). Spearman correlation analysis showed that BMI was significantly correlated with BMI and AHI, MSpO2, LSpO2, and SIT90 (all P < 0.05). AHI will increase 4.88 % when BMI added to 1kg/m2. In addition, logistic regression analysis showed the risk of patients suffering from moderate to severe OSAHS increased 21.3% by 1kg/m2 added in BMI. The cut-off value of BMI for diagnosis moderate to severe OSAHS was 27.8kg/m2, and the sensitivity and specificity were 62.85% and 69.79%, respectively. Conclusions: Obesity is related to the degree of sleep-disordered breathing and hypoxia in OSAHS patients. AHI and the degree of hypoxia aggravated with the increase of BMI. CPAP treatment combined with weight loss may reduce the severity of OSA.

Keywords OSAHS; Obesity; Sleep-disordered breathing index; Intermittent hypoxia.

Chinese herbal medicine for post–stroke insomnia: a systematic review and meta–analysis

Xiaojia Ni,Qing Su,Qin Li,Danmei Zou,Bojing Zhang,Yefeng Cai

Guangdong Provincial Hospital of Chinese Medicine，Guangdong Provincial Academy of Chinese Medical Sciences，The Second School of Guangzhou University of Chinese Medicine，Guangzhou 510120，China

Objective: The systematic review was to evaluate the efficacy and safety of Chinese herbal medicine (CHM)

for post-stroke insomnia. Methods: The English and Chinese literature databases were searched to identify the randomized controlled trials (RCTs) on CHM for post-stroke insomnia in March 2021. The risks of bias were assessed by using RoB 2.0. Meta-analysis was performed by using RevMan 5.3. Subgroup analyses were conducted to explore the sources of heterogeneity if necessary. Results: Thirty-one RCTs were included in the systematic review and 26 were included in meta-analyses. Only one trial used placebo as the control and double-blinding to reduce the performance bias. The meta-analysis indicated that CHM alone was more effective than placebo (MD: -6.50, 95%CI: -9.07 to -3.97; 1 RCT, 60 participants) and non-benzodiazepine drugs (BZDs) (MD = -2.63, 95%CI: -3.39 to -1.87, I2 = 92%; 10 RCTs, 786 participants) in terms of Pittsburgh Sleep Quality Index (PSQI). However, CHM did not outperform non-benzodiazepine drugs (non-BZDs). Meta-analysis also suggested that the adjunct use of CHM provided additional effects to BZDs (MD = -3.01, 95%CI: -3.63 to -2.39, I2 = 22%; n = 2 RCTs, 160 participants), non-BZDs (MD = -4.11, 95% CI: -5.82 to -2.40, I2 = 94%; n = 3 RCTs, 280 participants), and antidepressants (MD = -3.60, 95%CI: -5.49 to -1.70, I2 = 61%; n = 2 RCTs, 240 participants) regarding PSQI scores. CHM was without major adverse events and with fewer adverse events than pharmacotherapies. The most prevalent CHM formula was Chaihu Longgu Muli Decoction, the most widely used CHM drugs was Bailemian Capsule and the most frequent herb was ZIZIPHI SPINOSAE SEMEN (i.e., Suanzaoren). Conclusions: Oral CHM may improve subjective sleep quality for post-stroke insomnia and it is safe. The effect size varies on the types of CHM and the therapeutic duration. However, few RCTs were of high methodological quality and an outstanding CHM drug with solid evidence was needed in the future.

Keywords Stroke, Insomnia, Chinese herbal medicine, Meta-analysis, Evidence-based medicine.

Effects of sleep disordered breathing in patients with decompensated heart failure：an adverse endpoint analysis

Xiaomin He,Jing Wang,Kaida Guo,Qiaojun Wang, Fei Han,Rui Chen

Second Affiliated Hospital of Soochow University

Objective: To study the effect of Sleep disordered breathing (SDB) in patients with decompensated heart failure, to assess the effects of respiratory parameters and hypoxic parameters on adverse endpoints in patients with decompensated heart failure, and to determine the risk factors for decompensated heart failure in SDB patients. Methods: A prospective study was conducted. Patients with decompensated heart failure who hospitalized in the Department of Cardiology of the Second Affiliated Hospital of Soochow University were recruited from September 2018 to October 2020.Medical history, medication history, hematological indicators and cardiac ultrasound indicators of all patients were collected.The hematological indicators mainly included N-terminal pro-BNP(NT-proBNP), biochemical indicators, electrolytes and other indicators were all collected. After decompensated heart failure was managed and stablised, Apnealink (ResMed) sleep monitoring was performed prior to their discharge. The SDB group included the patients

with　AHI≥15/h, while the non-SDB group included those with AHI<15/h. After discharge, patients were systematically followed up every 3 months with follow-up records or telephone-interview. The time and type of the endpoint events was recorded, including all-cause death, heart transplantation, implantation of cardiac pacing devices, and rehospitalization, etc.The study compared the clinical characteristics, sleep respiratory parameters, blood and cardiac ultrasound indices, and adverse endpoints between patients with SDB complicated with decompensated heart failure and patients with decompensated heart failure alone. We analyzed the effects of combined SDB on adverse endpoints in patients with decompensated heart failure. Results: A total of 113 patients who met the inclusion criteria were included, consiting of 60 patients (53.1%) in the SDB group (AHI≥15/h) and 53 patients (46.9%) in the non-SDB group (AHI<15/h). Levels of body mass index (BMI), abdominal circumference and serum sodium in the SDB group were significantly higher than those in the non-SDB group (P<0.05), but there were no significant differences in gender, age, cardiac function grade, previous medical history, glucose and lipid metabolism indices and NT-proBNP between the two groups (P>0.05). Aortic diameter assessed with cardiac ultrasound indices increased in the SDB group compared to the non-SDB group (P<0.05), but there were no significant differences in the left atrial diameter, left ventricular diameter and left ventricular ejection fraction between the two groups (P>0.05). Comparing the sleep parameters in the two groups, RI, ODI, AI, HIand T90% in the SDB group were significantly higher than that of the non-SDB group (P<0.05). A total of 37 patients were followed up every 3 months after discharge, including 9 patients who died, 2 patients who were implanted of cardiac pacing devices, and 26 patients who readmitted. There were no significant differences in the incidence of each endpoint event between the SDB group(23 cases) and the non-SDB group (14 cases) (P>0.05). Kaplan-Meier survival analysis showed worse endpoint event-free survival in the SDB group than the non-SDB group (AHI≥15/h vs AHI<15/h：log rank P = 0.039). The endpoint-free survival rate of patients with T90% ≥ 6% was significantly lower than that of the patients with T90%<6% (T90%≥6% vs T90%<6%: log rank P = 0.018). Multivariate Cox analysis showed that T90% as a continuous variable had a statistically significant effect on endpoint events (HR 1.030, 95%CI 1.010-1.051, P = 0.004). Using a median cut-off at 6% of T90% ,patients with T90%≥6% had a 2.57-times increased risk to develop an endpoint event compared to those with T90%<6% (HR 2.566, 95%CI 1.150-5.723, P = 0.021). AHI as a continuous variable significantly predicted the endpoint events (HR 1.145, 95%CI 1.033-1.269, P = 0.010). However,when AHI (AHI≥ 15/h vs AHI<15/h) was similar in both groups. . Conclusion: Patients with SDB comorbid decompensated heart failure had more obvious abdominal obesity and wider the inner diameter of the aorta than those with decompensated heart failure alone. Sleep disordered breathing was a important factor in patients with decompensated heart failure. Patients with nocturnal hypoxia had lower endpoint-free survival and poor prognosis. This study indicated that nocturnal hypoxemia is a good predictor of adverse endpoint events in patients with decompensated heart failure.

Keywords

The mediating role of anxiety and depression in the relationship between perceived stress and sleep quality among medical students

Wanmin Huang1,3,Jiyang Pan2,Chunliu Luo2

1.Guangzhou Panyu Central Hospital

2.The First Affiliated Hospital of Jinan University

3.Jinan University

Objectives: To investigate the perceived stress and sleep status of medical students and to explore the relationship between anxiety, depression, sleep, and perceived stress among medical students. Based on the theoretical model of the relationship between stress and sleep quality and the cognitive quality-stress model theory, we employed anxiety and depression as mediators, to explore the mechanism of perceived stress on sleep quality and the underlying mediating effects of anxiety and depression. Methods: We used an online electronic questionnaire survey in the platform of Wenjuanxing and asked the participants to fill out the questionnaire on site. The medical students were investigated by using the Pittsburgh Sleep Quality Index Scale, Perceived Stress Scale, 9-item Patient Health Questionnaire, and 7-item Generalized Anxiety Disorder Scale. A total of 1021 medical students were surveyed. Results: The mean score of perceived stress, sleep quality, anxiety, and depression among medical students were (17.01 ± 4.805), (5.88 ± 3.574), (4.73 ± 4.285), and (5.39 ± 4.906). Perceived stress significantly and positively predicted poor sleep quality ($\beta=0.305$, $t=10.221$, $p<0.001$). Anxiety significantly and positively predicted stress perception ($\beta=0.286$, $t=5.943$, $p<0.001$). Anxiety significantly and positively predicted poor sleep quality ($\beta=0.504$, $t=18.612$, $p<0.001$). Depression significantly and positively predicted perceived stress ($\beta=0.114$, $t=2.231$, $p<0.05$). Depression significantly and positively predicted poor sleep quality ($\beta=0.224$, $T=11.208$, $p<0.001$). Anxiety and depression play a partially mediating role in the influence of perceived stress on sleep quality. Conclusions: The level of medical students' perceived stress is at low level relatively. It is a serious problem for the sleep quality of medical students. Anxiety and depression have a significant mediating effect on the impact of perceived stress on sleep quality, and they play a partial mediating role.

Keywords

Joint Sleep Stage Classification and Prediction in Obstructive Sleep Apnea Using Deep Learning Method

Fan Li1,2,Rui Yan3,4,1,Lai Wei5,Rong Liu1,Fengyu Cong1,6,4

1. School of Biomedical Engineering，Faculty of Electronic Information and Electrical Engineering，Dalian University of Technology，
2. RWTH Aachen University
3. School of Information Science and Engineering，HebeiUniversity of Science & Technology
4. Faculty of Information Technology，University of Jyva ̈ skyla ̈
5. Otolaryngology Department，Affiliated Zhongshan Hospital of Dalian University
6. School of Artificial Intelligence，Faculty of Electronic Information and Electrical Engineering，Dalian University of Technology

This study presents a deep neural network for sleep stage scoring and prediction on patients with OSAHS with different level of AHI using single-channel EEG. To investigate the difference in performance between subjects with different level of AHI, an end-to-end 1-D convolutional neural network combing with CRF is designed. The model considers three consecutive EEG epochs as the model input determining three corresponding stages in the output. For sleep staging task, the central label of the three consecutive epochs is viewed as the ground truth of each input, and the left and right neighbors of the central label are for left and right sleep stage prediction. So, it is a many-to-many strategy compared with the standard one-to-one or many-to-one methods. The designed model was trained and tested on different level of AHI subjects selecting from SHHS dataset, respectively. The obtained mean accuracies for normal, mild, moderate, and severe subjects are 0.86, 0.834, 0.829, and 0.809, respectively. The observed performance decreased gradually with subjects'AHI increasing. Compared with one-by-one sleep staging results, 90-s based input can improve the accuracy of NREM stage from all level subjects. However, for other sleep stages, changes in accuracy of each subset are not uniform. Especially for N1 stage, the performance increases on normal and moderate subsets, while, the other two subsets observe the reduced accuracy. The results demonstrate that the proposed method is not only effective for normal subjects but also available on patients with OSAHS. To our knowledge, this is the first research focusing on exploring the automatic sleep staging difference in different level of AHI. Thus, it can be utilized to monitor sleeping and screen subjects with high probability of OSAHS. Besides, many-to-many strategy is first introduced into automatic sleep staging. This strategy provides the way to real-time sleep staging and sleep intervention.

Keywords OSAHS, Sleep Staging, Deep Learning

Effect of lithium chloride on anxiety–depression–like behavior induced by acute and chronic sleep deprivation and its mechanism

Wenping Zhang, Jing Wang, Wenlin Bai, Nan Zhang, Yingying Zhang

Shanxi Medical University, China

Objectives Investigating the ameliorative effect of LiCl on anxiety-depressive behavior in mice caused by sleep deprivation (SD) and its possible regulatory mechanisms. Methods 10-week-old C57BL/6J male mice were selected and randomly divided into chronic sleep deprivation (CSD) and acute sleep deprivation (ASD) groups, CSD group contains: control group, LiCl group, CSD and LiCl intervention group (CSD+LiCl-40 mg/kg), and control group, LiCl group, ASD and LiCl intervention group (ASD+LiCl-120 mg/kg) for ASD group. Except for the control and LiCl groups, the modified multi-platform water environment method (MMPM) was used to construct a 28-day CSD and 3-day ASD model in remaining groups, meanwhile, the intervention group was administered by intraperitoneal injection once every other day for CSD and every day for ASD. During the experiment, the weight changes of mice were recorded weekly. At the end of the experiment, six mice from each group were taken for behavioral tests such as high plus maze, tail suspension and forced swimming test; further HE staining was performed on the hippocampal tissues of each group to observe the pathological morphological changes of hippocampal neurons in each group of mice; another six were used to detect the protein expression of p-GSK-3β, GSK-3β, β-catenin and p-β-catenin in hippocampal tissues. Results There was no statistical difference between the control and other groups in ASD model, but with the prolonged sleep deprivation time, the body weight of the mice in the CSD group showed a downward trend, and the difference was statistically significant at 21 and 28 days. Anxiety-like behavioral experiments revealed that in the high plus maze test, the ratio of the number of times mice entered the open arm and the percentage of time spent in the open arm decreased significantly in the ASD and CSD groups compared to the control group, and the mice in the intervention group showed a significant increase in all of the above indicators compared to their ASD and CSD groups. The depression-like behavior experiment via forced swimming and tail suspension test showed that the percentage of hanging immobility time and floating immobility time of mice in the CSD group were significantly increased compared with the control group, and both of these indexes were significantly decreased in the intervention group compared with the CSD group, while there were no significant differences in the above indexes in the ASD group. Pathological observations showed that the neurons in the dentate gyrus of the hippocampus in the ASD and CSD group showed pathological changes such as misalignment, nuclear consolidation, indistinct nucleoplasmic demarcation and deepening of staining, which were improved in the intervention group. Western blot results showed that p-GSK-3β expression was decreased, GSK-3β expression was increased, and β-catenin was decreased in hippocampal tissues of mice in the ASD and CSD group compared with the control and LiCl groups, and the LiCl intervention significantly reversed the changes in the above indices caused by ASD and CSD. Conclusions SD can lead to the development of anxiety and depression-like behaviors in mice, and ASD is

characterized by anxiety-like behavior changes, CSD is anxiety and depression-like behavior, accompanied by neuronal pathological changes in hippocampal tissue and abnormal expression of molecular markers, and LiCl intervention has significantly improved the above biological processes, and the mechanism may be related to the inhibition of GSK-3β by LiCl, which in turn affects β-catenin expression.

Development and Effects of Cognitive Behavioral Therapy for Insomnia in College Students with Irritable Bowel Syndrome

Yang,Yun-Yi

Department of Nursing，Dongeui University，Busan，Korea

Background: This study aimed to develop and evaluate cognitive behavioral therapy for insomnia (CBT-I) in college students with irritable bowel syndrome (IBS).   Methods: We used a randomized pretest-posttest control group design. A total of 60 college students with IBS comorbid insomnia were recruited from D city in South Korea and were randomly assigned to experimental or control groups. The experimental group (n = 29) participated in CBT-I for 90 minutes once a week for 4 weeks. The control group (n = 30) received a handout regarding CBT-I at the end of the study. Data were analyzed using descriptive statistics, Chi-square, Fisher's exact test, independent t-test, and repeated measures ANOVA test using SPSS/WIN 22.0.

Results: The experimental group showed significant decreases in insomnia severity (F = 32.84, p < 0.001), sleep onset latency (z = -4.15, p < 0.001), total time in bed (t = -2.44, p = 0.018), pre-sleep cognitive arousal (F = 37.71, p < 0.001), pre-sleep somatic arousal (F = 32.18, p < 0.001), GI symptoms during sleep (z = -3.79, p < 0.001), sleep-related dysfunctional cognitions (F = 85.73, p < 0.001), maladaptive sleep habits (F = 42.92, p < 0.001), and IBS symptom severity (F = 32.84, p < 0.001) compared to the control group. The experimental group showed significant increases in sleep efficiency (t = -4.12, p < 0.001) and IBS quality of life (IBS QOL) (F = 15.34, p < 0.001) compared to the control group. There were no significant differences between the groups in the levels of Interleukin-6 (IL-6) (z = -1.60, p = 0.058) and C-Reaction Protein (CRP) (z = -0.91, p = 0.363).

Conclusions & Inferences: The CBT-I for college students with comorbid IBS and insomnia was effective in improving insomnia, IBS symptom severity, and IBS QOL.

The relationships of sleeping with lights on with sleeping difficulty and the occurrence of diseases

Villamejor,Eric、Eric Villamejor

Cebu Normal University

Objective: To evaluate the effect of sleeping with lights on and the occurrence of diseases.

Methods: The survey was conducted at Cebu Normal University with 80 respondents with an equal number of both sleeping habits: sleeping with lights on and sleeping with lights off. The respondents were all CNU students, aged 16-24 years. The chi-square was used to compare inter-group differences.　Results: Sleeping with lights on was significantly related to the occurrence of diseases (P < 0.05). However, there is no significant relationship between sleeping with lights on and sleeping difficulty (P > 0.05).

Conclusions: Sleeping with lights on has effects on the occurrence of diseases, but not sleeping difficulty.

Associations between sleep arousal, nocturnal hypoxemia and mild cognitive impairment

Hsu,Wen-Hua1、Tsai,Cheng-Yu2,4、Liu,Wen-Te 1,4、Kuan,Yi-Chun 3、Lo,Kang4

1. School of Respiratory Therapy，College of Medicine，Taipei Medical University

2. Department of Civil and Environmental Engineering，Imperial College London

3. Department of Neurology，Shuang Ho Hospital，Taipei Medical University

4. Sleep Center，Shuang Ho Hospital，Taipei Medical University

Objective: Neurodegenerative diseases are correlated with sleep disorders. However, the associations between hypoxia, arousal and neurodegeneration remain unclear. This study investigated sleep parameters between mild cognitive impairment (MCI) and normal subjects. Besides, the associations between sleep parameters and cognitive assessment results were explored.

Methods: The participants completed Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR). Next, polysomnography was performed within seven days for their sleep parameters. All the derived data were divided into two groups: the normal group (CDR = 0) and MCI group (CDR = 0.5). Mean comparison analysis, Spearman correlation and Logistic regression models were used to examine their associations.

Results: There were 36 MCI and 37 Normal subjects in this study. For the MCI patients, the means of arousal index (ArI), ArI in NREM (ArINREM), spontaneous arousal index (SpArI), SpArINREM and SpArI in REM (SpArIREM) were significantly higher than those of normal subjects. Conversely, there was no significant difference between the two groups in the apnea-hypopnea index (AHI), oxygen level in arterial blood (SaO2), duration of apnea and hypopnea. The MMSE score presented significant negative correlations to the ArI,

ArINREM, respiratory arousal index (RArI), RArINREM, AHI, apnea index (AI), AINREM, hypopnea index (HI), HINREM, desaturation index and apnea duration, whereas the minimum SaO2 showed a significant positive correlation. Besides, an increased risk of MCI was associated with an increase in 1 events/h of ArI (OR-adjusted = 1.10; 95% CI = 1.03 - 1.18), ArINREM (OR-adjusted = 1.10; 95% CI = 1.03 - 1.17), SpArI (OR-adjusted = 1.12; 95% CI = 1.03 - 1.21), SpArINREM (OR-adjusted = 1.11; 95% CI = 1.03 - 1.21) and SpArIREM (OR-adjusted = 1.10; 95% CI = 1.03 - 1.19).

Conclusions: The MCI subjects had significantly higher ArI and SpArI. The arousal response may be associated with the increased risk of MCI.

Prevalence of obstructive sleep apnea syndrome among Filipino children who habitually snore and have undergone polysomnography

Dela Eva,Rolando

St Luke's Medical Center Quezon City

Objective: To examine the outcomes of polysomnography (PSG) studies investigating Obstructive Sleep Apneas (OSAS) in Filipino children in a sleep laboratory. This is the first study conducted in Filipino children.

Methods: PSG results were reviewed for consecutively referred, habitually snoring children who underwent PSG in a sleep laboratory. The retrospective review analyzed for factors increasing the likelihood of a positive diagnosis.

Results: 413 children aged 7.20 ± 4.17 yrs (70 % males) were studied from December 2014 to March 2016. Common comorbidities included obesity (50%, BMI >95th percentile for age & gender) & nasal allergy (32%). The prevalence of OSAS was 89%. 60% of participants had severe OSAS (AHI >10/hr). Mean apnea hypopnea index (AHI) overall was 25.6 ± 33.3/hr. Chi-Square test showed no association between the presence of OSAS and other variables (p > 0.05). Logistic regression showed that, after adjusting for age, sex and other variables, Z score of BMI was an independent predictor for OSAS (or = 18.6; 95% CI 1.8-190.0, p = 0.014).

Conclusions: OSAS may be common in Filipino children referred to a sleep laboratory. Obesity may be a common comorbidity and BMI has a significant impact on the likelihood of OSAS in this population.

The effect of fruits and vegetables on improving sleep quality among the elderly: A systematic review

Dias Labibah,Hasna Iffah1、*Saleh,Arman Yurisaldi2*、*Pramono,Andri Pramesyanti3*、*Hasna Iffah Dias Labibah*

1. Universitas Pembangunan Nasional Veteran Jakarta
2. Department of Neurology Faculty of Medicine Universitas Pembangunan Nasional Veteran Jakarta
3. Department of Microbiology Faculty of Medicine Universitas Pembangunan Nasional Veteran Jakarta

Objective: To investigate the effect of fruits and vegetables on improving sleep quality among the elderly.

Methods: This study used a systematic review design. A literature search was conducted through several databases such as PubMed, EBSCO, Cochrane, and through hand-searching. The identified articles were selected using eligibility criteria, then reselected gradually using the PRISMA-P method to be further analyzed qualitatively.

Results: Five relevant literatures were obtained. Four literatures showed an influence of fruits and vegetables consumption on improving sleep quality in the elderly, while one literature reported an influence on sleep quality only on vegetables consumption and women gender only. The improvements in sleep quality included improved sleep duration, improved sleep efficiency, decreased sleep latency, decreased sleep disorders and improved overall sleep quality.

Conclusions: Fruits and vegetables consumption has an influence on improving sleep quality among the elderly.

Risk perception, Unhealthy Behavior, and Anxiety due to Viral Epidemic among Healthcare Workers: The Relationships with Depressive and Insomnia symptoms during COVID−19

Chung,Seockhoon1、*Lee,Jukab2*、*Lee,Hyuk Joo2*、*Hong,Youjin3*、*Shin,Yong-Wook1*、*Park,Jangho2*

1. Department of Psychiatry，Asan Medical Center，University of Ulsan College of Medicine，Seoul，Korea
2. Department of Psychiatry，Ulsan University Hospital，University of Ulsan College of Medicine，Ulsan，Korea
3. Department of Psychiatry，GangNeung Asan Hospital，University of Ulsan College of Medicine，Gangneung，Korea

Objective: We aimed to investigate the relationship between mental health problems and unhealthy behaviors among healthcare workers in response to the COVID-19 pandemic.

Methods: Using an online survey, we collected data on healthcare workers' perceptions regarding COVID-19 exposure in a work unit. Workers' depression, insomnia, and anxiety symptoms were assessed using the Patient Health Questionnaire-9, Insomnia Severity Index, and Generalized Anxiety Disorder-7 scale respectively. Work-related stress and anxiety in response to the viral epidemic were measured using the Stress and Anxiety to Viral Epidemic-9 (SAVE-9) scale.

Results: We found that work-related stress and anxiety in response to the viral epidemic were associated with female sex, perception of the workplace as being dangerous, and depressive symptoms. Unhealthy behaviors, such as smoking and drinking as coping behaviors during the pandemic, were associated with male sex, young age, depression, and insomnia.

Conclusions: During the COVID-19 pandemic, it is necessary to closely observe the patterns of work-related stress and anxiety reactions among healthcare workers to reduce their burnout.

Depression, Anxiety, Insomnia to Viral Epidemic and Accessibility to Healthcare Service of Cancer Patients in COVID–19 Pandemic Era

Chung,Seockhoon、 Kim,Kyumin、 Kim,Harin

Department of Psychiatry，Asan Medical Center，University of Ulsan College of Medicine，Seoul，Korea

Objective: There is a paucity of literature concerning cancer care utilization after a massive outbreak of COVID-19 in South Korea. We aimed to investigate accessibility to healthcare services for cancer patients as well as depression, anxiety, and insomnia among them in COVID-19 pandemic era.

Methods: This online survey compiles questions for the disturbance of cancer patients to utilize the medical facilities in the pandemic era. The current mental health of cancer patients was assessed using the Stress and Anxiety to Viral Epidemic - 6 (SAVE-6) scale, Patient Health Questionnaire - 9, Insomnia Severity Index, Brief Resilience Scale, Cancer-related Dysfunctional Beliefs about Sleep scale, and one-item question of "Are you more afraid of coronavirus than cancer?".

Results: Among 221 responders, 95 (43.0%) reported that they felt disturbed to use the hospital utilities during the COVID-19 pandemic era. Logistic regression analysis revealed that no operation within 3 months (OR=2.60, 95% CI [1.20 - 5.64]), now need help for mood or anxiety state (OR=0.32, 95% CI [0.15 - 0.69]) and the high score of SAVE-6 scale (OR=1.15, 95% CI [1.06 - 1.24]) were significant predictors of the patients' disturbance for hospital utilization. Moreover, afraid more about COVID-19 than cancer (OR=1.23, 95% CI [1.07 - 1.47]), depressive symptoms (PHQ-9) (OR=1.13, 95% CI [1.03-1.25]) and dysfunctional beliefs about sleep (C-DBS) (OR=1.13, 95% CI [1.01 - 1.27]) were meaningful predictors of the patients' anxiety response to viral epidemics in COVID-19 pandemic.

Conclusion: In this pandemic era, cancer patients felt disturbed to visit hospitals. We should manage the care system for cancer patients during the pandemic era.

Assessing the Sleep–wake Pattern in Cancer Patients for Predicting a Short Sleep Onset Latency

Chung,Seockhoon、 Yi,Kikyoung、 Lee,Joohee、 Yeo,Sungook、 Kim,Kyumin

Department of Psychiatry，Asan Medical Center，University of Ulsan College of Medicine，Seoul，Korea

We investigated sleep parameters and clinical factors related to short sleep onset latency in cancer patients. We retrospectively reviewed 235 cancer patients' medical records. Patient Health Questionnaire-9, State and Trait Anxiety Inventory (State subcategory), Insomnia Severity Index(ISI), Cancer-related Dysfunctional Beliefs about Sleep, and Fear of Progression scale scores were collected. Sleep indices including sleeping pill ingestion time, bedtime, sleep onset time, and wake-up time were collected. These duration variables were calculated including durations from taking pills to bedtime, to sleep onset time, and to wake-up time; durations from wake-up time to bedtime and to sleep onset time; and time in bed in 24 h. Among cancer patients not taking sleeping pills (n = 145), early wake-up time (adjusted odds ratio [OR]: 0.39, 95% confidence interval [CI] 0.19-0.78), early sleep onset time (OR: 0.50, 95% CI 0.27-0.93), and low ISI score (OR: 0.82, 95% CI 0.71-0.93) were identified as the expecting variables for sleep latency ≤30 min. Longer duration from wake-up time to bedtime (OR: 2.49, 95% CI 1.48-4.18) predicted sleep latency ≤30 min. Among those taking sleeping pills (n = 90), early sleep onset time (OR: 0.54, 95% CI 0.39-0.76) and short duration from pills to sleep onset time (OR: 0.05, 95% CI 0.02-0.16) predicted sleep latency ≤30 min. Cancer patients who fell asleep quickly showed less time in bed during the day. Before prescribing sleeping pills to cancer patients with insomnia, we should explore their sleep parameters to improve their sleep onset latency.

Prevalence of Sleep Disturbances and Its Associated Factors in Children with Autism Spectrum Disorder

Eow,Shiang Yen、 Gan ,Wan Ying 、 Mohd Shariff,Zalilah、 Awang,Hamidin、 Lim,Poh Ying、 Shiang Yen Eow

Universiti Putra Malaysia

Objective: Sleep disturbances are common co-morbidities in children with Autism Spectrum Disorder (ASD). Alleviation of sleep problems is important to improve daytime functioning of children and reduce the burden of their caregivers. This study aimed to assess sleep disturbances and their associated factors among children with ASD in Malaysia.

Methods: A cross-sectional study was conducted on 261 children (83.5% males and 16.5% females) aged 3-18 years old at nine autism intervention centers by using convenience sampling. A mother-administered questionnaire on sociodemographic background, parenting style, parental feeding practices, parenting stress, autism severity, and sleep disturbances was completed and on-site measurement of body weight and height of the children was conducted.

Results: The means of bedtime and wake time of children with ASD in this study were 9.16 pm (SD=3 h 25 min) and 7.24 am (SD=1 h 12 min), respectively. The mean sleep duration was 9h 30min (SD=2 h 18 min), with 47.1% of children having a sleep duration less than 9 hours. The prevalence of potential clinical sleep disturbances among children with ASD was 90.3%, with the major sleep problem being bedtime resistance (73.9%). Multiple logistic regression results showed that perceived child weight (AOR=3.95, 95% CI=1.21, 12.88, p<0.05), parenting stress (AOR=0.98, 95% CI=0.95, 1.00, p<0.05), and satiety responsiveness (AOR=4.07, 95% CI=1.56, 10.63, p<0.05) were significantly associated with sleep disturbances among children with ASD.

Conclusion: The high prevalence of sleep disturbances among children with ASD in this study was alarming. Educational programs involving child weight management and regulation of satiety should be organized for mothers to improve sleep habits of children.

Self–rated sleep quality is associated with hemodynamics in prefrontal cortex in the first sleep cycle

LIANG,ZILU

Kyoto University of Advanced Science

Objective: To investigate the correlation between subjective sleep quality and the hemodynamics in the prefrontal cortex during the first sleep cycle.

Methods: An N-of-1 data collection experiment was conducted with a healthy male subject aged 36-year-old for 15 days. The subject was asked to rate his sleep quality on a five-level scale (1=very poor sleep; 5=very good sleep) in the morning after waking up. The hemodynamic response of the prefrontal cortex during sleep was measured using an Artinis Brite 24 fNIRS device with a sampling rate of 50 Hz and a template of 54 channels. Only the raw optical density signals in the first 1.5 hours (i.e., the average length of a sleep cycle) was used for analysis. Bad channels were removed using the SCI method with a cut-off threshold of 0.75. A bandpass filter with the frequency range from 0.02 Hz to 0.18 Hz was applied to remove the heart rate and breath components from the signals. The modified Beer-Lamberts' law was applied to compute the changes in oxy-hemoglobin (HbO) and deoxy-hemoglobin (Hb). A set of time and frequency domain features were constructed from the channel-wise HbO and Hb changes. These features were then averaged across all channels. Spearman's correlation coefficients were computed between self-rated sleep quality and the hemodynamic features.

Results: Self-rated sleep quality was negatively and significantly correlated with the mean absolute change (r=-0.514, p=0.050), skewness (r=-0.516, p=0.049) and kurtosis (r=-0.516, p=0.049) of the changes in HbO. No correlation was found between self-rated sleep quality and the features of the changes in Hb. Conclusion: The characteristics of the changes in HbO in the prefrontal cortex during the first sleep cycle may be used as objective indicators of subjective sleep quality.

Alerting Network Alteration in Idiopathic Rapid Eye Movement Sleep Behavior Disorder Patients with Mild Cognitive Impairment

Jeong,El1、Cha,Kwang Su2、Sunwoo,Jun-Sang3、Jung,Ki-Young2、El Jeong

1. Interdisciplinary Program in Bioengineering，College of Engineering，Seoul National University，Seoul，South Korea
2. Department of Neurology，Seoul National University Hospital，Neuroscience Research Institute，Seoul National University College of Medicine，Seoul，South Korea
3. Department of Neurosurgery，Seoul National University Hospital，Seoul，South Korea

Objective: It is reported that idiopathic REM sleep behavior disorder (iRBD) is associated with alteration of attention, executive functions, and visuospatial abilities. In addition, it is known that about half of the iRBD patients have mild cognitive impairment (MCI). The aim of this study was to explore the differences between iRBD patients with MCI and ones without MCI.

Methods: 14 healthy controls (HC), 24 iRBD patients without MCI (iRBD-nMCI), and 24 iRBD patients with MCI (iRBD-MCI) were recruited. The attention network task (ANT) was used to assess three attention network effects (alerting, orienting, and executive control). Event-related potentials (ERPs) and behavioral performances were recorded during the ANT. EEG data were recorded using 60 scalp electrodes. ERP N1 and P3 components were used to assess the three attention network effects.

Results: In comparison with HC, iRBD-nMCI showed similar neuropsychological, behavioral, and ERP results. On the other hand, iRBD-MCI showed an overall decline in cognitive domains and the alerting effect impairment [HC (no cue: -0.17 $\pm$ 1.10 μV vs. center cue: -0.66 $\pm$ 1.18 μV, p=0.043); iRBD-nMCI (no cue: -0.33 $\pm$ 1.07 μV vs. center cue: -0.77 $\pm$ 1.16 μV, p=0.014); iRBD-MCI (no cue: 0.07 $\pm$ 0.86 μV vs. center cue: -0.20 $\pm$ 0.99 μV, p=0.130)]. Compared to iRBD-nMCI, iRBD-MCI showed impairment in executive function and verbal memory domains and responded slower when performing the ANT. Although it was not significant, there was a trend that the iRBD-nMCI showed better performances and larger ERP response in ANT than the HC.

Conclusions: Our results suggest that the attention network particularly alerting component is impaired when MCI occurs in iRBD patients. On the other hand, attention network and cognition may be maintained because of the compensatory mechanism in iRBD patients.

Abnormal dream–related brain network in patients with isolated REM sleep behavior disorder (RBD)

Cha,Kwang Su1、Sunwoo,Jun-Sang2、Jung,Ki-Young1、Kwang Su Cha

1. Seoul National University Hospital

2. Neurosurgery，Seoul National University Hospital

Objective: Isolated REM sleep behavior disorder (iRBD) is characterized by disinhibition of motor control facilitating dream enactment behaviors. It has been reported that decreased activity of posterior regions is associated with experiencing dreams, and increased neuronal bistability in the frontal regions leads to protecting the continuation of sleep (Siclari et al., 2017). Although electrophysiological abnormalities during sleep have been investigated, characteristics of the dream-related network in iRBD are still unknown. Therefore, we evaluated electroencephalography (EEG) functional connectivity during REM sleep to identify the characteristics of the dream-related network in patients with iRBD.

Methods: Seep EEG data from 13 people with iRBD (mean age, 66.3 years; men, 84.6%) and 10 controls (mean age, 62.3 years; men, 70%) were analyzed. We estimated cortical source activities using sLORETA during N2 and REM sleep. For functional connectivity analysis, we calculated the weighted phase lag index (wPLI) and conducted a pixel-based permutation test to compare connection strength between the groups. wPLI was selectively applied for 8 ROIs (anterior cingulate cortex, lingual cortex, parahippocampal cortex, and precentral cortex), which has been known to be associated with dream-related cortical regions. To determine the dream-related functional connections, wPLI during the REM stage was normalized to the N2 stage.

Results: Overall connectivity strength did not differ between the two groups in the delta, theta, and beta frequency bands. However, in the sigma frequency-band, the strength of functional connectivity between the left precentral and left lingual cortex was significantly increased in the iRBD group than the control group (iRBD: 0.96 ± 0.03, control: 0.92 ± 0.06). In the gamma frequency-band, functional strength between the left anterior cingulate and left lingual cortex was significantly increased in the iRBD group (iRBD: 1.02 ± 0.02, control: 1.00 ± 0.02).

Conclusion: Hyper-excitability of brain network in the motor cortex and visual association cortex may be associated with the generation of dream-enacting behaviors in iRBD.

Long term effects of insomnia prevention program in at–risk adolescents over a 3–year follow–up

CHAN,Rachel Ngan Yin1、Li,Shirley Xin 2,3、Zhang,Jihui1、Yu,Mandy Wai Man1、Tsang,Chi Ching1、Wing,Yun Kwok1、Rachel Ngan Yin CHAN

1. The Chinese University of Hong Kong
2. Department of Psychology，The University of Hong Kong
3. The State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong

Background: Our previous study has indicated that insomnia can be prevented in at-risk adolescents over 12-month follow-up. This study is the extension of the previous study with the aim to evaluate the long-term efficacy of the insomnia prevention program in at-risk adolescents over a 3-year period.

Methods: A total of 242 adolescents (mean age: 14.9 yrs) who had a positive family history and presented with sub-threshold insomnia symptoms were randomized to a 4 weekly group-based insomnia prevention program or non-active control group. They were followed up at post-intervention, 6-, 12-, 18-, 24, and 36-month after the intervention. Survival analysis was used to compare the cumulative incidence of insomnia disorder ($\geq$ 3 times per week) between the 2 groups. Intervention effects were compared using linear mixed models.

Results: The follow-up rates at 18m, 24m, and 36m were 80%, 65%, and 60% respectively. The intervention group had a significantly lower incidence rate of insomnia disorder compared to the control group over the 3-year follow-up (Hazard Ratios = 0.42; p = 0.004) but the difference were not shown when chronic insomnia criteria were used. Significant interaction effect (P = 0.027) was observed in Insomnia symptoms (measured by insomnia severity index) with the intervention group having lower insomnia symptoms at 36 m follow up compared to the control group. However, other measures that have demonstrated significant effect at 12-month follow up including vulnerability to stress-related sleep disturbance (P = 0.12), daytime sleepiness (P = 0.58), and dysfunctional belief (P = 0.083) were not maintained over the 3-year periods.

Conclusions: A brief 4 weekly group-based insomnia prevention program seems to have enduring benefits in insomnia symptoms over the long term. However, the effect on other functional outcomes and vulnerability factors gradually decayed, suggesting the need for a booster intervention to maintain the intervention effect.

Excessive Daytime Sleepiness: A Case Report of Cognitive Behavioral Therapy for Sleep Deprivation

Bui-Diem,Khue、Nguyen,Binh-Thu、Thuy Le,Minh-An、Khue Bui-Diem

University of Medicine and Pharmacy at Ho Chi Minh City，Vietnam

Excessive daytime sleepiness (EDS) is a troublesome symptom and leads to increasing risk of traffic and work-related incidents. The most frequent causes of EDS are obstructive sleep apnea, narcolepsy, restless leg syndrome, sleep deprivation, and usage of the sedative drugs. In sleep medicine, cognitive behavioral therapy (CBT) is used primarily for insomnia (CBT-I) but not for EDS. However, in this case, we have found the problem is behavioral sleep deprivation, therefore CBT-I was implemented for this case. This patient is a 20-year-old medical student. He forced himself to sleep less in order to have more time to study. He had 5 traffic accidents due to sleepiness, and drowsy in class every day about one year. There are no evidence of snoring or leg movement before and during sleep, or any usage of sedative medication in this patient. The baseline body mass index was 19.3 kg/m2. Other histories included seizure episodes in childhood and night awakenings with dreams (not nightmares), then falling asleep easily. The patient visited a neurologist to exclude epilepsy. Polysomnography had not been implemented yet due to economic issues. Clinically, we had less suspicion of other sleep disorders. We applied CBT-I to this patient for 8 sessions with the intervals every 1-3 weeks. At the two first visits, the Epworth Sleepiness Score (ESS) was 18, and mean Total Sleep Time (TST) was 5.75 hours/day via sleep diary. We added melatonin to make the bedtime earlier as the patient expected. This patient had a 1.5-hour napping habit. We did not ask the patient to give up his napping, but required him to reduce it to 45 minutes gradually. After 3 months of CBT-I with melatonin, this patient reduced night awakenings and EDS (ESS=12), mean TST (6.9 hours/day). Through this case, we hope to contribute an effective tool to evaluate and treat EDS, especially in patients with sleep deprivation. However, it would be better if we had the data of polysomnography.

The relationship of drug dream phenomenon, drug withdrawal and religiosity among muslim amphetamine–type stimulant patients during recovery period in Klang Valley, Malaysia

Hamizi,Muhammad Asqalani1、Rashid,Rusdi Abd 1,3、Hutagalung,Fonny Dameaty2

1. Universiti Malaya Centre for Addiction Science Studies，Universiti Malaya，Malaysia
2. Department of Educational Psychology & Counselling，Universiti Malaya，Malaysia
3. Sleep Disorder Society Malaysia，Malaysia

Drug abuse is a global burden. The recovery journey requires a lot of resources and comprehensive strategies were needed in order for this effort to be effective. Since this is a complex issue, it needs to be viewed from

multiple angle which is an eclectic perspective of biopsychosocial-spiritual paradigm rather than solely on biomedical approach. Ex-drug user experienced drug dream phenomenon during withdrawal period. Some patient complained that they're having craving sensation after the dream occurs and some other reported otherwise. The effect of drug dream towards patient is remain unsolved among dream researchers. The type of drug dream imageries and its various contents might trigger the mesocorticolimbic dopamine pathway and may contribute to drug cravings after awakening. Social support and religious factor may be an important moderator that reducing and even inhibit drug relapse to take place if the patient reported the occurrence of stimulating drug dream. The objective of this study is to find the relationship of drug dream phenomena, drug withdrawal and religiosity activities among amphetamine-type stimulant patients during recovery period in Klang Valley, Malaysia. This research was divided into two phases. First, a stratified sampling of cross-sectional study was conducted among patients across various stages of drug recovery period. Validated self-administered questionnaires of sleep quality, drug dream content, addiction severity, drug withdrawal, quality of life and religiousity will measured. Then, a focus group from each strata of withdrawal period will be selected to compare the EEG pattern of recalled dream memory in contrast to the baseline. The expected outcome and findings of this research would integrate an additional layer into the holistic coping mechanism of biopsychosocial-spiritual paradigm. It would be beneficial to prevent patients from relapsing after experiencing drug dream phenomena.

Respiratory profiling of community–dwelling individuals many years after polio infection

Xiao Li1,5、 Meng Wang5、 Qidi Ding2、 JingYu Wang2、 Ting Sun5、 YunLiang Sun2、 Yan Yu5、 XiaoSong Dong2、 Jing Li2、 Long Zhao5、 XueLi Zhang2、 JinXian Wu3、 LiJuan Ren1、 ChangJun Lv1、 Kingman P. Strohl4、 Fang Han2

1. the university of Hong Kong

2. Department of Pulmonary Medicine，Peking University People's Hospital，Beijing，China;

3. Department of Pediatrics，DongYang People's Hospital，DongYang，China

4. Division of Pulmonary，Critical Care and Sleep Medicine，Department of Medicine，Case Western Reserve University，and Cleveland Louis Stokes VA Medical Center，Cleveland，OH

5. Department of Pulmonary and Critical Care Medicine，Binzhou Medical University Hospital，BinZhou，China

Objective: To determine the presence of respiratory impairment in community-living subjects with a history of poliomyelitis.

Methods: In a study conducted from July 2013-December 2015, we used a national database to recruit individuals in China with a known prior poliomyelitis infection > 25 years previously. They were assessed by overnight oximetry to collect the number/hr of drops in oxygen saturation >4% (ODI4), chest x-ray

(CXR), spirometry and maximal voluntary ventilation (MVV), and Epworth Sleepiness Scale (ESS). Those who had an ODI4 ≥ 5/hr with sleep apnea-related symptoms were randomly selected to undergo overnight polysomnography (PSG) in sleep clinics.

Results: A total of 298 subjects (age 47.8 ± 6.7, 71.1% males) completed overnight oximetry. As defined by ODI4 ≥ 5/hr, the frequency of sleep-disordered breathing (SDB) was 37.2% (n = 111);of the whole sample, 9% (n = 27) had an ODI4 ≥ 15/hr. ESS was within the normal range, but was higher in patients with SDB compared with those without (6.8 ± 5.0 vs. 5.2 ± 4.0, p < 0.01) . Scoliosis on the CXR was present 26.1% of those with SDB and 14.4% of those without (p = 0.038). Spirometry and MVV were similar between those with vs. those without SDB. Thirty-four participants with an ODI4 ≥ 5/hr completed PSG. Thirty (88.2%) had an apnea hypopnea index (AHI) ≥ 5/hr, twenty-five (73.5%) had an AHI ≥ 15/hr. None of the participants met the diagnostic criteria for central sleep apnea. A strong positive correlation was found between ODI4 and AHI (r = 0.802, p<0.001).

Conclusion: Mild (37.2%) and to a smaller extent moderate-severe (9%) SDB and PSG confirmed OSA are present many years after surviving poliomyelitis. In most, sleepiness is low but scoliosis is often present. It needs to be aware of the potential impact of SDB and post-polio sequelae in the aging population worldwide.

Longitudinal examination of the directionality association between chronotype and insomnia

Cheung,Forrest Tin Wai1、 Chan,Ngan Yin2、 Chan,Wing Yan Joey2、 Li,Xiao1、 Zhang,Jihui3,4、 Wing,Yun Kwok2、 Li,Shirley Xin1,5、 Forrest Tin Wai Cheung

1. The University of Hong Kong

2. Department of Psychiatry，The Chinese University of Hong Kong

3. Guangdong Mental Health Center，Guangdong General Hospital and Guangdong Academy of Medical Sciences，

4. Zhujiang Hospital，Southern Medical University/The Second School of Clinical Medicine，Southern Medical University，

5. The State Key Laboratory of Brain and Cognitive Sciences，The University of Hong Kong

Objective: Evening chronotype and insomnia are common in youth and are often closely linked. However, the existing research on the causal relationship between chronotype and insomnia is limited. The current study aimed to examine the directionality of the association between chronotype and insomnia using a set of longitudinal community samples.

Methods: Three hundred and thirty-seven youth participants (mean age at baseline = 21.5, SD = 2.52; % Female = 75.1%) completed the measures on insomnia severity (i.e., Insomnia Severity Index) and chronotype (i.e., mid-point of sleep derived from Munch Chronotype Questionnaire) at baseline and

12-month follow-up. A series of cross-lagged pathway analyses were tested to examine whether insomnia at baseline could predict chronotype at follow-up, or vice versa, or whether insomnia and chronotype are bidirectionally linked.

Results: The chronotype to insomnia cross-lagged model was deemed to be the parsimonious best fitted model (Chi2 [1] = 0.005, p = .946, CFI = 1.000, SRMR= 0.001, RMSEA= 0.000; AIC = 6067.118). Greater tendency towards eveningness at baseline predicted more insomnia symptoms at 12-month follow-up (β = 0.317, p = .044). The alternative, insomnia to chronotype cross-lagged model was not supported (β = -0.00, p = .098).

Conclusions: This current study provided evidence that there was a directional relationship between chronotype and insomnia, where evening chronotype leads to more insomnia problems. This directional relationship suggested the potential role of circadian preference in the aetiology of insomnia and highlighted the need to consider circadian factors in the clinical prevention and intervention of insomnia.

Unified Regional Brain Volume Changes in Patients with Restless Legs Syndrome

Kim,Tae-Joon1、Kim,Jeonghun2、Sohn,Chul-Ho3、Seong,Joon-Kyung2、Jung,Ki-Young4、Tae-Joon Kim

1. Department of Neurology，Ajou University School of Medicine，Suwon，Republic of Korea
2. Department of Bio-convergence Engineering，Korea University，Seoul，Republic of Korea
3. Department of Radiology，Seoul National University Hospital，Seoul，Republic of Korea
4. Department of Neurology，Seoul National University Hospital，Seoul，Republic of Korea

Objective: The pathomechanism of restless legs syndrome (RLS) is brain-specific iron insufficiency and associated dopamine system abnormality. RLS patients suffers from sensorimotor symptoms characterized by an irresistible urge to move, and periodic limb movements. Volumetric changes of subcortical structures and sensorimotor cortices of RLS patients were investigated and found to be altered in separate studies. However, the integrated analysis of the entire brain including brainstem and cerebellum has never been performed in RLS patients. This study aimed to analyze the whole brain of RLS patients using volumetric studies compared to the healthy control, and before and after intravenous iron therapy. Methods: We enrolled 32 RLS patients and 20 healthy controls. All the participants had undergone the Creceived intravenous iron therapy and had follow-up imaging and test at 6- and 24-weeks. Three-dimensional morphometric surface analysis evaluated average thickness for cortex and cerebellum, and local shape volume for subcortical regions and brainstem. Results were adjusted for age and intracranial volume. Correlation analysis was done between the volumes and clinical parameters.

Results: In subcortical structures, caudate and putamen in RLS patients increased significantly (p < 0.05) compared to the healthy control. Whole brainstem including midbrain and medulla was increased whereas

cerebellum especially left hemisphere was decreased. Only postcentral cortex among cerebral cortices was significantly increased in RLS patients. Lingual, fusiform, and inferior and middle temporal gyri were significantly increased after intravenous iron therapy. Caudate and left cerebellum was correlated with quality of life or RLS severity scales.

Conclusion: Large sensorimotor network including subcortex, brainstem, cerebellum and primary sensory cortex altered in restless legs syndrome. Visual cortices were associated with intravenous iron therapy. These unified and regional brain volume changes support sympto-mechanism of RLS.
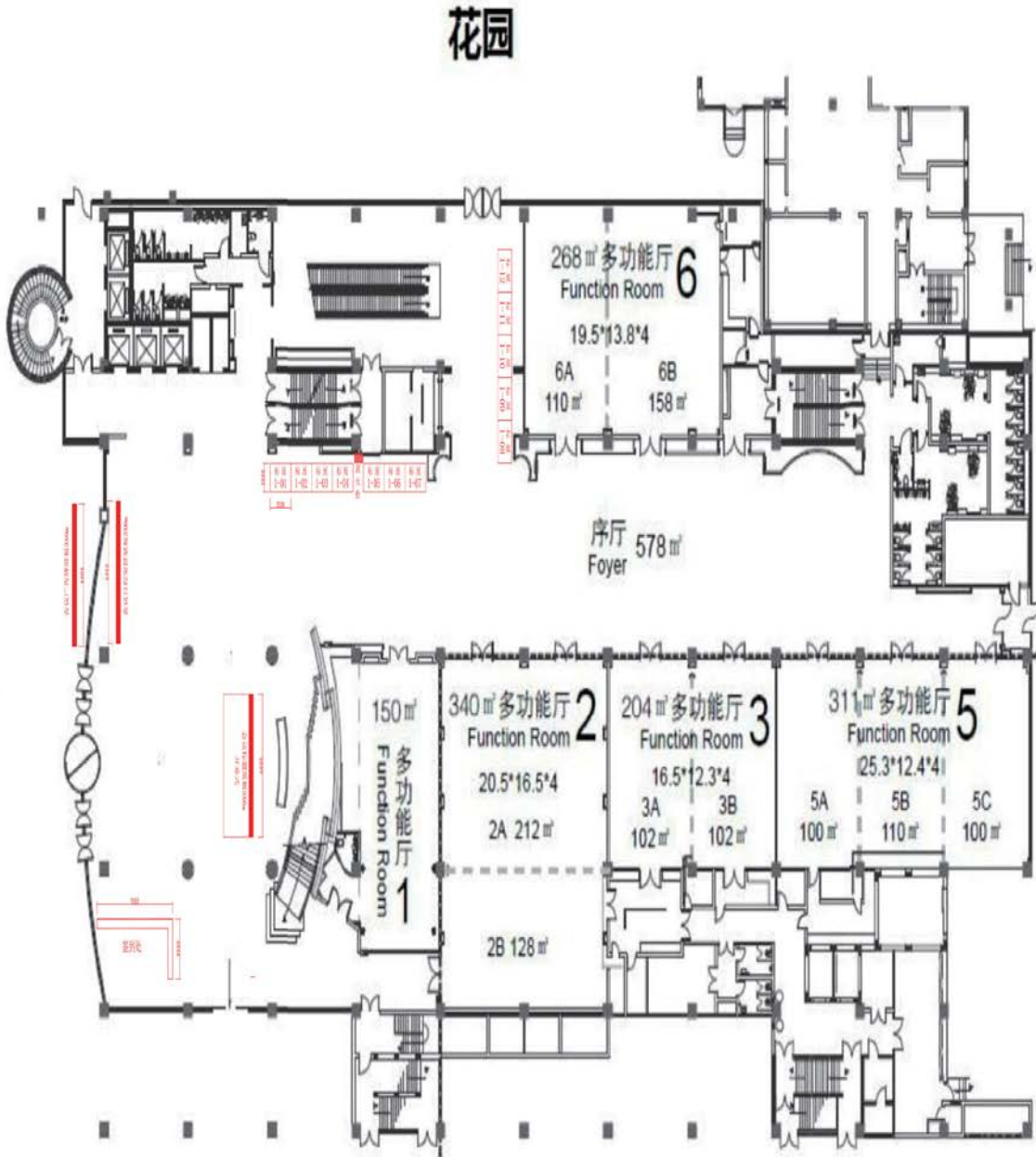
Overview diagram

Legend: Workshop | Technical Training Course | Oral Presentation | Educational Session | Keynote Lecture | Symposium | Lunch Seminar | Event | Case Discussion

Program at a Glance

Programs are subject to change

14-May

Date	Time	Auditorium, 2F	Function Room 8, 2F	Function Room 9, 2F	Function Room 2A, 1F	Function Room 2B, 1F	Function Room 3, 1F	Function Room 5AB, 1F	Function Room 6, 1F	Function Room 5C, 1F	Function Room 10, 2F
14-May	08:00-10:00	Workshop 1	Technical Training Course 1	Oral Presentation 1	Oral Presentation 3	Oral Presentation 5	Oral Presentation 9	Oral Presentation 11		Oral Presentation 17	
	10:00-12:00	Workshop 2	Technical Training Course 2	Oral Presentation 2	Oral Presentation 4	Oral Presentation 6	Oral Presentation 10	Oral Presentation 12		Oral Presentation 18	
	12:00-13:00	Lunch Symposium (Supported by GZ Zaoke)									
	13:00-13:30	Poster & Exhibition Viewing									
	13:30-15:30	Case Discussion 1	Technical Training Course 3		Workshop 4	Oral Presentation 7	Oral Presentation 13	Educational Session 2	Oral Presentation 15		
	15:30-15:45	Tea Break									
	15:45-17:45	Case Discussion 2	Technical Training Course 4	Educational Session 1	Workshop 5	Oral Presentation 8	Oral Presentation 14	Education Session 3	Oral Presentation 16		
	18:00-19:00	Opening Ceremony (Grand Hall, 3F)									
	19:00-21:00	Gala Dinner (Supported by Yangtze River Pharm. Co.)									

15-May

Date	Time	Auditorium, 2F	Function Room 8, 2F	Function Room 9, 2F	Function Room 2A, 1F	Function Room 2B, 1F	Function Room 3, 1F	Function Room 5AB, 1F	Function Room 6, 1F	Function Room 5C, 1F	Function Room 10, 2F
15-May	08:00-08:35	Keynote Lecture 1	Keynote Lecture 2								
	08:40-10:40	International Sleep Research Training Program & Scientific Work from ISRTP Trainees	Precision Medicine in OSA	Circadian Rhythms and Circadian Medicine	Traditional and Complementary Medicine for Insomnia	Wearable Devices and Telemedicine in Sleep	Surgical Intervention for Obstructive Sleep Apnea Based on Phenotype Classification	Various Sleep Disordered Breathing Derived from Various Diseases	Pediatric Sleep Breathing Disorder: Growth, Development and Targeted Treatment	Advances in neural circuitry of wakefulness	The Interaction of Upper-Lower Airways and OSA: The Role of Multidisciplinary Healthcare Actors in Contemporary Century
	10:45-11:20	Keynote Lecture 3	Keynote Lecture 4								
	11:25-12:00	Keynote Lecture 5									
	12:00-13:00	Lunch Seminar (Supported by Phillips)	Lunch Seminar (Supported by SH Langhua)								

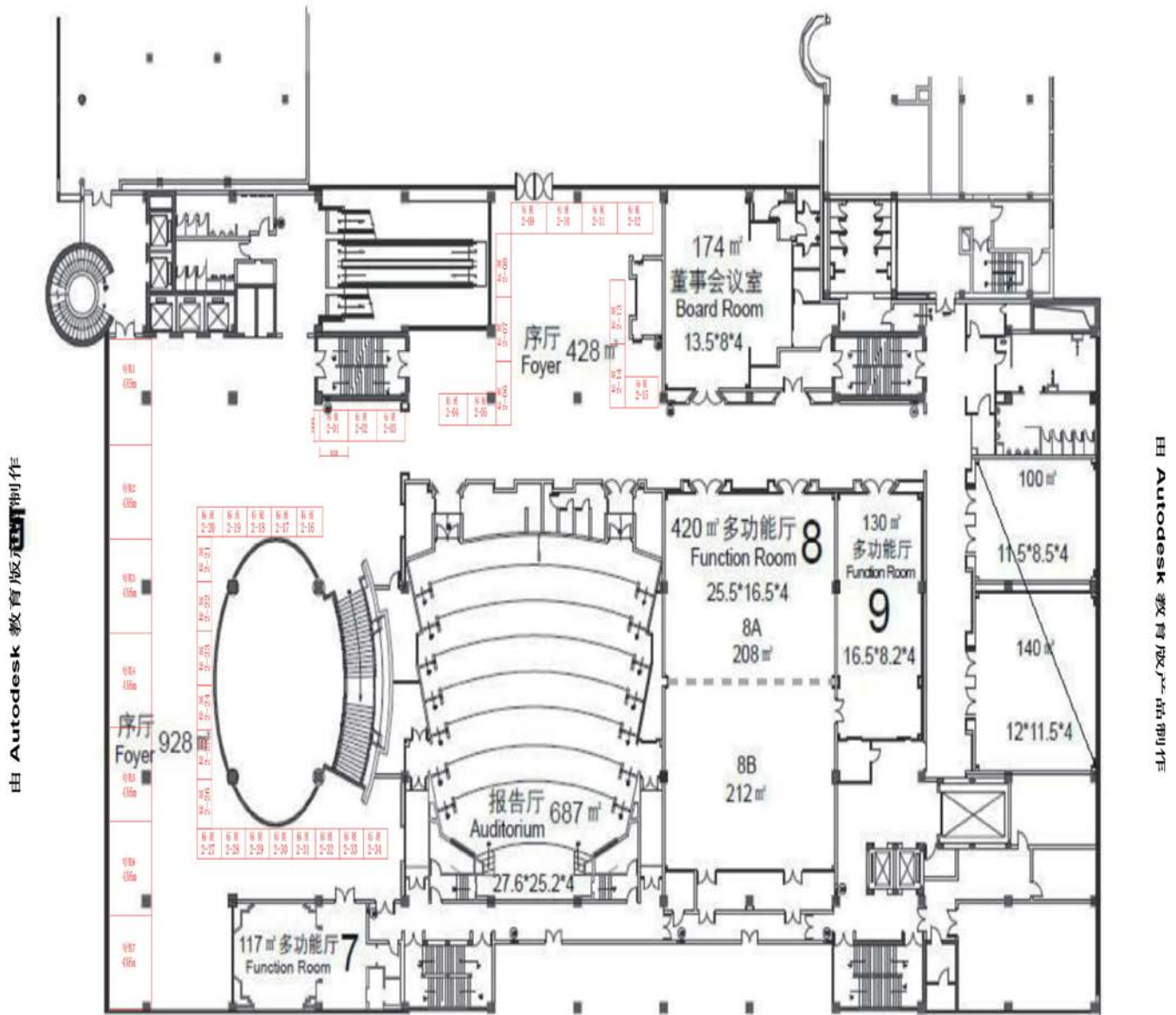| Date	Time	Auditorium, 2F	Function Room 8, 2F	Function Room 9, 2F	Function Room 2A, 1F	Function Room 2B, 1F	Function Room 3, 1F	Function Room 5AB, 1F	Function Room 6, 1F	Function Room 5C, 1F	Function Room 10, 2F
	13:00-14:00	Poster & Exhibition Viewing									
	14:00-16:00	Sleep in Professionals	Treatment of Sleep Disordered Breathing in Different Comorbidities	Impact of Eveningness and Efficacy of Bright Light Therapy	New Techniques of Sleep Research	Smart Sensing for Sleep Health	Sleep Problems in Youth – What's New?	Update on Comorbidities of Narcolepsy	Pediatric Sleep Hypoventilation Syndrome	Sleep Deprivation in Asian Children and Adolescents – Any Evidence? What Should We Do?	Fatigue – State of Art, Epidemiology and Therapeutical Interventions
	16:00-16:15	Tea Break									
	16:15-18:15	Work and Intervention Accomplished in Hospitals During the COVID-19	Artificial Intelligence (AI) for Sleep Analysis	Cross Talk Between Ramadan Intermittent Fasting, Mealtime, Sleep, and Circadian Rhythm	Pathophysiological Mechanism and Non-Pharmacological Treatment of Restless Leg Syndrome	Sleep Disorders and Psychiatric Disorders	Current Evidence and Trend in CPAP Therapy in Sleep-Disordered Breathing	Sleepiness & Narcolepsy: Wake-Promoting Therapies, with a Focus on H3-Receptor Inverse Agonist Pitolisant	Treatment Approaches for Childhood Obstructive Sleep Apnea	Glymphatic System and Sleep	Sleep Patterns and Metabolic Effect
	19:00-21:00	CRSR Business Meeting									
16-May	08:00-08:35	Keynote Lecture 6	Keynote Lecture 7								
16-May	08:40-10:40	Sleep and Metabolism	Insights into The Diagnosis and Management of OSA with Upper Airway Imaging	Sleep, Circadian Rhythms and Neurodegeneration-a Multidisciplinary Perspective	Translational Studies for Orexin and Receptors	New Trends for the Relationship of Sleep with Human Cognition and Emotion	Oral Therapy and Sleep Disordered Breathing	The Epidemiology and Heterogenity of REM Sleep Behavioral Disorder (RBD)	Child and Adolescent Sleep: Conceptualization, Assessment, and Emotional Outcomes	Multi-omics Approaches for Sleep Research	Neurological Disease and Sleep
16-May	10:45-11:20	Keynote Lecture 8	Keynote Lecture 9						Anesthesia, Pain and Sleep Close-Door Meeting		
16-May	11:25-12:00	Keynote Lecture 10									
16-May	12:00-13:00	Lunch Seminar (Supported by Yangtze River Pharm. Co)	Lunch Seminar (Supported by ResMed)								
16-May	13:00-13:30	Poster & Exhibition Viewing									
16-May	14:00-14:35	Keynote Lecture 11									
16-May	14:40-16:40	The Latest Progress in the Field of REM Sleep: from Basic Research to Clinics	Hypoventilation Derived from Rare Respiratory Genetic Disorders	The Gating and Maintenance of Sleep and Wake: New Circuits and Insights	Understanding, Modulating and Enhancing Sleep Process with Novel Neurotechnologies and Models	Sleep Status, Socio-Behavioral Factors, and Comorbidies in Korean Adolescents	High Altitude and Sleep Medicine	REM Sleep Behavioral Disorder(RBD) and Neurodegeneration	Sleep Habits and Sleep Problems in Children	MCI and OSA: Common Problems in iRBD. How to Recognize and Manage It	Genetics of Sleep: Insights to The Function and Evolution of Sleep
16-May	16:45-17:00	Closing Ceremony									

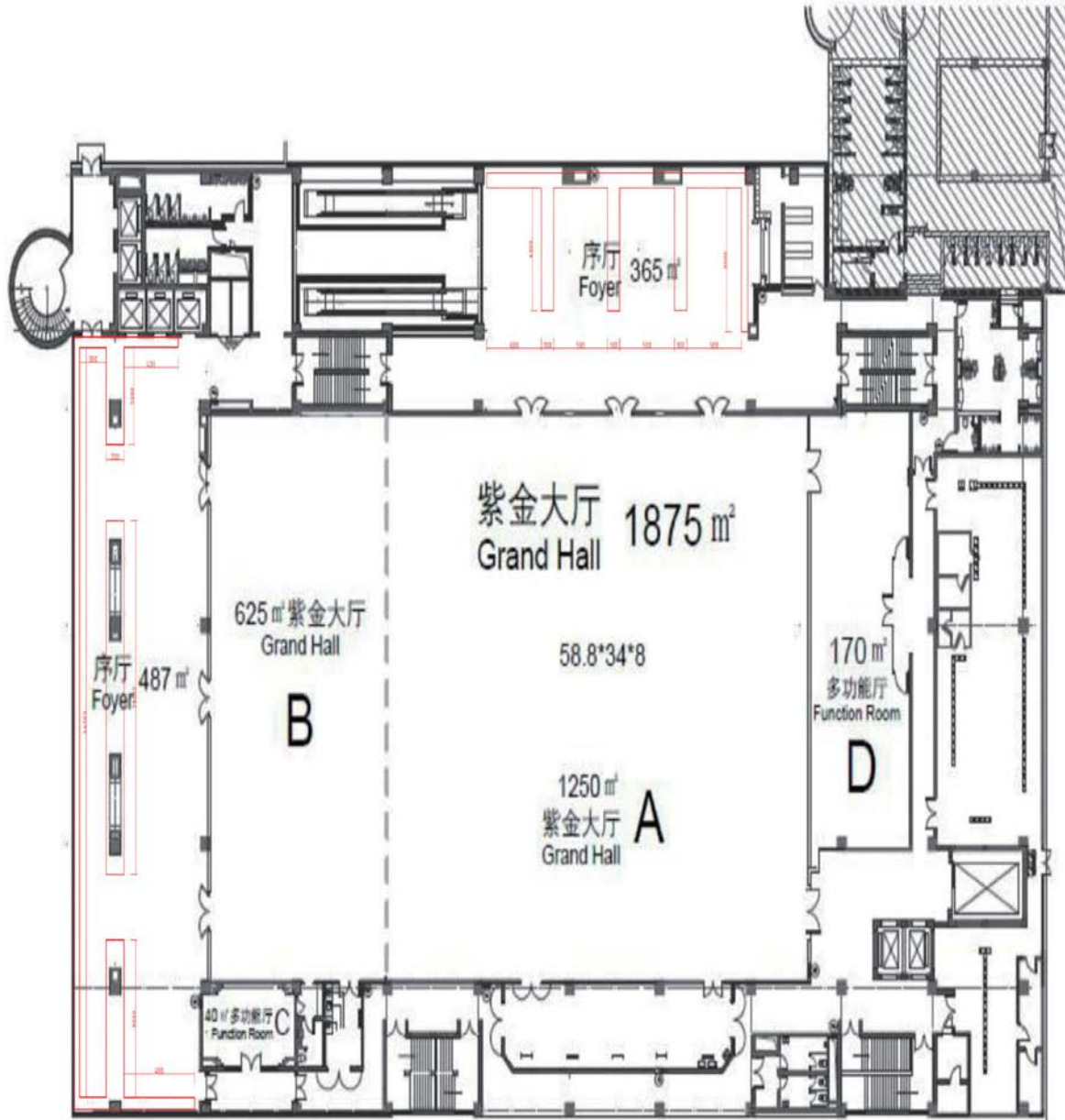# The Floor Plan

Beijing International Hotel Convention Center

会议中心一层厅房名称及格局图

Beijing International Hotel Convention Center

会议中心二层厅房名称及格局图

Beijing International Hotel Convention Center

序厅 Foyer 365 ㎡

紫金大厅
Grand Hall 1875 ㎡

58.8*34*8

625 ㎡ 紫金大厅
Grand Hall

序厅 Foyer 487 ㎡

B

1250 ㎡
紫金大厅
Grand Hall A

170 ㎡
多功能厅
Function Room

D

40 ㎡ 多功能厅
Function Room C

会议中心三层厅房及格局图

Virtual conference

Website: www.assm2021.com

Contact:

ASSM2021 Congress Secretariat c/o No.40 Gaoliangqiao Xiejie, Haidian District, Beijing, China

TEL +86–18612147117   FAX +86–10–65230156

Email secretariat@assm2021.com

Sponsors

Philips (China) Investment Co., Ltd

飞利浦（中国）投资有限公司

Yangtze River pharmaceutical group

扬子江药业集团有限公司

Citrine Medicine (Shanghai) Co., Ltd.

琅铧医药（上海）有限公司

Curative Medical Technology (Beijing) Ltd.

凯迪泰（北京）医疗科技有限公司

Lee's Pharmaceutical Holdings Limited

李氏大药厂控股有限公司

DeRUCCI

慕思健康睡眠股份有限公司

ASSM 2021