Sleep Research Review™

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Abbreviations used in this issue:

AHI = apnoea-hypopnoea index; **CNS** = central nervous system; **COVID-19** = coronavirus disease 2019; **HR** = hazard ratio; **iRBD** = idiopathic/isolated rapid eye movement sleep behaviour disorder; **MRI** = magnetic resonance imaging; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2.

Welcome to the latest issue of Sleep Research Review.

In this issue, a clinical decision support tool proves useful for allowing hospitalised patients a greater opportunity to sleep, a US study looks at the benefits of sleep extension in overweight patients, and Swiss investigators evaluate the impact of COVID-related school closures on adolescents' sleep patterns. Also in this issue, a US study investigates the impact of sleep-disordered breathing and sleep-related hypoxaemia on COVID-19 outcomes, an Italian cohort study examines the impact of different shift patterns on sleep quality in nurses, and an Australian study finds that poor sleep quality is common in patients with an acute exacerbation of cystic fibrosis.

We hope you find these and the other selected studies interesting, and look forward to receiving any feedback you may have.

Kind Regards,

Associate Professor Belinda Miller
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Effectiveness of an analytics-based intervention for reducing sleep interruption in hospitalized patients

Authors: Najafi N et al.

Summary: This US trial investigated whether a clinical decision support tool in the electronic health record helps physicians identify clinically stable hospitalised patients and thereby reduce sleep interruption by safely discontinuing their overnight vital sign checks. 1930 inpatient encounters in 1699 patients were randomised 1:1 to the intervention or usual care. For the intervention arm, a clinical decision support notification informed the physician if the patient had a high likelihood of night-time vital signs within reference ranges (using real-time patient data). The notification allowed the physician to discontinue measure of night-time vital signs or dismiss the notification. There was a significant decrease in the mean number of night-time vital sign checks in the intervention group compared with the control group (0.97 vs 1.41; p<0.001) without an increase in intensive care unit transfers (5% of patients in each group) or code blue alarms (0.2% vs 0.9%; p=ns). The incidence of delirium (primary outcome) was not significantly affected (11% vs 13%; p=ns).

Comment: Hospitals are difficult places to sleep; ambient noise, shared rooms, unfamiliar environments, night-time medications and procedures and vital sign observations all contribute to sleep disturbance overnight. Maintenance of a normal sleep cycle may help prevent delirium, particularly in older patients. This study was a randomised clinical trial examining the effectiveness of a clinical decision support tool in the electronic health record to enable physicians to identify patients for whom the frequency of vital sign measurement can be safely reduced at night. The primary end-point, reduction in delirium, was not achieved. However, hospital delirium has many contributors, and the reduction in vital signs checking was relatively small (average checks per night 0.97 in the intervention arm and 1.41 in the control arm, p<0.001). Also, there was 35% discordance in checking vital signs regardless of sleep-promoting orders. Nonetheless, the intervention arm experienced no increase in intensive care unit transfers or code blue alarms. With greater fidelity to the intervention, avoidance of night-time vital sign measurement could be an important factor in a delirium prevention strategy, as well as increasing patient satisfaction and allowing staff to focus on more useful interventions.

Reference: JAMA Intern Med 2022;182(2):172-7
Abstract

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Effect of sleep extension on objectively assessed energy intake among adults with overweight in real-life settings

Authors: Tasali E et al.

Summary: This US study investigated the impact of a sleep extension intervention on energy intake, energy expenditure, and body weight in adults with overweight who usually curtailed their sleep duration. 80 individuals aged 21–40 years with a body mass index between 25.0 and 29.9 who had a habitual sleep duration of <6.5 h/night were randomised to either a sleep extension intervention or to continue their habitual sleep (controls). Those in the intervention arm received an individualised sleep hygiene counselling session that was intended to extend their bedtime to 8.5h. After 4 weeks, sleep duration increased by approximately 1.2 h/night in the intervention group compared with the control group, accompanied by a significant decrease in energy intake (–270 kcal/d; p<0.001), and a reduction in weight. Total energy expenditure did not differ between groups.

Comment: Short sleep duration is associated with an increased risk of obesity, coronary artery disease and type 2 diabetes. Previous studies have indicated a dose-response relationship between sleep duration and risk of obesity, with a 2019 meta-analysis suggesting lowest risk at 7–8h sleep/night and a 9% increase in obesity risk for each 1-h sleep decrement below 7h. This controlled study assessed whether an increase in sleep duration resulted in a negative energy balance, and thus potential weight loss. 80 overweight participants with habitual sleep time of <6.5h per night were randomised to either sleep extension of 1.2 h/night or usual sleep duration, for 4 weeks. There was a significant decrease in energy intake of 270 cal/day in the sleep extension group as compared to controls, without a change in energy expenditure. The mechanisms linking short sleep duration and obesity are complex, and may include changes in leptin, ghrelin, cortisol and melatonin levels, irregular or altered eating patterns when fatigued, and time-restricted feeding when more sleep is obtained. A deliberate increase in sleep duration may be a measure to counter weight gain.

Reference: JAMA Intern Med 2022;182(4):365-74
Abstract

Association between homeschooling and adolescent sleep duration and health during COVID-19 pandemic high school closures

Authors: Albrecht JN et al.

Summary: This Swiss study investigated associations between sleep and health-related characteristics in adolescents during school closures due to the COVID-19 pandemic. Cross-sectional online surveys were circulated among 21 public high schools in Zurich, Switzerland. 5308 students who completed the survey under regular, prepandemic conditions (May to July 2017; control group) were compared with 3664 students who completed the survey during school closures (May to June 2020; lockdown group). Sleep-wake patterns, health-related quality of life (HRQoL), substance use, and depressive symptoms were compared between the 2 groups. During lockdown, the sleep period on scheduled days was 75 min longer, and was associated with better HRQoL and less caffeine consumption. In the lockdown sample, an inverse association was found between depressive symptoms and HRQoL, and a positive association was found with caffeine consumption.

Comment: The negative mental health impacts in adolescents of school closures and social isolation due to the COVID-19 pandemic have been well documented. However, a potentially conflicting finding has also appeared consistently: adolescents slept significantly longer during school closures than before them. Sleep plays a crucial role in mental and physical health, and thus a positive association of increased sleep with adolescent well-being may be present. This Swiss study of adolescent sleep patterns before and during the pandemic found an average 75-min increase in sleep duration with school closures. Longer sleep duration was associated with better HRQoL and reduced caffeine intake. However, depressive symptoms were associated with poorer quality of life and increased caffeine consumption and thus diminished the beneficial associations with sleep. This study may help to inform the impacts of school start timing, sleep duration and mood disorders in adolescents.

Reference: JAMA Netw Open 2022;5(1):e2142100
Abstract

Association of sleep-related hypoxia with risk of COVID-19 hospitalizations and mortality in a large integrated health system

Authors: Orbea CP et al.

Summary: This US case-control study investigated the influence of sleep-disordered breathing (SDB) and sleep-related hypoxia on SARS-CoV-2 infection and COVID-19 outcomes. The study was conducted within the Cleveland Clinic Health System and included all patients who were tested for COVID-19 between Mar 8 and Nov 30, 2020, who had an available sleep study record. Of 350,710 individuals tested for SARS-CoV-2, 5402 had a prior sleep study, and 1935 (35.8%) of these individuals tested positive for SARS-CoV-2. Individuals who were positive for SARS-CoV-2 had a higher AHI score (median 16.2 vs 13.6 events/h; p<0.001) and increased sleep-related hypoxia (p=0.02) than those who were negative for SARS-CoV-2. However, no SDB measures were associated with SARS-CoV-2 positivity after overlap propensity score-weighted logistic regression. Sleep-related hypoxia was associated with a 31% higher rate of COVID-19-related hospitalisation and mortality (adjusted HR 1.31, 95% CI 1.08–1.57; p=0.005).

Comment: Many risk factors have been identified for development of severe disease after infection with SARS-CoV-2, including male gender, hypertension, obesity and cardiopulmonary disease. This case-control study of a US database of about 350,000 patients tested for COVID-19 assessed whether a prior diagnosis of SDB and sleep-related hypoxia was associated with risk of SARS-CoV-2 infection or disease severity. SDB and sleep-related hypoxia were not associated with increased risk of infection. However, if infected, sleep-related hypoxia, but not AHI, was a risk factor for severe COVID-19 disease, even after controlling for confounders including obesity and hypertension. Sleep-related hypoxia may more accurately capture SDB-related physiological stress compared with the AHI, which does not reflect duration and severity of hypoxic exposures. The findings suggest that baseline sleep-related hypoxia is associated with progression of hypoxic insult and hypoxia-related injury. Intermittent hypoxia is implicated in sympathetic activation, endothelial dysfunction, systemic inflammation, and oxidative stress, all pathways postulated to contribute to COVID-19 morbidity and mortality.

Reference: JAMA Netw Open 2021;4(11):e2134241
Abstract

Association of SARS-CoV-2 infection with psychological distress, psychotropic prescribing, fatigue, and sleep problems among UK primary care patients

Authors: Abel KM et al.

Summary: This UK cohort study evaluated the risk of psychiatric illness, fatigue, and sleep problems after SARS-CoV-2 infection. Cohorts were assembled from a UK primary care registry (Clinical Practice Research Datalink Aurum). Individuals with positive results on a SARS-CoV-2 test were matched with up to 4 controls with negative SARS-CoV-2 test results. After adjusting for confounders, there was an association between positive SARS-CoV-2 test results and psychiatric morbidity (adjusted HR [aHR] 1.83, 95% CI 1.66–2.02), fatigue (aHR 5.98, 95% CI 5.33–6.71), and sleep problems (aHR 3.16, 95% CI 2.64–3.78). However, there was a similar risk of incident psychiatric morbidity for individuals with a negative SARS-CoV-2 test result (aHR 1.71, 95% CI 1.65–1.77) and a larger increase in those with influenza (aHR 2.98, 95% CI 1.55–5.75).

Comment: Long COVID-19, generally described as lingering symptoms that persist for more than 4 weeks post COVID-19 diagnosis, is commonly associated with fatigue and sleep disturbance. Additionally, there is concern that SARS-CoV-2 infection itself may cause psychiatric disease. This UK study assembled matched cohorts from a large primary care registry of individuals with positive results on a SARS-CoV-2 test, both with and without prior mental illness, with controls with negative test results. SARS-CoV-2 infection was associated with increased risk of incident psychiatric morbidity, sleep problems, and fatigue in the following months. However, those with a negative SARS-CoV-2 test result also had a substantial increase in risk of incident psychiatric morbidity, of similar magnitude to that observed in people with positive test results. These findings suggest that confounders, including health anxiety, workplace, financial and other stressors associated with the pandemic may be as responsible for psychiatric morbidity in the pandemic era as SARS-CoV-2 infection itself.

Reference: JAMA Netw Open 2021;4(11):e2134803
Abstract

Comparison of sleep and attention metrics among nurses working shifts on a forward- vs backward-rotating schedule

Authors: Di Muzio M et al.

Summary: This Italian cohort study investigated the association of shift patterns with tiredness, sleepiness, and sustained attention among nurses working forward- and backward-rotating shifts. Data were collected from 144 nurses working at 5 midsized Italian hospitals. The nurses had either a forward-rotating schedule (i.e. morning to afternoon to night; n=80) or a backward-rotating schedule (i.e. afternoon to morning to night; n=64). Nurses working backward-rotating shifts had significantly greater sleepiness and cognitive slowing than those working forward rotations; the differences were not affected by age, years of employment, or sleep quality. 93.8% of nurses working on a backward-rotating schedule reported elevated sleepiness (Karolinska Sleepiness Scale score ≥7) after the night shift. Reaction times of nurses on backward-rotating schedules also indicated a lower level of vigilance.

Comment: Shift work, while essential in health care, is recognised to have a negative effect on many health parameters, including sleep quality, cognitive performance and cardiovascular risk. Shifts can be slow rotation, over 2–4 weeks, which allow for circadian rhythm adjustment, or fast, changing every 3–5 days, which allow workers to maintain constant circadian rhythm. Shifts can rotate forward (clockwise) or backward (counterclockwise). This Italian field study of nurses working fast rotation shifts compared forward and backward-rotating shifts and their effects on sleep quality, tiredness and vigilance. Both forward and backward rotations were associated with similarly poor sleep quality. However, nurses on backward rotations had comparatively higher levels of sleepiness and worse performance on cognitive testing, especially after night shifts. Better outcomes with forward rotations have been previously reported; forward rotation may be easier for physiological adaption as the human circadian rhythm tends to move forward. These findings suggest optimisation of shift rotations for nurses is needed to decrease the negative outcomes associated with shift work.

Reference: JAMA Netw Open 2021;4(10):e2129906
Abstract

Cohort study of sleep quality in adult patients with acute pulmonary exacerbations of cystic fibrosis

Authors: Henderson D et al.

Summary: This prospective observational study in Australia evaluated sleep quality in adults admitted to hospital with an acute pulmonary exacerbation of cystic fibrosis (CF). Sleep quality was defined by the Pittsburgh Sleep Quality Index (PSQI). 66% of patients were found to have impaired sleep quality, mostly due to pain and insomnia. Univariate modelling showed relationships between PSQI and symptoms of depression and anxiety as well as with sleep disruption due to pain, general noise and nursing observations. A multivariable model revealed that insomnia severity index was the only variable significantly associated with PSQI.

Comment: Sleep and the circadian rhythm exert a regulatory influence on immune functions. Evidence has accumulated over the past 25 years that sleep enhances immune defences and sleep deprivation adversely affects multiple components of the immune response and reduces vaccination responses. This prospective observational Queensland study of adult patients admitted to hospital with an acute pulmonary exacerbation of CF showed a high prevalence of impaired sleep quality. About two-thirds of patients reported poor sleep quality. The major issue was insomnia symptoms, with pain, depressive symptoms, dyspnoea, restless leg symptoms and ambient noise possible contributing factors. Previous studies in patients with stable CF suggest about 50% have impaired sleep quality. Although there have been no direct studies assessing the effects of impaired sleep quality or duration on immune function in patients with CF, it is possible that sleep impairment may contribute to poor patient outcomes, and attention to sleep quality may help improve these outcomes.

Reference: Intern Med J 2022;52(1):63-8
Abstract

Internet addiction, headache, and insomnia in university students

Authors: Rangel TC et al.

Summary: This cross-sectional study in Brazil investigated the association between headache, insomnia, and internet addiction. 420 university students (51.4% male, median age 21 years) were evaluated using a semi-structured questionnaire, Headache Impact Test, Hospital Anxiety Depression Scale, Insomnia Severity Index, and Internet Addiction Test. 95.0% of participants had suffered from headaches in the previous year, 20% had internet addiction, and 22.6% had insomnia. Logistic regression analysis revealed that internet addiction was associated with anxiety (OR 2.3, 95% CI 1.3–4.0; p=0.003), insomnia (OR 3.0, 95% CI 2.0–4.6; p<0.001), and migraine with aura (OR 1.8, 95% CI 1.1–2.9; p=0.066). Multiple linear regression analysis showed that the severity of internet dependence was associated with the impact of headache (p=0.047) and with the severity of insomnia (p<0.001).

Comment: Electronic device and social media use have transformed the ways in which people socialise and interact, and have enhanced social connections during the COVID-19 pandemic. However, the downsides include reduced sleep quality and duration, especially if electronic device use is in the evenings. "Internet addiction" describes a pathological compulsive use of the internet, and can be associated with depression, anxiety, and problems in interpersonal relationships. This cross-sectional study of university students in Brazil was conducted pre-pandemic. About 20% of students (of whom 27% were medical students) were considered to have internet addiction. There was a significant association of internet addiction with insomnia, anxiety and migraine, such that a student with these symptoms had a 50% probability of internet addiction compared with an 8.6% probability of internet addiction if they did not have them. Review of electronic device use in patients of all ages with insomnia symptoms is an important part of assessment.

Reference: Neurol Sci 2022;43(2):1035-41
Abstract

Risk factors for phenoconversion in rapid eye movement sleep behavior disorder

Authors: Zhang H et al.

Summary: This multicentre study evaluated risk factors for α-synuclein-related neurodegenerative diseases in patients with iRBD. Patients with iRBD from 12 centres were assessed for potential environmental and lifestyle risk factors via a standardised questionnaire at baseline. They were then assessed for parkinsonism or dementia during up to 11 years of follow-up. Of 319 patients who were free of parkinsonism or dementia at baseline, 281 provided follow-up information and were included in the analysis. After a mean follow-up of 5.8 years, 46.3% of patients developed neurodegenerative disease. The overall phenoconversion rate was 24.2% after 3 years, 44.8% after 6 years, and 67.5% after 10 years. Cox regression analyses adjusted for age, sex, and centre showed that older age (adjusted HR [aHR], 1.05) and use of nitrate derivatives (aHR, 2.18) increased the risk of phenoconversion, whereas prior pesticide exposure, rural living, lipid-lowering medication use, and respiratory medication use were associated with lower risk of phenoconversion. Risk factors for conversion to primary dementia and parkinsonism were generally similar.

Comment: The authors of this multicentre study followed patients with iRBD for up to 11 years to assess for predictive factors for development of α-synuclein–related neurodegenerative diseases. After a mean follow-up of 5.8 years, 46.3% of patients developed Parkinson disease or dementia, a similar risk of phenoconversion to that seen in prior studies. Risk factors for development of either condition were similar, and included older age and use of nitrate-containing medication, with protective factors including rural living, use of lipid-lowering medication and respiratory medication. Previous studies have suggested that RBD in patients with known Parkinson disease is a risk factor for development of mild cognitive impairment and additional dementia. This study adds to the literature by identifying some predictive values of environmental factors and comorbid conditions to help identify RBD patients at higher risk of phenoconversion.

Reference: Ann Neurol 2022;91(3):404-16
Abstract

Association of sleep, neuropsychological performance, and gray matter volume with glymphatic function in community-dwelling older adults

Authors: Siow TY et al.

Summary: This study explored the associations between human glymphatic function, sleep, neuropsychological performance, and cerebral grey matter volumes. Data for 84 community-dwelling individuals aged ≥60 years (mean 73.3 years, 56.0% female) who had participated in the Integrating Systemic Data of Geriatric Medicine to Explore the Solution for Health Aging study between Sep 2019 and Oct 2020 were analysed. Grey matter volumes were estimated based on MRI, and diffusion tensor imaging analysis along the perivascular space (DTI-ALPS) index was used as an MRI marker of glymphatic function. A multivariate linear regression model determined that age (p=0.02), N2 sleep duration (p=0.04), and AHI (p=0.03) were independently associated with DTI-ALPS. Higher DTI-ALPS was associated with better neuropsychological test scores (after adjustment for age and education) and with higher grey matter volume (after adjustment for age, sex, and total intracranial volume).

Comment: The CNS lacks lymphatic drainage. In 2012, the glymphatic system was first demonstrated in a mouse model, and human research into the system remains limited. The glymphatic system is a waste clearance system that utilises perivascular channels, formed by astroglial cells, for removal of soluble proteins and metabolites, including β-amyloid, from the CNS. The glymphatic system functions mainly during sleep and is largely disengaged during wakefulness. This cross-sectional study included community-dwelling individuals 60 years or older and assessed sleep via questionnaire and polysomnography, neuropsychological tests and brain grey matter volume via MRI, with MRI analysis as a marker of glymphatic function. Advancing age, shorter N2 sleep duration, abnormal neuropsychological test performances, lower grey matter volumes and higher AHI were all associated with impaired glymphatic function. The results suggest a close interaction between glymphatic function, sleep, and cognition, highlighting the relevance of sleep as a potential target for dementia prevention or treatment.

Reference: Neurology 2022;98(8):e829-38
Abstract

Independent commentary by Associate Professor Belinda Miller

Associate Professor Belinda Miller is a Respiratory and Sleep Physician at The Alfred Hospital, Melbourne. Her areas of clinical and research interests include respiratory failure, oxygen therapy, sleep disorders and COPD.