Sleep Research Review™

Making Education Easy

Issue 13 - 2022

In this issue:

Abbreviations used in this issue:

AHI = apnoea-hypopnoea index; **BMI** = body mass index; **CPAP** = continuous positive airway pressure; **OSA** = obstructive sleep apnoea; **REM** = rapid eye movement; **SaO_2** = oxygen saturation.

Welcome to the latest issue of Sleep Research Review.

In this issue, a secondary analysis of the REST-ON trial reports that extended-release sodium oxybate improves disrupted night-time sleep in patients with narcolepsy, a cross-sectional study in China adds to our understanding of the impact of outdoor artificial light at night on sleep disturbance in children, and a cross-sectional study in Japan confirms that accumulated unhealthy behaviours increase the risk of insomnia. Also in this issue, Korean investigators find that smartphones may be useful for identifying OSA, and a study in China finds that night shift workers with shift work disorder should try and sleep in the evening rather than the morning where possible.

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

Kind regards,

Dr Sean Tolhurst
sean.tolhurst@researchreview.com.au

Effect of FT218, a once-nightly sodium oxybate formulation, on disrupted nighttime sleep in patients with narcolepsy

Authors: Roth T et al.

Summary: This secondary analysis of the REST-ON trial investigated the effects of an extended-release, once-nightly sodium oxybate formulation on disrupted night-time sleep in adults with narcolepsy. 190 adults (aged ≥16 years) with narcolepsy were randomised 1:1 to receive extended-release sodium oxybate (4.5g at night for 1 week, 6g at night for 2 weeks, 7.5g at night for 5 weeks, and 9g at night for 5 weeks) or placebo. End-points were assessed for the 6g, 7.5g, and 9g sodium oxybate dosages. All 3 dosages were associated with a clinically meaningful decrease in the number of transitions from sleep to wake (or N1) from N1, N2, and REM stages and the number of nocturnal arousals. Sleep quality also improved significantly with all 3 dosages.

Comment: Sodium oxybate has an established role in narcolepsy management, decreasing night-time sleep disruption and reducing cataplexy. Currently available formulations have a short half-life requiring a second dose to be administered in the middle of the night-time sleep period to achieve maximal effect. Narcoleptic night-time sleep is already disrupted and the required awakening for the second night-time dose exacerbates this. Furthermore, patients often sleep through the mid-sleep alarm and wake later in the night, often too late for the second dose. This study was a phase 3 trial of once-nightly extended-release sodium oxybate in sodium oxybate-naïve patients with narcolepsy type 1 or type 2, examining the impact on polysomnographic and subjective measures of night-time sleep disruption. All 3 doses of the once-nightly formulation resulted in fewer transitions to wake and fewer nocturnal arousals, less time in N1 and more time in N3, with increased REM latency. Subjective sleep quality indices all improved compared to placebo. These results are encouraging and broadly consistent with the data on twice-nightly sodium oxybate, but this extended-release formulation has the benefit of not requiring awakening for the second dose which could provide additional improvements to the sleep patterns of patients with narcolepsy compared to the available short-acting preparations.

Reference: CNS Drugs 2022;36(4):377-87
Abstract

Claim CPD/CME points Click here for more info.

RACP MyCPD Program participants can claim **one credit per hour** (maximum of 60 credits per year in Category One – Educational Activities) **for reading and evaluating Research Reviews.**

Please CLICK HERE to download CPD Information

Association between exposure to outdoor artificial light at night and sleep disorders among children in China

Authors: Wang L-B et al.

Summary: This population-based cross-sectional study (part of the National Chinese Children Health Study) evaluated the association between outdoor artificial light at night (ALAN) and sleep disorders in children. 201,994 children and adolescents aged 2–18 years (mean 11.3 years, 52.7% male) were included in the analysis; 7166 (3.5%) participants had sleep disorder symptoms. Outdoor ALAN exposure within 500m of each participant's residential address was obtained using satellite imagery data, and ranged from 0.02 to 113.48 nW/cm^2/sr. Compared with the lowest quintile (Q1) of outdoor ALAN exposure, higher quintiles of exposure were associated with odds ratios for sleep disorder of 1.34 (95% CI 1.23–1.45) in Q2, 1.43 (95% CI 1.32–1.55) in Q3, 1.31 (95% CI 1.21–1.43) in Q4, and 1.25 (95% CI 1.14–1.38) in Q5. Greater effects were seen in children aged <12 years.

Comment: Outdoor ALAN is thought to have a detrimental impact on sleep pattern and duration in children and adolescents, but data are limited. This large epidemiological study involving more than 200,000 children and adolescents investigated the association of satellite assessments of outdoor ALAN to the sleep of the children and adolescents using the Sleep Disturbance Scale for Children (SDSC). The main findings were that increasing ALAN was associated with sleep disorders in children less than 12 years of age. With increasing urbanisation and populations, outdoor ALAN is increasing, making the detrimental impacts of ALAN on sleep more significant. This important study adds to our understanding of the role of ALAN in sleep disturbance in children and identifies a potential target for intervention in both individual cases and more broadly in the general population. This is particularly important for children sleeping in metropolitan areas who are generally exposed to higher levels of outdoor ALAN. Further research is needed to evaluate the association of indoor ALAN on sleep in children and also the impact that reducing ALAN (e.g., with total blockout blinds) has on these sleep indices.

Reference: JAMA Netw Open 2022;5(5):e2213247
Abstract

Accumulated unhealthy behaviours and insomnia in Japanese dwellers with and without cardiovascular risk factors

Authors: Kato S et al.

Summary: This cross-sectional study examined the impact of accumulated unhealthy behaviours on insomnia in Japanese adults. 9565 Japanese individuals aged 35–74 years living in a rural community who participated in annual municipal or work site health check-up programmes were included. They were categorised into 3 groups according to their number of unhealthy behaviours (no exercise habit, smoking, alcohol drinking, skipping breakfast and overweight [BMI >25 kg/m^2]): 0–1, 2–3, and ≥4. 13.3% of males and 19.3% of females had insomnia according to the Athens Insomnia Scale. After adjustment for potential confounders, men with ≥2 unhealthy behaviours were more likely to have insomnia than those in the least unhealthy group (trend p=0.013), and women with ≥4 unhealthy behaviours were more likely to have insomnia than those in the 2 lowest groups.

Comment: This study investigated the association of accumulated unhealthy behaviours with insomnia, primarily using self-reported questionnaires. Smoking, sedentary lifestyle, skipping breakfast, overweight (BMI >25 kg/m^2) and alcohol consumption were identified as the "unhealthy" behaviours and their impact was assessed according to the number of accumulated unhealthy behaviours in 3 categories (0–1, 2–3, 4 or more). Not surprisingly, the study demonstrated that having a high number of unhealthy behaviours was associated with a higher likelihood of insomnia. Skipping breakfast alone was associated with an increased risk of insomnia in both sexes. Most of the other unhealthy behaviours alone were not associated with insomnia, but the combination of multiple unhealthy behaviours increased the risk of insomnia. Additional research is required to demonstrate a causal link and assess whether addressing these modifiable factors leads to an improvement in insomnia.

Reference: BMJ Open 2022;12:e052787
Abstract

Effect of an interdisciplinary weight loss and lifestyle intervention on obstructive sleep apnea severity

Authors: Carneiro-Barrera A et al.

Summary: The INTERAPNEA trial investigated the effect of an interdisciplinary weight loss and lifestyle intervention on OSA and comorbidities in adults with moderate to severe OSA and overweight or obesity. 89 Spanish males aged 18–65 years with moderate to severe OSA and a BMI ≥25 kg/m^2 who were receiving CPAP therapy were randomised to receive usual care (CPAP therapy) or an 8-week weight loss and lifestyle intervention in addition to CPAP therapy. The lifestyle intervention comprised nutritional behaviour change, aerobic exercise, sleep hygiene, and alcohol and tobacco cessation. After 8 weeks, the intervention group had a greater change in AHI (–21.2 events/h) than the control group (+2.5 events/h), with a mean between-group difference of –23.6 events/h. When assessed 6 months after the intervention, the mean between-group difference was –23.8 events/h. 45.0% of patients in the intervention group no longer required CPAP therapy after 8 weeks, and 15.0% had complete OSA remission. Compared with the control group, the intervention group also had greater improvements in body weight and composition, cardiometabolic risk, and health-related quality of life.

Comment: Obesity is a major risk factor for OSA. Weight loss and lifestyle interventions are frequently recommended (but less often achieved) for patients with OSA. The INTERAPNEA study interventions consisted of nutritional behaviour change, moderate aerobic exercise, smoking cessation, alcohol avoidance and improvements in sleep hygiene. The study found a 51% reduction in AHI in the intervention group and the authors propose this multidisciplinary intervention as a primary treatment, with more than half of the intervention group no longer needing CPAP at delayed (6 months) follow-up. The intervention resulted in a 7kg reduction in bodyweight, a significant increase in daily exercise, and a reduction in alcohol intake. In addition, 70% of smokers had successfully quit at the 6-month follow-up. These results are remarkable and are probably not attainable in routine clinical practice outside of an intensive intervention programme, but highlight the important contribution that successful behavioural interventions have in the management of OSA.

Reference: JAMA Netw Open 2022;5(4):e228212
Abstract

Evaluating prediction models of sleep apnea from smartphone-recorded sleep breathing sounds

Authors: Cho S-W et al.

Summary: This cross-sectional study evaluated OSA prediction models using smartphone-recorded breathing sounds. 423 patients who underwent full-night, in-laboratory polysomnography at the sleep centre of Seoul National University Bundang Hospital for evaluation of snoring or sleep apnoea in 2015–2019 had audio recordings taken during sleep using a smartphone. Sleep breathing sounds recorded by a smartphone created reasonably accurate OSA prediction models; accuracies were 88.2%, 82.3%, and 81.7%, and the areas under the curve were 0.90, 0.89, and 0.90 for an AHI threshold of 5, 15, and 30 events/h, respectively.

Comment: Smartphones have become ubiquitous and have permeated into many aspects of routine life, with an increasing role in health. Snoring is often captured by bed partners using the audio recording capabilities of the smartphone as "evidence" of the severity of the problem. This study investigated whether audio recordings of snoring and noises during sleep using a smartphone can be used to identify OSA. Patients simultaneously had their sleep breathing noises recorded by a smartphone during routine in-laboratory polysomnography. The results are encouraging – the sensitivity and specificity of AHI >15 were similar to more formal portable home sleep monitoring. One major limitation is the underestimation of AHI in those patients with low sleep efficiency because time rather than total-sleep-time is the only duration parameter available for smartphones. The role of these ubiquitous devices in sleep monitoring is likely to increase in the years ahead.

Reference: JAMA Otolaryngol Head Neck Surg 2022;148(6):515-21
Abstract

Sleep duration predicts subsequent long-term mortality in patients with type 2 diabetes

Authors: Li C-I et al.

Summary: This study investigated whether sleep duration predicts long-term mortality in patients with type 2 diabetes. 12,526 patients aged ≥30 years with type 2 diabetes were identified from the Diabetes Case Management Programme of a medical centre in Taiwan. 2918 patients died during 10 years of follow-up (1328 from cardiovascular disease). A J-shaped association was observed between sleep duration and mortality, with the lowest risks in patients with 5–7h of sleep.

Comment: Sleep duration is associated with mortality. Across various populations, increased mortality has been demonstrated in both long-sleepers and short-sleepers. This study examined the association between sleep duration and mortality in patients with type 2 diabetes, primarily using sleep-duration questionnaires and national death data sets. During the nearly 11-year study, there were almost 3000 deaths in enrolled patients. The data demonstrated J-shaped mortality for sleep durations, with those reporting a sleep duration of 7h having the lowest mortality. The authors highlight the potential role that assessing sleep duration in patients with type 2 diabetes may have in identifying high-risk patients. Interventions to improve sleep hygiene and treat sleep disorders in this population may address both short- and long-sleepers and are worth considering.

Reference: Cardiovasc Diabetol 2022;21:60
Abstract

Polysomnographic markers of obstructive sleep apnea severity and cancer-related mortality

Authors: Kendzerska T et al.

Summary: This Canadian cohort study evaluated the association between OSA severity and cancer-related mortality in individuals with previously diagnosed cancer. 2222 adults who underwent a diagnostic sleep study in 1994–2017 in 4 Canadian academic hospitals and who had previously been diagnosed with cancer were included. During a median follow-up of 5.6 years, 11.7% of participants with prevalent cancer died from cancer-related causes. Some polysomnographic measures of OSA severity (hypoxaemia and sleep fragmentation, but not AHI) were found to be significantly associated with cancer-related mortality after adjustment for potential confounding factors.

Comment: This study used historical polysomnograms and linked provincial cancer and death databases to identify patients that had a diagnosis of cancer before the polysomnogram was performed. They then evaluated the sleep study results to assess for an association with mortality in those patients. Nocturnal hypoxaemia and sleep fragmentation were significantly associated with cancer-related mortality, but AHI was not. Percentage of time with SaO_2 <90% demonstrated an increasing hazard ratio for each 5% increase in time. Percentage of stage 1 sleep increased the hazard ratio with each additional 16% increase. The lack of association with AHI probably indicates that abnormal respiratory events that do not result in significant reduction in SaO_2% and/or sleep fragmentation are probably less concerning than those that do. In this patient cohort, additional focus on SaO_2% and sleep fragmentation (rather than AHI) in treatment decisions is probably warranted.

Reference: Ann Am Thorac Soc 2022;19(5):807-18
Abstract

Incidence of VTE in patients with OSA

Authors: Genuardi MV et al.

Summary: This cohort study investigated whether OSA is an independent risk factor for venous thromboembolism (VTE). 31,309 patients (mean 50.4 years, 50.1% female) with sleep-disordered breathing who were undergoing overnight polysomnography were included. 1791 VTE events occurred during a mean follow-up of 5.3 years. Each 10-event/h increase in AHI was associated with a 4% increase in incident VTE risk (hazard ratio 1.04, 95% CI 1.02–1.06), but the association disappeared after adjusting for BMI. In contrast, nocturnal hypoxaemia was independently associated with incident VTE. Patients with >50% sleep time spent with SaO_2 <90% had a 48% increased risk of VTE compared with those without nocturnal hypoxaemia (hazard ratio 1.48, 95% CI 1.16–1.69).

Comment: OSA and VTE share several risk factors, especially obesity. It is unclear whether OSA poses an additional independent risk of VTE, or whether the increased incidence of VTE in OSA cohorts is explained by the coexisting obesity. This study followed 31,000 patients who had 1791 VTE events and found that for each 10-event/h increase in AHI there was a 4% increase in incident VTE risk. However, once adjusted for obesity there was no increased VTE risk associated with increasing AHI. Nocturnal hypoxaemia did display an independent association with incident VTE. Patients with more than half of their sleep time with SaO_2 <90% are at 48% increased VTE risk compared to those without hypoxaemia. Although there is a clear association between VTE risk and OSA, it appears that most of that association is due to coexisting obesity. However, prolonged nocturnal hypoxaemia may be a more relevant marker of VTE risk than AHI.

Reference: Chest 2022;161(4):1073-82
Abstract

Neural mechanisms that promote food consumption following sleep loss and social stress: An fMRI study in adolescent girls with overweight/obesity

Authors: Jensen CD et al.

Summary: This study examined the effects of acute sleep restriction on female adolescents' neural responding during social stress and their subsequent eating behaviour. 42 adolescent females aged 15–18 years with overweight or obesity completed a social stress induction task in which they were told they would be rated by peers based on their photograph and profile. They were then randomised to 1 night of sleep deprivation or 9h of sleep the night before undergoing functional magnetic resonance imaging while receiving positive and negative evaluations from their peers. After this they had an ad libitum buffet meal. Compared with non-sleep deprived participants, those who were sleep deprived had distinct patterns of neural engagement to positive and negative evaluation in anterior, mid, and posterior aspects of midline brain structures. In the sleep-deprived group, greater engagement during negative feedback was associated with lower caloric intake. This was not observed in the non-sleep deprived group.

Comment: Insufficient sleep, social stress, weight gain and obesity are all common issues impacting adolescent girls. Insufficient sleep is associated with obesity and this may be due to altered eating patterns when sleep deprived. This study explored the links between sleep deprivation, social stress and caloric intake, and demonstrated that sleep-deprived adolescent girls had patterns of neural engagement that were not present in non-sleep deprived girls. The study results imply that sleep deprivation and social stress play a significant role in emotional response and food choices in adolescent girls. Behavioural interventions and societal changes could play a meaningful role in reducing obesity in this cohort, especially those that increase total sleep time.

Reference: Sleep 2022;45(3):zsab263
Abstract

Impact of sleep timing on attention, sleepiness, and sleep quality among real-life night shift workers with shift work disorder

Authors: Cheng W-J et al.

Summary: This crossover trial examined the effect of a sleep timing intervention on sleep quality among night shift workers with shift work disorder. 60 night shift workers with confirmed shift work disorder were designated to follow evening sleep (15:00–23:00) and morning sleep (09:00–17:00) schedules in a randomised order. Participants slept for longer durations during the evening sleep schedule than during the morning sleep schedule. After adjustment for light exposure and sleep duration, participants had lower sleepiness scores, higher sleep quality, and shorter reaction times in the psychomotor vigilance test when following evening sleep versus morning sleep schedules.

Comment: Night shift workers are required to sleep during the day or evening when the remainder of society is most active, and often struggle to achieve prolonged sleep due to noise, light and family/social interactions. Night shift results in circadian misalignment to a variable degree among almost all night shift workers. This crossover study assessed whether morning sleep or evening sleep is more beneficial for night shift workers with shift work disorder and assessed the impact of different chronotypes. Actigraphy monitored sleep behaviours and light-exposure, questionnaires assessed sleepiness, and performance was assessed with psychomotor vigilance tests. Evening sleep was superior, with longer sleep duration, lower sleepiness scores and faster reaction times. The impact was greatest among those with late chronotypes. This study indicates that, where possible, night shift workers with shift work disorder should sleep in the evening period.

Reference: Sleep 2022;45(4):zsac034
Abstract

Independent commentary by Dr Sean Tolhurst

Dr Sean Tolhurst is a Consultant Respiratory and Sleep Physician working in private practice at Greenslopes Private Hospital. He graduated first in science (with First Class Honours) from The University of Queensland, then completed his medical training at The Flinders University of South Australia (again at an Honours level). He completed his basic and advanced training in Queensland and New South Wales, gaining his fellowship from the Royal Australasian College of Physicians (FRACP) in 2006 with specialist qualification in Respiratory and Sleep medicine. He was formerly the Head of Department of Respiratory and Sleep medicine at Greenslopes Private Hospital.

Dr Tolhurst is one of Australia's most experienced Sleep Physicians with an extensive Sleep Medicine practice and was previously the lead Clinician in Australia's largest diagnostic sleep service provider. His particular areas of clinical interest include conservative treatment options for OSA (without the need for CPAP therapy), assessing sleepiness, narcolepsy, idiopathic hypersomnolence and central sleep apnoea. He has co-authored several peer-reviewed publications and case-studies related to Sleep Medicine and was one of the co-authors of the Australasian Sleep Association's previous guidelines on the performance of Sleep Studies in adults. Dr Tolhurst regularly provides expert medico-legal opinion in cases involving Sleep Medicine and is a member of the Medico-legal Society of Queensland.

Australian Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our CPD page.

Research Reviews are prepared with an independent commentary from relevant specialists. To become a reviewer please email geoff@researchreview.com.au.
Research Review Australia Pty Ltd is an independent Australian publisher. Research Review receives funding from a variety of sources including Government depts., health product companies, insurers and other organisations with an interest in health. Journal content is created independently of sponsor companies with assistance from leading local specialists. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.
Research Review publications are intended for Australian health professionals.