

Sleep Research Review

Making Education Easy

Issue 9 - 2018

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Abbreviations used in this issue:

AHI = apnoea-hypopnoea index; **CPAP** = continuous positive airway pressure;
CVD = cardiovascular disease; **OSA** = obstructive sleep apnoea;
PSG = polysomnography; **REM** = rapid eye movement;
SDB = sleep-disordered breathing.

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Welcome to the latest issue of Sleep Research Review.

In this issue we report that adequate sleep duration is important for overweight or obese individuals who are trying to lose weight, CPAP therapy may improve optic nerve function in patients with severe OSA who are adherent to treatment, and a novel forehead temperature-regulating device shows potential in the treatment of insomnia. Australian researchers look at the impact of cerebral oxygenation on behaviour in children with sleep-disordered breathing, US researchers report that clinical interventions for OSA may prevent amyloid build-up in cognitively normal elderly individuals, and a meta-analysis finds that short sleep duration is a risk factor for obesity in children. Comments for this issue have been provided by Dr Peter Solin (Melbourne).

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

Kind regards

Dr Janette Tenne

Medical Research Advisor

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Influence of sleep restriction on weight loss outcomes associated with caloric restriction

Authors: Wang X et al.

Summary: This study evaluated the effects of moderate sleep restriction on bodyweight in individuals undergoing caloric restriction. 36 overweight or obese adults were randomised to an 8-week caloric restriction regimen alone (CR group; n=15) or combined with sleep restriction (CR+SR; n=21). All participants were instructed to restrict daily calorie intake to 95% of their measured resting metabolic rate. Those in the CR+SR group were also instructed to reduce time in bed on 5 nights per week and to sleep *ad libitum* on the other 2 nights per week. The CR+SR group reduced sleep by a mean 57 min/day on sleep restriction days and increased sleep by a mean 59 min/day on the *ad libitum* sleep days, resulting in a mean sleep reduction of 169 min/week. Both groups lost similar amounts of weight, lean mass, and fat mass, but the proportion of total mass lost as fat was significantly greater in the CR group.

Comment: More evidence emerges that healthy content as well as adequate duration of sleep is important for overall health. In this study an important question was raised. Typical of many individuals, can catch-up sleep on the weekend but sleep restriction during the week be harmful? In this case is it harmful to the goal of weight loss? In this study, overweight or obese adults underwent 8 weeks of calorie restriction. One group was randomised to instruction of sleep restriction on 5 of 7 days, with catch-up sleep in the remaining 2 days; the other group to ordinary sleep. This would be mimicking the scenario of busy individuals being sleep deprived during the week, but then trying to catch up on the weekends. Strict measurement of sleep restriction was not robust so results need to be interpreted with caution. Absolute weight loss appears to be very similar. However the interesting finding from this paper was that the proportion of fat loss in the sleep restriction group was less than the non-sleep restriction group. The study teases us with the concept that should you wish to lose weight, then focus on getting an adequate duration of sleep, because if you don't you will be losing less fat mass and potentially more lean body mass! Not really the ideal outcome.

Reference: *Sleep* 2018;41(5):zsy027

[Abstract](#)

Continuous positive airway pressure treatment may improve optic nerve function in obstructive sleep apnea

Authors: Liguori C et al.

Summary: This electrophysiological study examined the effects of CPAP treatment on optic nerve function in patients with severe OSA. Visual evoked potential (VEP) was recorded at baseline and after 1 year of CPAP treatment in 20 patients with severe OSA; patients were divided into two groups based on CPAP adherence, and compared to a healthy control group (n=26). At 1 year, patients with good adherence to CPAP therapy had significantly higher VEP P100 amplitude than patients with poor adherence to CPAP therapy. VEP responses in patients with good adherence to CPAP therapy were similar to those in the control group.

Comment: Sleep disorders clinicians should be receiving referrals from ophthalmologists. Why? In ophthalmological press, a number of conditions have been associated with untreated OSA. Most popular is floppy eyelid syndrome. This condition is more obvious, as the gaping eyelid is readily identifiable in the mirror! Non-arteritic anterior ischaemic optic neuropathy (NAION), glaucoma, central serous chorioretinopathy (CSCR), papilloedema, and hypoxia-related revascularisation of diabetic retinopathy are the other concerns for ophthalmologists and sleep physicians. These conditions have been associated with untreated sleep apnoea. Is there a way of measuring visual dysfunction or potential dysfunction in OSA? One metric is VEPs. This relies on a functional lens and retina, optic nerve conduction, and visual cortex activity. In this fascinating study, severe OSA patients were measured before and after 1 year of CPAP treatment. Those that utilised CPAP effectively had normalisation of VEP, as compared to the poor adherence group. Although the numbers are small (10 in each CPAP group), the study provides a tantalising corroboration of optic tract health in well-treated OSA, in contrast to poorer optic tract health in undertreated or untreated OSA. For the sleep clinician, the study supports the notion that if an ophthalmologist is concerned about eye health, so should we.

Reference: *J Clin Sleep Med* 2018;14(6):953-58

[Abstract](#)



A novel forehead temperature-regulating device for insomnia

Authors: Roth T et al.

Summary: This randomised controlled trial evaluated the safety and efficacy of a novel forehead temperature-regulating device for the treatment of insomnia. 106 adults with insomnia wore the forehead temperature-regulating device (maintaining frontal cerebral temperature at 14–16°C) or a sham device for 2 consecutive nights. The co-primary end-point (latency to persistent sleep and absolute sleep efficiency) did not differ significantly between groups. However, frontal cerebral thermal therapy produced improvements over sham in relative change from baseline in latency to persistent sleep, latency to stage 1 non-REM sleep, latency to stage 2 non-REM sleep, and the minutes of sleep during the first hour of the night.

Comment: Nonpharmacological treatment is the holy grail for insomnia. Body temperature circadian manoeuvres have involved baths or showers 4–6 hours prior to sleep onset, and certainly the cold bedroom environment is a useful and beneficial manoeuvre. Vestibular stimulation devices have come and gone. Other passive manoeuvres include white noise, meditation and various distraction methods. If a cool bedroom environment at night is beneficial, what about cooling the scalp? In this study, there were small and suggestive improvements with the use of forehead temperature regulation. A urethane forehead bladder (think camelback drink bladder) with infused liquid at 15°C was applied 1 hour prior to sleep, and kept on the forehead for the duration of the night. A sham vestibular stimulate was used. In the treatment group, there was an improvement in latency to stage I, latency to stage II, but not overall sleep efficiency or latency to persistent sleep. The number of participants was small. It was uncertain whether the investigators had any financial links to the device, which may undermine the conclusions and validity. Larger efficacy studies need to confirm the benefit. Interestingly the sham treatment also had a benefit, underscoring the placebo effect.

Reference: *Sleep* 2018;41(5):zsy045

[Abstract](#)

Age effects on cerebral oxygenation and behavior in children with sleep-disordered breathing

Authors: Tamanyan K et al.

Summary: This Australian study examined cerebral tissue oxygenation and oxygen extraction in children with SDB. Children referred for suspected SDB (n=159) and non-snoring controls underwent overnight PSG with near-infrared spectroscopy. Children were categorised according to age (3–6 years and 7–12 years), and OSA severity (primary snoring, mild OSA or moderate/severe OSA). In children aged 3–6 years, cerebral oxygenation and oxygen extraction did not differ significantly between severity groups. In those aged 7–12 years, cerebral oxygenation and oxygen extraction were significantly lower in snorers than controls, but there were no differences between primary snorers and OSA groups. Cerebral oxygenation was not associated with cognitive performance in either of the age groups or with behaviour in children aged 3–6 years, but was associated with behaviour in school-aged children.

Comment: This paper extends the knowledge base in children with sleep disorders. In this case, SDB with respect to cerebral oxygenation. The Ritchie Centre has been pursuing the determinants of breathing in children, infants, and newborns, initially looking into the cause of cot death, and over the last 20 years, looking at growth and maturation of the cardiorespiratory system. Oximetry and spectroscopy performed noninvasively derived the relevant measurements. The interesting question addressed by this study was whether the small drops in oxygen saturations in childhood sleep disorders would correlate with cognitive and behavioural performance. It appears that in the younger age group (3–6 years) with some SDB, there isn't a change in oxygen i.e. derived cerebral oxygenation. In the older age group (7–12 years) there was a small drop in oxygenation, and this did correlate with behavioural measures. The study advances the notion that cerebral injury (in this case minimal hypoxaemia from SDB) can have a measurable functional impact. It suggests that SDB in older children carries more detriment than in younger children.

Reference: *Am J Respir Crit Care Med* 2018;197(11):1468-77

[Abstract](#)

Obstructive sleep apnea severity affects amyloid burden in cognitively normal elderly

Authors: Sharma R et al.

Summary: This longitudinal study examined the association between OSA severity and amyloid burden in cognitively normal elderly individuals. Community-dwelling cognitively normal elderly (aged 55–90 years) were evaluated over a 2-year period. OSA was monitored using a home sleep recording device. Linear regression analysis adjusted for confounding factors found that OSA severity was associated with markers of increased amyloid burden over the 2-year follow-up.

Comment: The association between accelerated cognitive decline and SDB namely OSA has emerged over the last 10 years, and represents a major impetus for patients and clinicians to consider treatment for longer term cognitive function. This study looked at community dwelling elderly, without depression, who then had cerebral spinal fluid (CSF) sampled for amyloid protein (amyloid β), and positron emission tomography (PET) scanning for target areas in Alzheimer disease. SDB was identified from home sleep testing. Interestingly, the amyloid protein in CSF correlated with AHI and with AHI associated with 4% oxygen desaturation (after adjustment for confounding variables and measurement variables). The imaging study using PET did not correlate although there was a trend suggesting that a larger sample size would have shown an association. This study therefore suggests that untreated OSA in individuals between the ages of 55 and 90 years increases rates of amyloid production. It doesn't demonstrate amyloid deposition on visual scanning, but suggests the CSF levels are likely associated with their position. Therefore, another piece of evidence showing that treatment of OSA in older groups is worthwhile. Whether OSA treatment in this age group can arrest or reverse abnormalities remains to be determined.

Reference: *Am J Respir Crit Care Med* 2018;197(7):933-43

[Abstract](#)

Patient engagement using new technology to improve adherence to positive airway pressure therapy

Authors: Malhotra A et al.

Summary: This retrospective study compared CPAP adherence in sleep clinic patients assigned to active patient engagement (APE) technology or usual care monitoring (UCM). Adherence data were analysed for a total of 128,037 patients. Baseline characteristics were typical of a sleep clinic cohort. More patients achieved adherence criteria in the APE group than in the UCM group (87.3% vs 70.4%; $p < 0.0001$), and CPAP therapy was used for a mean 5.9 vs 4.9 h/night in the respective groups ($p < 0.0001$). Patients with sleep apnoea who were "struggling" with therapy adherence had a 17.6% absolute improvement in adherence when using APE compared with UCM.

Comment: The presence of de-identified online databases on CPAP utilisation carries some scary connotations. Will health monitoring be used to disadvantage or at worst punish individuals whose data has been uploaded? Conversely, can automated programmes providing feedback for individuals improve outcomes? Through access to 2 large CPAP biomedical companies' online portals, this question was addressed. APE refers to supportive interaction for the outcome or therapy at hand. Conceptually it is recognised as a major driver for behavioural change in health care. These feedback tools can be readily seen on portals for CPAP treatment (personal perspective: seeing these positive messages certainly feels encouraging rather than intrusive). When compared with usual care treatment in a large cohort of individuals starting CPAP treatment within 7 days, there was a substantial improvement in usage of CPAP by 1 h/night (from 4.9h up to 5.9h). Additionally US Medicare adherence definition was improved from 70% up to 87%. The study supports the notion that feedback, although algorithm-generated and intrinsically impersonal, has a positive effect on CPAP therapy utilisation.

Reference: *Chest* 2018;153(4):843-50

[Abstract](#)



Independent commentary by Dr Peter Solin, MBBS FRACP PhD

Dr Peter Solin is the medical director of the Sleep & Respiratory Group and a highly trained authority in sleep and respiratory medicine. Covering all facets of sleep medicine, he has a particular interest in the effects of cardiovascular and cerebrovascular diseases on sleep and performance, the impact of ill-health and infirmity on sleep, how medications interfere with sleep and rest, as well as unusual causes of fatigue and sleepiness, particularly in young adults. Dr Solin is also a dedicated teacher, educating medical students, GPs, as well as public and professional audiences. In recent years, he has delivered expert healthcare and sleep diagnostic services in more regional and remote centres, such as his program of home sleep testing through National Sleep Diagnostics.



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References: **1.** CIRCADIN® Product Information, 9 June 2016. **2.** Zisapel N. Sleep and sleep disturbances: biological basis and clinical implications *Cell Mol Life Sci* 2007;64:1174-1186. **3.** http://search.tga.gov.au/s/search.html?collection=tga-artg&profile=record&meta_i=153959 (Accessed 30th April 2018) **4.** EPAR. Assessment report for Circadin. *Procedure No EMEA/H/C/695* 2014.

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Sustained benefits of delaying school start time on adolescent sleep and well-being

Authors: Lo J et al.

Summary: This study investigated the impact of a 45-min delay in school start time on sleep and well-being in adolescents. 375 students in grades 7–10 (mean age 14.6 years) at an all-girls' secondary school in Singapore that delayed its start time from 07:30 to 08:15 were included. Self-reports of sleep timing, sleepiness, and well-being were obtained at baseline, and at approximately 1 and 9 months after the delay was implemented. After 1 month, bedtimes on school nights were delayed by 9.0 min, while rise times were delayed by 31.6 min (resulting in a 23.2 min increase in time in bed). At 9 months, the increase in time in bed was sustained, and total sleep time had increased by 10 min relative to baseline. Participants reported less subjective sleepiness and improvement in well-being at both follow-ups. A greater increase in sleep duration on school nights was associated with greater improvement in alertness and well-being.

Comment: The problem of the sleepy child and teenager purposefully delaying sleep onset (despite all encouragement or threats), is common to almost all parents. There is a push to 'wave the white flag', and push out school times i.e. start later and finish later, to coincide with the delayed sleep phase and circadian clock in adolescents and teenagers. This concept was put into practice in a Singaporean girls' school in years 7–10 (mean age 14 years). A 45-min delay in the start of school was initiated. Self-reports of mood as well as actigraphy for sleep were obtained. Time in bed improved by 23 min, despite sleep onset being 9 min later. Self-reports of alertness and well-being improved. As mentioned in the abstract, this environment may not be typical of some Western societies, due to the pressure for success in this culture. Nevertheless, the study supports the notion that delayed school start time is beneficial for students rather than detrimental. How this may impact on the family environment and dynamics was not really addressed.

Reference: *Sleep* 2018;41(6):zsy052

[Abstract](#)

Insomnia with objective short sleep duration and risk of incident cardiovascular disease and all-cause mortality

Authors: Bertisch S et al.

Summary: This analysis of data from the Sleep Heart Health study examined the association between insomnia or poor sleep (with short sleep duration) and the risk of CVD and mortality in the general population. Questionnaires and at-home PSG were performed in 1994–1998 for 4994 participants (mean age 64 years) who were then followed for a median 11.4 years. 14.1% of participants reported insomnia or poor sleep, and 50.3% of this group slept for <6h. Compared with a reference group, those with insomnia or poor sleep who slept for <6h had a 29% higher risk of incident CVD but were not at increased risk for all-cause mortality.

Comment: The Sleep Heart Health study is a large dataset of individuals tested by home sleep testing between 1994 and 1998 with ongoing surveillance, with a slight bias for snorers. Various trends can be picked up by observing these individuals over time, although there is of course dropout, and observational studies are prone to bias that is difficult to control. Amongst 5000 individuals with a mean age of 64, 14% reported insomnia according to defined criteria, and of this group, 50% slept <6h. Those that slept for <6h had a 29% increase in all-cause CVD events. All-cause mortality was not elevated. Therefore, insomnia with PSG-proven sleep of <6h appears to have a detrimental impact on cardiovascular health, but not necessarily mortality. This study provides further support that reduced sleep duration is detrimental through the mechanism of CVD. It supports other population observational studies, but is a little at odds with these due to the absent signal for mortality.

Reference: *Sleep* 2018;41(6):zsy047

[Abstract](#)

Sleep duration and incidence of obesity in infants, children, and adolescents

Authors: Miller M et al.

Summary: This systematic review and meta-analysis evaluated the association between sleep and obesity in infants, children and adolescents. A search of PubMed, Embase, Web of Science, and Cochrane identified 42 prospective studies that were suitable for inclusion. Meta-analysis of the data showed that short sleep was associated with a greater risk of developing overweight or obesity in infancy, early childhood, middle childhood, and adolescence.

Comment: Short sleep duration is a risk factor or marker of the development of obesity in infants, children, and adolescents. In a meta-analysis of 42 studies, a reasonably convincing association was seen between sleep duration and obesity, in younger children through to adolescents. A calculated risk was determined and expressed in terms of hours of reduced sleep. There was an increase in body mass index (BMI) for reduced sleep times, and there was a decrease in BMI for increased sleep duration. The study supports observations over the last 20 years that short sleep duration is a risk factor for obesity in children, as well as in adults.

Reference: *Sleep* 2018;41(4):zsy018

[Abstract](#)

Phenotyping pharyngeal pathophysiology using polysomnography in patients with obstructive sleep apnea

Authors: Sands S et al.

Summary: Pharyngeal collapsibility determines the ventilation at normal ventilatory drive during sleep, and pharyngeal compensation determines the rise in ventilation accompanying a rising ventilatory drive. This study used PSG to quantify the phenotypic traits of pharyngeal collapsibility and compensatory muscle responsiveness in 29 patients with OSA. PSG-derived collapsibility and compensation estimates correlated favourably with those quantified using gold standard ventilatory drive, and using CPAP manipulation. PSG estimates effectively stratified patients into high versus low subgroups.

Comment: Despite our own advances, the oropharynx remains a mysterious box. Most clinicians can understand structural imaging (computed tomography scans, magnetic resonance imaging, functional ultrasound). However it remains a challenge to understand the interactive complexity of respiratory drive, collapsibility and responsiveness. The two main authors have spent the last decade defining and determining measurements for these important components of upper airway patency. From this endeavour, the copious physiological signals in PSG recordings can provide metrics to define upper airway collapsibility and compensatory muscle responsiveness. Clinicians are performing far less CPAP titrations, and relying far more on automated CPAP with its downloadable features. Clinicians constantly battle with (and are looking for some metric to validate) what settings the patient might be optimally comfortable on. Soft algorithms? Upper airway resistance algorithm is? Baseline CPAP? Expiratory pressure relief? Boost settings? Sense awake settings? What do we choose and why? Moreover, what characteristics of the patient should point us towards fine tuning their individual settings? Should we undertreat a little bit and allow for some arousability? The clinical relevance of Sands and colleagues is that deriving metrics from PSG is a step further to individual patient tailored treatment. This sort of work may end up making the generic CPAP prescription far more precise for the individual: for example a specific range rather than a general range, and the responsiveness of the CPAP unit in terms of algorithms provided by manufacturers.

Reference: *Am J Respir Crit Care Med* 2018;197(9):1187-97

[Abstract](#)

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