Abstracts

Disorders of Sleep

Given space limitations and varying reprint permission policies, not all of the influential publications the editors considered reprinting in this issue could be included. This section contains abstracts from additional articles the editors deemed well worth reviewing.

The Effects of Shift Work on Sleeping Quality, Hypertension and Diabetes in Retired Workers
Guo Y, Liu Y, Huang X, Rong Y, He M, Wang Y, Yuan J, Wu T, Chen W.
PLoS One 2013 Aug 16; 8(8):e71107

Background: Shift work has been associated with adverse health effects by disturbing circadian rhythms. However,its potential long-term health effects and the persistent effects after leaving shifts have not been well established. **Methods and Results:** We studied 26,463 workers from Tongji-Dongfeng Cohort in China. All the participants are retired employees of Dongfeng Motor Company. Information on demographics, occupational history and medical history were gathered through questionnaires. After adjusting potential confounders in the logistic regression models, shift work was associated with poor sleeping quality, diabetes and hypertension independently. We observed significant effects of shift work on poor sleeping quality, diabetes and hypertension; the ORs (95%CI) are 1.18 (1.09-1.27), 1.10 (1.03-1.17) and 1.05 (1.01-1.09) respectively. In the further analysis, we found elevated ORs (95%CI) for participants with poor sleeping quality, the ORs (95%CI) are 1.34 (1.08-1.60), 1.13 (1.05-1.21), 1.05 (1.03-1.07) and 1.05 (1.01-1.09) for 1-4, 5-9, 10-19, ≥20 years of shift work respectively. However, with the extension of leaving shift work duration, the effects of shift work on sleep quality gradually reduced. **Conclusions:** Shift work may be an independent risk factor for sleeping quality, diabetes and hypertension even in retired workers. Applicable intervention strategies are needed for prevention of sleep loss, diabetes, and hypertension for shift workers.

Behavioral Treatment of Insomnia in Bipolar Disorder
Kaplan KA, Harvey AG
Am J Psychiatry 2013; 170:716–720

Sleep disturbance is common in bipolar disorder. Stimulus control and sleep restriction are powerful, clinically useful behavioral interventions for insomnia, typically delivered as part of cognitive-behavioral therapy for insomnia (CBT-I). Both involve short-term sleep deprivation. The potential for manic or hypomanic symptoms to emerge after sleep deprivation in bipolar disorder raises questions about the appropriateness of these methods for treating insomnia. In a series of patients with bipolar disorder who underwent behavioral treatment for insomnia, the authors found that regularizing bedtimes and rise times was often sufficient to bring about improvements in sleep. Two patients in a total group of 15 patients reported mild increases in hypomanic symptoms the week following instruction on stimulus control. Total sleep time did not change for these individuals. Two of five patients who underwent sleep restriction reported mild hypomania that was unrelated to weekly sleep duration. Sleep restriction and stimulus control appear to be safe and efficacious procedures for treating insomnia in patients with bipolar disorder. Practitioners should encourage regularity in bedtimes and rise times as a first step in treatment, and carefully monitor changes in mood and daytime sleepiness throughout the intervention.

A Trial of Prazosin for Combat Trauma PTSD With Nightmares in Active-Duty Soldiers Returned From Iraq and Afghanistan.
Raskind MA, Peterson K, Williams T, Hoff DJ, Hart K, Holmes H, Homas D, Hill J, Daniels C, Calohan J, Millard SP, Rohde K, O'Connell J, Pritzl D, Feiszli K, Petrie EC, Gross C, Mayer CL, Freed MC, Engel C, Peskind ER
Am J Psychiatry 2013; 170:1003–1010

Objective: The authors conducted a 15-week randomized controlled trial of the alpha-1 adrenoreceptor antagonist prazosin for combat trauma nightmares, sleep quality, global function, and overall symptoms in active-duty soldiers with posttraumatic stress disorder (PTSD) returned from combat deployments to Iraq and Afghanistan. **Method:** Sixty-seven soldiers were randomly assigned to treatment with prazosin or placebo for 15 weeks. Drug was titrated based on nightmare response over 6 weeks to a possible maximum dose of 5 mg midmorning and 20 mg at bedtime for men and 2 mg midmorning and 10 mg at bedtime for women. Mean achieved bedtime doses were 15.6 mg of prazosin (SD=6.0) and 18.8 mg of placebo (SD=3.3) for men and 7.0 mg of prazosin (SD=3.5) and 10.0 mg of placebo (SD=0.0) for women. Mean achieved midmorning doses were 4.0 mg of prazosin (SD=1.4) and 4.8 mg of placebo (SD=0.8) for men and 1.7 mg of prazosin (SD=0.5) and 2.0 mg of placebo (SD=0.0) mg for women. Primary outcome measures were the nightmare item of the Clinician-Administered PTSD Scale (CAPS), the Pittsburgh Sleep Quality Index, and the change item of the Clinical Global Impressions Scale anchored to functioning. Secondary outcome measures were the 17-item CAPS, the Hamilton Depression Rating Scale, the Patient Health Questionnaire-9, and the Quality of Life Index. Maintenance psychotropic medications and supportive psychotherapy were held constant. **Results:** Prazosin was effective for trauma nightmares, sleep quality, global function, CAPS score, and the CAPS hyperarousal symptom cluster. Prazosin was well tolerated, and blood pressure changes did not differ between groups. **Conclusions:** Prazosin is effective for combat-related PTSD with trauma nightmares in active-duty soldiers, and benefits are clinically meaningful. Substantial residual symptoms suggest that studies combining prazosin with effective psychotherapies might demonstrate further benefit.

Sleep Disturbances as the Hallmark of PTSD: Where Are We Now?
Germain A
Am J Psychiatry 2013; 170:372–382

The hypothesis that rapid eye movement (REM) sleep disturbances are the hallmark of posttraumatic stress disorder (PTSD), proposed by Ross and colleagues in 1989, has stimulated a wealth of clinical, preclinical, and animal studies on the role of sleep in the pathophysiology of PTSD. The present review revisits this influential hypothesis in light of clinical and experimental findings that have since accumulated. Polysomnographic studies conducted in adults with PTSD have yielded mixed findings regarding REM sleep disturbances, and they generally suggest modest and nonspecific sleep disruptions. Prospective and treatment studies have provided more robust evidence for the relationship between sleep disturbances and psychiatric outcomes and symptoms. Experimental animal and human studies that have probed the relationship between REM sleep and fear responses, as well as studies focused more broadly on sleep-dependent affective and memory processes, also provide strong support for the hypothesis that sleep plays an important role in PTSD-relevant processes. Overall, the literature suggests that disturbed REM or non-REM sleep can contribute to maladaptive stress and trauma responses and may constitute a modifiable risk factor for poor psychiatric outcomes. Clinicians need to consider that the chronic sleep disruption associated with nightmares may affect the efficacy of first-line PTSD treatments, but targeted sleep treatments may accelerate recovery from PTSD. The field is ripe for prospective and longitudinal studies in high-risk groups to clarify how changes in sleep physiology and neurobiology contribute to increased risk of poor psychiatric outcomes.

Controversies in the Use of Second Generation Antipsychotics as Sleep Agent
Shah C, Sharma TR, Kablinger A
Pharmacol Res. 2013 Nov 1; 79C:1–8. doi: 10.1016/j.phrs.2013.10.005. [Epub ahead of print]

A growing number of patients present in clinics with complaints of insomnia. Over the past century, great advances have been made in our knowledge of mechanisms of sleep and wakefulness. Understanding sleep neurochemistry has led to better management of different types of insomnias with a variety of non-pharmacological and pharmacological treatments. Unfortunately, the increasing development and availability of second generation antipsychotics (SGA) have prompted their frequent use exclusively for insomnia. However, to date, no large randomized-controlled or placebo-controlled studies have shown the utility of SGAs in the realm of treating insomnia. Many clinicians use SGAs as "off-label" for sleep induction and maintenance, but this practice needs to be readdressed given their potential risks and the current lack of

evidence base. This review will highlight the neurochemistry related to sleep, the mechanisms of action by which SGA may have some benefit in treating insomnia, and the risks associated with their utilization.

A Practical Guide to the Therapy of Narcolepsy and Hypersomnia Syndromes
Mignot EJ
Neurotherapeutics 2012 Oct; 9(4):739–752

Narcolepsy and other syndromes associated with excessive daytime sleepiness can be challenging to treat. New classifications now distinguish narcolepsy/hypocretin deficiency (also called type 1 narcolepsy), a lifelong disorder with well-established diagnostic procedures and etiology, from other syndromes with hypersomnolence of unknown causes. Klein-Levin Syndrome, a periodic hypersomnia associated with cognitive and behavioral abnormalities, is also considered a separate entity with separate therapeutic protocols. Non hypocretin-related hypersomnia syndromes are diagnoses of exclusion. These diagnoses are only made after eliminating sleep deprivation, sleep apnea, disturbed nocturnal sleep, and psychiatric comorbidities as the primary cause of daytime sleepiness. The treatment of narcolepsy/hypocretin deficiency is well-codified, and involves pharmacotherapies using sodium oxybate, stimulants, and/or antidepressants, plus behavioral modifications. These therapies are almost always needed, and the risk-to-benefit ratio is clear, notably in children. Detailed knowledge of the pharmacological profile of each compound is needed to optimize use. Treatment for other syndromes with hypersomnolence is more challenging and less codified. Preferably, therapy should be conservative (such as modafinil, atomoxetine, behavioral modifications), but it may have to be more aggressive (high-dose stimulants, sodium oxybate, etc.) on a case-by-case, empirical trial basis. As cause and evolution are unknown in these conditions, it is important to challenge diagnosis and therapy over time, keeping in mind the possibility of tolerance and the development of stimulant addiction. Kleine-Levin Syndrome is usually best left untreated, although lithium can be considered in severe cases with frequent episodes. Guidelines are provided based on the literature and personal experience of the author.

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