A Review of Obstructive Sleep Apnea, Shift Work, Gender

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Executive Summary -
The purpose of the review is to make connections between obstructive sleep apnea (OSA) and shift work while giving special attention to the factor of gender and rapid eye movement sleep. Obstructive sleep apnea is a common sleep disorder that has various detrimental effects on health and cognitive functioning. The prevalence and symptoms of OSA appear to be gender specific. The current clinical guideline has not yet included the evaluation of fatigue, the common symptoms among women with OSA, which may lead to an under diagnosis of OSA among women. Rapid eye movement sleep is associated with more severe OSA episodes. Shift work has a similar range of effects on health and cognitive functioning, however, it affects workers through both sleep disturbance and circadian disruption. Gender specific effects have also been observed among shift workers. Night shift interacts with REM sleep and may lead to a higher risk of cardiovascular disease. Finally, we proposed the question, “Is there a difference in the REM sleep of male and female night shift workers with OSA,” and “How is cognitive functioning of these two groups affected by the interaction of OSA and shift work?”

Keywords: obstructive sleep apnea (OSA), shift work, REM sleep

1. Introduction

Obstructive sleep apnea is a common sleep disorder that is caused by complete or partial functional impairment of the upper airway dilator muscle, which leads to apnea/hypopnea-induced oxygen desaturation, repetitive micro-arousals, and disturbed sleep (Kloepfer et al., 2009; Rajagopalan, 2011). Thus, OSA patients suffer from sleep fragmentation and chronic sleep deprivation, with common symptoms of daytime sleepiness, tiredness, snoring, etc. When adequate apneas and hypopneas episodes are presented together with these symptoms, OSA is labeled as obstructive sleep apnea syndrome (OSAS) (Eliasson et al., 2014). Various factors have been identified as predictors of OSA including oropharyngeal narrowing, neck circumference, and BMI. In general, factors that predispose individuals to increased collapsibility of the upper airway are major risk factors for OSA. Among all of them, obesity is the greatest risk factor for OSA due to its high prevalence (Veasey, 2012). Clinical diagnosis of OSA requires baseline polysomnography of patients and a CPAP titration study, although home studies are increasingly being used as screening test.
even argue that OSA can be considered a component of metabolic syndrome (Rajagopalan, 2011).

Additionally, OSA plays a role in neurologic disorders, for example, the onset and worsening of seizure. Besides its detrimental effects on physical health, OSA is also associated with mood disturbance, with the most common symptom reported being depression. Among patients with relatively severe OSA, about half of them meet the clinical diagnosis criteria of depression (Veasey, 2012).

3. Obstructive Sleep Apnea and Cognitive Impairment

Fulda and Schulz found a 36.9% reduction in performance of psychological functions among patients with sleep related breathing disorders (SRBD). This is in line with other studies that suggest a consistent pattern of cognitive impairment among patients with SRBD (Schneider et al., 2004). Patients with sleep apnea syndrome often exhibit neuropsychological deficits such as frontal lobe related abnormalities (Munoz et al., 2000). Particularly, individuals with OSA have been observed with abnormalities in cognitive functions, including impaired verbal memory, planning, reasoning, vigilance and mood control. For memory impairment, Kloepfer et al. (2009) found a significantly lower verbal retention rate and a non-significantly reduced visual retention rate among OSA patients. While visual memory is not affected by OSA, verbal memory, either in the domain of semantic, episodic, or working memory, is impaired.

The cognitive functioning deficits in OSA patients may be explained by the long-term sleep disturbance and hypoxia that lead to functional or structural alterations in brain circuits (Kloepfer et al., 2009). Hypoxia increases neurotoxic substances that can cause neural dysfunction. Brain structures such as mesial temporal lobe, basal ganglia, and the neocortex may be affected and result in deficits in declarative and procedural memory consolidation (Kloepfer et al., 2009). The effect of treatment for OSA on memory is not clear. In general treatment for OSA has been found to improve some but not all neurobehavorial test performance, suggesting the direct impact of OSA on cognitive functioning as well as the potentially irreversible impairment to specific parts of the brain from OSA. Note that obesity is a risk factor for both OSA and poor cognitive functioning. Further studies need to be done to determine how OSA and obesity affect cognitive functioning (Veasey, 2012).

Sleep disturbance also affects cognitive functioning by altering relevant brain circuits, thus factors that cause sleep disturbance may interact with OSA and affect cognitive functioning together. Patients with only moderate OSA already exhibit some deficits in their cognitive functioning and among those with severe OSA, more cognitive functioning deficits of greater severity have been observed. Kloepfer et al. (2009) looked at a sample of patients with moderate OSA and observed no significant differences in alertness, divided attention, and psychomotor speed as compared to individuals without OSA. Engleman and Joffe (1999) observed attenuated attention, psychomotor performance, and executive functioning in patients with severe OSA.

Night shift work has been found to aggravate OSA by causing significant increase in the total duration of obstructive apneas during REM sleep, mean duration of obstructive apneas during arousal, and apnea index during arousal (Laudencak et al., 2007). As previous studies have established the association between sleep disturbance and impairment of cognitive functioning, night shift work may intensify the cognitive deficits that have already been found in patients with moderate-severe OSA. The interaction between OSA and shift work on cognitive functioning and physical health must be further studied.

3.1. Treatment for Obstructive Sleep Apnea

The most effective and widely adopted treatment for OSA is continuous positive airways pressure (CPAP) therapy, which opens the upper airway with positive pressure (Veasey, 2012). Other treatments such as pharyngeal surgery that reduces soft tissue are less effective for severe OSA and therefore, CPAP is recommended for patients with moderate to severe OSA (Veasey, 2012). It has been found that after CPAP treatment, the performance level of patients with OSA almost returned to the same with individuals who never had OSA, especially for self-rated sleepiness/tiredness (Schneider et al., 2004).

Short-term CPAP therapy can immediately improve daytime sleepiness but complete reversal of the sleepiness is unlikely if it is too severe before the treatment. This is in line with other studies that found no improvement of some neurobehavioral outcomes after CPAP treatment, suggesting irreversible damage to the brain from OSA (Veasey, 2012). Long-term CPAP treatment has been found to significantly improve somnolence and vigilance but fail to modify anxiety and depression. It is possible that patients remain anxious and depressed while using CPAP because they realize that they need to rely on this symptomatic rather than curative treatment for a unforeseeably long period of time (Munoz et al., 2000). However, it is also possible that the mechanism behind mood disturbance caused by OSA is different from that of cognitive functioning deficits caused by OSA.

3.2. Obstructive Sleep Apnea and REM Sleep

The pathophysiology of OSA can be summarized as intermittent occlusions of the upper airway during sleep (Veasey, 2012). In rapid-eye-movement (REM) sleep, muscle atonia and reduced chemosensitivity occur and result in increased
frequency of apneas and more severe oxygen desaturations (Skatrud et al., 1990). Thus, more severe OSA may happen during REM sleep. Kloepfer et al. (2009) found significantly decreased subjective sleep quality, reduced REM density, increased frequency of micro- arousals, more severe apnea-hypopnea in OSA patients compared to individuals without OSA. In summary, there is a two-way effect between REM sleep and OSA.

3.3. Obstructive Sleep Apnea and Gender

OSA is a prevalent sleep disorder that affects people across age groups but it affects males in middle age the most. Among the population of 25 years old and over, 4% men are affected by OSA, which is twice the chance of women having OSA (Kloepfer et al., 2009). Female sex hormones such as progesterone affect respiratory control and correlate with upper airway stability, thus may have protective effect against OSA (Netzer et al., 2003).

Besides the gender difference in the prevalence of OSA, the symptoms OSA are also gender-specific. Women with OSA are more likely to report fatigue and men with OSA are more likely to report sleepiness, while men and women without OSA have similar level of fatigue and sleepiness (Eliasson et al., 2014). The finding suggests the importance of assessing fatigue in order to capture the experience of women with OSA. Nonetheless, unlike the widely endorsed sleepiness evaluation, the assessment of fatigue has not yet been included in recent clinically guideline for the diagnosis and control of OSA. Furthermore, it is suggested that sleepiness and fatigue are two independent symptoms that patients with similar severity of OSA may experience both or either or none of the two (Eliasson et al., 2014). In addition, women have been found to prefer describing their experience of sleep-disordered breathing using terms like fatigue and lack of energy than sleepiness. The possible under diagnosis of OSA among women has been brought to attention and study has showed that the number might be as high as 90% (Lichuan et al., 2009). The under-recognition of OSA in women also has socioeconomic impact. The Centers for Medicare and Medicaid Services (CMS) consider CPAP therapy necessary for patients with mild OSA when appropriate symptoms are present, which include sleepiness but not fatigue. As CMS also set the standard for Medicare coverage which is adopted by other insurance providers, patients with mild OSA but experience fatigue rather than sleepiness may not get appropriate allowance from their insurance providers for CPAP treatment (Eliasson et al., 2014). It is possible that some of the patients with mild OSA that expresses as fatigue, most likely women, will choose not to get CPAP therapy and thus suffer from the detrimental physical health effect and cognitive impairment due to OSA. As mentioned before, night shift promotes the development of OSA symptoms. Therefore, certain occupations that require night shift and rotating shift may have greater need of CPAP treatment. The inappropriate documentation of OSA symptoms and the insufficient insurance allowance because of that may affect these occupations more, such as nurses, who are still predominantly women and work in shifts.

It is mentioned earlier that more severe OSA episodes happen during REM sleep and patients with OSA also have significantly reduced REM sleep. Recent study took a close look at the relationship between REM sleep and OSA and found significant gender differences. Women with OSA experienced significantly less REM sleep and longer latency to the onset of REM sleep compared to men with OSA (Jefferson et al., 2014). The particularly strong interaction between OSA and REM sleep among women may be related to female sex hormone. Netzer et al. (2003) found an association between female sex hormone reduction and higher risk of sleep-disordered breathing (SDB). Specifically, significantly lower levels of progesterone, estradiol, and 17-OH progesterone have been found in women with obstructive sleep apnea/hypopnea syndrome (OSAHS). Therefore, hormone therapy may be an option to treat OSA and abnormalities in REM sleep.

4. An Overview of the Effect of Shift Work

Early study has found that shift workers tend to experience higher level of job stress, more alcohol use, more emotional problems, and poor sleep quality compared to non-shift workers (Gordon, et al., 1986). Female shift workers also reported problems in their social life and an increased use of sleeping pill and tranquilizer. Compared to day shifts, night shifts were found to be associated with higher risk of sleep and digestive disorders as well as disrupted social life (Gordon, et al., 1986). The fact that a large segment of the modern western workforce work on non-standard schedules such as night shifts and rotating shifts has driven an increased volume of clinical and psychology studies on the effect of shift work on workers’ physical and psychological wellbeing for the past few decades (Flo et al., 2012). It has been identified that shift work affects workers in various ways by causing sleep disturbance and circadian rhythm disruption (Marquie and Foret, 1999; Ohayon et al., 2002).

4.1. Shift Work and Sleep Disturbance

Sleep disturbance is among the most important problems of shift work that lasts a long period of time. Workers who currently work during irregular hours reported the highest rates of having difficulties in falling asleep and early awakening compared to former shift workers and non-shift workers, with former shift workers falling in between (Marquie and Foret, 1999). Even after people resume to normal work hours, the sleep disturbance caused by
previous shift work experience does not simply go away. Current shift workers are affected the most by sleep disturbance and have high risk of work-related accidents. Specifically, Ohayon et al. (2012) found that compared to rotating daytime shift, fixed nighttime shift and fixed daytime shift, workers on rotating daytime shift have the highest rate of work-related accidents and sick leave, followed by fixed nighttime shift workers, and with the fixed daytime shift the least prone to accidents. The US National Transportation Safety Board reported that 20-30% of all transportation accidents with injury are due to fatigue, which is one of the most common results of sleep disturbance (Akerstedt et al., 2002). In their population-based study among Canadians, Kling et al. (2010) found the highest increased risk for work injury associated with trouble sleeping among women who work on rotating shifts. Consistent findings have suggested that among all work schedules, rotating shift affects work performance and work safety the most, with changes in relevant variables including higher level of fatigue, loss of concentration, higher rates of heavy smoking, coffee/tea consumption, constipation, job stress, and poor sexual performance (Ohayon et al., 2002; Fido and Ghali, 2008).

The effect of shift work varies a lot from individual to individual. Factors such as gender, age, morningness/eveningness, circadian flexibility/linguidity, and resilience against environmental stressors all play a role in how shift work affects individuals (Flo et al., 2012). Indeed, the effect of shift work shows trait-like qualities that parallels to the effect of OSA, with the subjective experience of individuals differs significantly in correspondence to their personal traits (Eliasson et al., 2014).

Some shift workers exhibit enough symptoms to be diagnosed with shift work disorder (SWD), which is characterized by sleepiness and insomnia due to work schedule. Flo et al. (2012) found that about one third of nurses reported symptoms that meet the criteria of SWD, which is significantly higher than the prevalence found within community sample by Drak and colleagues. This might be partially explained by the interaction between gender and work stress. Akerstedt et al. (2012) has identified female gender, hectic work and physically strenuous work as the shared predictors of sleep disturbance and fatigue, suggesting that women, especially those who has stressful and physically demanding job, are more susceptible to sleep disturbance and fatigue. As nurses are still predominantly female, they fall exactly into this category and are therefore more likely to have SWD than the overall shift worker population. In addition, while non-night shift work is also associated with increased risk of SWD, there is a positive correlation between the number of night shifts and risk of SWD among nurses (Flo et al., 2012). Thus, the researchers recommended putting a limit on the total number of night shifts per year as a way to protect nurses from SWD.

4.2. Shift Work and Circadian Rhythm Disruption

Shift workers experience circadian disruption as their internal circadian rhythm is desynchronized with the circadian rhythm of the outer environment due to their irregular work hours. Nojkov et al. (2010) found that nurses in shift work, particularly rotating shift work, have higher risk of irritable bowel syndrome (IBS) and abdominal pain, of which the pathogenesis is not related to sleep problem but more likely to be a function of circadian rhythm disturbances. In this sense, the stronger association between rotating shift and IBS can be interpreted as that more disrupted circadian rhythm is associated with more severe digestive problem.

4.3. Shift Work and Metabolic Syndrome

Shift workers have been found to have higher risk of cardiovascular disease, obesity, gastrointestinal problems, and abnormal in blood sugar levels, etc (Tucker et al., 2012). These health-related risks of shift work greatly overlap with the symptoms of metabolic syndrome and thus suggest a strong linkage between shift work and metabolic syndrome. Previous studies in Sweden, Italy and Japan have found converging results that support the association between shift work and metabolic syndrome. Tucker et al. (2012) found that individuals with over 10-years experience of rotating shift work have significantly higher risk of metabolic syndrome compared to those who never had shift work experience. Factors that may play a role in the development of metabolic syndrome among shift workers include disrupted circadian rhythms, stress, sleep debt, altered health behaviors, and increased anxiety and depression (Tucker et al., 2012).

4.4. Shift Work and Cognitive Impairment

Sleep problem and circadian rhythm disruption are both identified to have detrimental effect on cognitive functioning. As mentioned in the effect of OSA, sleep disturbance can cause deficits in executive functions, working memory, long-term memory, attention, etc. Current shift workers were found to lower scores in cognitive speed, selective attention and memory than workers who had never worked on shift (Rouch et al., 2005). However, the researchers argued that the reduced cognitive efficiency may be due to the circadian rhythm disruption alone rather than together with sleep disturbance, because no association was found between subjective sleep quality and cognitive performance among the male shift workers assessed. The lack of the association between sleep disturbance and cognitive functioning in this study may be partially due to the effect of gender, since males are less likely to report sleepiness and fatigue compared to females.
Another explanation may be that the instrument used to assess subjective sleep quality is not comprehensive enough to capture the sleep problem of those shift workers and the strong effect of circadian rhythm disruption on cognitive functioning made the effect of the less severe sleep problems undetectable. Studies on jet lag have identified alteration of brain structure that paralleled the memory deficits due to circadian rhythm disruption. Reduced cognitive performance, significantly higher salivary cortisol and smaller volume of the right temporal were observed among flight attendants with more than 3 year’s experience of the job (Rouch et al., 2005). It was also found by Rouch et al. (2005) that former shift workers who have resumed to normal work schedule for more than 4 years showed increased cognitive performance, which may suggest the reversibility of cognitive impairment due to shift work. At the cellular level, Gibson et al. (2010) observed reduction in hippocampal cell proliferation and neurogenesis that paralleled jet-lag induced memory deficits, suggesting that in suggesting that circadian rhythm disruption impairs cognitive functioning by impeding the birth and maturation of new cells.

5. Shift Work, REM Sleep and Obstructive Sleep Disorder

Recent study on medical interns found significantly increased REM sleep, reduced stable sleep, and longer latency of stable sleep during the on-call night shift (Lin et al., 2013). Similar reduction of stable sleep has also been found in patients with OSA. According to Lin et al. (2013), the reduced stable sleep and increased REM sleep during night shift are consistent with the increased sympathetic activity and reduced vagal tone observed in acute sleep deprivation. The increased sympathetic activity and reduced vagal tone are also associated with higher risk of cardiovascular disease which suggests the negative effect of night shift on cardiovascular system. Night shift was also found to worsen OSA by leading to the increase of total duration of obstructive apneas during REM sleep, mean duration of obstructive apneas during arousal, and apnea index during arousal (Laudencka et al., 2007). However, the mechanism behind the adverse effect of night shift on OSA is not clarified yet. Further studies may conduct more parallel analysis of shift work and OSA to identify their interaction on the cellular level.

5.1. Gender and Shift Work and Obstructive Sleep Disorder

Women were found to have higher rate of sleep related complaint due to shift work. As they get older, women are more affected by sleep disturbance due to shift work compared to men as there is a significantly larger increase in women’s consumption of sleeping pills (Marquie and Foret, 1999). The results of Marquie and Foret’s (1999) study, together with the higher rates of SWD and IBS found among nurses (who are mostly women), suggest that women are more severely affected by sleep disorders caused by shift work. As night shift was found to be associated with increased REM sleep and women with OSA were found to have significantly reduced REM sleep compared to men with OSA, it is possible that there are are also gender differences in REM sleep among OSA patients who work night shifts. Future research may work in this direction to find out more about the interactions between OSA, shift work, and gender in REM sleep. Moreover, researchers may investigate if there are any gender differences in cognitive functioning among OSA patients due to the interaction of OSA and night shift.

6. References


