THE UNIVERSITY OF IOWA

LITERATURE REVIEW

Sleep Apnea

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1 PREVALENCE AND DESCRIPTION, RISK FACTORS

Sleep apnea is a common disorder affecting many Americans. One estimate is that 24% of male and 9% of female middle-aged adults suffer from sleep apnea (Friedman, Tanyeri, La Rosa, Landsberg, Vaidyanathan, Pieri and Caldarelli, 1999). Men have a higher apnea risk than females in all age groups. Obesity is a significant risk factor for the disorder (Young, Palta, Dempsey, Skatrud, Weber and Badr, 1993).

An incident of sleep apnea occurs when a patient's upper airway becomes obstructed during sleep. Sleep apnea patients awake frequently during the night as they struggle to breathe. Another symptom is blood oxygen desaturation. Many (but not all) patients experience excessive daytime sleepiness (EDS) as a result of sleep apnea; this symptom is the major complaint of most sufferers (Dement, Carskadon and Richardson, 1978). Airway constriction in sleep apnea is also associated with loud snoring and tossing and turning as the patient repositions him or herself upon awakening. Therefore, sleep apnea is sometimes recognized by a patient's spouse or bed partner before the patient himself makes the connection between his EDS and a possible a sleep disorder. Other reported outcomes of sleep apnea include respiratory failure, hypertension, heart attack, neuropsychological dysfunction, stroke and heart disease (Marrone, Bonsignore, Insalaco and Bonsignore, 1998).

2 MEASUREMENT

There is debate over the most diagnostic criterion on which to judge the severity of sleep apnea. A number of different measurement techniques exist, including:

- oxy-hemoglobin/oxygen desaturation index
- apnea/hypopnea index
- partial arterial pressure of oxygen
- partial arterial pressure of carbon dioxide
- sleep fragmentation
- subjective sleepiness

The apnea/hypopnea index (AHI) is widely used to judge the severity of sleep apnea. It is the number of apneas and hypopneas per hour of sleep. An AHI of 5 is frequently cited as the cutoff for normal breathing during sleep. AHIs over 5 are clinically significant, although one study showed that apneas become more common in old age, and many healthy elderly adults are classified as apneics by this criterion (Berry, Webb and Block, 1984). A study involving a number of measures of sleep apnea indicators showed significant correlations of partial arterial pressure of oxygen and median oxygen desaturation with cognitive impairment as indicated by several psychomotor tests (Findley, Barth, Powers, Wilhoit, Boyd and Suratt, 1986). The number of oxygen desaturations per hour of sleep was not significantly correlated with impairment, and neither were measures of sleep fragmentation. Subjective sleepiness is generally found not to relate to other measures of sleep apnea severity (Dement *et al*., 1978). Sleep apnea sufferers may lose their ability to rate their sleepiness after experiencing long-term daytime sleepiness; Dement *et al*. state that this ability may return with treatment.

3 NEUROPSYCHOLOGICAL EFFECTS

It is not clear what causes performance deficits in sleep apnea patients. The most obvious explanation is that the patients are simply too exhausted to perform well on cognitive and psychomotor tests. If this is the case, sleep apnea patients should not perform differently from normal study participants who have been deprived of sleep. Apnea patients were compared with people who suffered from EDS but who did not exhibit apnea (Greenberg, Watson and Deptula, 1987). The apnea patients scored worse than the other participants with EDS on 15 out of 17 neuropsychological tests, including a number of tests from the Wechsler Adult Intelligence Scale—Revised and some memory tasks. The authors attributed apneics' greater difficulty with the neuropsychological tests to hypoxemia, from which the apneics suffered but the controls did not. Similar performance deficits are often seen in chronic obstructive pulmonary disorder patients, who experience consistent hypoxemia. Sleep apnea patients experience oxygen desaturation only during the night, but interestingly, in this study, performance was significantly positively correlated ($r = 0.59$) with the duration of the sleep apnea illness. This may indicate a cumulative effect of oxygen desaturation in sleep apnea.

Sleep apnea patients suffering from hypoxemia scored significantly worse than apnea patients without hypoxemia on a number of cognitive tests in one study (Findley *et al.*, 1986). These tests included memory tasks, vigilance and coordination tasks and Trails B from the WAIS-R, which measures attention and concentration. In another study with 10 apnea patients and 10 controls (Feuerstein, Naegele, Pépin and Levy, 1997), sleep apnea appeared to have no effect on tests of very short duration requiring focused attention (such as Trails A and B and letter cancellation). Short- and long-term visual and verbal memory tasks were impaired in the apnea patients, and the authors speculate that the memory problem in sleep apnea stems from difficulty in encoding information rather than forgetting it.

4 DRIVING INCIDENTS

In one study of sleep clinic referrals, one third of sleep apnea patients reported "near misses" or accidents, compared to 7% of control patients, who completed sleep studies at the clinic but were shown not to have sleep apnea (Gonzalez-Rothi, Foresman and Block, 1988). Case studies (Findley, Weiss and Jabour, 1991) also indicate that untreated sleep apnea, marked by loud snoring and chronic fatigue, is regarded as a cause of accidents occurring when the driver falls asleep at the wheel. Severe sleep apnea (as evidenced by AHI>40) has been associated with increased accident risk (George and Smiley, 1999), while the disorder in its less severe manifestations did not appear to impact accident rates.

Seventy-seven patients referred to a sleep clinic completed sleep studies; 38 were diagnosed with sleep apnea, and 39 did not exhibit apneas during sleep (Findley, Unverzagt and Suratt, 1988). All of the patients had been referred to the clinic with complaints of daytime sleepiness, loud snoring and sleep disturbances. DMV records were requested for all 77 of the patients for the five years prior to referral. The sleep apnea patients had seven times the rate of car accidents of the non-apneic referrals. Apnea patients also had significantly more at-fault accidents than and had accumulated more traffic citations than the other group. Accident rates in the apnea patients were also much higher than those in the general population of the state in that time period. Five of the apnea patients admitted to having caused accidents by falling asleep; none of the other patients admitted having done so. Twenty-five percent reported falling asleep at least once a week while driving.

An on-the-road driving study with an instrumented vehicle showed that a group of ten professional bus drivers who suffered from mild and untreated sleep apnea had significantly longer mean blink durations than healthy control bus drivers (Häkkänen, Summala, Partinen, Tiihonen and Silvo, 1999). No performance measures or other eye measures were collected in this study.

5 SIMULATED DRIVING

A PC-based vigilance task called "Steer Clear" (Findley, Unverzagt, Guchu, Fabrizio, Buckner and Suratt, 1995) is the most commonly cited "driving simulation" used in the sleep apnea literature. Participants in a Steer Clear study "drive" for 30 minutes, during which an animated vehicle moves along a road on a computer screen. The only response required of the participant is that he or she press the space bar in order to change lanes and miss obstacles that appear on the road. Obstacles are presented at pseudo-random intervals between 2 seconds and 2 minutes apart. Seven hundred eighty of these obstacles appear during the 30-minute task. The single performance measure in Steer Clear is the number of obstacles hit (not avoided). Steer Clear is not a particularly good driving simulation; it does not have the divided attention requirements of the driving task. However, performance on Steer Clear is related to the number of accidents caused by sleep-disordered drivers (Findley *et al.*, 1995).

In Steer Clear testing, sleep apnea patients hit more obstacles than matched control participants hit. Percentage of obstacles hit by the sleep apnea patients also increased linearly with apnea severity, as measured by oxyhemoglobin desaturation. Steer Clear performance was also significantly positively correlated with oxyhemoglobin desaturations per hour of sleep and apneas plus hypopneas per hour of sleep (Findley *et al.*, 1995).

Seven hundred eighty obstacles per 30 minute drive equates to obstacles appearing 26 times per minute. Therefore, it is not accurate to describe Steer Clear as a vigilance task in the tradition of Mackworth, who presented participants with much more infrequent signals in his vigilance tasks. To address this problem, three hundred obstacles per 30 minute drive were presented in another study (Randerath, Gerdesmeyer, Siller, Gil, Sanner and Rühle, 2000), but even this change does not make Steer Clear a vigilance task with very infrequent signals. In this study, non-apneic participants who suffered from occasional breathing obstructions during sleep hit significantly more obstacles than participants who only snored or did not snore or have occasional apneas.

6 TREATMENT AND ITS EFFECTS ON DRIVING AND PERFORMANCE

There are two main treatments for sleep apnea. One is nasal continuous positive airway pressure (CPAP), in which patients wear a mask while they sleep and receive constant flow of air pressure from a bedside machine; this keeps a patient's airway from closing and obstructing breathing. CPAP is generally well tolerated. Common complaints include sore throat and chafing associated with the mask that covers mouth and nose. Nasal congestion has been reported in as many as 35% of patients (George, 2001).

In a study of consecutive admissions to a sleep clinic, fourteen patients elected not to begin CPAP therapy and were used as controls for 36 patients who agreed to try it. DMV records were obtained for all of the patients for the two years prior to and the two years following diagnosis. Seven of the 50 patients had been involved in accidents involving more than $500 property damage and a citation for the patient in the two years prior to diagnosis. This resulted in a high crash/driver/year rate compared to the rest of the population of the state. Post-diagnosis, none of the CPAP patients were involved in accidents, and two of the CPAP refusers were involved in accidents. Steer Clear performance (in Findley, Fabrizio, Knight, Norcross, Laforte and Suratt, 1988; see above) improved significantly with 3-5 months of CPAP therapy—patients hit significantly fewer obstacles after treatment than before. However, patients with very mild sleep apnea apparently do not benefit greatly from CPAP treatment—neither subjective sleepiness nor sleep latency in the Multiple Sleep Latency Test improved in patients with fewer than 15 apneas/hypopneas per hour of sleep (Engleman, Martin, Deary and Douglas, 1997).

A PC-based simulator has been used by Hack and colleagues (Hack, Davies, Mullins, Choi, Ramdassingh-Dow, Jenkinson and Stradling, 2000) to test the effects of CPAP on "driving" performance. This simulator has a steering wheel with which participants guide a simulated vehicle down a road while responding to digits that appear in the corners of the screen. Therefore, it taps some of the divided attention aspects of real driving not addressed in Steer Clear. Apnea patients treated with CPAP for one month improved their performance significantly in terms of standard deviation of lateral position in this task, but reaction time and number of off-road events did not change significantly.

Significant reductions in accident rates per patient per year were maintained for as long as three years in a group of 182 CPAP-treated patients. Accident rates in a group of matched controls did not change over the same period of time (George, 2001). The greatest reductions were observed occurred in patients who had been involved in multiple accidents in the three years before their apnea diagnoses.

A more invasive approach to sleep apnea treatment is a surgery called uvulopalatopharyngoplasty (UPPP). UPPP is directed at physically removing the parts of the throat that may obstruct breathing when patients sleep. Soft tissue from the back of the throat, the tonsils, the uvula and any extra tissue is removed. The surgery increases the size of the airway so that it is more difficult for it to close completely. The surgery requires general anesthesia and an overnight hospital stay, and recovery is prolonged, so it is not an ideal choice for every patient. Additionally, one study has shown that patient mortality following UPPP is no different from mortality in untreated sleep apnea, while

CPAP and tracheostomy (discussed below) led to increased survival rates (He, Kryger, Zorick, Conway and Roth, 1988). This finding was attributed by the authors to the fact that UPPP patients receive less follow-up care after undergoing the surgery. CPAP and tracheostomy patients were followed up more thoroughly.

However, UPPP does seem to impact driving performance in a positive manner. Thirteen middle-aged male patients drove in a moving-base driving simulator in Sweden before undergoing surgery. They drove on a curving, narrow road for about 90 minutes and had to respond to 25 visual brake stimuli during the drive. Performance was measured in terms of lane position deviation, off-road incidents and brake reaction time to the brake stimuli. Self-reported drowsiness was also assessed with a visual analogue scale. Patients showed significant improvement on all of these measures when they were retested an average of 45 months after receiving UPPP surgery (Haraldsson, Carenfelt, Lysdahl and Törnros, 1995).

A less common surgical therapy for sleep apnea is tracheostomy. Tracheostomy brings relief from airway closure in some sleep apnea patients because it opens the airway below the point at which the apneic blockage typically occurs. However, tracheostomy may be rejected by many patients because of the "social and permanent maintenance problems involved" with having a visible opening in the neck and preventing it from closing over time (Haapaniemi, Larikainen, Halme and Antila, 2001; p. 132). It is often a treatment of last resort after UPPP has failed to produce lasting results and when patients reject CPAP. Tracheostomy can be a dangerous procedure in obese patients (and many sleep apnea patients are obese). Recurrent respiratory infections are also observed in patients who have undergone a tracheostomy.

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