The Effects of Untreated and Treated Obstructive Sleep Apnoea on Subjective

Sleepiness, Microsleeps, Simulated Driving Performance and Neurocognitive

Functioning

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Declaration

"I declare that this report is an original piece of research, conducted by myself and does not contain data or materials which have been previously submitted by myself or anyone for academic credit. I further declare that this report does not contain any materials previously presented by myself or another persons, except where due reference is made in the text. This study was conducted with the full approval of the ethics committee of the Department of Psychology, of Victoria University."

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Acknowledgements

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Abstract

Obstructive sleep apnoea (OSA) is a complex disorder of neural respiratory control and upper airway dysfunction that results in repeated complete and partial occlusion of the upper airway during sleep. Obstructive sleep apnoea has been linked to fatigue, increased rates of road and work-related accidents and deficits across a range of neurocognitive domains. The most widely used treatment for OSA is continuous positive airway pressure (CPAP). This study aimed to compare neurocognitive functioning, simulated driving performance, vigilance, objective and subjective sleepiness in patients with moderate to severe OSA with control participants before and after treatment with CPAP. It was hypothesised that patients with OSA would report higher levels of subjective sleepiness, perform poorer on a simulated driving task and neurocognitive tests, demonstrate reduced vigilance and reaction times, and show increased objective sleepiness in comparison to control participants. It was also hypothesised that performance in these tasks would improve in OSA patients following CPAP treatment. Fifteen patients (12 males and 3 females) with moderate to severe OSA between the ages of 40 and 71 were recruited from the Austin and Repatriation Medical Centre and 15 healthy controls (12 males and 3 females) aged between 37 and 70 matched for gender and closely matched for age and weight were recruited from the community. Participants were assessed on a driving simulator, psychomotor vigilance task and a battery of neurocognitive tests. The results showed that OSA patients displayed significant impairments related to daytime sleepiness and a novel finding of this study was that OSA patients demonstrated a lowered capacity for procedural learning. The current study also found that following CPAP treatment, OSA patients improved on measures of sustained attention, reaction time, simulated driving performance, memory and procedural learning. Findings of the present study

indicate the importance of detecting impairments relating to performance in OSA patients in order to minimise the risk of accidental injury to themselves or others. Increased sleepiness and deficits in simulated driving and neurocognitive tasks may be alleviated with CPAP treatment. Continued research into this area is warranted so that significant consequences for the quality of life of patients and for other road users can be identified.

Introduction

Sleep

Sleep is a universal phenomenon and is essential for survival. Human sleep has three basic characteristics: (1) it is a brain process; (2) it is an active process; and (3) it is not a single process (Ambrogetti, 2000; Hirshkowitz, Moore, & Minhoto, 1997; Shneerson, 2000). However, the behavioural inactivity that occurs during sleep has led to the belief that mental activity also ceases during this process (Ambrogetti, 2000). This misconception is based on the idea that, since humans cannot recall their thoughts or the events that occurred during the interval between going to bed and rising, they are mentally inactive during this period. This is not the case; the fact that humans have some memory for dreams suggests that mental activity occurs during the sleep phase (Hirshkowitz et al., 1997).

Electroencephalogram and Sleep

While spontaneous electrical discharges in the brains of animals were reported as early as 1875 by English physiologist Richard Caton, the first recordings from human brains were performed by Austrian psychiatrist Hans Berger in 1929 (Bear, Connors, & Paradiso, 2001). A series of papers followed and confirmed that the electrical activity was derived from neuronal tissue, that it responded to sensory stimulation and that abnormal discharges occurred during epileptic seizure (Mendelson, 1987). Berger used the term electroencephalogram (EEG) to refer to his recordings of electrical activity of the cerebral cortex.

Electroencephalogram activity is characterised by both the amplitude and the frequency of the waves. Amplitude refers to how high the waveform is on the paper tracing and indicates how much electrical activity is occurring at any one time (Widmaier, Raff, & Strang, 2004). These waveforms are usually measured in microvolts (μV) and may range from 0.5 to 100 μV. Frequency refers to how often the wave cycles from its maximal amplitude to its minimal amplitude and back, and is measured in Hertz (Hz or cycles per second) (Bear et al., 2001). The more cycles per second, the faster the EEG frequency.

Electroencephalogram rhythms vary dramatically and often correlate with particular states of behaviour, such as level of attentiveness, sleeping or waking and pathological states, such as seizures or coma (Widmaier et al., 2004). The EEG rhythms are generally divided into the following four categories according to their frequency range: beta rhythms are fastest (greater than 14 Hz) and signal an activated cortex; alpha rhythms (8-13 Hz) are associated with quiet, waking states; theta rhythms (4-7 Hz) occur during some sleep states; and delta rhythms (less than 4 Hz), which are quite slow, are a hallmark of deep sleep (Bear et al., 2001).

Stages of Sleep

Sleep is commonly studied by recording brain electrical activity with EEG. In 1937, Loomis, Harvey, and Hobart described the results of 30 all night human EEG recordings and discovered that sleep is made up of a series of discontinuous stages (Mendelson, 1987). Although the classification has since evolved, the basic principle that sleep is made up of discrete, recurring stages, regulated by neural mechanisms, is fundamental to modern sleep research (Mendelson, 1987).

Full-night polysomnography studies are commonly performed on most patients suspected of having a sleep-related breathing disorder (Bassiri & Guilleminault, 2000). The polygraph records three types of data: the EEG (brain-wave), the electrooculogram (EOG; eye movement), and the electromyogram (EMG; submental chin muscle tone) (Ancoli-Israel, 1997). However, other information is also gathered, including respiratory effort, airflow from nasal pressure, nasal temperature, expired carbon dioxide, oxygen saturation, heart activity (electrocardiogram), pulse rate, posture, sound or objective snoring intensity and video recording (Bassiri & Guilleminault, 2000; Douglas, 2000). Determination of sleep stage is based on the combined information from the EEG, EOG, and EMG (Ancoli-Israel, 1997).

Waveform activity is read over a specified time frame, called an epoch (usually 20 or 30 seconds long). The most widely accepted criteria for categorising different sleep stages were published by the National Institutes of Health in 1968 (Hirshkowitz et al., 1997). Each polygraphic epoch is classified as wake, Stage 1, Stage 2, Stage 3, Stage 4 or rapid eye movement (REM) sleep. As described by Douglas (2002) and Widmaier et al. (2004), these stages are characterised as follows.

Wake

During alert wakefulness, with the eyes open, the EEG shows beta rhythm (faster than 13 Hz) predominantly in frontal and parietal areas. During relaxed wakefulness, with the eyes closed, the EEG is characterised by alpha waves (8-13 Hz), which is especially apparent over the occipital area, intermixed with lower amplitude irregular beta waves. With increased sleepiness, alpha slows and may

extend forward over the head, with beta activity becoming more prominent frontally. Slow rolling eye movements are a prominent feature of drowsiness.

Non-REM Sleep

  Stage 1.

  Alpha activity in stage 1 (Figure 1) is significantly decreased to less than 50 percent of the participant's 'normal' recording. A low-amplitude, mixed-frequency pattern is predominantly beta with the development of slower, central theta activity (4-7 Hz). Slow eye movements are evident on the EOG and there is a gradual reduction in EMG tone. As the person progresses toward stage 2 sleep, the slower activity predominates.
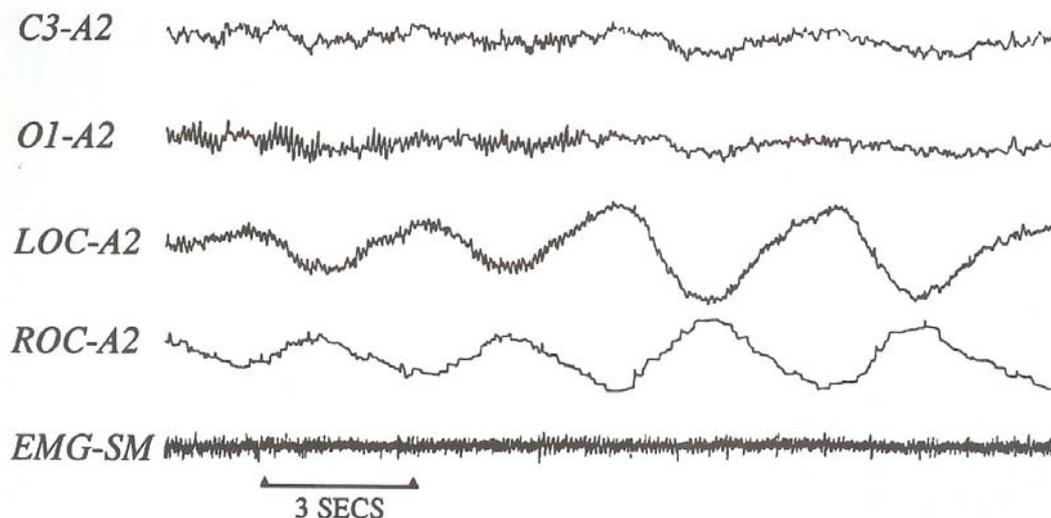
Figure 1. Sleep onset with EEG alpha disappearance and slow eye movements present. The two top tracings show central (C3) and occipital (O1) EEG activity electrically referenced to the mastoid (A2). Eye movement activity is provided by LOC-A2 and ROC-A2, which refer to the left and right outer canthi, respectively. Submental electromyographic activity (muscle tone) is denoted by EMG-SM. (Hirshkowitz et al., 1997)

Stage 2.

Stage 2 consists largely of theta background, and is characterised by the appearance of two types of intermittent events: spindles and K complexes (Figure 2). A spindle is a brief burst of rhythmic 12-14 Hz activity, with a duration of 0.5 seconds or more. A K complex is a high-amplitude sharp negative (upward) wave directly followed by a positive (downward) wave, the whole complex lasting at least 0.5 seconds. Sleep spindles often follow a K complex. The presence of spindles and K complexes in the absence of significant slow wave activity (20 percent of the epoch) essentially defines Stage 2 sleep.
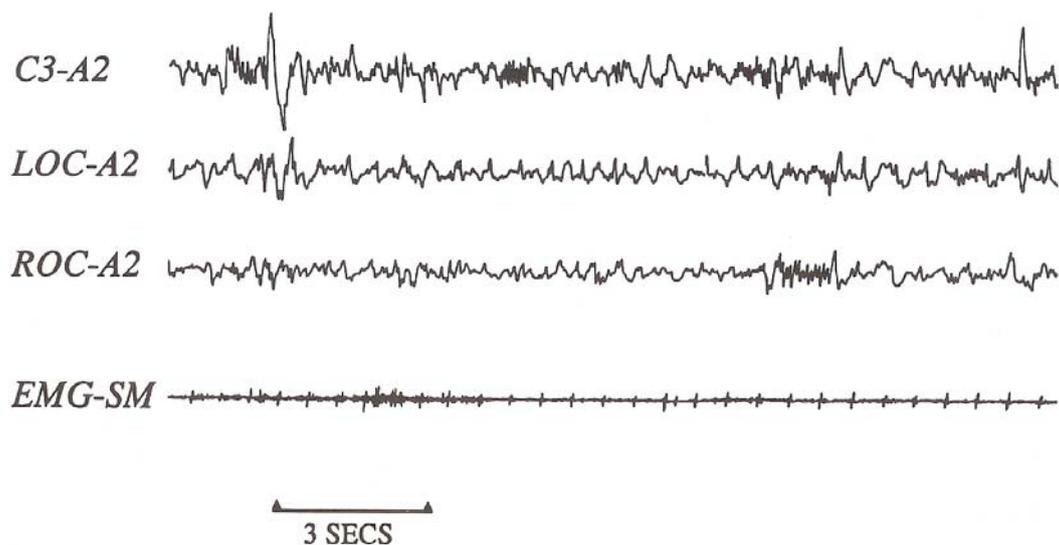
Figure 2. K complex and sleep spindle activity during Stage 2 sleep. The recording segment illustrates a K complex preceded by a spindle (the first 3 secs of recording). C3 is monopolar central EEG referenced to the mastoid (A2); LOC-A2 is left electrooculogram; ROC-A2 is right electrooculogram; and EMG-SM is submental electromyogram. (Hirshkowitz et al., 1997)

Stages 3 and 4.

Stage 3 and 4 are characterised by the appearance of high amplitude and slow delta waves (less than 4 Hz). Together, these stages are often referred to as slow-wave sleep (SWS) or delta sleep. Delta activity (Figure 3) is the slowest EEG activity to occur during sleep and may be the most salient sleep-related EEG feature in humans. Stage 3 sleep is determined when delta activity occurs for between 20 to 50 percent of the epoch. In Stage 4, delta activity makes up more than 50 percent of the recording epoch. Sleep spindles may or may not be present during Stages 3 and 4. In both stages slow eye movements are absent and EMG tone is reduced to a similar extent as it is during Stage 2.
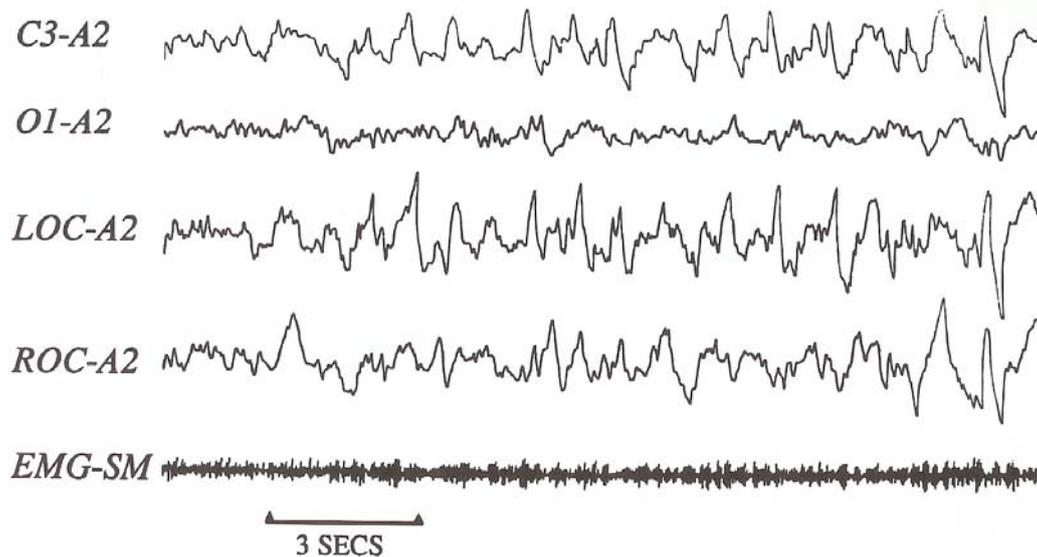
Figure 3. EEG delta activity during slow-wave sleep. C3 and O1 are monopolar central and occipital EEG, respectively, referenced to the mastoid (A2); LOC-A2 is left electrooculogram; ROC-A2 is right electrooculogram; and EMG-SM is submental electromyogram. (Hirshkowitz et al., 1997)

REM Sleep

During REM sleep (Figure 4), the EEG returns to a low-amplitude, mixed frequency pattern similar to that seen in Stage 1. This activity is thought to reflect generally increased cerebral activation. In contrast to Stages 2, 3 and 4, there are no sleep spindles, K complexes, or significant delta activity. There is a marked reduction in EMG tone and if intermittent conjugate rapid eye movements are present, REM sleep is scored.
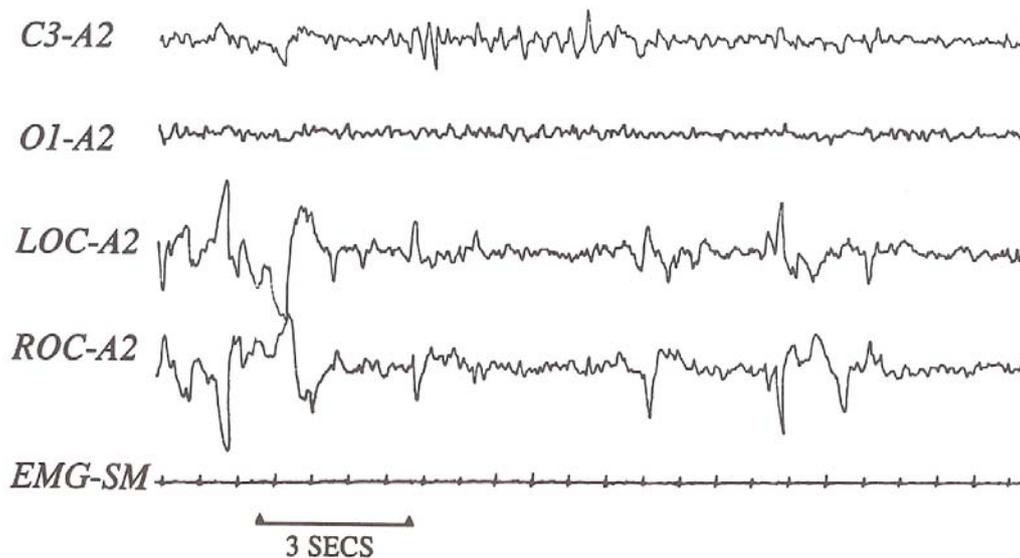
Figure 4. REM sleep with EEG theta activity. The partial epoch begins with a burst of rapid eye movements apparent from the deflections recorded on LOC-A2 and ROC-A2 (left and right outer canthi, respectively, referenced to the mastoid). Central EEG (C3-A2), but not occipital (O1-A2), shows well formed theta activity approximately in the centre of the tracing. Submental electromyogram (EMG-SM) shows typical near absence of activity associated with REM sleep. (Hirshkowitz et al., 1997)

Normal Sleep Pattern

When sleep stages are plotted as a function of time, distinct patterns emerge. The most obvious pattern is an alternation of NREM and REM sleep stages, occurring approximately every 90-120 minutes (Figure 5). Most SWS occurs in the first third of the night, and most REM sleep occurs in the second half of the night. Sleep normally begins with a progression through NREM sleep stages, followed by REM sleep, which occurs in approximately four to six discrete episodes each night.
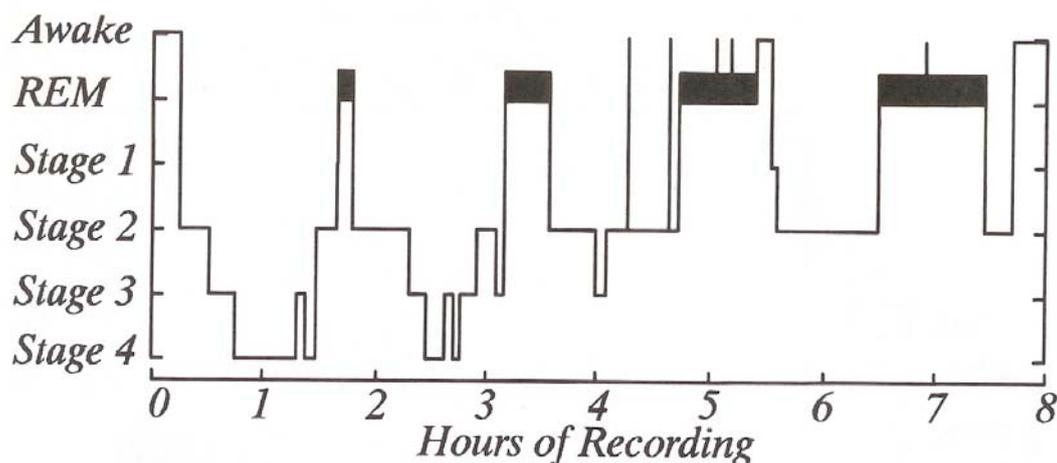
Figure 5. The normal sleep pattern of a young adult over 8 hours of sleep. (Hirshkowitz et al., 1997)

Circadian Rhythms

Daily rhythms in behavioural, physiological and biochemical processes are observed in all living organisms. The most common type is the circadian rhythm, which recurs more or less at a regular interval (Campbell, 1997). In response to the natural alternation of day and night, most species have developed an endogenously

mediated circadian rhythms that vary on a cycle of approximately 24 hours (Kleitman, 1987; Widmaier et al., 2004). These rhythmic processes appear to be vital to the overall well-being of organisms (Campbell, 1997).

Many of these endogenous rhythms are controlled by mechanisms within the organism, that is, by an internal pacemaker, oscillator or biological clock, which is located in the supra-chiasmic nucleus of the hypothalamus (Bear et al., 2001; Shneerson, 2000). Recent research on human circadian rhythms has been concerned with issues regarding the mechanisms and implications of these rhythms, such as on shift workers (Akerstedt, 1988; Monk et al., 1997). Physiological variables are often based upon an analysis of blood or urine of the subject, enabling the concentration of various hormones, such as cortisol and melatonin, or electrolytes, such as sodium and potassium, to be obtained over time (Mendelson, 1987).

Core body temperature (Tc) is often recorded because of its stability and relative ease of measurement (Bear et al., 2001). For these reasons, Tc has essentially become the benchmark rhythm used in most human circadian rhythm research (Campbell, 1997; Mendelson, 1987; Monk et al., 1997). Studies of the Tc rhythm have indicated that maximum alertness occurs near the peak (Monk et al., 1997) and as Tc starts to fall, drowsiness ensues. When Tc reaches the nadir, defined as the point at which the Tc is at its minimum (Campbell, 1997), sleepiness can be overwhelming. When Tc starts to rise, sleepiness decreases and alertness increases. The cycle begins again when Tc reaches its maximum during the day.

Humans show a diurnal rhythm, where they have a need to sleep at night, and to become active and productive as they wake from sleep in the morning (Monk et al.,

1997). A lack of synchrony between this biological rhythm and the scheduled bedtime can impair nocturnal sleep (sometimes producing insomnia) and diurnal alertness (sometimes causing hypersomnolence) (Kleitman, 1987). In addition, human sleep is viewed as a diphasic system (Campbell, 1997). In other words, there are two specific episodes of peak sleepiness in the circadian cycle which coincide with the Tc rhythm (Lavie & Weler, 1989); one between 1400 and 1600 hours, and the other between 0100 and 0600 hours (Aschoff, 1994). These periods lead to an increase in sleepiness and a decrease in performance, vigilance and emotional output (Monk et al., 1997).

Obstructive Sleep Apnoea

The maintenance of life depends on a continual supply of oxygen. Oxygenation of all bodily tissues is achieved by means of the reciprocal exchange of oxygen and carbon dioxide in the lungs (Sherwood, 1997). Oxygenation of cerebral tissues is particularly critical. The brain only accounts for two percent of total body mass, but consumes approximately 20 percent of the oxygen taken in by the body in resting state (Sherwood, 1997). Cessation of oxygen to cerebral tissues (anoxia), such as experienced in cardiac arrest, can have a devastating effect on the brain and other tissues (Kelly, Claypoole, & Coppel, 1990). Sustained reduction of oxygen supply (hypoxia or hypoxemia), such as experienced in chronic obstructive pulmonary disease, results in reduced tissue oxygenation that can also impair brain function (Kelly et al., 1990). The effects of intermittent hypoxia in patients with sleep disordered breathing are less well understood.

Obstructive sleep apnoea (OSA) is a complex disorder of neural respiratory control and upper airway dysfunction that results in repeated complete and partial occlusion of the upper airway during sleep (Orr, 1997). It is associated with quantity and quality of sleep (Sauter et al., 2000) and is a common cause of excessive daytime sleepiness. Obstructive sleep apnoea has become the most frequently studied condition in sleep clinics.

What is now commonly known as the OSA syndrome was initially described by Burwell in 1956 (Burwell, Robin, Whaley, & Bikelman, 1956). Burwell and colleagues described an obese patient who presented with carbon dioxide retention, somnolence, and polycythemia (marked increase in red cell mass and blood volume). The fundamental pathogenesis was attributed to simple hypoventilation, secondary to obesity-related chest wall constriction (Burwell et al., 1956). The authors originally termed this the Pickwickian syndrome, after the character in the Dickens novel who could not stay awake on the job (Kelly et al., 1990). It was not until several years later that individuals meeting the criteria, as described by Burwell, were found to actually have upper airway obstruction during sleep (Gastaut, Tassinari, & Duron, 1965).

Obstructive sleep apnoea has been linked to daytime sleepiness, impaired daytime concentration, fatigue, increased irritability and depression, hypertension, stroke, ischemic heart disease, and premature death (Douglas & Polo, 1994). The incidence of OSA increases after the age of 40 and is more common in men than in women. In the middle-aged population, it has been shown to affect approximately 25 percent of males and 9 percent of females (Young et al., 1993). An Australian study showed the prevalence of OSA in men was 8.5 percent and in women it was 4.7

percent (Bearpark et al., 1993). The combination of relatively high prevalence and

serious health consequences has led to the view that OSA may be just as big a public

health hazard as cigarette smoking (Walling, 1997).

Obstructive sleep apnoea is characterised by apnoea and hypopnea and is

associated with daytime hypersomnolence, impaired daytime concentration, increased

rates of road and work-related accidents, and a predisposition to cardiovascular

disease and cerebrovascular accidents (Douglas & Polo, 1994; Tangugsorn, Krogstad,

Espeland, & Lyberg, 2000). An apnoeic event is defined as an involuntary cessation

of breathing due to narrowing of the upper airway during sleep, that usually lasts for

at least 10 seconds (Bassiri & Guilleminault, 2000; Wright, Johns, Watt, Melville, &

Sheldon, 1997). Hypopnea refers to a reduction in airflow to less than 50 percent of

baseline for a minimum of 10 seconds and is usually associated with arterial oxygen

desaturation of 4% or 3% in some laboratories (Bassiri & Guilleminault, 2000;

Tangugsorn et al., 2000). In symptomatic OSA, a repetitive series of events occurs

many times each night while the person is asleep (Bradley & Phillipson, 1985).

In understanding how the upper airway remains patent or becomes

progressively diminished in circumference, eventually leading to complete occlusion,

it is necessary to understand the factors that occur naturally to keep the airway open

(Orr, 1997). In healthy individuals, each inspiratory effort is associated with a

collapsing negative pressure and a simultaneous burst of activity from a variety of

upper airway muscles that serve to prevent collapse (Orr, 1997). When an individual

with OSA falls asleep, there is an occlusion in the upper airway that results in the

cessation of airflow, even though respiratory efforts are continued (Bradley &

Phillipson, 1985). As a consequence of the apnoeic events, asphyxiation progresses

until the patient is briefly aroused from sleep, in which case the apnoea is terminated, upper airway patency returns to normal and airflow resumes (Bradley & Phillipson, 1985). With breathing restored to normal and asphyxia terminated, the patient usually returns to sleep promptly. This sequence of apnoeic events is repeated throughout the night. A number of pathogenetic mechanisms contribute to this primary sequence of events (Bradley & Phillipson, 1985). Bradley and Phillipson (1985) identified the following three phases: (1) the onset of the apnoea; (2) the progression of asphyxia during the apnoea; and (3) the termination of the apnoea.

With the onset of sleep in normal individuals, there is a gradual increase in upper airway resistance that can lead to a decrease in inspiratory airflow (Wiegand, Zwillich, & White, 1989). The airway is anatomically narrow however it is limited in normal individuals during sleep by compensatory mechanisms such as increases in upper airway tone reflexes (Chadwick, Crowley, Fitgerald, O'Regan, & McNicholas, 1991). Cerebral arousal into wakefulness increases the activation of dilator muscles in order to restore airway patency (Chadwick et al., 1991).

At sleep onset in OSA patients, an increased susceptibility to upper airway closure because of abnormal anatomical structure and/or an imbalance of forces between maintaining upper airway patency and collapse results in a reduction in tone of the dilator muscles (Bradley and Phillipson, 1985). The airway narrowing results in snoring, hypoventilation and complete occlusion of the upper airway (Wiegand et al., 1989). The increase in upper airway resistance and decrease in inspiratory airflow is particularly apparent during REM sleep, thus explaining the tendency for OSA to first progress in, and to be most severe during, this particular stage of sleep (Boudewyns et al., 1999). During apnoeic periods significant oxygen desaturation

may occur. In order to compensate, the diaphragm increases effort to resolve the imbalance, leading to the development of more negative intrathoracic and oropharyngeal pressures in most cases until arousal from sleep occurs and obstruction to the airway is overcome by increased tone of the upper airway dilator muscles (Guilleminault, 1987). When sleep resumes airway obstruction may recur, resulting in a cycle of airway obstruction and arousal from sleep.

This cyclical process accounts for the large number of episodes experienced during an average night of sleep. The repetitive apnoeic events change the structure of sleep. Abnormal amounts of time are spent in Stage 1 or Stage 2 sleep and there is significantly reduced or absent periods of slow wave sleep (Stages 3 and 4) (Kelly et al., 1990). Sleep fragmentation and intermittent cerebral hypoxia increases the duration of apnoeic episodes and results in daytime sleepiness (Kelly et al., 1990). The number of apnoeic events suffered per hour of sleep is the most common method measuring the severity of OSA and has also been considered the best predictor of daytime sleepiness by some authors (Bedard, Montplaisir, Richer, Rouleau, & Malo, 1991; Tangugsorn et al., 2000).

Diagnosis of obstructive sleep apnoea.

There is some disagreement amongst clinicians regarding the diagnosis of OSA. The American Academy of Sleep Medicine proposed that a respiratory disturbance index (RDI) of at least five apnoeic events per hour along with daytime sleepiness defines OSA, although a number of clinicians use an RDI of at least 10 (American Academy of Sleep Medicine, 1999; Cirignotta, Zucconi, Mondin, Gerardi, & Lugaressi, 1989).

Snoring is a near-universal feature of OSA and is probably the most common cause of referral for sleep evaluation (Mendelson, 1987). When hypoxia and hypercapnia worsen during an apnoeic event, respiratory efforts become vigorous. Noisy pharyngeal snoring, associated with staccato-like snorts, serves to break the apnoea, albeit temporarily (Kelly et al., 1990). Other nocturnal manifestations of OSA include motor restlessness, excessive sweating, enuresis, sleep talking, sleep walking, and cerebral hypoxic attacks resembling seizures (Kelly et al., 1990).

Excessive daytime sleepiness (hypersomnolence) is another ubiquitous feature of the disorder, making such activities as driving or operating machinery extremely hazardous (Bearpark et al., 1995). Individuals with OSA are often in a 'twilight zone' much of the time, having difficulty differentiating sleep and quiet wakefulness (Kelly et al., 1990). Other diurnal manifestations associated with OSA include persistent headaches, irritability and mood disturbance, personality changes, severe vocational and marital problems, and reduced concentration and attention (Harding, 2000). Impotence in males and decreased libidinal drive in both sexes is common (Hirshkowitz, Karacan, Gurakar, & Williams, 1989).

Obstructive sleep apnoea and hypoxemia.

Obstructive sleep apnoea not only induces multiple awakenings during the night, but the syndrome also causes desaturation of blood oxygen levels (Bedard et al., 1991). Bradley and Phillipson (1985) suggest that oxygen desaturation occurs during the progression of asphyxia and produces the most serious immediate clinical features of upper airway occlusion. Therefore, daytime somnolence and impaired

cognitive function may either be a reflection of sleep disruption or nocturnal

hypoxemia, or a combination of the two factors.

Recent studies have investigated the relative contribution that sleep disruption

and nocturnal hypoxemia make to daytime sleepiness (Bedard et al., 1991; Poceta,

Jeong, Ho, Timms, & Mitler, 1990). Poceta et al. (1990) found that hypoxemia may

be the primary pathogenetic factor of somnolence in more severe cases of OSA.

However, in more mild forms of the syndrome, sleep disruptions contribute more to

daytime sleepiness. Therefore, both factors appear to contribute to vigilance

impairment in people with OSA, with the relative contribution of each factor

dependent on the severity of the disorder (Poceta et al., 1990). Bedard et al. (1991)

also found measures of hypoxemia to be the best predictors of daytime sleepiness and

alertness in moderate to severe OSA patients.

Anatomical changes in obstructive sleep apnoea.

In patients with OSA, the regions behind the soft palate and the tongue are the

major sites of airway collapse (Bradley & Phillipson, 1985). Imaging studies

examining this area have found that the cross-sectional area of the airway is

consistently reduced in patients with OSA in comparison to normal control subjects

(Bradley & Phillipson, 1985). In OSA patients, the physiological changes induced in

upper airway muscle function during sleep and their structurally smaller pharynx

significantly increases the tendency for their airway to collapse (Bradley & Phillipson,

1985).

Two mechanisms have been proposed to account for the smaller airway lumen in patients with OSA (Bradley & Phillipson, 1985; Miyamoto et al., 1999). Firstly, an important anatomical factor, often related to the development of OSA, is the dimensions of the lower face, which tends to be smaller in patients with the syndrome (Miyamoto et al., 1999). Secondly, obesity plays a major role in accounting for a smaller lumen (Bradley & Phillipson, 1985; Tangugsorn et al., 2000) and will be discussed in the next section.

Detailed cephalometric measurements in patients with OSA have shown subtle degrees of underdevelopment and changes in the craniofacial bony structure (Bradley & Phillipson, 1985). Paoli (2001) found that retropositioning of the maxilla and mandible resulted in narrowing of the upper airway. Mandibular posture is believed to be related to upper airway narrowing, due to mouth opening being associated with movement of the mandible in an inferior-posterior fashion (Miyamoto et al., 1999). Miyamoto et al. (1999) found that mandibular posture was more open during sleep in OSA patients and this was more progressive during apnoeic episodes. Other studies have also found differences in craniofacial morphology between obese and non-obese patients, which may contribute to both the development and severity of OSA (Paoli et al., 2001; Tangugsorn et al., 2000).

Obstructive sleep apnoea and obesity.

In Western societies, obesity is rapidly becoming a major public health problem and a body mass index ([BMI] weight in kg/height in m^2) of greater than 28 is present in approximately 60 percent of patients diagnosed with OSA (Bissiri & Guilleminault, 2000; Richman et al., 1994). With increased obesity, oxyhaemoglobin

saturation decreases due to lung restriction and increased work of breathing, and may in turn, result in OSA (Richman et al., 1994).

Upper airway apnoeas have been found to result from purely structural abnormalities such as excessive fat deposits (Horner et al., 1989) and an abnormally thick soft palate (Battagel, Johal, Smith, & Kotecha, 2002; Kelly et al., 1990). Tangugsorn et al., (2000) analysed skeletal and upper airway tissue morphology of obese and non-obese patients. A comparison between the two groups revealed different features as the cause of airway obstruction. The obese patients displayed more abnormalities relating to upper airway soft tissue morphology and deviated head posture (Tangugsorn et al., 2000). The soft tissue of the upper airway was larger in obese patients, particularly that involving the tongue and soft palate. Furthermore, some deviations in the craniofacial skeletal morphology prevailed, including short cranial base, narrow bony nasopharynx, retruded chin, increased facial height, and lower position of hyoid bone (Tangugsorn et al., 2000). Except for the hyoid bone position, these features were less pronounced in the non-obese group.

Horner et al. (1989) examined the sites and sizes of fat deposits around the pharynx in obese patients with OSA compared to weight-matched control subjects. Using magnetic resonance imaging (MRI), these authors found that more fat was evident in areas surrounding the collapsible portions of the pharynx in OSA patients (Horner et al., 1989). They suggested that the presence of such fat deposits might compromise the function of the upper airway muscles by causing the narrowed airspace to be more dependent on the muscle activity for patency (Horner et al., 1989).

Performance Measures

Excessive daytime sleepiness (hypersomnolence) is reported in the majority of individuals with OSA and has been associated with difficulty in maintaining adequate arousal to complete occupational and domestic activities (Ulfberg, Jonsson, & Edling, 1999). Sleepiness during driving is particularly problematic, with studies reporting impaired performance on simulated driving tasks, as well as on tests for vigilance and reaction time (Findley, Fabrizio, Knight et al., 1989; Findley et al., 1995; Williamson & Feyer, 2000). These deficits result in a higher risk of accidental injury for people with sleep disordered breathing. OSA-related deficits have also been reported across a range of neurocognitive domains, including motor speed, attention, information processing speed, working memory and executive control (Bedard et al., 1991; Findley et al., 1986; Naegele et al., 1995). The aetiology of such impairments is believed to be the result of nocturnal hypoxemia and oxygen desaturation and/or sleep fragmentation associated with multiple arousals during sleep (Findley et al., 1986).

Sleepiness.

It is generally accepted that after an extended period of wakefulness there is a concomitant increase in fatigue and sleepiness (Lumley, Roehrs, Zorick, Lamphere, & Roth, 1986). Fatigue and sleepiness are caused by factors such as time of day, duration of prior wakefulness and prior sleep deprivation (Bonnet & Arand, 1995). Excessive daytime sleepiness is a serious effect of OSA. Its clinical features are a strong feeling of abnormal daytime tiredness, reduced wakefulness and vigilance (Sauter et al., 2000). The negative effects of sleepiness on performance and

subjective sleepiness have been observed in a number of studies (Gillberg, Kecklund, & Akerstedt, 1994; Lamond & Dawson, 1999).

A series of studies by Bonnet (1985, 1987, 1989), in which sleep was intermittently disrupted to the extent of producing behavioural awakenings, indicated impaired daytime performance following sleep disruption. However, OSA subjects rarely waken to this level following sleep disruption with brief cortically detected arousals being much more common (Martin, Brander, Deary, & Douglas, 1999). One night of sleep fragmentation, as detected by cortical arousal, makes normal subjects sleepier during the day (Roehrs, Merlotti, Petrucelli, Stepanski, & Roth, 1994). These results were confirmed by Martin, Engleman, Deary and Douglas (1996) who found that one night of acoustically induced cortical sleep fragmentation causes normal subjects to report increased objective daytime sleepiness and impaired mood and cognitive function, similar to that observed in patients with OSA.

The most reliable physiological consequence of sleep deprivation or disruption is physiological sleepiness, or the tendency for an individual to fall asleep in the absence of competing stimuli (Walsh & Lindblom, 1997). In both clinical and experimental settings, the Multiple Sleep Latency Test (MSLT) is widely used to measure physiological sleepiness (Walsh & Lindblom, 1997). The MSLT uses EEG recordings to measure the time it takes for sleep onset to occur on four to six sleep opportunities at 2-hour intervals during the day (Strohl et al., 1994). The more rapidly sleep onset occurs, the greater the physiological sleepiness (Strohl et al., 1994). Unfortunately, tests such as the MSLT are expensive and time-consuming, and are therefore not always carried out on patient populations (Johns, 1993).

For these reasons, subjective ratings are often the only possible methods for assessing sleepiness in field and clinical studies (Gillberg et al., 1994). However, it is important to stress that subjective methods, apart from being practical in field settings, also evaluate an important aspect of sleep. In work situations with more or less passive supervision, such as simulated driving or control room tasks, the individual has no continuous feedback on the quality of performance (Gillberg et al., 1994). The subjective signals of sleepiness are the only information on which the individual bases his/her decisions about when to discontinue work to avoid mistakes or accidents.

In order to subjectively measure a general level of chronic daytime sleepiness, Johns (1991) devised a simple questionnaire called the Epworth Sleepiness Scale (ESS). It asks the subject to rate the chance of falling asleep in eight different situations (Johns, 1991). Johns (1993) reported that sleepiness, as measured by the ESS, was positively related to the severity of OSA and snoring. Johns found that ESS scores increased with the severity of OSA, and that patients with OSA were distinguishable from primary snorers on the basis of ESS scores. It was concluded that the ESS is a useful tool for measuring sleepiness, compared to other more time-consuming laboratory based tests such as the MSLT (Johns, 1993).

The nine-point Karolinska Sleepiness Scale (KSS) is another tool that has been used to subjectively assess state related sleepiness by asking individuals to rate how sleepy they feel right now. The KSS requires the patient to integrate and translate a number of sensations to a continuum that is fairly abstract in spite of the verbal descriptions (Gillberg et al., 1994). Akerstedt and Gillberg (1990) evaluated levels of sleepiness in train drivers, truck drivers and shift workers using both

subjective and objective measures of sleepiness. The results showed that the KSS was strongly related to EEG and EOG signs of sleepiness (Akerstedt & Gillberg, 1990).

Although subjective measures of sleepiness, such as the ESS and KSS have been successfully employed experimentally in the assessment of sleepiness, these measures correlate poorly with motor vehicle accident risk (George, Boudreau, & Smiley, 1997; Sauter et al., 2000; Young, Blustein, Finn, & Palta, 1997). Patients with OSA may be reluctant to disclose difficulties with driving as a result of sleepiness, either due to their unawareness of risks involved or because of the potential for loss of driving license and employment status (George et al., 1997; Horstmann, Hess, Bassetti, Gugger, & Mathis, 2000). Such inconsistencies complicate the task of determining the ability to safely operate a motor vehicle and thus, more objective measures may prove to be important to the process of determining the ability of OSA patients to work and drive safely.

While the ESS and KSS are useful tools for assessing subjective sleepiness and correlate closely to that of objective measures of sleepiness, a number of studies have shown that patients with sleep disordered breathing often underestimate the degree of sleepiness (Breugelmans, Ford, Smith & Punjabi, 2004; Dement, Hall & Walsh, 2003; Engleman, Hirst & Douglas, 1997).   Dement et al., (2003) suggested that patients who have lived with severe sleepiness for many years may underreport their sleepiness due to habituation. The authors also suggested that there may be variation in sensitivity to the sensations of sleepiness, such that some individuals fail to attribute the cues indicating a state approaching sleep as 'sleepiness'. Few studies have found the contrary, that patients with sleep disordered breathing actually overestimate their sleepiness.

Microsleeps.

Sleepiness and sleep related fatigue impair reaction times, vigilance and peripheral vision, and ultimately result in falling asleep inappropriately (Akerstedt, 1988; Dinges et al., 1997; Russo et al., 1999; Williamson, Feyer, & Friswell, 1996). Periods of falling asleep are initially very brief 'microsleeps' and may last from 3 to 15 seconds (Priest, Brichard, Aubert, Liistro, & Rodenstein, 2001). However, as sleepiness increases, longer periods of sleep occur (Riemersma et al., 1977). During microsleep, responsiveness to environmental stimuli is impaired or completely absent (Akerstedt, 1988). These episodes may occur with eyes open or closed, and they may occur without warning in sleep-deprived individuals. At highway speed, a motor vehicle traverses a distance equivalent to the length of a football field during a three to four second microsleep (Akerstedt, 1988). Consequently, these microsleeps can result in accidents due to failure to respond appropriately to hazards, such as avoiding obstacles, or adjusting steering and speed. Microsleeps also result in variability in speed and an increase in lane drift, which may, in turn, result in road accidents (Riemersma et al., 1977).

A number of factors can contribute to the development of sleepiness on an acute or chronic basis and result in microsleeps. Chronic partial sleep deprivation and acute sleep deprivation contribute to deficits in function (Dinges et al., 1997; Williamson et al., 1996). Specifically, the circadian rhythm influences fatigue with maximum sleep propensity occurring during the early hours of the morning and a second, less pronounced period, occurring in the early afternoon (post-lunch dip). This effect is especially evident in shift workers, who are over represented in fatigue-

related work and motor vehicle accidents (Fell & Black, 1997) as their sleep-wake cycles may be out of phase with their circadian cycle.

There are no set criteria for defining a "microsleep", with a number of classifications and methods of measurement in use. However, a microsleep should reflect impaired performance on objective tasks relevant to the process concerned and should ultimately predict important outcomes, such as subsequent accidents. Methods for measuring microsleeps include standard manual scoring of the EEG, spectral analysis of the EEG and video of the face to indicate sleep, and duration of eye closure (Hakkanen, Summala, Partinen, Tiihonen, & Silvo, 1999; Torsvall & Akerstedt, 1987). While each method has been beset with technical problems in obtaining adequate recordings and interpreting the data, eye closure has been shown to be reliable (Hakkanen et al., 1999).

Nevertheless, few field studies have been able to demonstrate correlations between measures of microsleep and performance despite having identified microsleeps.   Presumably many periods of microsleep can occur before an episode results in an accident or other measurable error in a field study (Lisper, Laurell, & van Loon, 1986). In a laboratory study, on the other hand, a more sensitive measure of performance can be used, such as reaction time to a frequently presented signal, which makes it easier to detect lapses in performance. Using these techniques, a few studies have clearly associated episodes of microsleep with performance failure (Hakkanen et al., 1999; Torsvall & Akerstedt, 1987; Wierwille & Ellsworth, 1994). In Torsvall and Akerstedt's (1987) study of train drivers on night shift, slow eye movements (vertical movement, which predominantly reflects eyelid movements, lasting more than one second) increased during the night.   In two drivers there were

episodes where increased slow eye movements (consistent with microsleeps) were present for a short period prior to failure to brake in response to a signal.

Morris and Miller (1996) used EOG to measure blink rate, blink duration, long eye closure rate (>500ms) and blink amplitude in ten partially sleep deprived pilots during simulated flying. Blink rate, blink duration and long eye closure rate increased with increased subjective sleepiness and correlated positively with performance errors (Morris & Miller, 1996). Blink amplitude correlated negatively with subjective sleepiness and performance and was actually the strongest predictor of performance. In another study, an increase in slow-eye-closure, as measured from EOG was evident after 16 hours of wakefulness during a 32-hour period of sleep deprivation (Cajochen, Khalsa, Wyatt, Czeisler, & Dijk, 1999). The greatest increase in slow-eye-closure occurred during the circadian rhythm nadir in the early hours of the morning. A number of studies have also found that blink duration and slow-eye-closure (>500 msec) also increases with increasing duration on a task (Morris & Miller, 1996).

In a study by Hakkanen et al., (1999) bus drivers with mild to moderate OSA showed increased daytime sleepiness in terms of blink frequency and duration on a simulated driving task when compared to control peers. Blink duration was measured using a video-scanning method. The findings indicated that blink frequency was increased by feelings of increased sleepiness. Similarly, driver drowsiness has also been assessed using video-images of the vehicle operator's face. Levels of drowsiness can be determined based on slow-eye-closure, as well as characteristics such as rubbing, yawning, nodding and facial tone (Wierwille & Ellsworth, 1994). However, it is difficult to establish validity using this method alone due to differences in rater assessments of drowsiness. Although there has been little work using these

measures with OSA patients, slow-eye-closure assessment for microsleeps has been used to objectively measure sleepiness in sleep-deprived normal individuals on a driving simulator and has been shown to correlate negatively with simulated driving performance (Wierwille & Ellsworth, 1994).

Another promising method for detecting microsleeps is Perclos, video scoring of eye closure to assess the percentage of time that the eyes are more than 80 percent closed (Wierwille & Ellsworth, 1994). Dinges, Mallis, Maislan, and Walker-Powell (1999) assessed the validity of six different methods, including Perclos, for detecting drowsiness or microsleeps in terms of lapses on a psychomotor vigilance task (PVT) (Dinges et al., 1999).   The authors used two EEG algorithms, Perclos, a head tracker device and two eye blink monitors, to assess subjects who had a prior 42-hour sleep deprivation period. Only Perclos produced a high correlation with PVT lapses for all subjects across all sessions. Perclos also correlated better with PVT lapses than individuals rating of sleepiness. These results are supported by studies that suggest that monitoring of eye closure is a promising way of detecting microsleeps that result in performance failure (Dinges et al., 1999; Wierwille & Ellsworth, 1994).

Sleepiness, obstructive sleep apnoea and motor vehicle accidents.

Motor vehicle accidents remain a major cause of death and injury, despite recent reductions related to enforcement of speed restrictions and maximum blood alcohol levels. In Australia, although the Victorian road toll has decreased by half since 1989, there are still up to 700 fatalities and 10,000 serious injuries per year from motor vehicle accidents (TAC, 1994). In Australia, road traffic accidents are the seventh highest cause of years of life lost due to premature mortality (Van Der

Weyden, 1999). Alcohol, excessive speed, inexperience, sleepiness and inattention have been implicated as major causes of motor vehicle accidents (Maycock, 1997). Driver sleepiness contributes to between 5 and 40 percent of vehicle accidents and 20 to 60 percent of truck accidents, with the cost estimated at $3 billion every year in Australia (Fell & Black, 1997; TAC, 1994).

The Australian Transport Safety Bureau (ATSB) examined the occurrence of fatigue related road crashes in Australia and found that these fatalities mostly occurred in the male population and in road users aged between 17 and 24 years (Dobbie, 2000). In addition, 16.6 percent of fatal crashes were attributable to driver sleepiness. Motor vehicle accidents that involve a driver falling asleep have been found to be more severe and have often included high speed, head-on collisions, or hitting a stationary object at high speed; (Dobbie, 2000; Findley, Unverzagt, & Suratt, 1988). Horne and Reyner (1995) found that death or serious injury occurred in 23 percent of sleep related vehicle accidents, compared with 15 percent of accidents not related to sleep.

Driver sleepiness contributes to motor vehicle accidents in two ways. The first is the driver actually falling asleep at the wheel. The second, which is considered to be a greater contributory factor, is driver inattention or judgment error (Philip & Mitler, 2000). Research overseas has shown that drivers in the United Kingdom and the United States of America have found fatigue to be a substantial problem (Feyer, 2001). An Australian survey showed 14 percent of truck drivers admitted to having fallen asleep at the wheel in the past nine months (Arnold et al., 1997). Twenty-two percent of long-haul truck drivers surveyed in Helsinki reported having dozed off at

the wheel at least twice during the preceding three months (Hakkanen & Summala, 2000).

Reduced daytime alertness and sleepiness is of direct relevance to driving risk in patients with OSA. Sleepiness is a common experience, although often under reported, and is associated with a lack of sleep and time of day effects (Engleman, Hirst et al., 1997; Horne & Reyner, 1995; Strohl et al., 1994). Motor vehicle accidents are more prevalent at particular times of the day (Folkard, 1997). Long-haul drivers in Helsinki reported greater sleepiness during the night (Hakkanen & Summala, 2000). The two major peaks in accident risk are in the early morning, between 0200 and 0600 hours and late afternoon, between 1500 and 1600 hours, compared with the rest of the waking day (Folkard, 1997; Horne & Reyner, 1996; Pack et al., 1995). It is interesting to note that these times correlate with the circadian peaks in sleepiness (Hakkanen & Summala, 2000). The duration of time spent driving and the amount of prior sleep loss further compound this problem (Philip et al., 1999).

Excessive daytime sleepiness can present in varying degrees, from mild to severe, and is affected by other factors such as age, drugs and/or medication, and sleep patterns, particularly insufficient nocturnal sleep (Strohl et al., 1994). In the presence of insufficient sleep, alcohol and specific medications may increase the tendency toward sleepiness (Strohl et al., 1994). Furthermore, the increased daytime sleepiness caused by OSA can result in impaired simulated driving performance equivalent to that produced by alcohol intoxication of at least a blood alcohol level of 0.05 percent (Dawson & Reid, 1997; Hack, Choi, Vijayapalan, Davies, & Stradling, 2001; Williamson & Feyer, 2000). These impairments in performance, judged to be

equivalent to the legal alcohol limit for safe driving, start to occur as early as 17 hours after waking in a non-sleep deprived state in those without a sleep disorder (Dawson & Reid, 1997; Williamson & Feyer, 2000).

Many studies have demonstrated an increased rate of motor vehicle accidents in those with sleep disordered breathing with a respiratory disturbance index as low as five to ten events per hour (Findley et al., 1988; Haraldsson, Carenfelt, Diderichsen, Nygren & Tingvall, 1990; Teran-Santos, Jimenez-Gomez, & Cordero-Guevara, 1999). A large prospective population based cohort study showed an odds ratio of 3.4 for having had an accident over a five year period in men with sleep disordered breathing (RDI over 15) (Young et al., 1997).

Sleepiness, obstructive sleep apnoea and simulated driving performance.

A limited number of studies have assessed the relationship between performance and objective sleepiness during simulated driving in OSA patients (Akerstedt, 1998; George, et al., 1997; Gillberg, et al., 1996; Lisper, Laurell & van Loon, 1986; O'Hanlon & Beatty, 1977). While a microsleep as short as three seconds may be long enough to result in driving off the road, periods as long as 16 seconds of continuous sleep and 520 seconds of stage one sleep have been recorded in simulated drivers on the road without crashing (Mitler, Miller, Lipsitz, Walsh, & Wylie, 1997; O'Hanlon & Beatty, 1977). Therefore, it is only when a microsleep occurs at a critical point, when the driver is required to perceive a problem, such as drifting off the road or avoiding an obstacle on the road, and take the relevant action, such as braking or correcting steering, that an accident results.

Other performance measures that indicate a problem with sleepiness and occur prior to accidents, such as drifting from the lane or increased speed variability, are likely to correlate better with measures of microsleep (Riemersma et al., 1977). During driving, the operator is required to process complex visual, tactile, and auditory information in order to produce a well-coordinated motor output (George et al., 1996). Among the many tasks involved in driving are the important features of vehicle control, which include maintaining the vehicle within the lane (tracking), and visual search, including scanning for pedestrians, other vehicles, traffic signs and lights (George et al., 1996). Attention is constantly divided between these tasks. Therefore, driving performance simulators have been designed to include these kinds of multiple demands (Gillberg, Kecklund, & Akerstedt, 1996). Using driving simulators, fatigue and microsleeps have been shown to cause speed variability and an increase in lane drift (Riemersma et al., 1977). Fatigue and mictrosleeps can lead to drifting into an adjacent lane or off the road and can result in accidents.

These results have been confirmed by other studies assessing subjects with OSA and impaired performance due to driver sleepiness on simulated driving tasks (Findley, Fabrizio, Knight et al., 1989; George et al., 1996; Nilsson, Nelson, & Carlson, 1997; Turkington, Sircar, Allgar, & Elliott, 2001). George et al. (1996) found that patients with OSA performed substantially worse on a test comprising both visual search and tracking in comparison to control subjects. The authors found a greater mean difference between the two groups on the tracking task, compared to the visual search measure, indicating that patients with OSA were unable to effectively divide their attention between the two tasks. These results strengthen the findings of Findley, Fabrizio, Knight, et al. (1989) who used two separate driving simulator tasks in order to compare the simulated driving performance of subjects with OSA to that of

healthy control subjects. The first task simulated highway driving, and the second

task simulated rural and city driving. Their results indicated that the OSA patients

performed worse on both simulated driving tasks and hit a greater number of road

obstacles in comparison to the control group (Findley, Fabrizio, Knight et al., 1989).

Vigilance.

Human performance following sleep loss or disruption varies with the nature

of the task at hand. It appears that people have the capacity to perform reasonably

well under the most trying of sleep loss circumstances provided the affected

individual is sufficiently stimulated or motivated and the behaviour required is not

overly complex (Walsh & Lindblom, 1997). A powerful determinant of lapsing and

decreased performance in a sleepy person is the duration of the task (Dinges &

Kribbs, 1991). The longer the task duration, the greater likelihood that performance

will show evidence of impairment early in sleep deprivation (Dinges & Kribbs, 1991;

Kribbs et al., 1993). For example, Lee and Kleitman (1993) observed that sleep-

deprived individuals could maintain normal performance for a few minutes on a

simple task like colour naming until the task duration was extended, resulting in

poorer performance at up to 15 minutes. Both the number of errors and time required

to provide responses increased (Lee & Kleitman, 1993).

Similar results were reported by (Dinges et al., 1997) using a psychomotor

vigilance task (PVT). The authors examined the effect of sleep restriction (only 4-5

hours sleep per night) on neurobehavioral alertness while awake. It was found that

cumulative sleep restriction resulted in slowed reaction times and increased lapse

frequency on the PVT (Dinges et al., 1997). Sleep deprived drivers have also been

studied in order to determine whether they display evidence of peripheral visual field

neglect (Russo et al., 1999). In this study, subjects were evaluated eight times during

64 hours of total sleep deprivation and exhibited impairments on a peripheral visual

attention task after 24 hours of sleep deprivation. This dysfunction in peripheral

visual field attention may be a behavioural manifestation of cerebral hypometabolism

due to sleep deprivation (Russo et al., 1999). This may help to explain motor vehicle

accidents, particularly single vehicle incidents, involving driving off the road.

Findley et al. (1995) designed a computer program that simulated a long and

monotonous highway presenting with obstacles. This program was used as a method

to determine impaired vigilance in patients with OSA. The results indicated that

patients had a poorer performance on the test of vigilance compared to control

subjects, and that vigilance was further impaired as the severity of OSA increased

(Findley et al., 1995). Impaired vigilance was also associated with higher motor

vehicle accident rates, where patients who hit more than 4.5 percent of obstacles had a

significantly greater motor vehicle accident rate than subjects with normal

performance (Findley et al., 1995). Therefore, poor vigilance performance in OSA

patients may be a predictor of high risk for motor vehicle accidents.

Neurocognitive deficits.

Theoretical and empirical interest in the effects of sleep on cognitive processes

can be traced back to shortly after the turn of the century (Tilley et al., 1992). The

interest was stimulated not so much by a fascination with sleep, but by issues

concerning the effect of sleep on cognition, particularly the consolidation of

information (Tilley et al., 1992). Since this time, OSA-related deficits have been

reported across a wide range of neuropsychological domains, including motor speed (Greenberg, Watson, & Deptula, 1987), attention (Bedard et al., 1991; Findley et al., 1986), information processing speed (Bedard et al., 1991), working memory (Naegele et al., 1995), long-term episodic memory (Bedard et al., 1991; Findley et al., 1986; Naegele et al., 1995), general intellectual functioning (Berry, Webb, Block, Bauer, & Switzer, 1986), and executive control (Bedard et al., 1991; Decary et al., 2000; Engleman & Joffe, 1999; Findley et al., 1986; Naegele et al., 1995).

Bedard and coworkers (1993) noted that the effects of nocturnal hypoxemia appear to differ depending on the neuropsychological abilities being assessed and depending on the region of the brain subserving these abilities. In neuropsychological literature, data supporting an association between impaired executive functions and frontal lobe damage date back to 1868 and the description of Phineas Gage (Eslinger, 1996). Many subsequent studies have strongly supported this neural-behavioural association and the terms 'executive function' and 'frontal lobe function' have sometimes been used interchangeably (Eslinger, 1996).

Bedard et al., (1991) found that nocturnal hypoxemia contributes to cognitive deficits in OSA. However, they also found that impaired vigilance played a role in producing such deficits, and that each of these two contributing factors produced differences in the nature of the cognitive dysfunctions. The authors suggested that a reduction of general intellectual performances, as well as deficits of executive functions, such as planning and shifting set, may have been attributable to respiratory impairments, while an increase in daytime sleepiness seemed primarily responsible for attention and memory deficits (Bedard et al., 1991). The study also showed that an increased severity of OSA not only intensified the neuropsychological deficits

present in patients with moderate OSA, but also produced additional deficits in more severe patients.

Progressively increasing dysfunction in moderate to severe patients included deficits in full scale and performance IQ (Wechsler Adult Intelligence Scale – Revised; WAIS-R), attention tasks (Trails A), immediate and delayed recall of both visual and verbal material (Wechsler Memory Scale; WMS), executive functioning (Trail B and verbal fluency), and planning and sequential thinking (Bedard et al., 1991). Thus, it has been postulated that the frontal cortex is particularly vulnerable to hypoxic effects associated with OSA (Bedard, Montplaisir, Malo, Richer, & Rouleau, 1993). The hippocampus, a brain region implicated as being important for long-term episodic memory, is also particularly susceptible to hypoxia (Bedard et al., 1993; Baddeley, 1999).

Memory is the biological process whereby information is registered, stored and retrieved (Markowitz & Jensen, 1999). One of the major functional distinctions of the memory system is its division into sensory memory, short-term or working memory, and long-term memory (Figure 6). Sensory memory refers to the memory trace that preserves the original information of a sensory stimulus for very brief periods, that is, less than one second for visual information and up to three seconds for auditory information, following the termination of the stimulus (Gray, 2002). Short-term memory (STM) or working memory (WM) is responsible for the temporary maintenance of information that is to be used immediately and is regarded as the 'active' component of memory (Nairne, 1996). Long-term memory (LTM), on
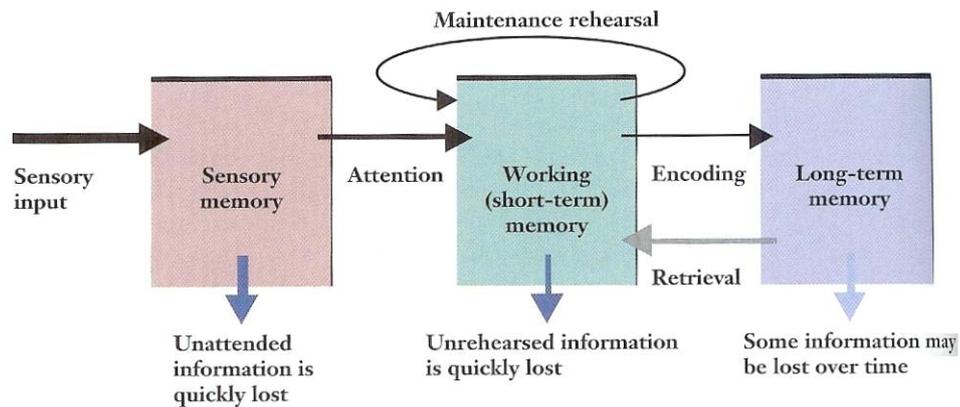
Figure 6. The main components of the human memory system. (Gray, 2002)

the other hand, represents information that is stored for considerable periods of time

(Baddeley, 1999). It refers to information that is stored sufficiently to be accessible

over time from periods as brief as a few seconds to many years (Baddeley, 1999).

The model represented in Figure 6 not only differentiates active (short-term or

working) memory from passive (long-term) memory, it also provides a basis for

defining the processes of attention, encoding and retrieval (Markowitz & Jensen,

1999). According to the model, new information can be encoded into long-term

memory only if it is first perceived consciously in short-term or working memory

(Gray, 2002).

Another simple classification (Figure 7) delineates long-term memory by the

manner in which it is encoded and retrieved, either consciously or instinctually

(Markowitz & Jensen, 1999). Explicit, or declarative, memory is the type of memory

that can be brought into a person's consciousness (Zillmer & Spiers, 2001).
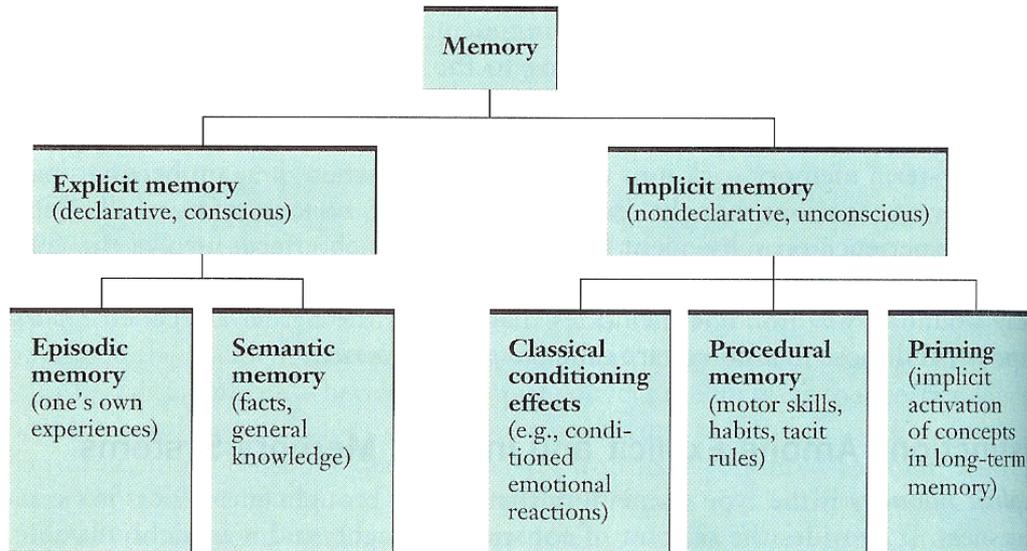
Figure 7. Types of long-term memory. (Gray, 2002)

It provides the content of conscious thought and is highly flexible. Figure 7 shows

explicit memory is also divisible into two subclasses; episodic and sematic memory.

Episodic memory, also known as autobiographical, refers to one's own experiences,

whereas semantic memory is that which is not tied mentally to a particular past

experience and includes facts, ideas, and general knowledge (Markowitz & Jensen,

1999).

Implicit, or non-declarative, memory, in contrast, is the type of memory that

does not enter into the contents of consciousness (Zillmer & Spiers, 2001). It consists

of all the unconscious means through which previous experiences can influence a

person's actions and thoughts. Implicit memory is also divided into subclasses

(Figure 7). One subclass consists of the memories that are produced by classical

conditioning, that is, the internal changes produced by conditioning experiences that

lead a person to respond to conditioned stimuli (Cohen & Eichenbaum, 1994).

Priming refers to the process by which a stimulus activates one ore more memories that already exist in long-term memory (Gray, 2002).

A third variety of implicit memory is procedural memory (Figure 7). Procedural memory is a form of learning that cannot or is very difficult to verbalise and is therefore expressed implicitly (Markowitz & Jensen, 1999). It refers to "the gradual acquisition and maintenance of motor skills and procedures" (Decary et al., 2000, p. 372). It represents the 'how to' of a memory task and, though procedural memory is embedded through practice, the skill becomes virtually automated over time (Markowitz & Jensen, 1999). The improvement is retained (remembered) from one practice session to the next. Examples of procedural memory include riding a bike, driving a motor vehicle and tying our shoelaces.

Almost all investigations of OSA patients' cognitive functioning include an evaluation of their memory, with the WMS being the most frequently used measure (Decary et al., 2000). Long-term memory deficits are frequently reported in patients with OSA, with studies finding that LTM efficiency is significantly decreased for both verbal and visual information (Bedard et al., 1991; Berry et al., 1986; Naegele et al., 1995). The delayed recall of the logical stories and design subscales of the WMS has been consistently shown to be deficient in OSA patients (Bedard et al., 1991; Berry et al., 1986; Findley et al., 1986). The poor recall of a word list (California Verbal Learning Test) has been found to be related to OSA patients' increased level of sleepiness (Salorio, White, Piccirillo, Duntley, & Uhles, 2003; Valencia-Flores, Bliwise, Guilleminault, Cilveti, & Clerk, 1996).

Short-term memory abilities are also decreased in patients with OSA, regardless of whether verbal or visual information is used (Findley et al., 1986; Naegele et al., 1995; Decary et al., 2000). For example, Naegele et al., (1995) found poor digit span performances in patients with severe OSA. Borak et al. (1996) found diminished digit span performance and poorer immediate visual and spatial memory. They also found verbal memory performance levels to be below normal (Borak et al., 1996). Performance on the Benton Visual Retention Test, a measure of immediate visual span, is reduced in moderate to severe OSA patients (Klonoff, Fleetham, Taylor, & Clark, 1987).

Despite considerable research on LTM and STM impairments in OSA patients, relatively little is known about the impact of disordered breathing on procedural memory. The basal ganglia, once thought to be solely associated with control of muscle movement, have been implicated in the learning of cognitive skills and procedural memory (Saint-Cyr, Taylor, & Lange, 1988). It has been suggested that movement reinforces memory by providing an anchor or external stimulus to match to the internal stimulus (Markowitz & Jensen, 1999). Given that the basal ganglia are linked to the frontal cortex, the frontal lobes may also play a role in the acquisition of procedural skills. Since the basal ganglia are among brain structures that are most vulnerable to hypoxemia, and that slowing of EEG in frontal regions has been identified in OSA patients, these patients may have an attenuated capacity for procedural learning (Decary et al., 2000). With damage to the basal ganglia, cognitive flexibility, the ability to generate and shift ideas and responses, is also reduced (Lezak, Howieson, & Loring, 2004).

Procedural memory has been examined in research studies using a variety of tasks, such as pursuit motor learning, mirror writing and maze learning (Butters, Salmon, Heindel, & Granholm, 1988; Bylsma, Brandt, & Strauss, 1990; Milner, 1965). The stylus maze task in Milner's (1965) study, which was similar to the Austin Maze (AM) used in the current study, posed a procedural learning problem primarily since it required the repeated 'tracing' of a constant path until the most direct route from starting-point to goal had been mastered. For this reason, performance was less affected by minor spatial deficits than by difficulty in remembering the correct sequence of turns from one trial to the next. Bylsma et al., (1990) also successfully used a push-button maze-learning task to assess procedural memory in a group of Huntington's disease patients and normal controls. Bowden and colleagues (1992) analysed the performance on the Austin Maze using a sample of healthy adults. The failure to observe a substantial effect of the WAIS-R Vocabulary subtest on the Austin Maze score reinforces the view that push-button maze performance is largely independent of verbal ability (Bowden et al., 1992).

In OSA patients, Decary et al. (2000) found that procedural memory, as assessed via the acquisition of a complex visuomotor task (Mirror Tracing), was deficient. These measures of procedural learning generate higher cognitive demands, therefore, suggesting that OSA patients have difficulty employing an efficient strategy when completing such tasks (Decary et al., 2000).

Diffuse cognitive dysfunction results in a decrease in new learning ability, impaired attention and concentration, visual-spatial deficits, and reduced capacity for planning, initiating and executing activities (Baddeley, 1999). However, the aetiology of such impairments in OSA patients is less well known. During apnoeic events,

periods of severe cerebral hypoxia occur (Borak et al., 1996). Combined with disordered sleep, this may result in behavioural changes in patients with OSA (Borak et al., 1996).

Findley and colleagues (1986) examined the cognitive functioning of patients who had OSA with associated hypoxemia compared to non-hypoxemic patients with OSA. They found that individuals with OSA-related hypoxemia had poorer cognitive functioning on four of the eight tests administered, as well as mean performance scores in the impaired range on measures of attention and concentration (Trails B), complex problem-solving (Paced Auditory Serial Addition Task, PASAT), short-term recall of verbal information (WMS delayed stories) and short-term recall of visuospatial information (WMS delayed designs). Individuals with OSA, but no hypoxemia, performed within normal limits in these domains (Findley et al., 1986). The degree of hypoxemia, during both sleep and wakefulness, correlated significantly with overall cognitive impairment, whereas measures of sleep fragmentation did not significantly correlate with overall cognitive impairment in patients with OSA (Findley et al., 1986). These findings not only indicate that patients with OSA display cognitive impairment, but also suggest that sleep fragmentation is a less important cause of neuropsychological impairment in comparison to hypoxemia (Findley et al., 1986).

Continuous Positive Airways Pressure (CPAP) Treatment

Nasal continuous positive airway pressure (CPAP) therapy was introduced by Sullivan in 1981 (Sullivan, Issa, Berthon-Jones, & Eves, 1981) and has since become the most widely used treatment for OSA (Jenkinson, Davies, Mullins, & Stradling,

1999). Nasal CPAP consists of a high-flow pump that delivers a continuous stream of room air into a sealed mask that the patient wears over the nose during sleep (Saskin, 1997). This infusion of positive air pressure creates a pneumatic splint, maintaining upper airway patency during sleep and preventing pharyngeal collapse (Sullivan et al., 1981). The success of nasal CPAP has been associated with its demonstrated ability to abolish most episodes of apnoea, eliminate associated oxygen desaturation, and decrease sleep fragmentation, all of which result in an improvement of nightly sleep quality and daytime function (Saskin, 1997; Sullivan, Issa, Berthon-Jones, McCauley, & Costas, 1984).

For approximately the first 10 years of CPAP use in sleep centres, most studies of adherence to CPAP therapy were conducted through patient interviews. Patients were consulted during follow-up visits regarding their level of CPAP use (Raucher, Popp, Wanke, & Zwillich, 1991). A more detailed study that analysed the cumulative time counters, which indicate the total amount of time the CPAP machine has been operated for, found that CPAP has enjoyed up to a 90 percent acceptance rate by patients and has been used everyday by up to 75 percent of patients (Rand & Wise, 1994). In addition, research has found a total CPAP use time of between five and six hours per night (Engleman, Martin, Deary, & Douglas, 1994; Meurice et al., 1994).

Sleepiness and impaired daytime function are major clinical features of OSA and the primary indication for treatment with CPAP is to try to improve these features (Engleman, Hirst et al., 1997). There is objective evidence that excessive daytime sleepiness improves significantly on treatment with nasal CPAP (George, 2001; George et al., 1997; Jenkinson et al., 1999). In addition, improvements in vigilance, attention, anxiety and depressive symptoms, work performance and quality of life

have been reported following treatment with CPAP (Engleman et al. 1994; Engleman et al., 1994; Montserrat et al., 2001; Ulfberg, Johsson, & Edling, 1999).

George et al. (1997) studied men with OSA, one to twelve months after initiating treatment with CPAP, in order to examine the effects of treatment on performance on a driving simulator and the MSLT for sleepiness. The treatment of OSA with CPAP resulted in significant improvement in simulated driving in this group of patients. Sleepiness was unchanged in control subjects, but improved significantly in patients treated with CPAP (George et al., 1997). Hack et al. (2000) found similar results, showing that nasal CPAP improves measures of steering performance and response to target stimuli. In addition, pre-treatment groups showed clear deterioration in steering performance across the 30-minute simulation period, and this was virtually abolished by treatment with nasal CPAP (Hack, Davies, Mullins, Choi, et al., 2000). This was reflected in the improved ability of subjects to stay on the road for longer periods of time and have fewer off-road events.

Daytime sleepiness, reduced alertness, and impaired concentration are believed to be important factors in increasing motor vehicle accident rates (George, 2001). Using an objective measure of motor vehicle accidents, Department of Motor Vehicle accident reports, (Findley et al., 2000) found patients who were treated with CPAP had a lower crash rate while being treated than before treatment and untreated patients with OSA continued to have a high crash rate. George (2001) also demonstrated a decrease in motor vehicle collisions in patients with OSA following successful treatment with CPAP. Collision rates for patients not having undergone treatment remained higher than in control subjects over the study period (George, 2001). However, while treatment of OSA with CPAP has been shown to reduce the rate of

motor vehicle accidents (Findley et al., 2000), it has been suggested that this risk does not completely return to normal, possibly due to some residual sleepiness or permanent deficits associated with long-term sleep deprivation (George, 2001).

The effect of CPAP on the cognitive status of OSA patients has also been evaluated. In a study by Borak et al. (1996), tests were performed before, after three months, and after twelve months of CPAP treatment. The investigation found that after one year of CPAP treatment there were improvements in visual and spatial memory, concentration, speed of work and verbal memory, with results for concentration and memory tests improving after only three months of CPAP treatment (Borak et al., 1996). In spite of this, after 12 months of treatment, no significant improvement was observed in diminished intelligence. Naegele et al. (1998) also assessed the effect of four to six months of CPAP treatment on attention, short-term memory span, learning abilities, planning capacities, categorising activities, and verbal fluency. The results showed that patients with OSA improved on most of the cognitive executive and learning tasks, but that all short-term memory test results remained unchanged (Naegele et al., 1998). These findings indicate that nasal CPAP treatment can result in early improvement of selective cognitive functions in patients with OSA, but that other functions may show little or no improvement.

While many studies have shown at least some degree of improvement in tests of cognitive function after treatment of mild, moderate or severe OSA with CPAP treatment (Borak et al., 1996; Engleman, Martin et al., 1997; Lojander et al., 1999), there is limited evidence that post-treatment values for performance on memory tasks are comparable to those of normal individuals.

Rationale

Objective measures of sleepiness tend to only assess sleepiness in passive situations, rather than while performing a task. This study explored sleepiness in patients with OSA using an objective measure of sleepiness (microsleeps/slow-eye-closure) measured during a simulated driving task. While a substantial number of studies have examined sleepiness and simulated driving performance (Bearpark, 1990; Findley et al., 1988, 1989, 1992, 1995; George et al., 1996; Hack et al., 2001; Lisper et al., 1986; O'Hanlon & Beatty, 1977; Williamson & Feyer, 2000), the subjective measures of sleepiness have not consistently correlated with accident risk and no objective measure has been shown to relate to accident risk in OSA patients. Moreover, these studies have not assessed sleepiness or brief sleep periods in this population while they are actually driving on a simulator. If sleepiness can be identified in an objective way during simulated driving it may prove to be a better predictor of accident risk in these patients and a means for assessing response to treatment.

In addition, this study may enhance our understanding of procedural memory deficits in patients with OSA. Long-term memory impairments are frequently reported in OSA patients. However, relatively little is known about procedural memory in this population.   Similarly, there is limited evidence that post-OSA-treatment values for performance on memory tasks are comparable to those of normal individuals.

Aims

The aim of this study was to compare simulated driving performance and objective and subjective sleepiness in patients with moderate to severe OSA with control participants. An additional aim of this study was to assess and compare neurocognitive functioning in these two groups, by measuring memory performance, vigilance, sustained attention, and reaction time. This study also aimed to ascertain the benefits of treatment of OSA with CPAP on simulated driving and neurocognitive performance. The following hypotheses were proposed:

Hypothesis 1: Effect of condition 1.

It was hypothesised that patients with OSA (prior to treatment) would perform poorer on the tests of simulated driving performance, vigilance and reaction time, and sustained attention, than control participants.

Hypothesis 2: Effect of condition 2.

It was hypothesised that patients with OSA (prior to treatment) would have higher levels of reported subjective sleepiness and would show increased objective sleepiness (microsleeps/slow-eye-closure) during the PVT and simulated driving tasks in comparison to control participants.

Hypothesis 3: Effect of condition 3.

It was hypothesised that patients with OSA (prior to treatment) would show poorer performances on tests of neurocognitive function in comparison to control participants.

Hypothesis 4: Effect of time.

It was hypothesised that there would be a decrease in simulated driving performance and vigilance, increased subjective sleepiness, and increased objective sleepiness (microsleeps/slow-eye-closure) throughout the night for both OSA patients and control participants.

Hypothesis 5: Effect of treatment 1.

It was hypothesised that patients with OSA would improve their simulated driving performance, vigilance and reaction time, and sustained attention following CPAP treatment. Control participants did not undertake treatment, therefore it was hypothesised that their simulated driving performance, vigilance and reaction time, and sustained attention would not change over time.

Hypothesis 6: Effect of treatment 2.

It was hypothesised that patients with OSA would show decreased objective sleepiness (microsleeps/slow-eye-closure) during the PVT and simulated driving tasks and lower levels of reported subjective sleepiness following CPAP treatment. Control

participants did not undertake treatment, therefore it was hypothesised that their objective sleepiness (microsleeps/slow-eye-closure) during the PVT and simulated driving tasks would not change over time.

Hypothesis 7: Effect of treatment 3.

It was hypothesised that patients with OSA would show an improvement in their performances on tests of neurocognitive function following CPAP treatment. Control participants did not undertake treatment, therefore it was hypothesised that their performance on tests of neurocognitive function would not change over time.

Method

Participants

The participants were 15 patients with moderate to severe OSA (RDI greater than 20) and 15 healthy control participants (RDI less than 5). The OSA sample included 12 males and 3 females between the ages of 40 and 71 (M = 54.6 years, SD = 10.76 years), with a mean Body Mass Index (BMI) of 34.34 (SD = 3.48). The control group consisted of 12 males and 3 females aged between 37 and 70 (M = 47.53 years, SD = 9.48 years), with a mean BMI of 27.54 (SD = 2.76).

All participants were required to be over 18 years of age, hold a current drivers licence and be capable of giving consent. Potential participants' medical records were examined by the sleep physician against the selection criteria and those with a history of chronic neurological illnesses, chronic liver disease, diabetes requiring insulin, renal impairment, pregnancy or breast-feeding, chronic psychiatric illness, visual acuity problems not correctable with glasses, or regular use of sedating medication were excluded. Participants unable to speak or read English were also excluded.

Participants were referred from a physician at the Austin and Repatriation Medical Centre (A&RMC) following a diagnosis of moderate to severe OSA from an overnight polysomnographic sleep study (an RDI of more than 20). Only those who planned to proceed to treatment with constant positive airway pressure (CPAP) were included. Control participants were recruited from the community via advertisements in the local newspaper and hospital newsletter (see Appendix A). Control participants

were matched as closely as possible to the OSA clinical patients by age, gender, and weight, and were screened for significant sleep disorders and/or excessive sleepiness.

Measures

Plain Language Statement. This statement was designed to explain the aims of the research, the requirements of participation and the possible risks of participating in the research (see Appendix B).

Consent Form. The consent form was an adapted version of the Austin and Repatriation Medical Centre standard consent form for participation in psychological/medical research (see Appendix C).

Demographics Questionnaire. The questionnaire was designed to elicit demographic information about gender, age, height, weight, number of days worked per week, number of kilometres driven per year and number of motor vehicle accidents over the past three years (see Appendix D).

Multivariate Apnoea Prediction Questionnaire (MAPQ) (Maislin et al., 1995). Control participants were screened for sleep disordered breathing by a sleep physician using the MAPQ. This questionnaire predicts sleep apnoea risk using a score between 0 and 1, with 0 representing low risk and 1 representing high risk. Potential control participants with a MAPQ score greater than 0.5 were excluded from the study.

Epworth Sleepiness Scale (ESS) (Johns, 1991). This scale is a self-reported measure of chronic daytime sleepiness and was used to identify participants who may

have been experiencing disordered sleep (see Appendix E). Participants were required to rate how likely they would be to doze off or fall asleep in eight everyday situations. Examples included sitting and reading, watching television, and in a car while stopped for a few minutes in traffic. Responses were rated on a scale ranging from 0 = never, to 3 = high chance. Possible scores ranged from 0 to 24, with higher scores reflecting more disordered sleep. A score between 0 and 10 is considered to be in the normal range (Johns & Hocking, 1997), therefore control participants with an ESS score greater than 10 were excluded. This scale has high internal consistency and test-re-test reliability. For example, Johns (1992) found a Pearson's *r* correlation coefficient of .82 when a group of healthy medical students were tested and re-tested five months later. Cronbach's alpha results were .88 for a patient sample and .73 for a student sample.

Sleep Diary. This is a measure of total sleep per night and time taken to fall asleep (see Appendix F). Participants were required to record time spent in bed prior to falling asleep, as well as time of sleep onset and awakening for a one-week period. Total time asleep and time taken to fall asleep was then calculated for each night and averaged across the week.

Karolinska Sleepiness Scale (KSS) (Akerstedt & Gillberg, 1990). This is a single item scale used to measure subjective sleepiness at a point in time (see Appendix G). Participants were required to place a cross next to a number that best described how sleepy they felt at the time they completed the KSS. The numbers ranged from 1 = extremely alert, 3 = alert, 5 = neither alert nor sleepy, 7 = sleepy-but no difficulty remaining awake, to 9 = extremely sleepy-fighting sleep, with even items having a scale value but no verbal label. Possible scores ranged from 1 to 9. Higher

scores represented higher subjective sleepiness. The KSS is highly correlated with

EEG and EOG measures of sleepiness and therefore has high validity (Akerstedt &

Gillberg, 1990). This scale was also found to be highly positively correlated with a

visual analogue scale of sleepiness and the Accumulated Time Sleepiness Scale

(Gillberg et al., 1994), which suggests good concurrent validity.

Alertness Questionnaire (AQ). This questionnaire was used to measure eleven

symptoms of sleepiness (see Appendix H). Participants were asked to indicate, on a

seven-point Likert scale, how often they noticed particular symptoms occurring during

the previous simulated driving session. Some examples of these symptoms include

struggling to keep your eyes open, nodding off to sleep, difficulty keeping to the

middle of the road, difficulty maintaining the correct speed, head dropping down,

stretching and yawning. The items ranged from 1 = not at all, 3 = occasionally, 5 =

frequently, to 7 = most of the time, with even items having a scale value but no verbal

label. Possible scores ranged from 11 to 77. Higher scores reflected higher

sleepiness. This questionnaire was developed at the Sleep Disorders Unit at the

Austin and Repatriation Medical Centre, Melbourne, Australia. Chronbach's alpha

for this questionnaire has been found to be .95, indicating a high degree of internal

consistency (Radford, 2001).

Stop Driving Questionnaire (SDQ). This two-part questionnaire was used as a

subjective measure of when drivers felt they would stop driving and a subjective

estimate of their simulated driving performance (see Appendix I). It required

participants to rate how alert they felt with regards to 1) driving for a short period in

suburban traffic and 2) driving for a continuous long distance. For each part, possible

scores ranged from 1 = I would continue driving, 2 = I would continue driving only if

pressured to do so, 3 = I would stop driving now even if under pressure to continue, to

4 = I would have stopped driving some time ago. This questionnaire was developed at

the Sleep Disorders Unit at the Austin and Repatriation Medical Centre, Melbourne,

Australia.

Perclos. Perclos is a device designed to measure eye closure using infrared

video recording. Perclos measures the percentage of time that the eyes are more than

80 percent closed over the duration of a given task (in this study, 30 minutes for the

driving simulator or 10 minutes for the PVT). Thus, slow-eye-closure would be

recorded and scored by the computer. Participants were asked to reposition the device

until their eyes were visible in the small screen to ensure that the device could detect

slow-eye-closure at all times throughout the task. The device was then switched on

prior to beginning the PVT and driving simulator tasks and switched off at the

completion of each task. Wierwille & Ellsworth (1994) found that Perclos (mean

percent of eye closure) most highly correlated with expert raters of drowsiness, with

an *r* value of 0.911.

Psychomotor Vigilance Task (PVT) (Ardmore, Dinges, Kribbs & Powell,

2000; Dinges et al., 1997; Jewett, Dijk, Kronauer, & Dinges, 1999). This task is a 10-

minute, hand-held, computerised vigilance reaction time (RT) task that evaluates

sustained attention and is sensitive to performance variations due to sleepiness

(Ardmore et al., 2000). The PVT was enclosed in a small plastic box with two push

buttons (right and left) on the bottom of the box and one display screen above the

buttons. Participants were required to press the right button if right-handed or the left

button if left-handed as quickly as possible when the numbers appeared in the display

window. The numbers appeared randomly at intervals from two to 10 seconds.

Reaction times equal to or greater than 500 milliseconds are considered lapses in attention and a button push prior to the clock starting is a false start. The PVT provides a number of indices of sustained attention. The following three were used in this study:

1. Median RT: the elapsed time between the presentation of each number in the display window and the button pressing by the participant (measured in milliseconds). Higher scores indicated lower levels of sustained attention.

2. Slowest 10 percent: the mean reaction time from the slowest 10 percent of reaction times. Lower scores indicated higher levels of sustained attention and faster reaction times.

3. Transformed lapses: lapses in attention were measured in milliseconds and transformed (the inverse square of the reaction time, plus one) to decrease the effect of very long lapses. Higher scores indicated lower levels of sustained attention.

The PVT task has been found to be a reliable vigilance task for assessing the effects of sleep deprivation and circadian phase (Jewett et al., 1999).

AusEd Sampler Driving Simulator (© Grunstein, Engleman, Joffe, & Constable, 1998) (Banks, Catcheside, Lack, Grunstein, & McEvoy, 2004; Howard, Worsnop, Campbell, Swann, & Pierce, 2001). The AusEd Sampler Driving Simulator assesses reaction time and vigilance while conducting a simulated motor vehicle driving task. It consisted of a 45-centimetre screen mounted to a table displaying a two-lane road at night from the perspective of the participant sitting in the drivers seat and looking out of the windscreen. A speedometer was displayed in the upper left hand corner of the screen and the speeds ranging between 60 kilometres per hour

(km/h) and 80 km/h were illuminated. Participants were instructed to remain in the

centre of the left lane and were required to maintain their speed between 60 km/h and

80 km/h. Attached to the table in front of the screen was a steering wheel. On the

floor was a pad with the brake and accelerator pedals. At 10 random times during the

half hour drive, a truck appeared on the screen in the left lane in front of the motor

vehicle. Participants were required to depress the brake pedal the moment they saw

the truck appear in front of them. The following performance indicators were used in

this study:

1. Average steering deviation from centre of left lane: higher scores

   represented larger deviations from the centre of the left lane and decreased

   vigilance.

2. Average velocity deviation from the 60 km/h to 80 km/h speed: higher

   scores represented larger deviations from the prescribed speed and

   decreased vigilance.

3. The number of vehicle accidents with trucks that occurred during each 30-

   minute simulated driving session.

Austin Maze (AM) (Milner, 1965). The Austin Maze was used to measure

procedural memory. The AM took approximately 20 minutes to complete the initial

20 learning trials. A further five minutes was required to complete the delayed recall

task (which occurred approximately 30 minutes after the initial trails were completed).

The AM is a computerised box with 100 buttons in a 10 by 10 array. The AM had a

set maze or path that was pre-programmed in the box. Participants were instructed to

start at the green start button and move towards the red stop button by only pushing

buttons in the forward, backward or sideway direction. They were not allowed to

move diagonally. Each time a correct button was pushed, a green light was

illuminated and the participant could continue with the path-finding. A red light was illuminated and a buzz sounded to indicate an incorrect button press and participants were instructed to move back to the previous correct button before continuing. The following performance indicator was used in this study:

1. Number of Errors: it is expected that participants will learn the maze and therefore make fewer errors with each successive trial.

Logical Memory (LM) (Wechsler, 1997). The Logical Memory task is a subtest of the Wechsler Memory Scale – Third Edition (WMS-III; Wechsler, 1997). The LM was used to assess auditory short-term memory and auditory long-term memory. The LM took approximately 10 minutes to complete and required participants to listen to two stories and to recall each story immediately after presentation and again following a 30-minute delay. Verbal short-term memory was assessed using the number of correct story units recalled after the initial presentation of each story and the score of each story was added. Verbal long-term memory was assessed using the number of correct story units recalled after a 30-minute delay for both stories. The LM task has been shown to have a reliability coefficient of .77 (Wechsler, 1997).

Visual Reproduction (VR) (Wechsler, 1997). The Visual Reproduction task is a subtest of the Wechsler Memory Scale – Third Edition (WMS-III; Wechsler, 1997). The VR took approximately 15 minutes to complete and was used to assess visual short-term memory and visual long-term memory. Participants were presented with a series of five black-and-white geometric designs and after viewing each design for 10 seconds were required to draw the design they had just seen (visual short-term memory). Participants were also asked to recall each of the designs following a 30-

minute delay (visual long-term memory). Each of the recalled designs were scored

using the scoring criteria outlined in the WMS-III administration manual (Wechsler,

1997). The VR task has been shown to have a reliability coefficient of .70 (Wechsler,

1997).

Trail Making Test (Trails A & B) (Lezak et al., 2004). The Trail Making Test

was used to measure working memory, a form of short-term memory, and set shifting.

The TMT took approximately 5 minutes to complete. Participants were given a pencil

and a sheet of paper with 25 randomly arranged encircled numbers on it (Trail A).

Participants were instructed to connect the numbers in numerical order from one to 25

as fast as they could without lifting their pencil off the paper. Upon completion of

Trail A, participants were given another sheet of paper with 25 encircled numbers and

letters (Trail B). Participants were instructed to connect the numbers and letters in

alternating order (i.e. 1, A, 2, B, etc) as fast as they could without lifting their pencil

off the paper. Number of errors made and completion time were recorded.

Procedure

Prior to conducting the study, ethical approval was obtained from the Victoria

University Department of Psychology Research Ethics Committee and the Austin and

Repatriation Medical Centre (A&RMC) Human Research Ethics Committee.

After agreeing to participate, an initial consultation between the participant

and researcher was organised. During this session, the study was explained to the

participants and they were given written information detailing the study. Participants

were specifically informed that they would be undertaking an initial study and a

follow-up study to be conducted five months later. Confidentiality was ensured and informed consent was obtained. Participants were instructed on how to complete the sleep diary and they completed the demographic questionnaire and the ESS.

For both the initial and follow-up studies, participants were asked to wake at 0700 hours on the morning of the study, and to have had their normal amount of sleep during the night prior to the study. Participants were instructed to record their sleep-wake activity on the sleep diary for the week prior to the initial and follow-up study. No caffeine or other stimulant medication was allowed on the day of testing until the study had been completed.

At 1800 hours on the day of the initial study, patients with OSA presented for implementation of CPAP treatment. Upon presentation, the participants were informed of the proceedings of the session and any questions the participants had were answered. Participants were instructed that they could withdraw from the study at any time. Testing throughout the study period was separated into four testing sessions (see Table 1).

Session 1 (1800h).

The first session was a practice session in order for the participants to become familiar with the equipment. The participants were seated at a computer desk in a quiet room, where the PVT was located and were instructed by the experimenter on the task requirements. Just prior to commencing the task, the experimenter turned on the Perclos in order to assess eye closure during the task. The participants were then

Table 1

Study Design for Pre-treatment and Post-treatment Sessions for OSA Clinical Patients and Control Participants

	Pre-treatment session number and session time in hours				Post-treatment session number and session time in hours			
	1	2	3	4	1	2	3	4
	1800h	1900h	2000h	2200h	1800h	1900h	2000h	2200h
Driving simulator	✓	✓		✓	✓	✓		✓
PVT	✓	✓		✓	✓	✓		✓
Perclos	✓	✓		✓	✓	✓		✓
KSS/AQ/SDQ		✓		✓		✓		✓
Neuro-cognitive Tests			✓				✓	

left alone in the room with the lights off in order to complete the task. The task ran

for 10 minutes, after which the participants were instructed to have a five-minute

break.

Participants were then called back into the room and were seated once again at

the computer desk, where a steering wheel was now located, with the accelerator and

brake pedals on the floor. The participants were asked to read a set of instructions

regarding how to use the driving simulator and the experimenter also briefly

explained the instructions verbally. Any questions the participants had were

answered. The participants were required to remove their shoes and watch, and were

asked to sit comfortably in the chair so that they could adequately operate the pedals.

Again, just prior to starting the driving simulator, the experimenter turned on the

Perclos and the participants were left alone in the room. The lights were turned off in order to simulate driving at night. The task lasted for 30 minutes, after which the participants were again given a break.

Sessions 2 (1900h) and 4 (2200h).

For the second and fourth test sessions, which were undertaken at approximately 1900 and 2200 hours, respectively, participants performed the same PVT and simulated driving tasks that were completed in the first session. However, after the simulated driving session, participants were administered the Karolinska Sleepiness Scale, the Alertness Questionnaire and the Stop Driving Questionnaire, in order to assess subjective sleepiness and alertness at that point in time. These testing times were chosen as they occurred on the falling limb of the Tc, therefore at a high propensity for sleep. The timing of the testing thus provided an opportune time to assess 'sleepiness'.

Session 3 (2000h).

Session 3 required participants to undertake a series of neurocognitive tests assessing working memory, set shifting, verbal short- and long-term memory and visual short- and long-term memory. Participants were taken to a quiet room and were seated at a one-meter table directly opposite the experimenter. The Trail Making Test (Trails A & B) was the first test administered. Participants were given a sample of each trail before being asked to complete the appropriate trail. The Logical Memory I (LMI) subtest was then administered, followed by the Visual Reproduction I (VRI) subtest. The Austin Maze (AM) was the next task to be administered and

took approximately 20-30 minutes to complete. This provided the delay required for the Logical Memory II (LMII) and Visual Reproduction II (VRII) subtests, which were administered next. Finally, the AM delayed trials were administered after the completion of the LMII and VRII subtests.

Session 4 concluded at approximately 2400 hours, following which the OSA clinical patients proceeded to their CPAP implementation study in the sleep laboratory as requested by their physician. Control participants did not have any overnight CPAP implementation study following Session 4 and were allowed to go home.

Post-treatment follow-up study.

The post-treatment follow-up study was undertaken five months following the initial study, during which the OSA clinical patients had been using CPAP. This study was an exact replica of the initial study (see Sessions 1-4 above), except that no CPAP implementation study was performed for OSA clinical patients following Session 4.

Results

Statistical Analysis

The data were downloaded from the PVT, Perclos and AusEd Driving Simulator devices and entered into the Statistical Package for Social Sciences (SPSS v11.0). Raw data from all questionnaires and neuropsychological tests were also

entered into the SPSS data file and descriptive statistics were computed to ensure that all data were in the specified ranges, and that there were no missing values. The data were found to be within the specified range and there were no missing values.

Descriptives

Means and standard deviations for the demographic variables and other sample characteristics are shown in Table 2. One-way analyses of variance (ANOVA) were conducted to assess any differences between OSA clinical patients and control participants.

Table 2 shows that in comparison to control participants, OSA clinical patients weighed significantly more, had a significantly higher body mass index, and spent significantly less time at work. OSA clinical patients also reported significantly less sleep on both work days and days off, were significantly less likely to feel refreshed, and reported significantly higher subjective sleepiness scores.

Paired samples *t*-tests were conducted to assess whether OSA clinical patients improved on sleep-log measures of sleep duration, sleep onset, frequency of awakening, and feelings of being refreshed following the CPAP implementation study. The results showed that although the mean number of hours that OSA clinical patients slept each night increased slightly (pre-treatment session $M = 6.51$, $SD = 1.25$; post-treatment $M = 7.15$, $SD = 1.25$), the difference was not significant, $t(13) = -1.96$, $p = .07$. The number of minutes taken for sleep onset was significantly lower post-CPAP implementation study ($M = 22.05$, $SD = 14.51$) than prior to it ($M = 30.43$, $SD = 18.19$), $t(13) = 2.61$, $p = .02$. There was no significant difference in the number

Table 2

Means and Standard Deviations for Demographic Variables and Other Sample Characteristics

	OSA Clinical Patients			Control Participants		
	N	Mean	SD	N	Mean	SD
Height (cm)	10	170.90	5.63	15	173.03.	5.33
Weight (kg)	11	98.68	18.20	15	82.42.**	9.56
Body mass index	9	34.34	3.48	15	27.54.***	2.76
Age (years)	15	54.60	10.76	15	47.53.	9.48
Days worked per week	15	2.60	2.41	15	4.40.*	1.40
Hours worked per week	15	22.73	22.00	15	37.40.*	15.46
Hours driven per week	15	14.40	16.98	15	32.80.	74.71
Kilometres driven per year	15	10357.33	12032.14	15	14546.67.	13103.86
Sleep hours per night (work days)	15	6.23	1.00	15	7.27.**	0.88
Sleep hours per night (days off)	15	6.73	1.12	15	8.27.**	1.03
Motor vehicle accidents in last 3 years	15	1.87	0.35	15	1.67.	0.49
Average hours of sleep each night	14	6.51	1.25	14	7.91.**	1.21
Time taken for sleep onset (minutes)	14	30.43	18.19	14	19.24.	10.70
Number of times woken up	14	9.21	5.37	14	5.36.	5.30
Probability of feeling refreshed out of seven days	14	0.10	0.12	14	0.78.***	0.36
Epworth Sleepiness Scale score	14	12.43	5.81	15	3.60.***	4.07

***$p<.001$, **$p<.01$, *$p<.05$

of times OSA clinical patients reported awakening during the night pre-treatment and post-treatment, $t(13) = 1.24$, $p = .24$, although they reported feeling significantly more refreshed post-treatment, $t(13) = -11.19$, $p = .0001$.

Data Analysis

Analyses were conducted using the SPSS split plot analyses of variance (SPANOVA) procedure. The SPANOVA is appropriate for research designs that employ mixed repeated measures and independent groups designs. The between-subjects factor was group (OSA clinical patients and control participants) and the within-subjects factor was time. The SPANOVA tests the main effects for time and group and the interaction between the two factors. There were nineteen dependent variables and one SPANOVA was used to test the main and interaction effects for each dependent variable.

The Karolinska Sleepiness Scale, Alertness Questionnaire, Stop Driving Questionnaire, Psychomotor Vigilance Task, AusEd Driving Simulator tasks, and the Perclos measures were all administered at four time points. These measures were taken at approximately 1900 hours (pre-treatment session 1) and 2200 hours (pre-treatment session 2) on the same pre-treatment study day and at 1900 hours (post-treatment session 1) and 2200 hours (post-treatment session 2) on the same post-CPAP implementation study day. Therefore, there were four levels of the within-subjects factor of time for the analyses of these dependent variables. The main effect of time tested the hypotheses that scores on the dependent variables significantly differed between pre-treatment sessions 1 and 2 and also between post-treatment sessions 1 and 2. The main effect of time also examined the effect of the CPAP implementation study on the dependent variables by investigating any differences in scores between pre-treatment session 2 and post-treatment session 2.

Assessment on the Logical Memory, Visual Reproduction, Austin Maze and Trail Making Test were conducted only once pre-treatment and once post-treatment. Therefore, there were only two levels of the within-subjects factor of time for these analyses. The main effect of time tested whether there was any significant difference in scores on the dependent variables between pre-treatment and post-treatment sessions.

For all analyses, the main effect of group tested whether there were any significant differences between OSA clinical patients and control participants on the dependent variables. The interaction effect tested whether any time effects were different between OSA clinical patients and control participants.

Box's M Test and Levene's Test were used to test the assumption of homogeneity of the variance-covariance matrices. In some cases the observed covariance matrices of the dependent variables were not equal. However, the SPANOVA tests were robust to violations of this assumption as sample sizes were equal (Tabachnick & Fidell, 2001). The assumption of sphericity was invoked where the dependent variables were measured over more than two different time periods. Where only two levels of time were analysed, the sphericity assumption was automatically met. Mauchly's Test of Sphericity, produced by SPSS, was used to test the assumption of sphericity. Where the assumption of sphericity was met, the Sphericity Assumed F-test was used, and where it was violated, adjustment was made by using the Greenhouse-Geisser F-test, as recommended by (Francis, 2004).

Karolinska Sleepiness Scale

The results of the SPANOVA showed a strong and significant main effect for time, $F(2,66) = 20.64$, $p = .0001$, $\eta^2 = .42$ (Table 3). There was no significant main effect for group, although there was a significant interaction effect between time and group, $F(2,66) = 9.04$, $p = .0001$, $\eta^2 = .24$.

To explore the significant main effect for time and the interaction effect, post-hoc comparisons were made using multiple 2 X 2 SPANOVA analyses. Scores on the Karolinska Sleepiness Scale for OSA clinical patients and control participants were compared across the two pre-treatment sessions (1900 hours and 2200 hours pre-treatment session), the two post-treatment sessions (1900 hours and 2200 hours post-treatment session), and between the final pre-treatment session (2200 hours) and the final post-treatment session (2200 hours).

The results showed that Karolinska Sleepiness Scale scores significantly differed across the two pre-treatment sessions, $F(1,28) = 22.58$, $p = .0001$, the two post-treatment sessions, $F(1,28) = 8.09$, $p = .008$, and between 2200 hours on the pre-treatment session and 2200 hours on the post-treatment session, $F(1,28) = 28.24$, $p = .0001$. There was a significant interaction effect between time and group type only between 2200 hours on the pre-treatment session and 2200 hours on the post-treatment session, $F(1,28) = 12.69$, $p = .001$. Figure 8 shows subjective sleepiness increased between 1900 hours and 2200 hours on both days for both OSA clinical patients and control participants. Subjective sleepiness at 2200 hours post-CPAP implementation study was significantly lower than subjective sleepiness at 2200 hours pre-treatment for OSA clinical patients only.

Table 3

Split Plot Analysis of Variance for Karolinska Sleepiness Scale for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	55.03	2.34	23.47	20.64	.0001	.42
Time X Group	24.09	2.34	10.28	9.04	.0001	.24
Error	74.63	84	0.89			
Group	3.68	1	3.68	0.31	.581	.01
Error	329.50	28	11.77			
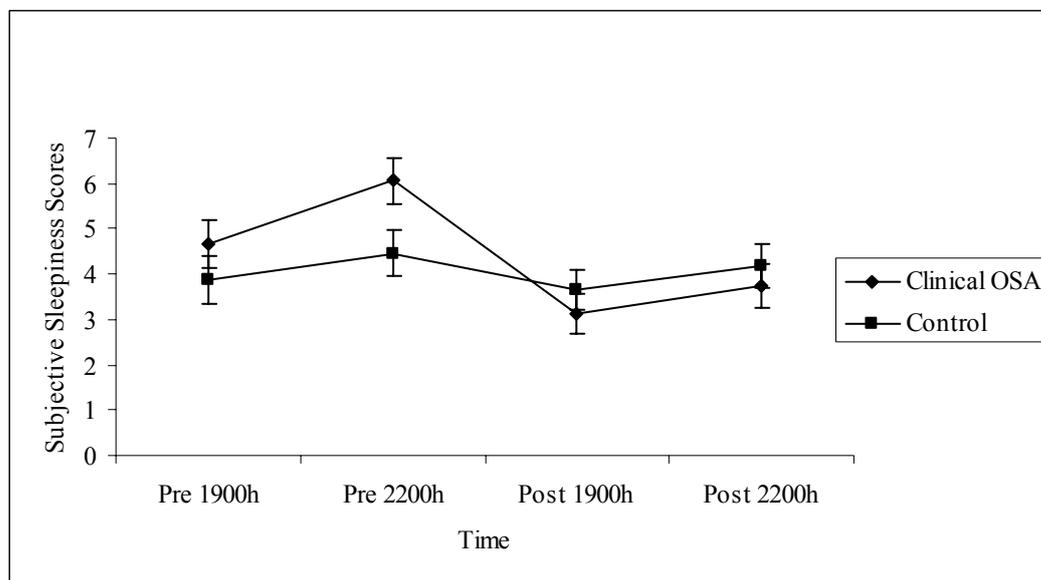
Figure 8. Adjusted marginal means for Karolinska Sleepiness Scale scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Alertness Questionnaire

There were significant and strong main effects for time, $F(2,57) = 16.67$, $p = .0001$, $\eta^2 = .37$, and for group, $F(1,28) = 10.56$, $p = .003$, $\eta^2 = .27$, and the interaction between these two factors, $F(2,56) = 17.95$, $p = .0001$, $\eta^2 = .39$. These results are shown in Table 4.

To further explore the main and interaction effects, three 2 X 2 SPANOVA analyses were conducted. Alertness Questionnaire scores were compared at 1900 hours and 2200 hours for both the pre-treatment and post-treatment conditions, and between 2200 hours pre-treatment and 2200 hours post-treatment. Between 1900 hours and 2200 hours during the pre-treatment session, Alertness Questionnaire scores significantly differed according to time, $F(1,28) = 13.59$, $p = .001$, by group, $F(1,28) = 24.79$, $p = .0001$, and by their interaction, $F(1,28) = 6.66$, $p = .015$. Between 1900 hours and 2200 hours during the post-treatment session, there were no significant effects for time, group, or their interaction. In relation to differences in Alertness Questionnaire scores between 2200 hours pre-treatment and 2200 hours post-treatment, there were significant main effects for time, $F(1,28) = 29.69$, p $= .0001$, and for group, $F(1,28) = 9.91$, $p = .004$. There was also a significant interaction effect between group and time $F(1,28) = 33.38$, $p = .0001$.

Figure 9 shows that symptoms of sleepiness, measured by the Alertness Questionnaire, increased significantly across the evening during the pre-treatment session for OSA clinical patients only. Symptom scores significantly decreased post-CPAP implementation study for OSA clinical patients, to be equal to the scores reported by the control participants.

Table 4

Split Plot Analysis of Variance for Alertness Questionnaire for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	1152.09	2.02	570.56	16.67	.0001	.37
Time X Group	1240.29	2.02	614.24	17.95	.0001	.39
Error	1934.87	56.54	34.22			
Group	1491.08	1	1491.08	10.56	.003	.27
Error	3955.27	28	141.26			
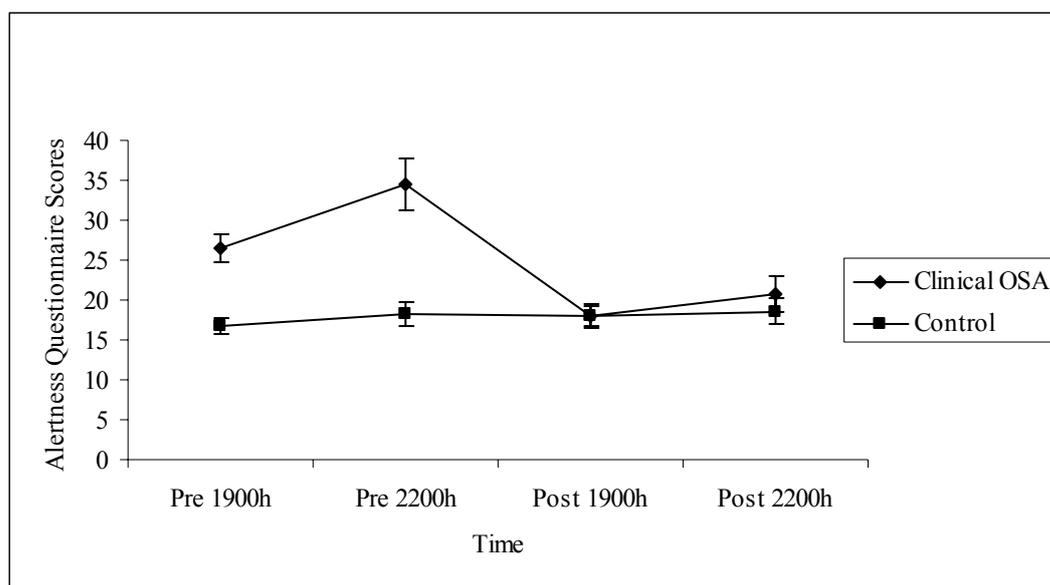
Figure 9. Adjusted marginal means for Alertness Questionnaire scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Stop Driving Questionnaire

Self-reports of driving performance in suburban traffic significantly differed according to time, $F(2,57) = 14.38$, $p = .0001$, $\eta^2 = .34$), by group, $F(1,28) = 8.14$, $p = .008$, $\eta^2 = .23$, and by their interaction, $F(2,57) = 13.38$, $p = .0001$ $\eta^2 = .32$. These results are shown in Table 5.

Post-hoc SPANOVA analyses showed that between 1900 hours and 2200 hours on the pre-treatment session days, driving performance in suburban traffic significantly differed over time, $F(1,28) = 15.59$, $p = .0001$, and by group, $F(1,28) = 13.26$, $p = .001$, and by the interaction between time and group, $F(1,28) = 8.39$, $p = .007$. Between 1900 hours and 2200 hours on the post-treatment session day, there were no significant differences in driving performance in suburban traffic by time, by group, or by the interaction. Between 2200 hours pre-treatment session day and 2200 hours post-treatment session day, driving performance in suburban traffic was significantly different over time, $F(1,28) = 18.31$, $p = .0001$, according to group, $F(1,28) = 9.30$, $p = .005$, and by the interaction of the two factors, $F(1,28) = 21.80$, $p = .0001$.

Figure 10 shows that on the pre-treatment session day, only OSA clinical patients reported that they would stop driving in suburban traffic sooner at 2200 hours than they reported at 1900 hours. Relative to pre-CPAP implementation study, OSA clinical patients' self-assessments of suburban driving latency significantly increased post-CPAP implementation study to be equal to those reported by the control participants.

Table 5

Split Plot Analysis of Variance of Stop Driving Questionnaire (Suburban Traffic) for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	13.80	2.03	6.78	14.38	.0001	.34
Time X Group	12.83	2.03	6.31	13.38	.0001	.32
Error	26.87	56.96	0.47			
Group	7.50	1	7.50	8.14	.008	.23
Error	25.80	28	0.92			
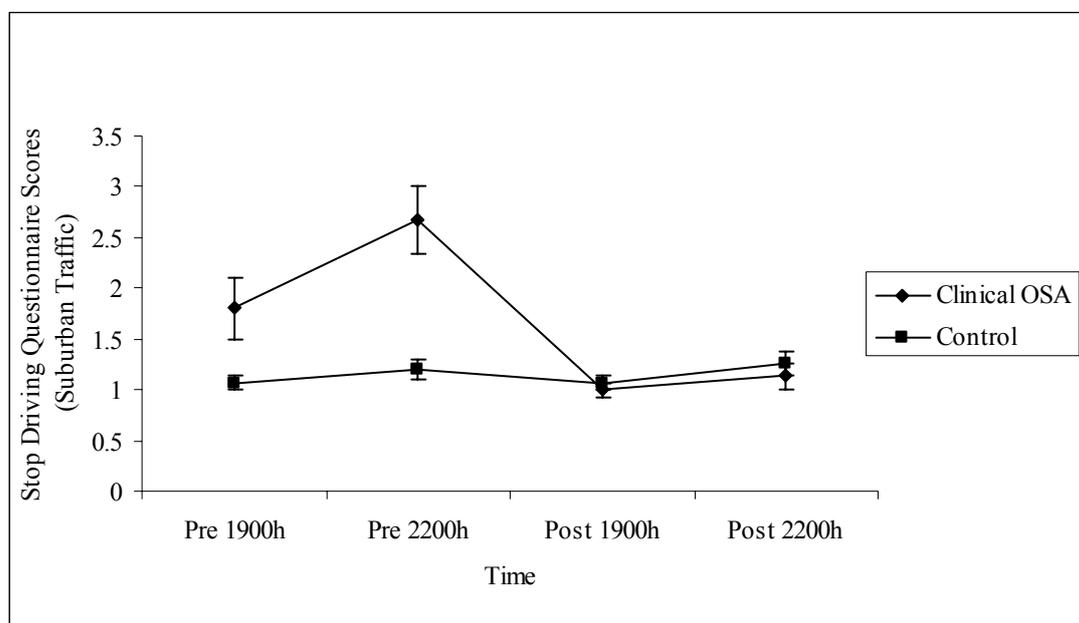
Figure 10. Adjusted marginal means for Stop Driving Questionnaire scores (Suburban Traffic) pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Responses to the Stop Driving Questionnaire for long distance significantly differed by time, $F(3,71) = 23.33$, $p = .0001$, $\eta^2 = .45$), by group, $F(1,28) = 11.29$, $p = .002$, $\eta^2 = .33$, and by the interaction of the two factors, $F(3,71) = 13.64$, $p = .0001$, $\eta^2 = .29$ (Table 6).

Post-hoc SPANOVA analyses showed that the during the two pre-treatment sessions, self-assessments of when participants would cease driving long distances significantly differed according to time, $F(1,28) = 11.56$, $p = .002$, by group, $F(1,28) = 18.28$, $p = .0001$, and by their interaction, $F(1,28) = 6.50$, $p = .017$. During the two post-treatment sessions, there was only a significant difference in cease driving long distance responses according to time, $F(1,28) = 9.21$, $p = .005$. Between 2200 hours pre-treatment session and 2200 hours post-treatment session, responses significantly differed according to time, $F(1,28) = 32.30$, $p = .0001$, by group, $F(1,28) = 14.18$, $p = .001$, and by the interaction between time and group, $F(1,28) = 23.48$, $p = .0001$.

Figure 11 shows that at 2200 hours on the pre-treatment session day, only OSA clinical patients reported that they would stop driving long distances significantly sooner than they would at 1900 hours. On the post-treatment session day, both OSA clinical patients and control subjects reported similar assessments of their driving performance and both groups reported that they would cease driving long distances sooner at 2200 hours than they would at 1900 hours. Between 2200 hours on the pre-treatment session day and 2200 hours on the post-treatment session day, OSA clinical patients' self-assessments of long distance driving latency significantly increased to be equal to those reported by control participants.

Table 6

Split Plot Analysis of Variance of Stop Driving Questionnaire (Long Distance) for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	25.13	2.55	9.87	23.33	.0001	.45
Time X Group	14.70	2.55	5.77	13.64	.0001	.33
Error	30.17	71.30	0.42			
Group	12.03	1	12.03	11.29	.002	.29
Error	29.83	28	1.07			
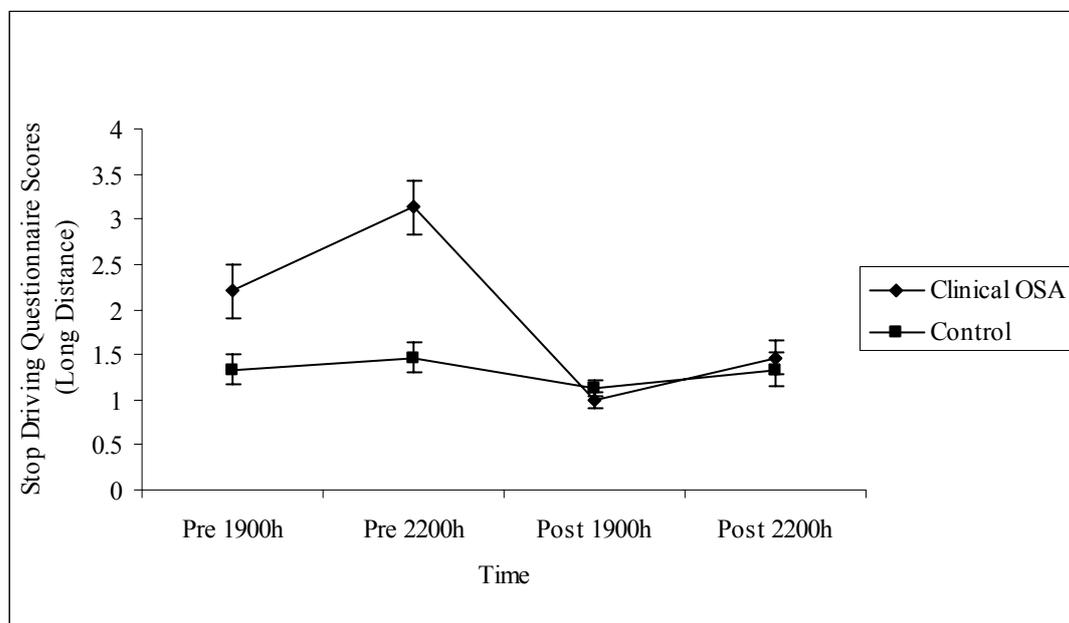
Figure 11. Adjusted marginal means for Stop Driving Questionnaire scores (Long Distance) pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Psychomotor Vigilance Task Performance

The results of the SPANOVA analyses showed no significant difference in the median reaction time or the mean number of lapses between the OSA patients and the control participants, or across time, or for the interaction on the PVT. These results are presented in Tables 7 and 8, respectively. Table 9 shows that there was a weak, but significant, interaction effect between time and group for sustained attention, $F(1,35) = 4.01.$ $p = .042,$ $\eta^2 = .13,$ but no significant main effects for group or time.

Subsequent post-hoc SPANOVA analyses revealed no significant group differences on sustained attention across the time periods for the hypotheses under investigation. However, further analyses revealed a significant interaction effect between group and time for PVT sustained attention scores between 2200 hours on the pre-treatment session day and 1900 hours on the post-treatment session day, $F(1,26) = 8.001, p = .009.$

The adjusted marginal means shown in Figure 12 shows that the time of night had no significant effect on PVT sustained attention. Furthermore, OSA clinical patients and control participants did not significantly differ in Psychomotor Vigilance Task performance except on the first trial post-CPAP implementation study where the OSA clinical patients reported significantly higher levels of sustained attention than the control participants.

Table 7

Split Plot Analysis of Variance of Median Reaction Time on the Psychomotor Vigilance Task for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	3873.63	1.36	2858.61	3.41	.061	.12
Time X Group	4098.28	1.36	3024.39	3.60	.054	.12
Error	29581.28	35.23	839.62			
Group	2735.38	1	2735.38	1.252	.27	.05
Error	56822.88	26	2185.50			

Table 8

Split Plot Analysis of Variance of Transformed Lapses on the Psychomotor Vigilance Task for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	14.39	1.96	7.35	1.85	.17	.07
Time X Group	8.92	1.96	4.56	1.14	.34	.04
Error	202.56	50.89	3.98			
Group	0.31	1	0.31	0.06	.80	.00
Error	124.06	26	4.77			

Table 9

Split Plot Analysis of Variance of Sustained Attention on the Psychomotor Vigilance Task for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	*F*	*p*	η^2
Time	3.22	1.34	2.41	2.87	.09	.10
Time X Group	4.50	1.34	3.36	4.01	.042	.13
Error	29.15	34.77	0.84			
Group	1.89	1	1.89	2.09	.16	.07
Error	23.72	26	0.91			
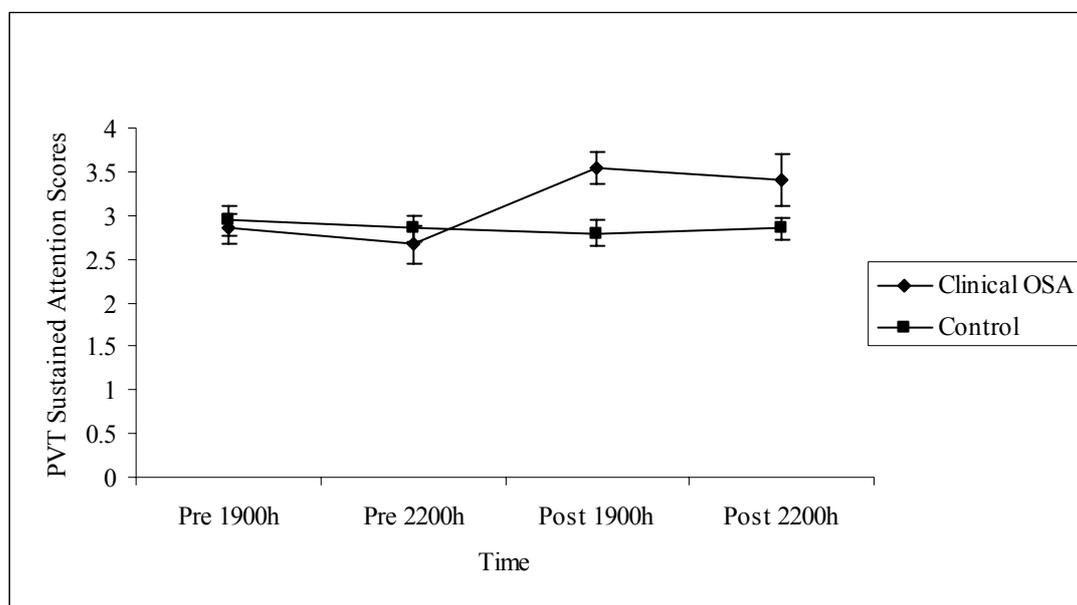
Figure 12. Adjusted marginal means for sustained attention on the Psychomotor Vigilance Task pre-treatment and post-treatment sessions for OSA clinical patients and control participants

AusEd Driving Simulator

The results in Tables 10 and 11 respectively show no significant main effects for time or group and no significant interaction effects between time and group for average velocity deviation and number of crashes measured by the AusEd Driving Simulator. In relation to average steering deviation, there were no significant main effects for time or for group. There was a significant interaction effect, $F(2,43) = 4.48$, $p = .023$, $\eta^2 = .15$ (Table 12).

Post-hoc SPANOVA analyses revealed a significant interaction effect between time and group for average steering deviations between 1900 hours and 2200 hours on the pre-treatment session day, $F(1,26) = 4.71$, $p = .039$, and between 2200 hours on the pre-treatment session day and 2200 hours on the post-treatment session day, $F(1,26) = 8.00$, $p = .009$. There was no significant interaction effect for average steering deviation between 1900 hours and 2200 hours on the post-treatment session day.

Figure 13 shows that prior to the CPAP implementation study, vigilance increased over the course of the evening for control participants, but decreased for OSA clinical patients. Post-CPAP implementation study, the opposite was true. Obstructive sleep apnoea clinical patients significantly increased vigilance whereas control participants significantly decreased vigilance.

Table 10

Split Plot Analysis of Variance of Average Velocity Deviation on the AusEd Driving Simulator for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	8.89	1.24	7.14	0.39	.58	.02
Time X Group	16.54	1.24	13.30	0.72	.43	.03
Error	598.96	32.35	18.51			
Group	272.47	1	272.47	2.03	.17	.07
Error	3482.43	26	133.94			

Table 11

Split Plot Analysis of Variance of Number of Crashes on the AusEd Driving Simulator for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	145.87	1.02	142.95	0.90	.35	.03
Time X Group	139.59	1.02	136.79	0.86	.37	.03
Error	4225.20	26.53	159.24			
Group	220.81	1	220.81	1.44	.24	.05
Error	3977.41	26	152.98			

Table 12

Split Plot Analysis of Variance of Average Steering Deviations on the AusEd Driving Simulator for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	*F*	*p*	η^2
Time	63.61	1.66	38.45	0.12	.85	.00
Time X Group	2447.18	1.66	1479.10	4.48	.023	.15
Error	14197.04	43.02	330.03			
Group	6519.47	1	6519.47	4.11	.053	.14
Error	41266.49	26	1587.17			
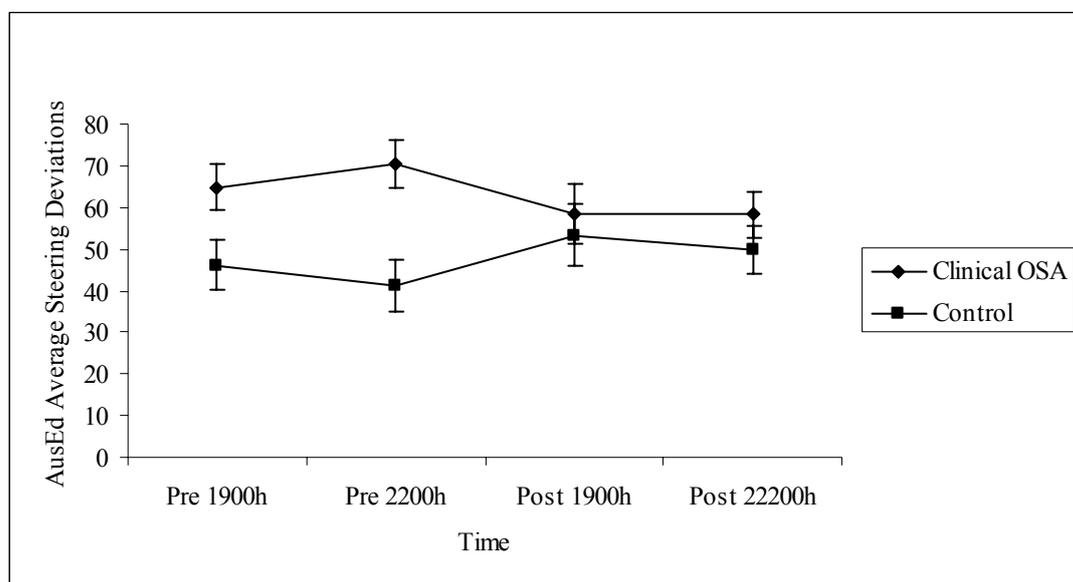
Figure 13. Adjusted marginal means for average steering deviations on the AusEd Driving Simulator pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Perclos

Figures 14 and 15 show that the percentage of time that participants' eyes were more than 80 percent closed was slightly greater among OSA clinical patients than the control group, and eye closure increased over time. However, there were no significant main or interaction effects during the driving simulator and PVT tasks. The results of the SPANOVA analyses are shown in Tables 13 and 14.

Logical Memory

Tables 15 and 16 respectively, show that there were strong and significant differences between pre-treatment and post-treatment for scores on the auditory short-term memory scale, $F(1,28) = 31.25$, $p = .0001$, $\eta^2 = .53$, and for scores on the auditory long-term memory scale, $F(1,28) = 46.37$, $p = .0001$, $\eta^2 = .62$.

There were no significant main effects for group for scores on the auditory short-term or long-term memory scales. There were significant interaction effects between time and group for the auditory short-term memory scale, $F(1,28) = 32.62$, $p = .0001$, $\eta^2 = .54$, and for the auditory long-term memory scale, $F(1,28) = 27.96$, $p = .0001$, $\eta^2 = .50$. Figures 16 and 17 show that auditory short-term and long-term memory scores significantly increased post-treatment for OSA clinical patients only.
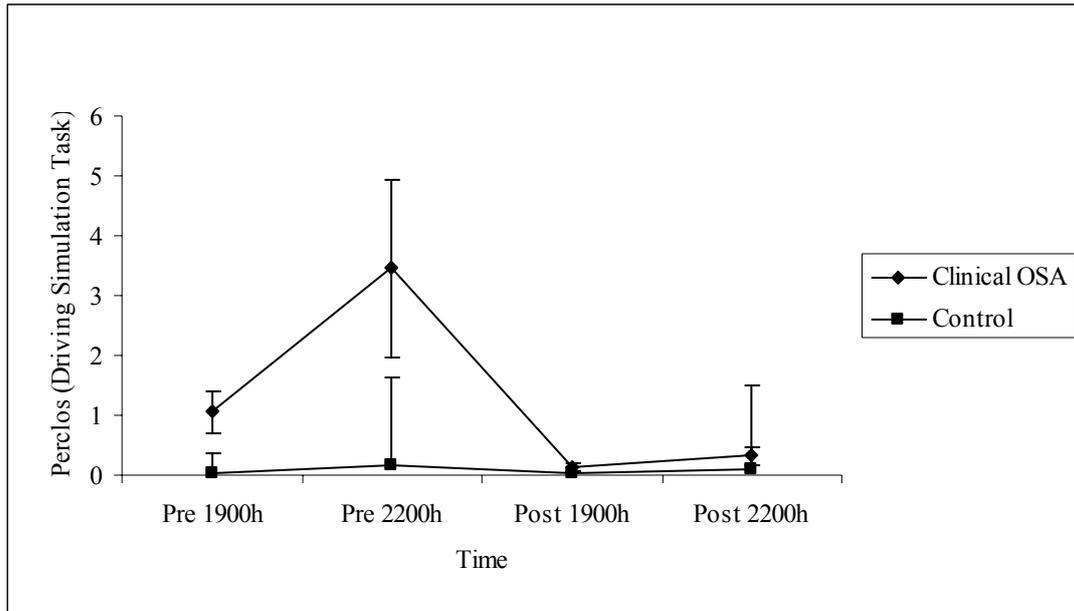
Figure 14. Adjusted marginal means for Perclos during driving simulator tasks pre-treatment and post-treatment sessions for OSA clinical patients and control participants
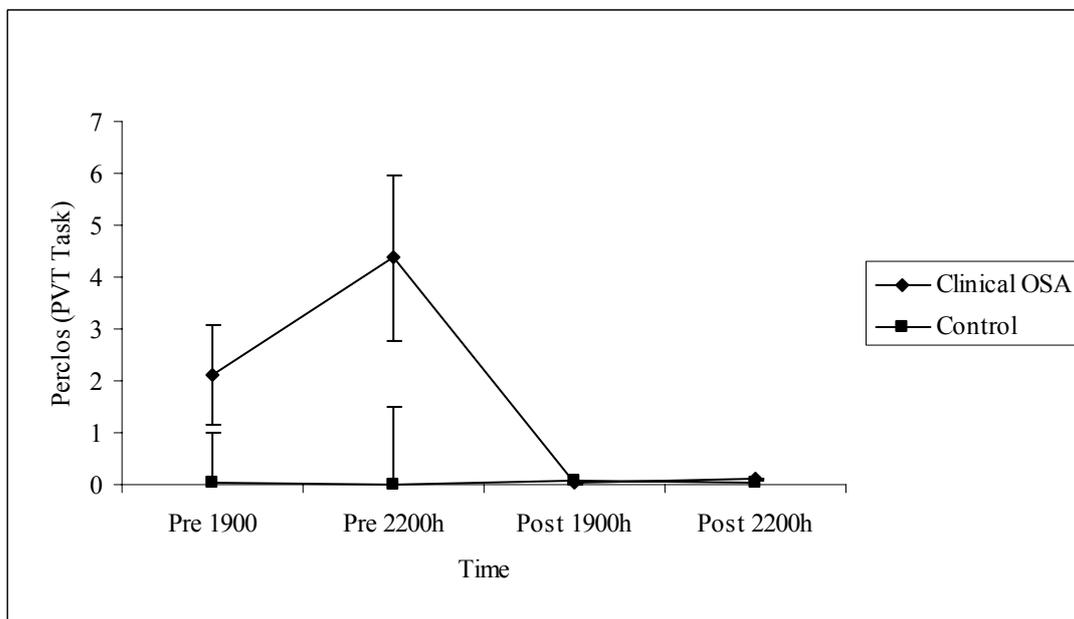
Figure 15. Adjusted marginal means for Perclos during PVT tasks pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Table 13

Split Plot Analysis of Variance of Perclos during Simulated Driving Task for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	*F*	*p*	η^2
Time	55.30	1.03	53.64	2.43	.13	.08
Time X Group	49.54	1.03	48.05	2.18	.15	.07
Error	636.47	28.87	22.05			
Group	40.49	1	40.49	3.22	.08	.10
Error	352.09	28	12.58			

Table 14

Split Plot Analysis of Variance of Perclos during PVT Task for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	*F*	*p*	η^2
Time	94.24	1.17	80.86	3.27	.07	.10
Time X Group	95.44	1.17	81.89	3.31	.07	.11
Error	807.85	32.64	24.75			
Group	81.69	1	81.69	3.57	.07	.11
Error	641.11	28	22.90			

Table 15

Split Plot Analysis of Variance of Auditory Short-term Memory Scores for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	564.27	1	564.27	31.25	.0001	.53
Time X Group	589.07	1	589.07	32.62	.0001	.54
Error	505.67	28	18.06			
Group	209.07	1	209.07	.56	.46	.02
Error	10384.87	28	370.89			

Table 16

Split Plot Analysis of Variance of Auditory Long-term Memory Scores for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η^2
Time	534.02	1	534.02	46.37	.0001	.62
Time X Group	322.02	1	322.02	27.96	.0001	.50
Error	322.47	28	11.52			
Group	252.15	1	252.15	1.22	.28	.04
Error	5802.60	28	207.24			
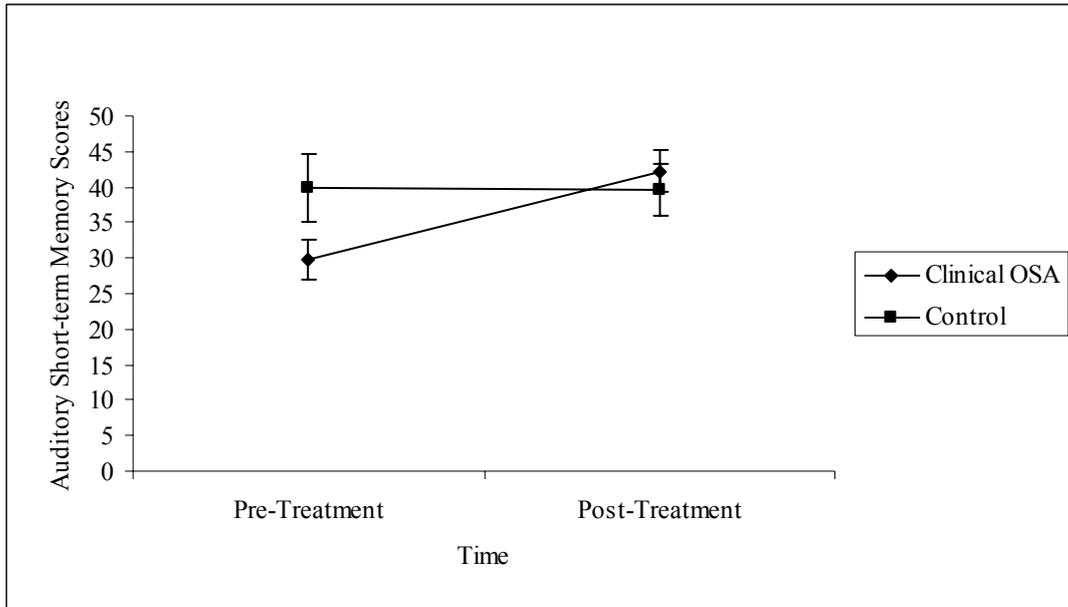
Figure 16. Adjusted marginal means for Auditory Short-term Memory scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants
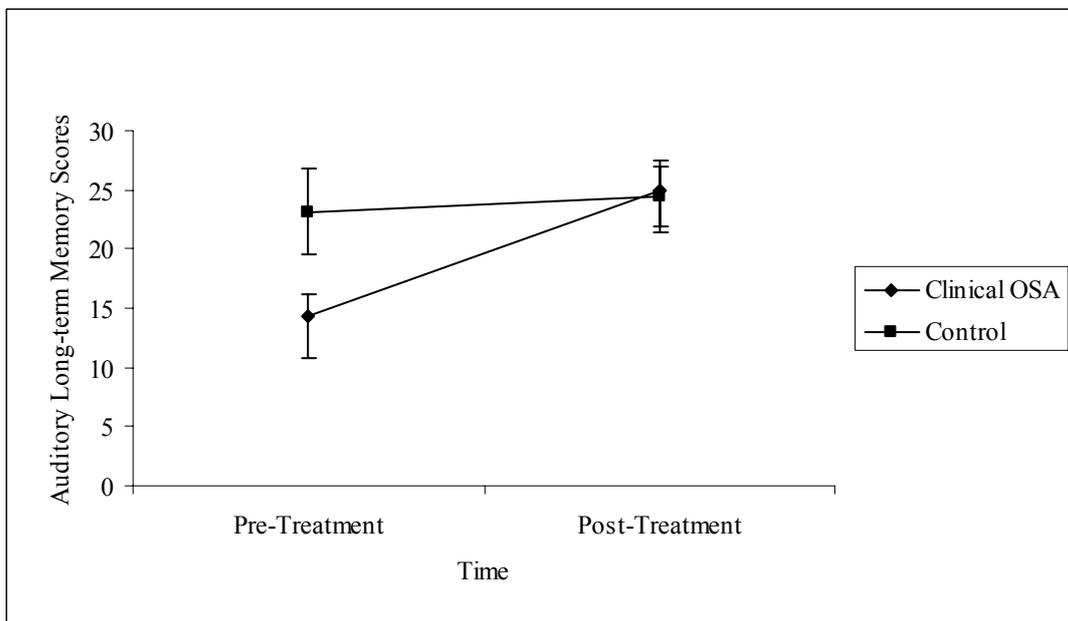
Figure 17. Adjusted marginal means for Auditory Long-term Memory scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Visual Reproduction

Tables 17 and 18 respectively, show that there were significant differences between pre-treatment and post-treatment for scores on the visual short-term memory scale, $F(1,28) = 27.85$, $p = .0001$, $\eta^2 = .50$, and for scores on the visual long-term memory scale, $F(1,28) = 30.96$, $p = .0001$, $\eta^2 = .53$. There were no significant main effects for group for scores on the visual short-term or long-term memory scales. There were significant interaction effects between time and group for the visual short-term memory scale, $F(1,28) = 33.30$, $p = .0001$, $\eta^2 = .54$, and for the visual long-term memory scale, $F(1,28) = 30.49$, $p = .0001$, $\eta^2 = .52$. Figures 18 and 19 show that visual short-term and long-term memory scores significantly increased post-treatment for OSA clinical patients only.

Austin Maze

Table 19 shows that scores on the Austin Maze moderately, but significantly, differed pre-treatment and post-treatment conditions, $F(1,28) = 10.01$, $p = .004$, $\eta^2 = .26$. There was also a significant difference in scores on the Austin Maze between OSA clinical patients and control participants, $F(1,28) = 13.82$, $p = .001$, $\eta^2 = .33$, but the interaction effect between time and group was not significant. Figure 20 shows that the number of errors recorded by both groups was significantly lower post-treatment than pre-treatment, but the OSA clinical patients recorded significantly more errors than the control participants at both times.

Table 17

Split Plot Analysis of Variance of Visual Short-term Memory Scores for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	1490.02	1	1490.02	27.85	.0001	.50
Time X Group	1782.15	1	1782.15	33.30	.0001	.54
Error	1498.33	28	53.51			
Group	252.15	1	252.15	.78	.38	.03
Error	9012.20	28	321.86			

Table 18

Split Plot Analysis of Variance of Visual Long-term Memory Scores for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	4752.60	1	4752.60	30.96	.0001	.53
Time X Group	4681.67	1	4681.67	30.49	.0001	.52
Error	4298.73	28	153.53			
Group	15.00	1	15.00	.03	.87	.001
Error	16218.33	28	579.23			
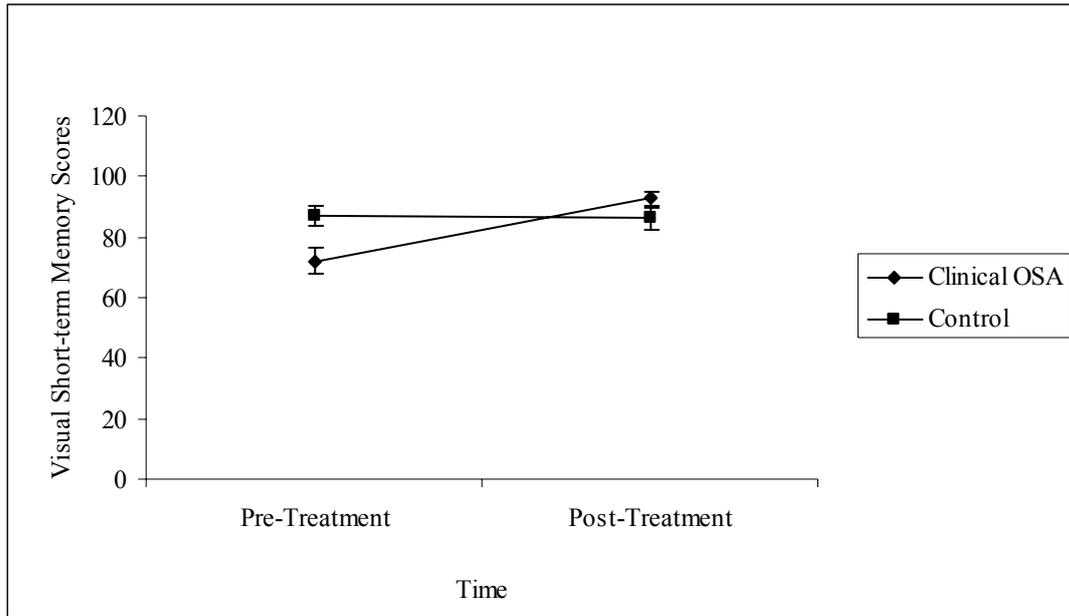
Figure 18. Adjusted marginal means for Visual Short-term Memory scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants
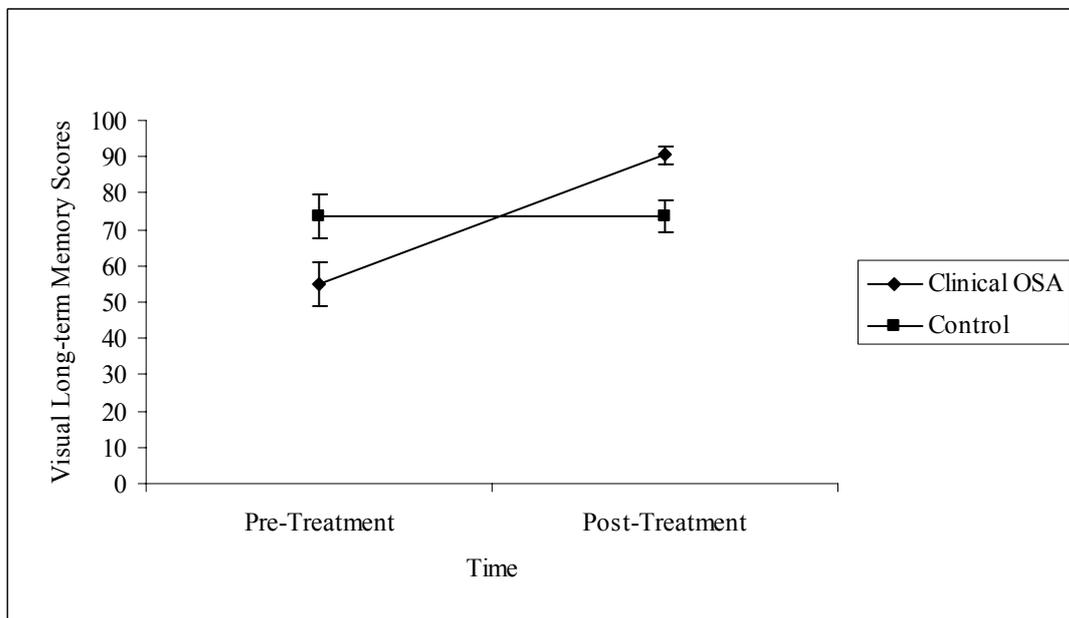
*Figure 19.* Adjusted marginal means for Visual Long-term Memory scores pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Table 19

Split Plot Analysis of Variance of Austin Maze Scores for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	*F*	*p*	η^2
Time	17204.27	1	17204.27	10.01	.004	.26
Time X Group	96.27	1	96.27	.06	.82	.002
Error	48103.47	28	1717.98			
Group	143277.07	1	143277.07	13.82	.001	.33
Error	290209.87	28	10364.64			
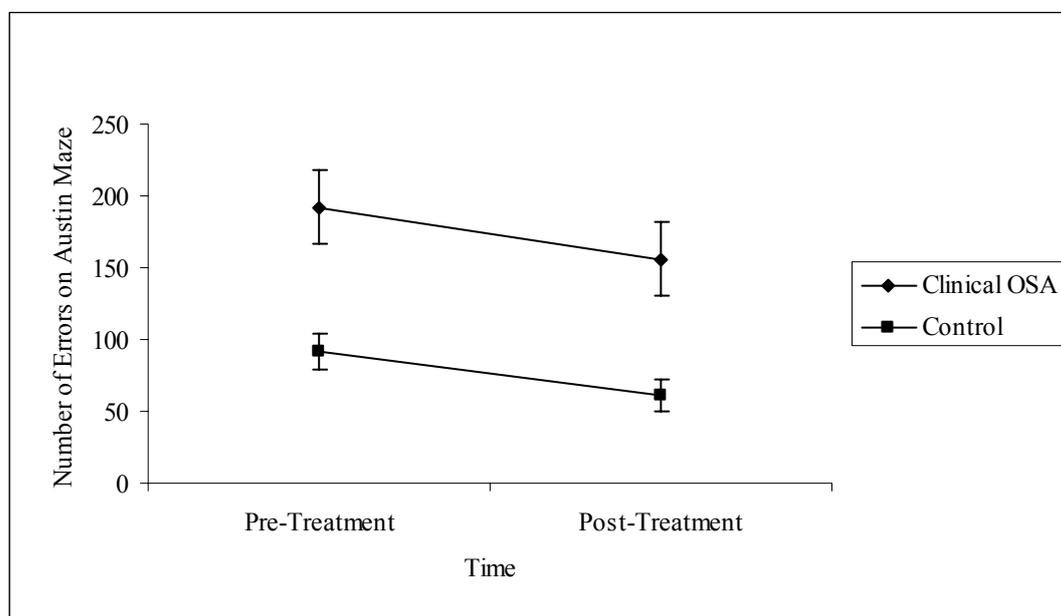
Figure 20. Adjusted marginal means for number of errors on Austin Maze pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Trail Making Test

The results of the SPANOVA analyses showed significant main effects for time on the measure of attention, $F(1,28) = 17.70$, $p = .0001$, $\eta^2 = .39$, and the measure of set shifting, $F(1,28) = 18.18$, $p = .0001$, $\eta^2 = .39$. There was a significant main effect for group on the measure of attention, $F(1,28) = 4.88$, $p = .036$, $\eta^2 = .15$, but not for set shifting. The interaction effects between time and group were statistically significant for the measure of attention, $F(1,28) = 14.27$, $p = .001$, $\eta^2 = .34$, and for the measure of set shifting, $F(1,28) = 8.10$, $p = .008$, $\eta^2 = .22$. The results of the SPANOVA analyses are shown in Tables 20 and 21.

Figure 21 shows that attention scores were significantly higher for OSA patients than for control participants pre-treatment and that scores significantly decreased post-treatment for OSA patients to be equal to the scores of control participants. Figure 22 shows that set shifting scores decreased post-treatment relative to pre-treatment for OSA clinical patients only.

Table 20

Split Plot Analysis of Variance of Trail Making Test Scores (Attention) for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	661.81	1	661.81	17.70	.0001	.39
Time X Group	533.36	1	533.36	14.27	.001	.34
Error	1046.81	28	37.39			
Group	718.50	1	718.50	4.88	.036	.15
Error	4122.94	28	147.25			

Table 21

Split Plot Analysis of Variance of Trail Making Test Scores (Set Shifting) for OSA Clinical Patients and Control Participants

Source of Variance	SS	df	MS	F	p	η²
Time	4418.19	1	4418.19	18.18	.0001	.39
Time X Group	1968.48	1	1968.48	8.10	.008	.22
Error	6806.54	28	243.09			
Group	3324.34	1	3324.34	2.54	.122	.08
Error	36614.85	28	1307.67			
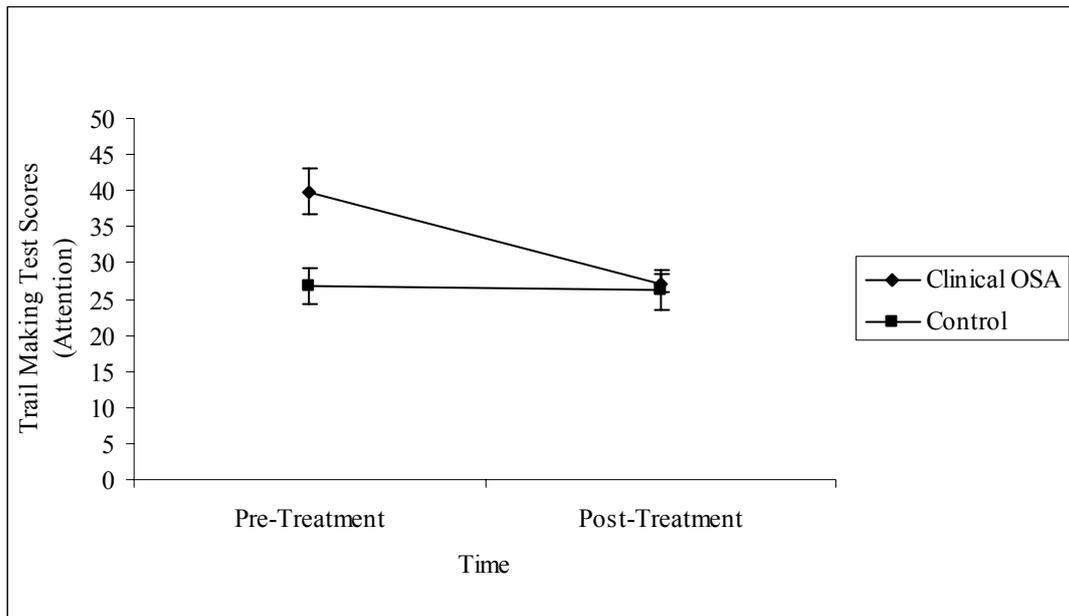
Figure 21. Adjusted marginal means for number of errors on Trail Making Test (Attention) pre-treatment and post-treatment sessions for OSA clinical patients and control participants
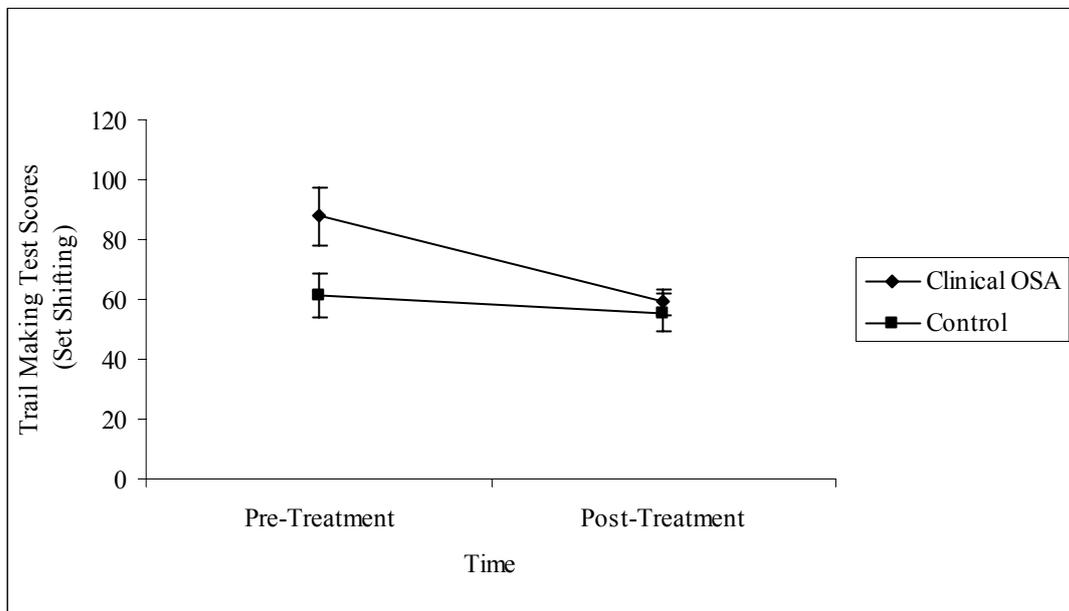
Figure 22. Adjusted marginal means for Trail Making Test (Set Shifting) pre-treatment and post-treatment sessions for OSA clinical patients and control participants

Discussion

The present study aimed to compare simulated driving performance and objective and subjective sleepiness in patients with moderate to severe OSA with control participants. This study also aimed to assess and compare neurocognitive functioning in these two groups by measuring memory performance, vigilance, sustained attention and reaction time. A further aim was to ascertain the benefits of CPAP treatment of OSA with respect to simulated driving and neurocognitive performance.

Measures of Subjective Sleepiness

As hypothesised (hypothesis 2), the subjective measures of sleepiness used in the present study indicated that OSA clinical patients reported significantly higher subjective sleepiness compared to control participants. Previous studies (Akerstedt & Gillberg, 1990; Engleman et al., 1997; George et al., 1996; Horstmann et al., 2000) have also identified higher than normal reports of subjective sleepiness in these patients. These results indicated that OSA clinical patients experienced increased daytime sleepiness, more symptoms of sleepiness and lower alertness compared to control participants.

Johns (1993) suggested that the clinically 'normal' range of ESS scores is two to 10. The OSA clinical patients in the present study had a mean ESS score of 12.43 indicating significantly more disordered sleep and a higher level of daytime sleepiness than control participants, who had a mean ESS score of 3.6. This is supported by Johns (1991), who found a mean ESS score of 11.7 for OSA patients compared to 5.9

for normal controls. Horstmann et al., (2000) also found higher ESS scores in patients with OSA than in a healthy control group. The findings of the present study demonstrated that in comparison to the control participants, OSA clinical patients were more likely to doze off in eight situations related to real-life activities. These included activities that were highly sleep-inducing, such as 'lying down in the afternoon when circumstances permit' and others that were less sleep-inducing, such as 'sitting and talking to someone'. This provided support for other studies that have found an inability of OSA clinical patients to stay awake during the day, at rest or even while performing a task (Bedard et al., 1991).

Daytime sleepiness has been linked to the degree of oxygen depletion in the blood during sleep in those who experience moderate to severe OSA (Bedard et al., 1991; Johns, 1991). Johns also found that ESS scores were correlated with both the RDI and the minimum arterial oxygen saturation. This finding suggests that daytime sleepiness may not only be an effect of hypoxemia associated with oxygen desaturation, but also the number of apnoea/hypopnoea events per hour of sleep.

While there was no significant difference in levels of subjective sleepiness, as measured by the KSS, between OSA clinical patients and control participants pre-treatment, there was a significant difference for both groups across the night. As hypothesised (hypothesis 4), subjective sleepiness was worse at the end of the night (2200 hours) than at the start of the night (1900 hours). Previous studies (Feyer, 2001; Gillberg et al., 1994; Lamond & Dawson, 1999) have also observed an increase in subjective sleepiness as a direct result of sleep deprivation and duration of wakefulness, as well as a circadian rhythm effect (Aeschbach et al., 1997).

The KSS was administered after completing the PVT and the driving simulator task, with the results suggesting that both OSA clinical patients and control participants were feeling sleepier after performing these tasks and significantly more tired at the end of the testing session than at the beginning of the testing session. Symptoms of subjective sleepiness, measured by the Alertness Questionnaire, also increased significantly across the evening during the pre-treatment session, but only for OSA clinical patients. Obstructive sleep apnoea clinical patients reported that they experienced more symptoms of sleepiness, such as struggling to keep their eyes open, blurred vision, stretching and yawning, more often than control participants. This suggests that OSA patients may be more susceptible to circadian rhythm effects after remaining awake for extended periods.

These findings were consistent with Gillberg et al. (1994) who found higher scores on the KSS for participants who were kept awake during the night. Specifically, the authors found that KSS ratings of sleepiness increased significantly across the night and early morning from 2100 hours to 0700 hours. The research literature suggests that higher scores on the KSS in OSA clinical patients and control participants at 2200 hours may reflect a small degree of sleep deprivation experienced by being awake for lengthy periods of time (Gillberg et al., 1994). In addition, similar levels of sleepiness across the testing session (from 1900 hours to 2200 hours) post-treatment for OSA clinical patients and control participants observed in the current study suggest that the CPAP treatment reduced the subjective sleepiness of OSA patients to be equal to those of normal participants.

Finally, the discrepancy between the significant KSS scores and the non-significant Alertness Questionnaire scores for control participants across the night

may be due to the different design of the questionnaires. The KSS is a single item

scale used to measure subjective sleepiness at that particular time (Akerstedt &

Gillberg, 1990) whereas the Alertness Questionnaire measures 11 different symptoms

of sleepiness. Therefore, while control participants may have been feeling sleepier

throughout the night, they may not have been experiencing the more severe symptoms

of sleepiness, such as struggling to keep eyes open, nodding off to sleep, difficulty

keeping to the middle of the road and difficulty maintaining correct speed.

Consistent with the Alertness Questionnaire findings, which indicated reduced

alertness for OSA clinical patients only, the SDQ was administered immediately after

the driving simulator task and indicated that OSA clinical patients experienced a

lower level of alertness throughout the course of night compared to control

participants. This was particularly evident since when asked how they felt about

driving for a short period in suburban traffic, the OSA clinical patients reported that

they would have stopped driving some time ago. Not surprisingly, this was also true

for driving for a continuous long distance.

As hypothesised (hypothesis 6), the current study found that subjective

sleepiness scores on the KSS and Alertness Questionnaire decreased significantly

post-treatment for OSA clinical patients, with scores equivalent to those of control

participants. Furthermore, relative to pre-treatment values, OSA clinical patients'

self-assessments of their ability to drive around suburbia or for long distances

increased post-treatment also to be equal to those levels reported by control

participants.

Treatment intervention studies utilising CPAP have also found improvements of varying magnitudes in daytime sleepiness (Bedard et al., 1993; Engleman et al., 1994; George et al., 1997; George, 2001; Jenkinson et al., 1999; Kribbs et al., 1993). Studies examining subjective ratings of sleepiness show relatively small changes with CPAP treatment (Johns, 1993; Kribbs et al., 1993). However, the ESS score for sleep propensity demonstrates a more marked change with treatment, falling to within the normal range (Johns, 1993). Kribbs et al., (1993) also found that CPAP treatment significantly improved subjective measures of daytime sleepiness. The current findings suggest that for OSA clinical patients, the ability to stay awake and maintain alertness, whether while driving or during day-to-day activities, is substantially improved by CPAP therapy.

Psychomotor Vigilance Task Performance

Probably the most salient assessment of daytime sleepiness is the ability to sustain attention. This impairment is perhaps the root cause of a potential source of mortality in these patients: driving accidents. The results of the current study found that while there was no significant difference in the median reaction time or the mean number of transformed lapses between OSA patients and control participants, there was a weak, but significant interaction effect for sustained attention (mean reaction time), which partially supports hypothesis 5.

Although tasks of long duration have previously been employed to expose deficits in sustained attention, there is evidence that shorter tasks, that is, of less than 30 minutes, can also reveal this impairment (Dinges & Kribbs, 1991). With increased task duration or demand, the ability to maintain attention deteriorates producing

unevenness in performance (Dinges & Kribbs, 1991). This is usually evident by slowing of response time, increased errors and periods of delayed or non-response (lapses). However, it is possible that the non-significant difference in transformed lapses may reflect the non-significant results obtained in relation to measures of slow-eye-closure (Perclos). A study has found that lapses on a reaction time task were particularly sensitive to microsleeps (Reyner & Horne, 1997).

The results of the present study were partially consistent with findings from previous research (Dinges et al., 1997; Kribbs et al., 1993). Dinges et al. found that after seven days of sleep restricted to five hours per night, duration of responses (mean reaction time) on the PVT increased significantly. These results suggested that individuals experiencing limited sleep durations, such as patients with OSA, might be at risk for developing neurobehavioral deficits during their waking hours. Despite this result, there was a significant time-of-day effect on PVT parameters (Dinges et al., 1997). Time-of-day was associated with poorest performance in the morning and best performance during the late evening. Given that the participants in the present study completed the PVT in the evening, the insignificant difference between groups was unexpected and may be related to the short 10-minute task that may not have been sufficiently long to induce sleepiness and/or fatigue. Furthermore, the PVT may not be sensitive enough to separate the two groups, therefore contributing to the insignificant difference.

As hypothesised (hypothesis 5), the results of the current study showed that OSA clinical patients demonstrated higher levels of sustained attention and faster reaction times post-treatment in comparison to control participants. These results were consistent with previous research, which showed that treatment of OSA with

CPAP can significantly improve vigilance and daytime sleepiness (Kribbs et al., 1993). Specifically, Kribbs et al., (1993) found that sleeping with CPAP for at least one month for an average of 5.7 hours per night had clear and positive effects, virtually eliminating apnoeas and hypopnoeas and resulted in significant improvements in objective measures of daytime sleepiness and performance (PVT). Although the number of respiratory events during sleep was less after a period of CPAP use, sleeping without CPAP for only one night fully reversed the effects of daytime sleepiness so that it was indistinguishable from pre-treatment values (Kribbs et al., 1993).

Driving Simulator Performance

As hypothesised (hypothesis 1), a significant difference was found between OSA clinical patients and control participants for average steering deviation from the centre of the left lane, but no significant difference was found for average velocity deviation and number of crashes measured by the AusEd Driving Simulator. The higher average steering deviation scores for OSA clinical patients indicated a decreased level of vigilance for this performance measure. Furthermore, pre-treatment values showed that performance increased over the course of the evening for control participants but decreased for OSA clinical patients (hypothesis 5).

This finding partly supports those of Findley et al. (1989) who found that OSA patients had a higher number of errors on steering during city, rural and highway simulated driving in comparison to control participants. Findley et al. also found that OSA patients had higher errors on speed, signalling and accelerating and a higher number of crashes. Thus, impaired simulated driving performance is not just limited

to when individuals actually fall asleep; rather, their response is also impaired when they are awake due to impaired vigilance and delayed reaction times (Hack et al., 2000).   In addition, George et al. (1996) found that patients with OSA performed significantly poorer than control subjects on a driving simulator task that incorporated two features considered essential for driving; tracking and visual search.

Turkington et al. (2001) identified an increased number of off-road events per hour, reduced tracking and poorer reaction time in patients with OSA during a simulated driving task. The authors indicated that the poorer performance was influenced by a number of factors not directly relating to OSA, including age, sex and alcohol consumption. The non-significant results found for the average velocity deviation and number of crashes performance metrics in the present study suggests that patients with OSA may have had well-developed fatigue-management strategies. For example, individuals may try to counteract the effect by increasing their normal sleep time by napping during the day. However, it is more likely that on a task of relatively short duration it was not possible to demonstrate an effect. Furthermore, there may have been inadequate power to demonstrate an effect given that there were differences in average performance even though they were not significant.

These findings suggest that other factors may influence vigilance and simulated driving performance. Known environmental factors affecting vigilance include noise, temperature and a variety of environmental pollutants (Turkington et al., 2001). In addition, since sleep deprivation produces feelings of increased sleepiness this process is related to circadian rhythms. Therefore, this should be an important consideration in the study of simulated driving performance.

Post-treatment values show that average steering deviation was significantly less for OSA clinical patients but was still slightly higher than for control subjects. These results support those of George et al. (1997), who found that one to 12 months of treatment with CPAP resulted in significant improvement in simulated driving performance in OSA patients. Hack et al. (2000) found similar results, showing that nasal CPAP improved measures of steering performance and response to target stimuli. In addition, pre-treatment groups showed clear deterioration in steering performance across the 30-minute simulation period and this was virtually abolished by treatment with nasal CPAP. This was reflected in the improved ability of subjects to stay on the road for longer periods of time and have fewer off-road events (Hack et al., 2000).

Findley et al. (1989) found that after three to five months of treatment with nasal CPAP, OSA patients had fewer accidents than they did before treatment and that the mean number of crashes post-treatment was not significantly different to those of the control subjects. Lending support to simulated driving performance findings, George (2001) found that on-road accident rates in OSA patients were reduced by 40 percent following at least six months of CPAP treatment. The improvement in performance following treatment suggests that the effects of OSA are a direct cause of poor driving simulator performance. That is, sleep fragmentation and/or nocturnal hypoxemia negatively affect these processes. The improvement in simulator performance after CPAP treatment suggests that patients with OSA may be better and safer drivers while maintaining treatment for OSA. However, this also suggests that stopping treatment may result in a return to premorbid levels of simulated driving performance and an increase in frequency and severity of motor vehicle accidents.

Microsleeps

Although the percentage of time that participants' eyes were more than 80 percent closed was slightly greater among OSA clinical patients than the control group (hypothesis 2) and eye closure increased over the course of the evening (hypothesis 4), there were no significant differences between these groups during the driving simulator and PVT tasks. Furthermore, contrary to what was hypothesised (hypothesis 6), there were no significant differences between pre-treatment and post-treatment values for OSA clinical patients and control participants on any Perclos measures.

Previous studies have shown an increase in the proportion of time that eyes are closed in sleepy subjects (Hakkanen et al., 1999; Wierwille & Ellsworth, 1994). Hakkanen et al. found a significantly longer mean blink duration in bus drivers with OSA and this was related to maintenance of speed and lane drifting on a driving simulator. The mean blink duration in patients returned to the level of control subjects after treatment of their OSA with CPAP. The non-significant results in the current study may reflect inadequate power for the study to detect a difference. It is also possible that the tasks involved were not of adequate duration to induce a degree of sleepiness that would be detected by the measurement of eye closure (Perclos).

The non-significant results in the present study may also be due to the fact that the participants' eyes were closed for less than four percent of the entire testing time and all participants had their eyes closed for less than one second. Given microsleeps last from three to 15 seconds (Priest et al., 2001), it is not surprising that the current study did not find any significant results for this measure as none of the participants demonstrated a true "microsleep".

Dinges et al. (1999) found that Perclos produced a high correlation with PVT lapses and that Perclos correlated better with PVT lapses than individuals rating of sleepiness. While the current study found significant differences in subjective ratings of sleepiness for both OSA clinical patients and control participants, it did not find significant differences for PVT lapses for either group. While individuals may have been experiencing symptoms of sleepiness, such as yawning and stretching, throughout the evening, they may have not been sleepy enough under the study conditions to develop a level of sleepiness required for a "microsleep". Since the present study ceased testing at 2330 hours, the presence of microsleeps and their associated effects on PVT lapses was not evident during the period of investigation.

Neurocognitive Performance

Significant differences between the OSA clinical patients and control participants on several tests of neurocognitive performance indicated that OSA patients had impairments in attention, set-shifting and procedural learning. These findings partially support the current study's hypotheses (hypothesis 3 and 7) as well as results found in previous literature (Bedard et al, 1991; Findley, et al., 1986; Kortte et al., 2002). In general, neuropsychological studies of individuals with OSA have revealed moderate cognitive impairments in the areas of concentration, attention, intelligence, memory and executive functioning. More convincingly, studies have shown marked improvements after six months of CPAP treatment, indicating that cognition was impaired by OSA (Engleman & Joffe, 1999; Naegele et al., 1998).

Logical Memory and Visual Reproduction.

When compared to control participants, OSA clinical patients did not show a deficit in their ability to remember information immediately after oral (Logical Memory I) or visual presentation (Visual Reproduction I). Furthermore, OSA clinical patients did not display a deficit in their ability to recall auditory (Logical Memory II) or visual (Visual Reproduction II) material following a 30-minute delay in comparison to control participants. While not significantly different, the OSA clinical patients' scores on all measures were less than those of the control participants.

The findings of the present study suggest that patients with OSA did not demonstrate impairments in visual and verbal short-term memory or visual and verbal long-term memory, compared to control participants. These findings were not supported by previous research (Bedard et al., 1991; Decary et al. 2000; Findley et al., 1986; Lojander et al., 1999; Naegele et al., 1995). Findley et al. reported cognitive functions in the impaired range for OSA patients on short-term recall of verbal and visuospatial information. Similarly, Bedard et al. found deficits relating to the delayed recall of memory tests between severe OSA patients and controls. Naegele et al. not only found that OSA patients displayed verbal and visual short-term memory deficits, but also that the patients' long-term memory efficiency was significantly decreased.

Despite the non-significant pre-treatment results, there were strong and significant differences between pre-treatment and post-treatment for scores on the auditory short-term memory scale (Logical Memory I) and for scores on the auditory long-term memory scale (Logical Memory II) for OSA clinical patients only and

scores were equivalent to those of control participants. In addition, there were

significant differences between pre-treatment and post-treatment for scores on the

visual short-term memory scale (Visual Reproduction I) and for scores on the visual

long-term memory scale (Visual Reproduction II) for OSA clinical patients only and

scores were equal to those of control participants.

These results were consistent with previous literature examining the effects of

CPAP on cognition of OSA patients (Borak et al., 1996; Naegele et al., 1998). Borak

et al. found that after one year of CPAP treatment there were improvements in visual

and verbal memory, concentration and speed of work, with results for concentration

and memory tests improving after only three months of CPAP treatment (Borak et al.,

1996).

Naegele et al. (1998) also assessed the effect of four to six months of CPAP

treatment on short-term memory span and learning abilities. The results showed that

patients with OSA improved on most of the cognitive learning tasks, but that all short-

term memory test results remained unchanged (Naegele et al., 1998). These findings

indicate that nasal CPAP treatment can result in early improvement of selective

memory functions in patients with OSA, but that other functions may show little or no

improvement.

Austin Maze.

Scores on the Austin Maze moderately, but significantly, differed for both the

pre-treatment and post-treatment conditions. Specifically, the number of errors

recorded for both groups was significantly lower post-treatment than pre-treatment,

but the OSA clinical patients recorded significantly more errors than control participants at both times. It has been suggested that the most valuable use of the Austin Maze is in relation to the study of patients' error utilisation (Walsh, 1991). Results of the current study indicate a deficit in OSA clinical patients' ability to utilise information from a particular behaviour in order to modify the next performance. For example, the OSA clinical patients showed an inability to learn the maze in order to decrease the number of errors as learning trials proceeded.

Crowe et al. (1999) used tasks of executive functioning, visuospatial memory and working memory in order to investigate the cognitive determinants of the Austin Maze. Their results indicated that performance on the Austin Maze was significantly dependent on visuospatial ability and memory. Crowe et al. found that individuals make use of their visuospatial abilities when they are becoming familiar with the path in early trials of the Austin Maze. In order to consolidate details of the path in later trials, individuals must operate visuospatial memory. Results for the present study suggest that OSA clinical patients had deficits in visuospatial ability and memory that interfered with learning of the path. This deficit does not return to normal levels after extended treatment with CPAP as evidenced by the results of the present study.

Prior to this study, procedural memory had not been studied in OSA patients. While researchers believe the primary activity of the basal ganglia regulates voluntary movements, specifically related to planning and initiating motor behaviour (Zillmer & Spiers, 2001), the basal ganglia have also been implicated in this form of memory. Given that reciprocal links have been found between this brain structure and the frontal cortex (Decary et al., 2000), the idea that the frontal lobes play an important role in the acquisition of procedural skills cannot be excluded.

Slowing of the EEG has been found in the frontal regions of OSA patients and research has demonstrated that the basal ganglia are particularly vulnerable to hypoxemia as experienced in OSA clinical patients (Svanborg & Gilleminault, 1996). The present study was the first to evaluate procedural learning in OSA patients using the Austin Maze and suggests that these individuals might have difficulties in initiating and recalling an efficient strategy for performing a task of this nature. Moreover, the current study found that OSA clinical patients' performance on the Austin Maze did not return to normal levels following extensive CPAP treatment, suggesting the possibility of residual damage to specific structures, such as the basal ganglia, the frontal lobes or the reciprocal connections between them, or cerebral function. These matters need to be further investigated with the use of appropriate radiological and physiological tools.

Trail Making Test.

Obstructive sleep apnoea patients completed the Trail Making Test Trail A (attention) subtest, but not Trail B (set-shifting), in a significantly longer time frame (measured in seconds) in comparison to the control participants. This indicates that OSA clinical patients lingered on the numbers only trail (Trail A) and took longer to move from one circled number to the next than they did on the numbers and letters trail (Trail B) in comparison to control participants. This suggests diminished conceptual and visuomotor tracking. Performance on both trails of the Trail Making Test has been reported to reflect a combination of several cognitive functions. These include visual scanning, motor agility and speed, sequencing abilities, attention and concentration (Findley et al., 1986), suggesting that OSA clinical patients have impairments in some, if not all, of these functions.

Studies have found that Trail B is more difficult to complete than Trail A and that impaired performance on this trail is apparent for OSA clinical patients in comparison to normal controls (Bedard et al., 1991; Findley, et al., 1986; Kortte et al., 2002). There may be certain cognitive demands that are placed on the patient by Trail B that are in addition to those required to perform Trail A, as demonstrated by the longer time period required for control participants to complete Trail B compared to Trail A.

Kortte et al. (2002) found that performance on Part B is more sensitive to cognitive flexibility, rather than the ability to maintain set. In addition, Trail B has been described as requiring the ability to switch repeatedly between two sequences (numbers and letters) in order to maintain two response sets simultaneously (Lezak et al., 2004). Therefore, the results of the present study suggest that OSA clinical patients have poorer attentional capacities than control participants for less demanding tasks as evidenced by the significant difference between the two groups on Trail A.

Attention and set-shifting scores significantly improved post-treatment relative to pre-treatment values for OSA clinical patients to equal those of the control participants. This supports previous research, which has found that patients with OSA improved on tasks of attention following four to six months of CPAP treatment (Naegele et al., 1998). These findings indicate that nasal CPAP treatment can result in early improvement of attention and concentration, as well as mental flexibility and set-shifting ability and that post-treatment performance returns to levels that were equal to normal levels of functioning.

Sleep Fragmentation vs. Hypoxemia

Since patients with OSA suffer from both night sleep fragmentation due to repetitive apnoeic episodes and intermittent nocturnal blood oxygen desaturation, the increased sleepiness, reduced performance and neuropsychological deficits displayed prior to treatment by these patients in the current study may be attributed to either or both of these factors. In addition, given that CPAP treatment improves sleep fragmentation and hypoxemia, many of the reversible neuropsychological deficits in OSA observed in the current study may be secondary to either of these symptoms.

Sleep disruption, as a result of the arousal response, is also accompanied by excessive motor activity, such as flailing of the arms, contractions of the leg muscles and changes in body position (Douglas et al., 1985; Findley et al., 1986). These responses to arousal may explain the significantly higher levels of daytime sleepiness reported by OSA clinical patients in this study. In turn, sleepiness has been implicated as the cause of increased risk of motor vehicle accidents in these patients (Findley et al., 1995; George et al., 1996).

Poceta et al. (1990) found that in mild forms of OSA, sleep disruption contributes more to sleepiness, whereas in more severe forms of the disorder hypoxia is the primary pathogenetic mechanism. It may also be that the contribution of each of these factors to vigilance and simulated driving performance is dependent on the severity of the disorder. Given that the OSA clinical patients in this study presented with moderate to severe forms of the disorder, hypoxia may have contributed more to performance impairment. It has also been found that sleep disruption plays a less important part in cognitive impairment than hypoxia in OSA (Findley et al., 1986).

Specifically, Findley et al. found that the degree of hypoxemia during sleep and wakefulness correlated significantly with the degree of overall cognitive impairment. Studies have suggested that the hypoxemia associated with OSA may affect the subcortical regions of the brain (Bedard et al., 1991). Anoxic brainstem dysfunction may occur due to abnormally low oxygen consumption and cerebral blood flow in all cerebral areas, but more severely in the brain stem (Derman et al., 1980).

In addition, short-latency auditory evoked potentials have been found in OSA patients indicating neural dysfunction (Wetmore, Henderson, Doshier, & Milligan, 1988). Given the anatomic proximity of respiratory centres, neural structure controlling vigilance and auditory relays in the brain stem, the impairments identified in these studies may indicate a hypoxia-induced brainstem dysfunction. As a result, the degree of hypoxemia, as measured by blood oxygen desaturation, may be a good predictor of the neuropsychological deficits observed in this study. Therefore, such measures should be evaluated in future studies and oxygen treatment should be considered as an alternative to CPAP treatment since recent research has shown that oxygen can eliminate the desaturations detected in sleep studies (Shneerson, 2000).

Methodological Issues

It is desirable for the control participants to be matched to the OSA patients by age, gender and weight; however, close matching for weight was not possible. This is because obesity is a predisposing factor to OSA. Therefore, it was difficult to find control participants with equivalent BMI's, but without evidence of OSA. Furthermore, premorbid abilities, including intelligence, educational and occupational attainment, were not recorded or compared and may have influenced neurocognitive

test scores. However, given the large effect sizes obtained, it is likely that the group differences obtained were due to the effects of OSA rather than sampling issues.

Analyses in this study employed multiple comparisons, increasing the likelihood of detecting a significant result by chance alone. However, it is unlikely that significance levels achieved in this study were false given the strong and significant results attained. In addition, the small sample size in this study may be viewed as a limitation. However, the repeated measures nature of this design increases the power of this study (Tabachnick & Fidell, 2001). Small sample sizes are not uncommon in studies of this nature. Many of the studies reviewed here (Bedard et al., 1991; Gillberg et al., 1996; Kribbs et al., 1993; Reyner & Horne, 1997) used sample sizes of 15 or less. Nevertheless, caution must be taken in generalising from this study, as it is difficult to estimate how representative this sample is of OSA clinical patients.

Given that the subjective component of sleep is very important, questionnaire investigations may be central to the study of driver sleepiness. Questionnaires can provide information about sleepiness such as feelings of alertness and symptoms of sleepiness. However, such research methods have limitations. For instance, self-report techniques cannot always be considered valid. In the present study, the self-report measures of subjective sleepiness paralleled the changes in physiological indicators of sleepiness, such as slow-eye closure. It would be preferable to include both subjective self-report and more objective measures of sleepiness when conducting sleepiness related research in order to verify sleepiness status.

With repeated testing, which is inevitable in before and after studies, there is potential for patients to learn from the preceding test. Given every participant in the study was re-tested after five or six months the testing effects should be comparable and therefore not significant. However, the post-treatment session results for control participants largely demonstrated a lack of practice effects for all measures used in the current study, except the Austin Maze, which is a measure of procedural learning and therefore anticipated to have a strong learning effect.

This study can perhaps be criticised for not directly measuring CPAP usage with a convert monitor. However, if there were participants who reported regular use of CPAP, but did not regularly use CPAP, these participants would be less likely to demonstrate improvements in sleepiness, simulated driving performance and neurocognitive functioning. This does not appear to be the case given the large number of strong and significant results following CPAP treatment found in the present study.

Further Research

There are theoretical and practical benefits of the current research. The results of this study add to the literature on sleepiness, simulated driving performance and neurocognitive functioning in OSA clinical patients before and after treatment with CPAP.

The multiple post-treatment deficits observed in this study in OSA clinical patients, particularly evident on the Austin Maze task, are perhaps the result of local or diffuse alterations to cerebral structure or function. These alterations are likely to

be reflected in neurochemical, neurophysiological, radiological or circulatory changes and should be further investigated in this population with the use of appropriate tools. The results of such research will advance the knowledge of the physical consequences of OSA, which in turn may aid in a better understanding of the psychological effects. It will also provide a foundation on which to explore different treatment options.

The causes of neuropsychological deficits in OSA, and the physiological pathways leading to daytime behavioural impairments, remain poorly understood and to an extent speculative. While the degree of hypoxemia appears to be a major factor in the pattern of cognitive dysfunction, sleep fragmentation and hypersomnia are also contributory. The correlation between hypoxemia and sleep fragmentation is likely to be high. Additional research is needed to separate the differential effects of these factors in OSA clinical patients. Unfortunately, investigation of the aetiology and mechanisms producing neuropsychological deficits is complicated by the fact that these are almost certainly multifactorial, both within and between individuals with OSA. Confounding the issue are the variable effects of co-morbidity in these individuals. For example, obesity, diabetes and hypertension can predispose OSA patients to cerebral infarction and smoking can lead to greater hypoxemia. These can create additional possible pathways leading to cerebral damage, which not only complicates the matter further but also reinforces the need for future research in this area.

Future field studies would undoubtedly be invaluable in the study of driving performance in OSA clinical patients and microsleeps. However, it is more difficult to detect microsleeps and assess their relationship with performance outside of a laboratory. Numerous factors can influence the level of alertness and the

development of microsleeps in fatigued subjects. In the laboratory many of these factors can be tightly controlled, such as the phase of the circadian rhythm, degree of sleep deprivation and factors that influence the level of arousal. These include environmental factors (e.g. noise, light and vibration), drugs (e.g. caffeine and alcohol), influence of the task (e.g. stimulating versus boring task), motivation and effort of the individual and emotional influences (Gaillard and Kramer, 2000). It is much harder to control these influences in field studies. Furthermore, artefact in EEG recordings and failure of electrodes for EEG recordings are common problems. Despite these obstacles, real-world research should be an aim for future research in this area.

Conclusion and Implications

Obstructive sleep apnoea is considered to arise as a result of the interaction between functional and anatomical changes that result in an apnoea-induced asphyxia. This results in recurrent arousal responses during sleep in order to terminate the obstructive event. This study was designed to investigate the effects of untreated moderate to severe OSA on subjective and objective sleepiness, simulated driving performance and neurocognitive functioning.

The main findings of this study were that OSA patients displayed significant impairments related to daytime sleepiness and levels of alertness, and experienced a number of symptoms of sleepiness. However, they did not indicate deficits on measures of objective sleepiness (slow-eye-closure). On a driving simulator task, the only difference in performance between OSA clinical patients and control participants was on steering deviation, with the OSA clinical patients deviating from the left lane

more often. A novel finding of this study was that impaired performance was observed for OSA clinical patients on the Austin Maze, which indicated a lowered capacity for procedural learning in this group. The current study also found that following CPAP treatment, OSA clinical patients improved on measures of sustained attention, reaction time, simulated driving performance, visual and auditory memory, set-shifting and procedural learning.

The significant deficits in performance on measures of simulated driving and neurocognitive function, demonstrated by OSA clinical patients, have commonly been attributed to levels of daytime sleepiness and hypoxemia characteristic of OSA. Specifically, the experimental and clinical evidence suggests that sleep fragmentation experienced during sleep in OSA may contribute directly or indirectly to deficits in all areas of daytime functioning. For neurocognitive performance, hypoxemia may provide an additional determinant. Hypoxemia is suggested to cause structural damage to the brain, thereby producing significant deficits in memory, attention, vigilance and concentration. The novel finding of this study, relating to the impaired performance on the task of procedural learning suggests that visuomotor and cognitive skill learning tasks should be included in the neurocognitive assessment of OSA clinical patients.

There is an emerging recognition that sleepiness contributes to deterioration in simulated driving performance, leading to a greater risk of accidents. Objectively measuring driving performance, using a driving simulator may help identify patients with OSA who are at risk of having a motor vehicle accident due to the effects of the disorder on sleepiness and neurocognitive functioning. However, knowledge regarding the relationship between OSA and simulated driving performance is

relatively inadequate, with literature often reporting conflicting results. Encouragingly, many studies have consistently demonstrated an increased risk of road accidents in patients with OSA and a reduction in risk following treatment. It is necessary for physicians to warn these patients of the potential dangers of driving while sleepy and the risks that this holds for them both personally and socially. Further work is required to better define those patients with OSA who are at particularly high risk of motor vehicle accidents.

Research literature has found clear improvements in daytime sleepiness, simulated driving performance and neurocognitive functioning after short periods of CPAP treatment. The current study also found that a number of post-treatment values for neurocognitive performance are comparable to performance in normal individuals. This suggests that several neurocognitive deficits observed in OSA clinical patients, such as visual and verbal short-term and long-term memory, attention and set-shifting, are completely reversible with CPAP treatment.

Recent data has also suggested that changes in brain morphology in patients with OSA may also have effects on neurocognitive functioning and may account for the small number of non-significant post-treatment findings in the current study. However, it is also reasonable to postulate that OSA effects may vary in the population, with certain subgroups more vulnerable to the effects of sleep disruption and/or hypoxaemia. It may be that a more comprehensive knowledge of OSA patients will allow further understanding of the underlying biological mechanisms that alter brain function and the extent to which individual differences in brain structure modulate the response to potentially negative physiological conditions experienced with OSA.

Findings of the present study indicate the importance of detecting impairments relating to performance in OSA patients, in order to minimise the risk of accidental injury to themselves or others. Increased sleepiness and deficits in simulated driving and neurocognitive tasks have negative effects on the quality of life of OSA clinical patients, but may be alleviated with CPAP treatment. Continued research into this area is warranted so that significant consequences for the quality of life of patients and for other road users can be identified.

In the future, implementation of neurocognitive testing will be useful in identifying individuals with OSA who are more likely to experience deficits in real-life on-road driving performance. Neurocognitive testing will help in identifying individuals who require CPAP treatment based on their neurocognitive deficits, those who can function better by learning compensatory strategies and under what circumstances individuals should be viewed as disabled or have restrictions placed on their driving and other activities.

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Appendix A

Appendix B

PARTICIPANT INFORMATION SHEET
FOR SUBJECTS WITH SLEEP APNOEA

**<u>ASSESSMENT OF THE EFFECTS OF UNTREATED AND TREATED SLEEP
APNOEA ON DRIVING PERFORMANCE AND MICROSLEEPS WHILST
DRIVING</u>**

Purpose of Study

You are invited to participate in a project to assess the effects of obstructive sleep
apnoea on driving performance and sleepiness whilst driving, and memory function.
In particular we are assessing some new methods of detecting sleepiness whilst
driving and changes in sleepiness and driving performance after treatment.

Your Involvement in the Study

Your participation will involve two separate sessions at the sleep laboratory.

▪ The first session will be held on the evening that you attend the sleep laboratory to
start treatment with CPAP and the second session will require a separate visit three
months after starting treatment. For these two sessions you will need to attend the
sleep laboratory at 5:45pm, having woken at 7:00am that morning. There will be
one practice session at 6pm, and two test periods at 7:00pm and 11:00pm, each
with a 30 minute driving simulation and 10 minute reaction test. Video monitoring
and monitoring of brain activity (using wires attached to the scalp with self
adhesive) will be performed during tests. A series of psychological tests assessing
memory will be administered throughout the night.

▪ You will need to keep a diary of your sleep pattern for the week prior to each
session and avoid caffeine on the day of the study.

Risks and Inconveniences

There may be minor discomfort associated with having leads and electrodes attached while sleeping. There are no invasive or painful procedures proposed. Time involved will be two single evening sessions three months apart. There will be a night in the laboratory to commence treatment with CPAP after the first session, as per treatment prescribed by a physician.

Voluntary Participation

Your participation in the project is entirely voluntary. You have the right to withdraw from the project at any time.

Confidentiality

Results will remain strictly confidential with individuals being identified by a coded number. Neither individuals nor individual results will be identified in publications. Records of the project will be kept under safe storage, locked in a filing cabinet for 7 years after completion. Records may be inspected for purposes of data audit by authorised persons within the institution (ethics committee), or external regulatory body's.

Questions

If you wish to contact someone, independent of the study, about ethical issues or your rights, you may contact Mr. Stephen Duns, Chairman of the Austin & Repatriation Medical Centre Human Research Ethics Committee, Phone (03) 5425 5475.

If you have any questions about the project please do not hesitate to contact me on the following numbers: Dr. Mark Howard: Ph: 03 94963871   Page: 03 9387 1000

PARTICIPANT INFORMATION SHEET
FOR CONTROL SUBJECTS

ASSESSMENT OF THE EFFECTS OF UNTREATED AND TREATED SLEEP APNOEA ON DRIVING PERFORMANCE AND MICROSLEEPS WHILST DRIVING

Purpose of Study

You are invited to participate in a project to assess the effects of obstructive sleep apnoea on driving performance and sleepiness whilst driving, and memory function. In particular we are assessing some new methods of detecting sleepiness whilst driving and changes in sleepiness and driving performance after treatment.

Your Involvement in the Study

Your participation will involve two separate sessions at the sleep laboratory.

- The first session will consist of a one hour visit to gain consent for the project, complete questionnaires relating to sleep habits and memory function and prior medical history, and practice on the driving simulator.

- For the second session you will need to attend the sleep laboratory at 5:45pm, having woken at 7:00am that morning. There will be one practice session at 6pm, and two test periods at 7:00pm and 11:00pm, each with a 30 minute driving simulation and 10 minute reaction test. Video monitoring and monitoring of brain activity (using wires attached to the scalp with self adhesive) will be performed during tests. A series of psychological tests assessing memory will be administered throughout the night.

- You will need to keep a diary of your sleep pattern for the week prior to each session and avoid caffeine on the day of the study.

Risks and Inconveniences

There may be minor discomfort associated with having leads and electrodes attached while sleeping. There are no invasive or painful procedures proposed. Time involved will be two single evening sessions three months apart. There will be a night in the laboratory to commence treatment with CPAP after the first session, as per treatment prescribed by a physician.

Voluntary Participation

Your participation in the project is entirely voluntary. You have the right to withdraw from the project at any time.

Confidentiality

Results will remain strictly confidential with individuals being identified by a coded number. Neither individuals nor individual results will be identified in publications. Records of the project will be kept under safe storage, locked in a filing cabinet for 7 years after completion. Records may be inspected for purposes of data audit by authorised persons within the institution (ethics committee), or external regulatory body's.

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Appendix C

Appendix D

Appendix E

Appendix F

Appendix G

Appendix H

Appendix I

Appendix J

List of Abbreviations

A&RMC	Austin and Repatriation Medical Centre
AM	Austin Maze
ANOVA	One-way analyses of variance
AQ	Alertness Questionnaire
BMI	Body mass index
CPAP	Continuous positive airway pressure
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
ESS	Epworth Sleepiness Scale
Hz	Hertz
KSS	Karolinska Sleepiness Scale
LM	Logical Memory
LTM	Long-term memory
MAPQ	Multivariate Apnoea Prediction Questionnaire
MRI	Magnetic resonance imaging
MSLT	Multiple Sleep Latency Test
OSA	Obstructive sleep apnoea
PVT	Psychomotor Vigilance Task
RDI	Respiratory disturbance index
REM	Rapid eye movement
RT	Reaction time

SDQ   Stop Driving Questionnaire

SPANOVA   Split plot analyses of variance

SPSS   Statistical Package for Social Sciences

STM   Short-term memory

SWS   Slow-wave sleep

Tc   Core body temperature

VR   Visual Reproduction

WAIS-R   Wechsler Adult Intelligence Scale – Revised

WM   Working memory

WMS   Wechsler Memory Scale

WMS-III   Wechsler Memory Scale – Third Edition