Information Processing In Narcolepsy

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THIS THESIS IS DEDICATED TO MY THREE CHILDREN

MATTHEW, TIMOTHY AND REBECCA

WITH ALL MY LOVE

ABSTRACT

Narcolepsy is a disorder of excessive daytime sleepiness. Previous attempts to investigate the relationship between this sleepiness and everyday cognitive function have been limited by both the ability of narcoleptics to contain their sleepiness for brief testing periods and the potential lack of sensitivity of routine performance tasks to sleepiness induced changes. The first study reported in this thesis developed a research protocol which allowed subjects with narcolepsy to express states of sleepiness and non sleepiness and to then compare the performance of subjects with narcolepsy to age, gender, and IQ matched controls on tasks evaluating automatic, attentional and complex cognitive functioning. The results indicate that at high arousal subjects with narcolepsy performed as well as controls on automatic tasks. This suggests that the capacity to perform for narcolepsy is not restricted by physiological factors but is secondary to the effects of sleepiness. Comparison of both the within subject effects for narcolepsy subjects of the transition between high and low arousal states, and the between subject effects of low arousal for narcolepsy subjects compared to controls, indicate that complex cognitive tasks are the most sensitive to arousal fluctuation. The second study compared the effects of low arousal for narcoleptic subjects, on selected performance tasks, with the effects of 32 hours of sleep deprivation for non pathologically sleepy subjects. The previously noted decrement for complex processing tasks secondary to low arousal in narcoleptic subjects was not demonstrated for the sleep deprived population. These differential performance outcomes for narcoleptic and sleep deprived controls are evaluated within a

theoretical model of the interaction between sleepiness and performance. The third study reported in this thesis evaluated the subjective impressions of narcoleptic subjects of diminished memory function associated with the disorder. Previous evaluations have been non specific, requiring subjects to simply provide a global rating of subjective memory function. The current study formalised this subjective analysis of memory function using the Metamemory in Adulthood Instrument to compare aspects of subjective memory dysfunction between (i) narcoleptic subjects, (ii) subjects with excessive daytime sleepiness not associated with narcolepsy, and (iii) controls . The analysis indicates narcoleptics have significantly diminished self efficacy for memory function, in comparison to the referent groups, despite demonstrating equivalent levels of memory knowledge. The three studies reported in this thesis all address new areas of research associated with cognitive function in narcolepsy. In addition an integrated model is developed that illustrates the postulated role of affective dysfunction and sleepiness in narcolepsy in contributing to both cognitive difficulties and dysfunction on complex processing tasks.

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TABLE OF CONTENTS

TABLE OF CONTENTS (CONTINUED)

TABLE OF CONTENTS (CONTINUED)

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

GLOSSARY OF ABBREVIATIONS

AEP	Auditory Evoked Potential
CFF	Critical Flicker Fusion
CNS	Central Nervous System
EDS	Excessive Daytime Sleepiness
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
ERP	Event Related Potential
HLA	Human Leukocyte Antigen
Hz	Hertz
MMPI	Minnesota Multiphasic Personality Inventory
MSLT	Multiple Sleep Latency Test
NODSS	Narcolepsy and Overwhelming Daytime Sleep Society
NREM	Non Rapid Eye Movement
PASAT	Paced Auditory Serial Addition Task
PET	Positron Emission Tomography
PSS	Polygraphic Score of Sleepiness
RAVLT	Rey Auditory Verbal Learning Task
REM	Rapid Eye Movement
RT	Reaction Time
RTSW	Repeated Test of Sustained Wakefulness
SCL	Skin Conductance Level

SOREM	Sleep Onset Rapid Eye Movement
SPECT	Single Positron Emission Computed Tomography
SPF	Sleep Propensity Function
SSS	Subjective Sleepiness Scale
SWS	Slow Wave Sleep
VAS	Visual Analogue Scale
WAVT	Wilkinson Auditory Vigilance Task

GLOSSARY OF DEFINITIONS

Many terms that are used in both the sleep and performance literature have, as yet, no substantive definition, but are used with the assumption that some "common sense of meaning" exists. This glossary will identify the meaning of some of these terms within the context of this thesis.

Arousal

Psychophysiological capacity of the individual to respond to the environment.

Attentional / Effortful Tasks

Tasks dependent on the input of attentional resources.

Automatic Tasks

Tasks performed independently of attentional resources and therefore sensitive to tonic arousal states.

Cognitive Model

A model of the relationship between sleepiness and performance that argues that sleepiness leads to reversible changes in the CNS capacity for information processing.

Core Sleep

Sleep essential for cerebral restitution. Represents the first few hours of sleep and comprises mainly SWS and some REM sleep.

Data Limiting Paradigm

A model of the impact of sleepiness on performance which argues that sleepiness decreases the capacity of the CNS to process stimulus material.

Fatigue

Performance decrement as a function of time on task.

Incremental Decline

A model of the interaction between sleepiness and performance that assumes a negative linear relationship between the variables.

Lapse Hypothesis

A model of the interaction between sleepiness and performance that assumes that performance decrements consequent to sleep loss occur as a result of subjects "missing" stimulus items.

Motivation

An increase in processing resources applied to a task as a consequence of heightened incentive to perform that task.

Optional Sleep

A period of sleep consequent to a behavioural drive to sleep. Comprises stage 2 and some REM sleep.

Phasic REM

Periodic bursts of neural activity during REM sleep such as rapid eye movements or middle ear muscle activity.

Resource Limiting

A model of the impact of sleepiness on performance that assumes that sleepiness decreases the attentional resources that a subject can apply to a task.

Sleepiness

A state of decreased arousal.

Sleep Need

A measure of the biological drive to sleep.

Sleep Latency

The time taken to sleep onset when the individual is given the opportunity to sleep.

Sleep Propensity

The psychobiological likelihood of an individual sleeping.

Tonic / Habitual Arousal

The resting arousal state.

Tonic REM

Background neural state during REM sleep.

Vigilance

Capacity of an individual to monitor their environment utilising tonic arousal resources.

STATEMENT OF THE PROBLEM

Narcolepsy is a disorder characterised by excessive daytime sleepiness. The central aim of this thesis is to evaluate the impact of this sleepiness on cognitive function for subjects with narcolepsy.

The impetus to explore this question emerges from the three diverse areas of i) the large body of research validating the impact of sleepiness on performance for non pathological sleepers and the characterisation of narcolepsy as a disorder of excessive daytime sleepiness, ii) self reports by narcoleptics of subjective experiences of cognitive dysfunction, particularly in the area of memory function, and, iii) the potential dual role of REM sleep in both normal information processing and the pathophysiology of narcolepsy.

The available research literature evaluating the impact of narcolepsy on information processing has failed to demonstrate cognitive impairments associated with the disorder. The validity of these previous findings remain limited however by the ability of narcoleptic subjects to contain their sleepiness for brief testing sessions. Experimental protocols have generally failed to 'capture' sleepiness in narcoleptics and therefore researchers have questioned the external validity of available laboratory based performance findings for this clinical population.

One of the primary aims of the study reported in this thesis is therefore to establish a 'sleepy' testing environment for narcoleptics that provides greater external validity than previous research. This methodology will allow for comparative analyses of performance measures for narcoleptic subjects under both sleepy and non sleepy testing environments. Performance change associated with sleepiness will be evaluated across automatic, attentional and complex cognitive tasks.

If performance deficits are demonstrated for subjects with narcolepsy then the question emerges whether these performance deficits are similar to those associated with sleep deprivation for non pathologically sleepy subjects. The second study reported in this thesis will attempt to evaluate this question by inducing a level of sleepiness in non pathologically sleepy subjects that equates with the reported sleepiness in subjects with narcolepsy. Performance decrements associated with this sleep deprivation will be evaluated and compared to effects for narcoleptic subjects reported in the first study.

To facilitate an understanding of the nature of sleepiness for subjects with narcolepsy, and the effects of this sleepiness on performance for both pathologically and non pathologically sleepy subjects, a model of the interaction of sleepiness and performance will be presented by the thesis author. This model, which is adapted from the work of Horne (1988a), provides an opportunity for comparative analyses of potential differences in both the qualitative and quantitative nature of sleepiness, and the impact of this sleepiness on cognitive functioning for narcoleptic and sleep deprived subjects.

The third study of this thesis will evaluate the subjective experience of memory dysfunction reported by subjects with narcolepsy. Recently there have been significant changes in the understanding of metacognitive processes and this study will compare aspects of metamemory between subjects experiencing excessive daytime sleepiness not associated with narcolepsy, subjects with narcolepsy and control subjects.

Finally this thesis will integrate the findings from this analysis of subjective memory dysfunction in narcolepsy with the previous objective analyses to generate an integrative model of the relationship between sleepiness and performance in narcolepsy.

CHAPTER 1

The Nature of Sleepiness

Which came first-the hen or the egg? In the alternation of sleep and wakefulness, which of the two states interrupts the other? Is the onset of sleep an active process or a mere cessation of wakefulness? (Kleitman, 1963, p. 363).

Introduction

Sleepiness is an ill defined biological phenomenon that has traditionally not been investigated as a discrete state but rather assumed to represent a "hybrid ... confusional" condition between the pivotal extremes of sleep and wakefulness (Pivik, 1991, p. 3). An early conceptualisation by Kleitman (1963) of the alternation between sleep and wake stages compares sleep and wakefulness to ice and water with transitional stages of melting or freezing representing the intermediate stages of drowsiness. Kleitman (1963) further suggests that the intensity of this transitional state may vary just as water may be

> near the freezing point or close to boiling point, so may alertness vary from semi - wakefulness to manic hyperactivity 'boiling mad'. Conversely, the depth of sleep, like the coldness of ice, may be close to the transition state or near coma (Kleitman, 1963, p. 5).

The sleep wake transition is therefore represented by Kleitman (1963) as a linear balance between states. More recently Johns (1993) has presented a model of sleep and wakefulness that refines this model and presents sleepiness as a fluctuating process between the competing drives of sleep and wakefulness. Johns (1993) states that the propensity for

sleep or wakefulness is determined by the interaction of sleep wake drives. These two drives which are mutually inhibiting are comprised of primary and secondary components. For both sleep and wake drives the primary component is the circadian sleep propensity. For sleep the secondary drive component is a function of prior wakefulness. The secondary drive component of wakefulness is enhanced by sensory stimulation and diminished by decreased physical and psychological activity, a process of preparing for sleep which Johns (1993) refers to as "sleepening". The absolute value of sleep or wakefulness is determined by the cumulative effect of the primary and secondary drives. The level of sleepiness therefore represents the balance between these absolute sleep wake drives.

Thus both Kleitman (1963) and Johns (1993) conceptualise sleepiness as a transitional state, the intensity of which is a function of the balance between the forces driving sleep and wakefulness. This representation of sleepiness implies that sleepiness is (a) temporally related to parent states of wakefulness and sleep and therefore occurs as a passive response to the balance of forces between these parent states and (b) sleepiness is a unitary physiological state varying quantitatively along a single dimension between sleep and wakefulness.

This chapter will attempt to evaluate the nature of sleepiness and will argue that models such as those proposed by Kleitman (1963) and Johns (1993) potentially underestimate the complexity of this physiological state. One of the difficulties in this analysis of sleepiness is the lack of theoretical literature devoted to non pathological sleepiness. In the early 1960's Kleitman presented a seminal review of aspects of sleep and wakefulness but of over 500 major topics cited in his text's subject index there was no entry for sleepiness. More recently, despite the growing acknowledgment of the functional significance of daytime

sleepiness, only 6 of approximately 1000 pages of the 1994 edition of "Principles and Practice of Sleep Medicine" discuss theoretical aspects of this state.

Measures of Daytime Sleepiness

Some of the difficulties of defining the construct of daytime sleepiness are reflected both in the range of instruments that have been used to measure sleepiness, and the discrepancies that emerge from differing measurement strategies. This section will review some of these instruments.

Subjective Measures of Sleepiness

The Stanford Sleepiness Scale (SSS) developed in 1972 by Hoddes, Dement, and Zarcone was the first instrument designed to quantify the sleepiness construct. The SSS is a self rating scale consisting of seven statements which describe varying states of sleepiness. For example item 1 is Feeling active and vital; alert; wide awake and item 4 is A little foggy; not at peak; let down (Hoddes, Zarcone, Smythe, Phillips & Dement, 1973, p. 431). Subjects are asked to record the scale value which best describes their subjective sleepiness state. Evaluation of the scale suggests it is able to reflect sleepiness changes over fifteen minute time intervals (Hoddes et al., 1973) and is sensitive to the effects of both total sleep deprivation and recovery sleep (Hoddes et al., 1973; Herscovitch & Broughton, 1981). Because the SSS is inexpensive and simple to administer and is appropriate for repeat administrations it has been used widely in clinical settings (e.g.. McCann et al., 1992; Mikulincer, Babkoff & Caspy, 1989). Interestingly the SSS is reported to have limited validity as a measure of sleepiness amongst clinically sleepy subjects. Sufferers of excessive daytime sleepiness (EDS) are reported to typically underestimate the severity of their

sleepiness (Roth, Hartse, Zorick, & Conway, 1980). This may reflect different baseline levels of sleepiness that develop for pathologically sleepy individuals or may occur as a consequence of EDS sufferers losing an appropriate frame of reference by which to measure their sleepiness state (Dement, Carskadon, & Richardson, 1978). The question of both the internal and external validity of self rating sleepiness scales is however difficult to address. Maclean, Fekken, Saskin and Knowles (1992) argue that psychometric analyses of the items on the SSS demonstrate a lack of internal consistency for descriptors associated with particular scale levels. In addition Maclean et al. (1992) demonstrate that factor analytic evaluation of the SSS results in the separation of the scale into two discrete factors which they characterise as 'activation' and 'sleepiness'. This finding from the factor analysis provides tentative support for the conceptualisation of sleepiness as a multidimensional construct. Additional support for this position of the multidimensionality of sleepiness comes from the lack of congruence between the SSS and objective measures of sleepiness such as the multiple sleep latency test (MSLT). Whilst this lack of congruence is used to argue for the decreased validity of self rating sleepiness in clinical groups, this lack of convergence between subjective and objective sleepiness scales may equally indicate that these measures tap different aspects of sleepiness and hence their lack of convergence in clinically sleepy populations may reflect fundamental differences in these sleepiness measures for pathological populations rather than the diminished validity of self report measures.

A less structured technique for assessing subjective sleepiness is the use of a Visual Analogue Scale (VAS) where subjects are asked to identify their level of sleepiness on a horizontal line between pivotal extremes of sleep and wakefulness. Because the instrument is quick to administer it has been used in settings, such as circadian rhythm studies, where repeated sleepiness measures are required (e.g. Babkoff, Caspy & Mikulincer, 1991).

Comparison of SSS and VAS measures indicate a significant correlation between the scales across an extended sleep deprivation paradigm (Babkoff et al., 1991).

Several other self rating sleepiness scales have been developed. The Thayer Activation Deactivation Check List (Thayer, 1978) consists of fifty adjectives and subjects are required to rate the relevance of each adjective to their immediate arousal state. Whilst the scale is suitable for single sleepiness evaluations the length of the scale makes it inappropriate for repeat administrations.

More recently Johns (1991) has developed the Epworth Sleepiness Scale which assesses sleep propensity in a variety of everyday settings. The scale aims at a global sleepiness rating and has been demonstrated to discriminate control from clinical groups and to reliably index severity of obstructive sleep apnea (Johns, 1992). The Epworth scale appears to have its major application as a screening device for EDS, measuring chronic behaviour rather than transitory sleepiness levels.

Objective Measures of Sleepiness

Pivik (1991) provides a summary of physiological responses associated with sleep onset. Of primary importance for the measurement of sleep propensity have been the physiological changes in brain activity measured using the electroencephalogram (EEG). The transition from wakefulness to sleep is marked by characteristic changes in the frequency and amplitude of electrical brain activity and these changes, when measured in conjunction with oculomotor and facial electromyographic activity, have been standardised to provide criteria for discriminating between wakefulness and subsequent sleep stages (Rechtschaffen & Kales, 1968).

Kamiya (1961) had noted the "self evident" measure of tendency to fall asleep as an index of level of sleepiness but discarded it as impractical for clinical assessment. Carskadon and Dement (1979) reevaluated sleep latency and demonstrated that it provided an objective measure of sleep propensity sensitive to sleepiness induced effects of sleep deprivation. Using sleep latency as the dependent measure, Carskadon and Dement (1979) developed the Multiple Sleep Latency Test (MSLT). The MSLT provides five discrete opportunities for subjects to sleep at 2 hour intervals over the day. Subjects, connected to a polysomnographic recording device, lie in a darkened, quiet room and are given the instruction to "please close your eyes, lie quietly and try to fall asleep" (Carskadon & Dement, 1979, p. 498). Sleep latency is measured from the point of lights out to the first epoch of any sleep stage and the test continues for 15 minutes after this first sleep epoch. If no continuous epoch of sleep occurs the test is terminated at the end of 20 minutes and a latency of 20 minutes is recorded in the analysis (Thorpy, 1992). The American Sleep Disorders Association provide the following guidelines for the definition of the severity of daytime sleepiness (Thorpy, 1992). A sleep latency of 10-15 minutes, measured as the mean latency over the five nap opportunities, indicates mild sleepiness with minimal associated impairment; 5-10 minute latencies represent a diagnostic "gray zone" (italics used in text) and a latency of less than 5 minutes provides the clinical criterion for pathological sleepiness.

In nonclinical subjects the MSLT has been demonstrated to be sensitive to diurnal changes in sleepiness (Carskadon & Dement, 1992; Clodore, Benoit, Foret, & Bouard, 1990); to the effects of sleep deprivation on daytime sleep tendency (Carskadon & Dement, 1982); to aspects of individual difference in sleep propensity (Roehrs, Timms, Zwyghuizen-Doorenbos, Buzenski, & Roth, 1990) and to the influence of maturation, aging, sleep pathology and drug ingestion on daytime sleepiness (Carskadon & Dement, 1987).

Hartse, Roth, and Zorick (1982) noted that discrepancies existed between subjective reports of daytime sleepiness and objective MSLT measures, and suggested that "it is possible that the ability to fall asleep quickly may have nothing to do with the ability to stay awake and alert" (p. 108). This argues that the ability to enter sleep may be controlled by different mechanisms to those which sustain wakefulness. To assess the difference between sleep latency and maintenance of wakefulness, Hartse et al. (1982) developed the Repeated Test of Sustained Wakefulness (RTSW). This test is structured in a similar manner to the MSLT but subjects, when lying down, are instructed to try and stay awake rather than trying to sleep. When instructed to stay awake subjects demonstrated significantly increased sleep latencies to the MSLT condition. Hartse et al. (1982) suggest that these RTSW findings indicate that daytime sleepiness may involve more subtle indices than those assessed using gross EEG measures.

Roth, Nevsimalova, Sonka, and Docekal (1986) suggest that just as sleep varies in intensity, so too may sleepiness. An understanding of daytime sleepiness may therefore involve not only a measure of latency to sleep but a quantitative analysis of the latency to, and duration of, all subsequent sleep stages. Just as sleep stages one to four represent increasing sleep intensity, then decreased latency to, and increased duration of, sleep stages three and four should represent increased levels of preceding sleepiness. Roth et al. (1986) argue that analysis of sleepiness could be based on a single 45 minute polygraphic recording of sleep. The percentage of total sleep time during the recorded period is scored as the Polygraphic Sleepiness Index (PSI). The latencies to, and duration of, subsequent sleep stages are included in a formula, the total of which represents the Polygraphic Score of Sleepiness (PSS). The PSS has been shown to be a valid measure of sleepiness discriminating sleep deprived subjects from normal controls (Banasiak, Bruck & Coleman, 1988).

The above section highlights the range of instruments used to measure sleepiness. What remains unclear is exactly what they are measuring and why a lack of association exists between various measures. One explanation for this lack of association is that sleepiness is not a unidimensional construct but a complex psychophysiological state and that instruments to date may be selectively tapping only discrete aspects of that state. The following section will evaluate these identified aspects of sleepiness.

Aspects of Sleepiness

This section will examine the factors which contribute to daytime sleepiness. These factors include sleep independent, or chronobiological parameters, and sleep dependent processes, such as the duration of prior wakefulness. These two aspects of daytime sleepiness will be evaluated separately and then the following section will overview the models of Borbély (1982) and Folkard and Åkerstedt (1992) which integrate these components of sleepiness into the working models which represent our current understanding of daytime sleepiness.

Chronobiological Parameters of Sleepiness

Circadian factors

At the most fundamental level sleep and wakefulness alternate with a circadian periodicity. Under normal conditions the sleep wake cycle becomes entrained, primarily via the zeitgeber of light - dark cyclicity to the 24 hour clock. However under conditions of temporal isolation the sleep wake cycle reverts to a free running rhythm of approximately 25 hours (Wever, 1984). Czeisler, Weitzman, Moore-Ede, Zimmerman, and Knauer (1980) investigated the duration and organisation of sleep patterns under conditions of temporal

isolation and found that the duration of sleep was independent of prior wakefulness but correlated highly with the circadian phase of the temperature rhythm at sleep onset. Some aspects of sleep and wakefulness therefore appear controlled by oscillatory rather than homeostatic mechanisms. If sleep is "switched on and off" by a central oscillator, then sleepiness, within this model, cannot be seen as only an incremental response to sleep debt.

Monk (1991a) suggests that subjective sleepiness may act as a "circadian messenger" to prepare the body for sleep. Emotional, cognitive and behavioural changes coincide to induce a feeling of readiness for sleep, allowing sleep to occur at an appropriate phase of the circadian cycle. Under conditions of temporal isolation where environmental cues cannot be used to initiate sleep readiness the decision to sleep reverts to dependence on the endogenous temperature rhythm with sleep onset decisions clustering around the phase of declining temperatures (Monk & Moline, 1989).

Whilst the relationship between sleepiness and circadian phase has been demonstrated under conditions of temporal isolation these laboratory situations do not reflect the everyday experience of sleepiness which is surrounded by numerous environmental zeitgebers. Psychophysiological "readiness for sleep" (which may need to be conceptualised as separate from physiological need for sleep) appears to provide an adaptive circadian function that, through a process of learning, links endogenous sleep need, based on circadian phase shifts, with exogenous environmental factors. Studies on pre adolescent children support this distinction between sleep readiness and sleep need, and suggest that sleepiness, as a preparative function for sleep, may in part be a learned phenomenon which is not a necessary condition of efficient sleep wake transitions, (Dement & Carskadon, 1982) but rather a proactive experience that facilitates circadian sleep wake mechanisms.

Ultradian Factors

Whilst the fundamental periodicity of sleep and wakefulness is a self evident phenomenon the finding by Aserinsky and Kleitman in 1955 of cyclical events of rapid eye movement (REM) sleep initiated not only an exploration of sleep architecture but a more focussed interest in the rhythmicity of sleep and wakefulness. Kleitman (1963) proposed that superimposed on the dichotomous states of sleep and wakefulness was a sleep wakefulness rhythm which he called the basic rest activity cycle (BRAC). Kleitman proposed that this 80-90 minute alertness rhythm was expressed during sleep as the periodicity between REM and nonREM (NREM) sleep cycles but continued with the same periodicity through waking as recurrent fluctuations in alertness.

Experimental support for an ultradian arousal rhythm was provided by Lavie and Scherson (1981), Lavie and Zomer (1984) and Lavie (1986) utilising an ultrashort sleep wake paradigm to investigate sleep propensity across the nychthermon. Sleep propensity was seen to provide an undefined but 'intuitively' valid measure of sleepiness (Bes, Jobert, Muller & Schulz, 1996). Lavie's methodology involved a 5/15 minute sleep wake schedule where across a 24 hour period subjects were provided with a 5 minute opportunity to sleep followed by a 15 minute awake period. The total amount of sleep, irrespective of sleep stage, obtained in the 5 minute sleep period provided a measure that Lavie (1991b) describes as the sleep propensity function (SPF). The principle findings from these initial studies by Lavie were that (a) approximately 90 minute rhythmic variations in SPF do occur throughout the day (Lavie & Scherson, 1981), (b) some phase relationship exists between sleeping REM and NREM cycles and waking 'sleepability' cycles, though incomplete phase convergence suggests that other cyclic factors apart from REM periodicity must impact on sleep propensity (Lavie & Zomer, 1984), and (c) superimposed on this ultradian cyclicity, circadian fluctuations in

sleepiness emerged with two major sleep propensity peaks, one nocturnal peak and one mid afternoon peak. These periods of major sleep propensity which Lavie describes as sleep gates were separated by a period of minimal sleep propensity, described by Lavie (1986) as a forbidden zone for sleep.

The nocturnal sleep gate is described by Lavie (1991b) as an almost all or none phenomenon rather than the end point of a gradual increment in sleepiness, suggesting that, at least for nocturnal sleep episodes, sleep may not necessarily be preceded by sleepiness and that sleep onset may represent the activation of brain stem inducing mechanisms (Lavie, 1985) rather than the end point of a gradual sleepening process.

More recent evidence for an ultradian oscillation in sleep propensity has been provided by Bes et al. (1996) who utilised a double nap technique to evaluate diurnal variations in both sleep onset latency and interactions between slow wave and REM sleep propensities. Subjects were given a 30 minute nap and then, following a 10 minute period of wakefulness, were given a second nap opportunity. The aim of the first nap period was to eliminate the pressure for SWS allowing the second nap to provide a measure of diurnal REM pressure independent of prior SWS. Whilst the double nap structure failed to exclusively separate SWS and REM sleep respectively into the first and second nap period the protocol demonstrated both overall diurnal fluctuations in sleep propensity, in addition to systematic variations in both SWS and REM components. Episodes of SWS increased across the day reinforcing the relationship between duration of prior wakefulness and SWS capacity. Latency to REM which also increased across the day was found to be associated with decreases in REM duration reaching minimum values between 18.00 and 20.00 hours. This distribution of REM demonstrated an inverse relationship with body temperature indices.

Lack and Lushington (1996) suggest that a common oscillator may regulate both body temperature and circadian sleep wake oscillatory mechanisms.

Despite the experimental demonstration of both circadian and ultradian components to sleepiness, the mechanism of interaction of these two components remains ill defined. Using fractional desynchronisation, a technique which allows for the separation of otherwise entrained rhythms, Wever (1985), has developed a model of the possible interaction between these chronobiological systems. Wever (1985) suggests that circadian and ultradian rhythms of sleep wakefulness are controlled by separate self sustaining oscillatory mechanisms. The oscillator driving circadian sleep wake function is divided by a threshold into two states - wake and sleep. As the amplitude of the wake cycle increases so too does wakefulness or alertness and below the threshold increasing wave amplitude represents increased sleep depth. The expression of the ultradian rhythm may be modulated by the amplitude of the circadian cycle. When the circadian system reaches a particular threshold value, which could be equivalent to the sleep wake threshold, then the ultradian rhythm is expressed. Above the threshold value of wakefulness, ultradian rhythms are suppressed. This model suggests that during sleep the ultradian REM and NREM cycle is expressed but periods of waking mask this ultradian rhythm (Wever, 1985).

Whilst Wever's model provides an explanation of the REM and NREM cyclicity of sleep as the expression of ultradian periodicity during the sleep cycle it, i) fails to account for the expression of the ultradian sleepiness rhythms of wakefulness and is therefore ii) at variance with the basic tenet of Lavie's (1981) theory that daytime sleep tendency is modulated by the interaction of both circadian and ultradian sleepiness rhythms. The theoretical models proposed by Wever (1985) and Lavie (1981) both have significant limitations. Lavie's (1981) methodology establishes a very artificial sleep wakefulness

environment. It is possible that this ultrashort sleep wake cycle disrupts normal regulatory mechanisms and allows for the expression of ultradian sleepiness that is usually masked by environmental stimuli. The model proposed by Wever (1985) also appears to have significant limitations in that it fails to account for the role of environmental factors in the expression of daytime sleepiness.

Sleep Dependent Parameters of Sleepiness

The previous section has reviewed the chronobiological factors that influence daytime sleepiness. These factors are controlled by endogenous oscillatory mechanisms which seem to operate independently of aspects of nocturnal sleep. Daytime sleepiness is however also dependent on both the quantity and quality of previous sleep episodes. Despite the face validity of this statement there is very little empirical research evaluating the nature of sleepiness following sleep deprivation. Dement and Carskadon (1982) highlight this omission by commenting that daytime sleepiness has been virtually ignored as a dependent variable in studies of the effects of sleep deprivation. The following section will evaluate the impact of reducing night time sleep duration on subsequent daytime sleepiness.

Quantitative changes to sleep

Carskadon and Dement (1982) assessed sleep latency in 12 adult subjects following acute sleep reduction to four hours for two nights and found that MSLT measures dropped significantly reaching pathological levels for three subjects on the first day of sleep restriction and in eight subjects on the second day. The effects of sleep restriction on sleepiness appear to be cumulative with a linear relationship between consecutive days of sleep restriction and subsequent decreasing sleep latencies. For subjects undergoing complete sleep deprivation in

the Carskadon and Dement (1982) study, "MSLT scores fell essentially to zero" (p. S78) following one night of sleep deprivation. These initial findings of a relationship between sleep restriction and sleepiness, as measured on the MSLT, have been replicated in many studies (e.g. Roehrs, Zorick, Sicklesteel, Wittig, & Roth, 1983) and provide support for the conceptualisation of daytime sleep latencies varying inversely as a function of sleep debt.

The relationship between sleep debt and the subsequent duration of recovery sleep is not however a monotonic one. Gulevich, Dement and Johnson (1966) report on a subject staying awake for 264 hours followed by 14.4 hours of catch up sleep. Similarly Dement and Carskadon (1982) demonstrated that 60 hours of sleep deprivation can be reversed with eight hours of recovery sleep. To explain this finding researchers evaluated the impact of sleep reduction on the architecture of recovery sleep and demonstrated that sleep deprivation led to significant changes in the qualitative structure of recovery sleep with an increase in slow wave sleep stages 3 and 4 and decreases in both REM and stage 2 sleep periods (Carskadon & Roth, 1991).

Several studies have evaluated the impact of selective sleep stage deprivation on the structure of recovery sleep. Beersma, Dijk, Blok and Everhardus (1990) deprived normal sleepers of REM sleep for the first five hours following sleep onset and then observed the implications of this deprivation on subsequent sleep. Following the deprivation a substantial REM rebound effect was noted with considerably increased REM duration across the recovery period. The compensation for REM deprivation did not however involve significant changes to the REM power spectrum but interestingly led to diminished intensity of NREM spectral energy. Similar findings of compensatory mechanisms for REM time were reported by Foret, Touron, Clodore, Benoit, and Bouard (1990) who noted that brief awakenings during REM episodes led to compensatory changes to subsequent inter REM intervals.

Manipulations of NREM sleep duration by Beersma et al. (1990) led, however, to compensatory changes, not to NREM duration, but to subsequent NREM intensity.

Glovinsky, Spielman, Carroll, Weinstein, and Ellman (1990) tried to assess the comparative implications of REM and Stage 2 sleep disruption on subsequent daytime sleepiness. Whilst a 30% reduction in sleep latency was noted following sleep interruption, comparable effects were noted between Stage 2 and REM conditions suggesting that reduced sleep time rather than sleep composition was the principle determinant of sleepiness. Daytime MSLT reductions of the order of 30% have also been reported following sleep fragmentation studies where total sleep time has remained intact (Roehrs, Merlotti, Petrucelli, Stephanski, & Roth, 1994) suggesting that sleepiness, as measured by the propensity for sleep initiation, is determined in part by both temporal and structural aspects of nocturnal sleep episodes.

Qualitatively distinct aspects of sleepiness

The work on the influence of sleep debt on subsequent sleep need presupposes that levels of sleepiness differ along some unitary quantitative dimension. Roth, Roehrs, Carskadon and Dement (1989) support this construction arguing that

> Sleepiness is a basic physiological state. It may be likened to hunger or thirst, which are physiological need states basic to the survival of the individual organism. The presence and intensity of the state can be inferred by how readily sleep onset occurs, how easily sleep is disrupted or how long sleep endures. Deprivation or restriction of sleep increases sleepiness, and as hunger or thirst is reversible by eating or drinking, respectively, sleep reverses sleepiness (p. 15).

Arguing that sleepiness increases or decreases along a continuum like hunger or thirst appears to be a flawed analogy. Surely we have all experienced hunger unrelated to the need for food, when one just feels like eating, or one eats as a response to changes in mood, or environmental cues. Hunger is surely not a unitary state, we can be hungry for any food, or we may only be hungry for a chocolate bar or for a cake. Can sleepiness also differ along qualitative dimensions? Is it possible that we may have need for different types of sleep under different circumstances, and that the nature of the sleep episode i.e. REM or NREM, is preceded by REM or NREM sleepiness states, and these sleepiness states are distinguishable along as yet perhaps unidentified dimensions?

Broughton (1982) argues that qualitatively different types of sleepiness do exist and that the construct therefore becomes multidimensional rather than a unitary state. Broughton and Aguirre (1987) suggest that sleepiness may be characterised by psychophysiological characteristics that represent selective pressure for subsequent sleep episodes. REM sleepiness would therefore be followed by REM sleep, NREM sleepiness by NREM sleep, and de arousal sleepiness representing diminished reticulo-cortical arousal mechanisms. In support of this argument Broughton and Aguirre (1987) compared event related potentials, MSLT and subjective sleepiness estimates for periods of wakefulness that preceded REM and NREM sleep episodes. On all three assessment protocols significant differences were found between REM and NREM sleepiness. REM sleepiness was associated with more intense sleepiness as measured by subjective ratings and shorter MSLT latencies. Event Related Potential (ERP) measures also discriminated between the two sleepiness states. One limitation of the Broughton and Aguirre (1987) study was their use of narcoleptic subjects in the study. Whilst this protocol allowed for the occurrence of both REM and NREM nap

periods, the extent to which findings from a pathologically sleepy population can be used to infer normal sleep processes must be questioned.

A second theorist to argue that sleepiness may be a multidimensional construct is Horne (1992). Horne proposes that sleep is comprised of two components - core and optional sleep, and these two components are associated with specific types of sleepiness. Core sleep is, according to Horne, the sleep that is essential for cerebral recovery and is made up of SWS and 50% of the total nightly REM sleep. The evidence for these sleep components having some essential role, comes, Horne argues, from the findings of recovery sleep where these sleep stages are selectively compensated for. A second argument for this core sleepiness component is that several studies (e.g. Horne & Wilkinson, 1985) have demonstrated that total sleep time can be reduced to approximately six hours without any increase in daytime sleepiness. This decrease in total sleep time involves the loss of the last one to two sleep cycles which are predominately REM and stage 2. Optional sleepiness is not essential for restitution but reflects circadian or behavioural influences. Horne also uses the hunger analogy to differentiate the two sleep components suggesting that there is a substantial difference between the daily subjective feeling of hunger, and the hunger associated with the need for food, "stomach pangs, the more "behavioural" component of hunger, may be likened to sleepiness produced by optional sleep loss, whereas the physical weakness and food need may be equivalent to the requirements for core sleep" (Horne, 1992, p. 28). Horne suggests that conceptualising sleepiness as comprising both core and optional components explains the observed discrepancy between the MSLT and RTSW (Hartse et al., 1982). The MSLT utilises instructions which encourage subjects to try to fall asleep whilst the RTSW encourages subjects to resist sleep. Horne suggests that latencies associated with the RTSW are indicative of core sleepiness whilst the MSLT includes an optional component

"the same may apply to oversleeping...If the opportunity is there, why not take it?" (Horne, 1992, p. 31). Johns (1994) supports this qualitative differentiation of sleepiness arguing that the propensity to sleep may differentially reflect a subject's usual propensity to sleep, or a sleepiness that emerges as secondary to soporific situational factors, the latter equating with Horne's optional sleepiness measure.

Horne suggests that core and optional sleepiness may be discriminated between using performance tasks that tap into differing psychological demands. If core sleep has the primary function of cerebral restitution then tasks with a high cognitive load, particularly frontal lobe tasks, will be sensitive to sleep deprivation that intrudes into core sleepiness. Performance on tasks demanding a lower cognitive load, such as vigilance or reaction time tasks, may be maintained even after some loss of core sleep. This suggestion seems at odds with much of the experimental literature on sleepiness and performance (refer Chapter 2) which suggests that these simple tasks provide the most sensitive indices of minimal sleep loss. Horne suggests that this sensitivity is not related to the cognitive task load but rather to the monotonous nature of these repetitive tasks and that the observed decrement reflects fatigue or boredom effects rather than cerebral dysfunction. The work of Horne and Pettitt (1985) supports this argument as they were able to reverse the effects of sleep deprivation on performance by adding monetary incentives to the task (refer Chapter 3).

Horne argues that optional sleepiness is largely controlled by motivational factors, whereas core sleepiness is independent of volitional control, and hence compensatory effort is only effective where sleep deprivation impinges on optional sleep time. Core sleepiness is indicated by deficits in intrinsically interesting tasks that demand higher cortical functioning. These tests are similar to neuropsychological tests of frontal lobe function, measuring abilities such as divergent thinking, creativity and distraction by irrelevant stimuli (Horne, 1992).

The principles of Horne's model of sleepiness will be central to this thesis' analysis of the relationship between sleepiness and performance in narcolepsy. The model will be reviewed at several points in the introductory chapters and applied in detail to the experimental work in Chapter 5.

Integrative Models of Sleepiness

The previous literature review demonstrates that sleepiness can be linked to both sleep independent (circadian) and sleep dependent processes. Several theorists have attempted to integrate these factors to provide a comprehensive model of sleepiness.

The first major model of sleep and sleep propensity to suggest that sleepiness may in part be independent from the sleep wake cycle was presented by Borbély (1982). Borbély proposed that sleep was regulated by two processes. At the most fundamental level the periodicity between night time sleep and daytime wakefulness is regulated by an endogenous oscillator and entrained by zeitgebers, especially light and dark, to a circadian rhythmicity. The sleep wake cycle is therefore primarily a sleep independent process which demonstrates a self sustaining sinusoidal rhythmicity. Borbély (1982) proposed that this sleep independent circadian factor, which he describes as process C, interacts with a sleep dependent factor, called process S, to regulate sleep propensity. Process S fulfils a homeostatic function and is represented by EEG slow wave activity which increases during waking and declines exponentially during sleep. The intensity of process S is therefore a function of prior waking time.

Borbély (1982) integrates these components of REM oscillatory mechanisms and SWS pressure into a sleep wake model which suggests that these parameters are not connected via a linear relationship but argues that the monotonic increase in Process S with

wakefulness can only be interpreted in relation to the phase of the circadian cycle and sleep propensity. A discussion of the mathematical aspects of this model of sleep regulation is beyond the scope of this thesis, an extensive review of the area is provided, however, by Borbély and Achermann (1992).

Figure 1 demonstrates the relationship between the two processes identified in the Borbély model. Process S, rising during wakefulness and falling exponentially during sleep, and process $\bar{C}$, which is the mirror image of process C varying with an endogenous circadian rhythmicity. The total sleep propensity is designated by the difference between curves $\bar{C}$ and S at any time point.

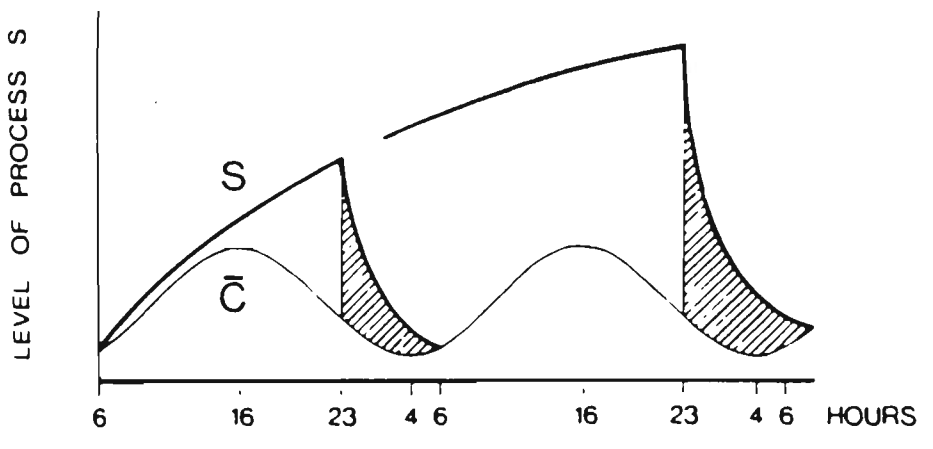

Figure 1 Diagrammatic representation of Borbély's two process model of sleep regulation (Borbély, 1982, p. 199).

Folkard and Åkerstedt (1992) refined the mathematical formulation of the two process model and argued for the inclusion of a third process, process W. This component represents a limited exponential decline from process S following enforced wakening. The term sleep inertia has been used to describe this feeling of sleepiness that immediately follows wakefulness and declines gradually over time.

Further refinement of the original two process model incorporates an ultradian process to allow for the REM, NREM cyclicity of sleep. An integrative model of processes S, C, W and the ultradian oscillator is provided by Acherman and Borbély in Figure 2. The major features of this model include (a) the independence of the circadian oscillator from the other processes (b) the impact of the phase of the circadian system on sleep dependent process S, on the ultradian REM cycle, and on alertness (c) the interaction of S and C in the timing of sleep, and (d) the dependence of the level of alertness on the combined input of process C, S and W wakefulness.

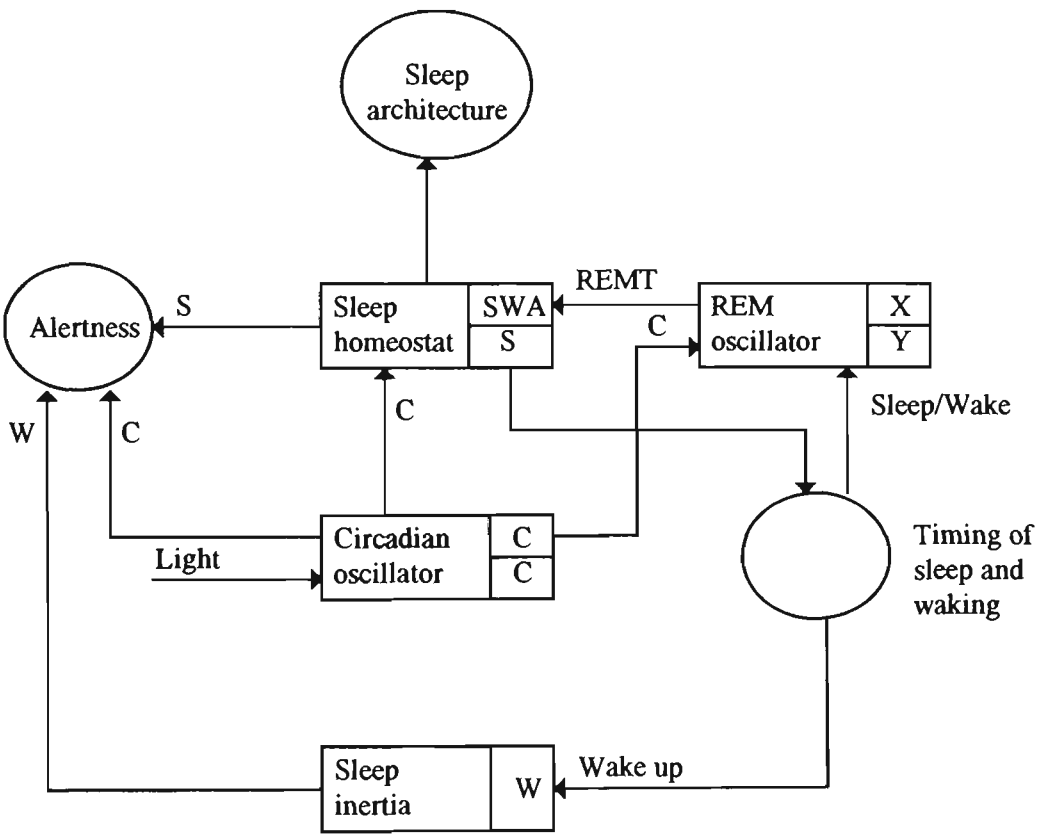

Figure 2 A combined model of sleep regulation (Achermann & Borbély, 1992, p. 145).

This model of sleep and wakefulness has been demonstrated to accurately predict waking levels of alertness as measured by both subjective and EEG parameters (Åkerstedt & Folkard, 1995).

Summary of the Nature of Sleepiness

Sleepiness is more than a passive response to the need to sleep, rather it appears as a complex psychophysiological state that potentially varies along both quantitative and qualitative dimensions. The nature of the state has been related to both homeostatic and chronobiological factors but models which integrate these processes are still unable to account for factors such as motivation, fatigue, boredom, or mood that may all impact on sleepiness states.

The complexity of sleepiness is indicated by the range of instruments designed to measure the state and the lack of congruence between measures suggests that they are tapping unitary aspects of a complex multidimensional state.

There seems to be a distinction between the concepts of sleep need and sleep propensity. How these differences are understood depends on the theoretical paradigm. To Horne (1992) such differences represent the propensities to core or optional sleep, with optional sleepiness containing a volitional component sensitive to exogenous factors. Perhaps subjective sleepiness is, as Thayer (1989) suggests, the most appropriate measure of sleepiness as it is surely the integration of volitional and physiological processes. Or as Monk and Moline (1989) write

> One way of conceptualising the subjective alertness rhythm is as the messenger between the circadian system and consciousness, integrating and transmitting the signals emanating from the various oscillatory and homeostatic processes. We are able to ignore those signals if we choose to (Monk and Moline, 1989, p. 309).

CHAPTER 2

Narcolepsy: A Disorder of Dissociated States of Sleep and Wakefulness

"We are more awake when we are asleep - and we are more asleep when we are awake - always wanting to move from one to another" (Personal communication, Subject J.H. in Study 1. August 1994).

Introduction

Narcolepsy is a disorder of sleep first described over 90 years ago by the French neuropsychiatrist Gélineau who wrote "it is a rare little known neurosis characterised by an imperative need to sleep of sudden onset and short duration, recurring at more or less close intervals" (as cited in Zarcone, 1973, p. 1156). Prior to this recognition by Gélineau of narcolepsy as a discrete medical disorder there was substantial written evidence of individuals with excessive daytime sleepiness. Graves (1851) described a gentleman "who always fell asleep in his soup" (as cited in Parkes, 1985, p. 277) and Edgar Allen Poe wrote of a character with "a species of exaggerated lethargy...without ability to stir" (as cited in Zarcone, 1973, p.1156).

Early theories of the disorder focussed on psychodynamic explanations, where sleep was seen as a defence against unacceptable urges such as sexual impulses or guilt. "Cataplexy...is a manifestation of conditioned inhibition, a response to the guilt that attends aggression even when it is only unconscious" (Levin, 1959, p. 136).

Narcolepsy remained ill-defined until Yoss and Daly (1957) presented the symptom tetrad of - excessive daytime sleepiness, cataplexy, hallucinations and sleep paralysis. These four primary symptoms still form the basis of current diagnosis of the disorder. Recognition

of these symptoms as characteristic of the disorder led to a formal definition of narcolepsy being drafted in 1975 at the First International Symposium on Narcolepsy

> A syndrome of unknown origin that is characterised by abnormal sleep tendencies, including excessive daytime sleepiness and often disturbed nocturnal sleep, and pathological manifestations of REM sleep. The REM sleep abnormalities include sleep-onset REM periods and dissociated REM sleep inhibitory processes, cataplexy, and less often sleep paralysis and hypnagogic hallucinations are the major symptoms of the disease. (Guilleminault, Dement & Passouant, 1976 [Preface]).

In the twenty years since this original definition of narcolepsy there have been considerable developments in knowledge about the disorder and this current knowledge base is evident in the International Classification of Sleep Disorders (ICSD, 1990) diagnostic criteria for narcolepsy. The 1990 ICSD criteria are listed below.

Diagnostic Criteria: Narcolepsy

A. A complaint of excessive sleepiness or sudden muscle weakness.

B. Recurrent daytime naps or lapses into sleep that occur almost daily for at least 3 months.

C. Sudden bilateral loss of postural muscle tone in association with intense emotion (cataplexy).

D. Associated features include:

1. Sleep paralysis;
2. Hypnagogic hallucinations;
3. Automatic behaviours;

4. Disrupted major sleep episode.

E. Polysomnography demonstrates one or more of the following:

1. Sleep latency less than 10 minutes;

2. REM sleep latency less than 20 minutes; and

3. An MSLT that demonstrates a mean sleep latency of less than 5 minutes:

4. Two or more sleep-onset REM periods.

F. HLA typing demonstrates DR2 positivity.

G. Absence of any medical or psychiatric disorder that could account for the symptoms.

H. Other sleep disorders may be present, but are not the primary cause of the symptoms, e.g., periodic limb movement disorder or central sleep apnea syndrome.

Minimal Criteria: B plus C, or A plus D plus E plus G.(ICSD, 1990, p. 42).

Many of these central features of the disorder are described in the available review articles on the disorder including, Aldrich (1990); Aldrich (1992); Broughton, (1990); Chaudhary and Husain, (1993); Cohen, (1988); Guilleminault, (1989); Kales, Vela-Bueno and Kales, (1987b); Manfredi, Brennan and Cadieux, (1987); Manfredi and Cadieux, (1987); Manfredi, Vgontzas and Kales (1989); Nahmias and Karetzky, (1989); Parkes (1985); Richardson, Fredrickson and Lin (1990); Roth, (1978); Zarcone, (1973).

Primary Characteristics of Narcolepsy

This section will examine the central features of the four primary diagnostic symptoms of narcolepsy which are, (a) excessive daytime sleepiness punctuated by sleep attacks, (b) cataplexy, (c) sleep paralysis and (d) hallucinations.

Excessive Daytime Sleepiness (EDS) and Sleep Attacks

The symptom of excessive daytime sleepiness punctuated by brief and irresistible sleep attacks is the principle feature of narcolepsy and is present in all narcoleptic subjects (Kales & Kales, 1974). Whilst daytime sleepiness is reported by 4% to 5% of the general population (Moldofsky, 1992), the daytime sleepiness and irresistible sleep attacks experienced by narcoleptic subjects can be discriminated from both non pathological sleepiness and other disorders of excessive sleepiness on several parameters. The first distinguishing feature for narcolepsy subjects is the *inappropriateness* of the sleepiness. Sleepiness and/or sleep attacks for narcoleptics can occur in situations such as eating, during a conversation, sexual intercourse, whilst standing up or whilst driving, as well as in more traditionally sleep inducing environments such as reading or watching television. The Epworth Sleepiness Scale (Johns, 1991) identifies this inappropriateness of narcoleptic sleepiness using items to test the propensity to fall asleep in situations such as - "in a car, while stopped for a few minutes in the traffic" (Johns, 1992, p. 379). Associated with this excessive daytime sleepiness narcoleptics experience recurrent sleep attacks. These involuntary sleep episodes can last between 30 seconds and 20 minutes with most attacks lasting from two to five minutes (Roth, 1978). Periods of daytime sleep appear to be maintained even in treated narcoleptic subjects. Rogers, Aldrich, and Caruso (1994a) found that even when medicated narcoleptics averaged 44 minutes of daytime sleep compared to under 5 minutes for controls. The study also demonstrated the high individual variability in daytime sleep tendency for narcoleptic subjects. There seems to be limited discussion in the literature as to whether sleep attacks for narcolepsy subjects are always preceded by sleepiness. Aldrich (1992) suggests that sleep attacks always represent the end point of sleepiness and that reports by narcoleptics of sleep attacks intruding into wakefulness simply

reflect the inability of the narcoleptic to monitor their own level of sleepiness. Whilst there is substantial support for people with pathological sleepiness being poor judges of their own sleepiness states (Browman & Mitler, 1988) personal observations of sleep attacks by this author suggest that sleep attacks may not always be associated with behavioural indices of sleepiness states. Nahamias and Karetzky (1989) support this observation stating that "some (sleep) attacks, however, occur quite suddenly with no prodromata" (p. 618). This phenomenon in narcolepsy warrants further investigation as it potentially helps differentiate the more general constructs of sleep and sleepiness. Polygraphic recordings of sleep attacks, as shown in Figure 3, typically demonstrate a Stage 1 type EEG, suppression of muscle tone and the rapid eye movements of REM sleep.

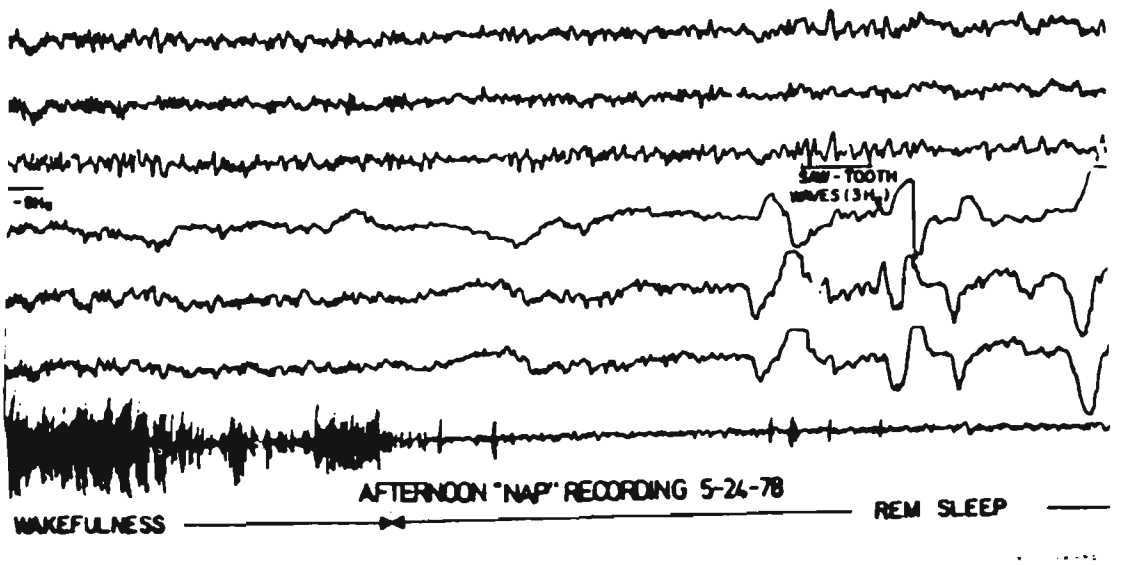

Figure 3 Sleep onset REM period during a sleep attack in a female narcoleptic patient (McGregor, Weitzman & Pollack, 1985).

In contrast to the sleep architecture of normal sleep, REM patterns characteristically appear at sleep onset in narcoleptic subjects. The relationship between night time and daytime sleep episodes and the circadian patterns of sleep and wakefulness in narcolepsy will be discussed later in this chapter.

Cataplexy

Cataplexy is the sudden loss of muscle tone and is experienced by approximately 70% of narcolepsy subjects (Kales & Kales, 1974). This effect may be generalised, affecting all striated muscles, and leading to the sufferer's total collapse, or it may be restricted to particular muscle groups. In the latter case the subject may experience rolling eyes or a sagging jaw (Parkes, 1985). Gelb et al. (1994) describe the wide range of cataplectic features and in addition to the classical symptoms described above by Kales and Kales (1974) Gelb et al. (1994) report less well defined symptoms such as "sudden jolts or interruptions in consciousness" and "waves of dizziness" (Gelb et al., 1994). Cataplectic attacks are initiated by strong emotional responses such as laughter or fear and last from a few seconds up to ten minutes. The characteristics of cataplexy are identified by Parkes, Dahlitz, Clift, and Chen (1994) with items from the postural atonia rating scale which estimate the likelihood of an attack under conditions such as - "telling a joke myself when I am standing up" or "if I was very angry, if I was standing up" (Parkes et al., 1994). In an evaluation of the distribution of cataplectic attacks over a twenty four hour period, Gelb et al. (1994) demonstrated that cataplexy rarely occurred during nocturnal periods and that, whilst high intersubject variability was evident in symptomology, across the day the frequency of attacks remained relatively stable.

Rechtschaffen and Dement (as cited in Zarcone, 1973) describe polygraphic recordings of cataplexy as demonstrating EEG activity unchanged from the waking state accompanied by almost total abolition of EMG potentials though extraocular muscles, as utilised in REM sleep are not affected. More recent recordings of cataplexy by Dyken, Yamada, Lin-Dyken and Seaba (1994) suggest that the normal waking 8-13 Hz alpha rhythm is replaced in cataplexy by a slower alpha/theta rhythm. Cataplectic attacks may gradually develop into sleep attacks, with the principle difference between the two states being the level of consciousness. During a cataplectic attack subjects maintain normal levels of consciousness and are aware of all coincidental visual and auditory stimuli, whereas after a sleep attack, a person is seldom aware of anything that occurred during the attack (Roth, 1978).

Sleep paralysis

Sleep paralysis also involves paralysis of the major striated muscle groups of the body and occurs in transition phases between sleep and wakefulness. The neurophysiological pathways mediating the motor inhibition of sleep paralysis appear distinct however from those triggering cataplexy (Lindsley, 1993). During an episode of sleep paralysis the person remains fully conscious but is unable to move. The state may be associated with intense feelings of fear which for some people with narcolepsy may escalate into panic (Lindsley, 1993). Episodes usually last only a few seconds and, in contrast to cataplexy, subjects may be aroused from this state by calling or touching (Zarcone 1973). The symptom of sleep paralysis is reported by approximately 50% of subjects with narcolepsy (Kales & Kales 1974).

Hypnagogic and hypnopompic hallucinations

These hallucinations which occur in transition states between sleep and wakefulness may be auditory, visual or tactile. Hypnagogic hallucinations are associated with sleep onset and hypnopompic, with awakening. Although these hallucinations have been reported in non narcoleptics they are considered more emotional and 'dreamlike' in narcolepsy (Mendelson, 1987). Hallucinations are the least frequently reported symptom of the tetrad occurring in approximately 25% of narcoleptic subjects - the full tetrad of daytime sleepiness, cataplexy, hallucinations and sleep paralysis occurring in only 10% of narcoleptics (Kales & Kales, 1974).

Onset and Prognosis of Narcolepsy

Manifestations of narcolepsy show high intersubject variability but the typical course of the disorder is that EDS and sleep attacks develop several years before cataplexy (Scrima, 1991) and symptoms tend to remain constant once they appear.

Age of onset of excessive sleepiness is typically in adolescence with a second peak in onset at about 30 years of age (Broughton, 1990). The literature reports diagnoses of narcolepsy in children as young as five (Bond, Frank, & Ware, 1993) or six (Reimao & Lemmi, 1991) and many reports exist of pre adolescent diagnoses (Kotagal, Hartse & Walsh, 1990; Allsopp & Zaiwalla, 1992; Walsleben & Rapoport, 1993; Dahl, Holttum & Trubnick, 1993; Challamel et al. 1994; Dahl, Holttum & Trubnick, 1994). A retrospective evaluation of the sleep history of an 11 year old child with narcolepsy suggests that increased sleepiness (compared to an identical twin) developed by age 2 to 3 (Dahl, 1992). The literature does indicate, however, a significant discrepancy between the small number of children diagnosed

with narcolepsy compared to the number indicated through retrospective reporting (Challamel et al. 1994).

Just as cases of narcolepsy may occur in children, late onset narcolepsy may present in the elderly. Diagnosis in the elderly may be confounded by the assumption that excessive daytime sleepiness is a natural consequence of ageing (Morewitz, 1988; Broughton & Broughton, 1994) or that the symptoms are secondary to age related cardiovascular disease (Kelly, Lowe & McTaggart, 1987).

Secondary Characteristics of Narcolepsy

Automatic behaviour

In addition to the primary features of narcolepsy the disorder also appears associated with secondary characteristics such as states of automatic behaviour "I was going to do the dishes. It was just after dinner. I remember walking in the kitchen and when I 'woke up' about thirty minutes later, the kitchen was a complete mess. I had put all the plates in the clothes dryer and turned it on!" (Guilleminault, Billiard, Montplaisir & Dement, 1975, p. 378).

Automatic behaviour seems to represent brief periods of altered awareness associated with complete retrograde amnesia. Electroencephalogram recordings of these periods demonstrate patterns of brief bursts of stage 1 sleep interspersed with wakefulness (Guilleminault et al., 1975).

Night Time Sleep Patterns

The first systematic recordings of nocturnal sleep patterns in narcoleptic patients were carried out by Rechtschaffen, Wolpert, Dement, Mitchell and Fisher in 1963. Their

study involved nine narcoleptics and nine controls in overnight laboratory recordings. The results, described by Rechtschaffen et al. (1963) are still recognised as central components of the narcoleptic syndrome. Their findings included, (a) the occurrence of REM periods at sleep onset - whilst normal sleep patterns demonstrate a 90-120 minute delay from sleep onset to the first REM period, up to 50% of sleep episodes for narcoleptic subjects will be characterised by sleep onset REM periods (SOREMPs), (Aldrich 1992). These SOREMPs being indistinguishable by polysomnographic inspection from REM periods experienced by controls later in the night, (b) the maintenance of normal sleep cycles. Apart from the occurrence of SOREMPs the narcoleptics did not differ from controls with respect to the major cyclical variations of sleep stages. Sleep cycles lasted approximately ninety minutes and periods spent in REM also did not vary between subjects and controls; (c) increased nocturnal body movements for subjects with narcolepsy compared to controls; (d) changes to the EEG patterns for subjects with narcolepsy with an increase in stage 1 activity and a concomitant decrease in slow wave sleep. Montplaisir et al. (1978) further demonstrated the fragmentation of night time REM sleep periods in narcolepsy. Whilst normal sleepers experience blocks of REM sleep throughout the night, narcoleptics appear to have great difficulty remaining in REM sleep. In narcoleptics REM periods are interrupted by several awakenings or stage 1 sleep periods. The effect of these interruptions is to fragment each REM period into several portions of short duration (REM fragments). The occurrence of fragmentation results in increased periods of stage 1 sleep or periods of awakening with decreases in stage 3 and 4 slow wave sleep. Comparative measures of motor activity and immobility between narcoleptics and controls indicates that night time sleep periods are characterised by increases in motor activity compared to controls whilst daytime periods demonstrate significantly decreased activity levels in comparison to control subjects measures

of motor activity and immobility in narcoleptics (Middelkoop et al., 1995). These studies of circadian mobility emphasise both the increased sleepiness associated with daytime functioning for narcoleptics and the coincident increase in night time sleep disruption.

Narcolepsy has also been shown to be associated with changes in nocturnal REM architecture, in particular there seems to be a disinhibition of REM phasic activity leading to increased REM phasic events for narcoleptics compared to controls (Geisler, Meier-Ewert & Matsubayshi, 1987). These characteristic nocturnal sleep patterns of REM in narcolepsy have been replicated in both laboratory (Tafti, Villemin, Carlander, Besset & Billiard, 1992; Zorick et al., 1986) and ambulatory home based studies (Broughton et al., 1988b).

The findings of Montplaisir et al. (1977) provide an objective explanation of the subjective experience of narcoleptic subjects of poor night time sleep. In a meta analysis of sleep indices for insomnia, depression and narcolepsy, narcolepsy was demonstrated to be associated with the most disturbed nocturnal sleep parameters (Hudson et al., 1992). Vivid, frightening and disturbing dreams are also associated with night time sleep for narcoleptics and may be consequent to REM fragmentation (Lee, Bliwise, Lebret-Bories, Guilleminault & Dement, 1993). The relationship between daytime sleep and nocturnal sleep disruption in narcolepsy remains controversial. Montplaisir et al. (1977) suggested that deprivation of daytime sleep, appears to decrease REM fragmentation, and hence increase the quality of nocturnal sleep in narcoleptics. Billiard et al. (1986) failed to demonstrate any relationship between the two states. Lamphere et al. (1989) evaluated the patterns of disturbance in nocturnal sleep for narcoleptics as a function of age and evaluated the impact of this fragmentation on the experience of daytime sleepiness. Whilst nocturnal sleep disruption for narcoleptic subjects increased as a function of age this increasing fragmentation was not associated with increased daytime somnolence. Similar results were reported by Broughton,

Dunham, Weisskopf and Rivers (1994) with no significant correlations between night time and daytime sleep indices. Both Broughton et al. (1994) and Lamphere et al. (1989) suggest that these findings provides support for the independence of EDS from disturbances of night time sleep in narcolepsy and that daytime sleepiness in narcolepsy may represent some *qualitatively* different phenomenon from sleepiness associated with sleep disruption in non narcoleptic subjects.

Smith and Cohen (1988a) suggest that the abnormal night time sleep patterns associated with narcolepsy resemble, in many aspects those of a three month old infant. Infants at three to five months experience a critical switch over period between ultradian and circadian dominance of sleep wake rhythms, and between neonatal and mature sleep characteristics (Bes, Fagioli, Peirano, Schulz & Salzarulo, 1994). Narcoleptic symptomology mimics this change over amalgam. The changes occurring during the infant's third month occur as a response to an increase in the inhibitory and modulatory functions of the forebrain, allowing in part for the prolonged maintenance of particular states. The analogy between infant sleep and narcolepsy may therefore provide support for the hypothesis that narcolepsy is not primarily associated with dysfunction of the brainstem, which governs the REM state, but reflects a dysfunction of higher levels of CNS organisation that permit inhibition of state changes. Zorick et al. (1986) support this hypothesis that narcolepsy reflects an inability to maintain a neural state and that this state imbalance is not specifically REM related as intrusions of wakefulness into sleep and vice versa appear to affect REM and NREM sleep components equally. Mahowald and Schenck (1992) also focus on the complex state transitions in narcolepsy describing the disorder as one of a dissociated state of wakefulness and sleep. Broughton et al. (1986) suggest that "the full narcolepsy-cataplexy syndrome may

best be conceptualised as a disorder of sleep/wake state boundaries rather than of REM sleep" (Broughton et al., 1986, p. 213).

Chronobiological Structures of Sleep and Wakefulness in Narcolepsy

As discussed in Chapter 1 periods of wakefulness for normal subjects are characterised by rhythmic oscillations in arousal levels and sleep stages also demonstrate structured oscillatory patterns. The overall relationship between the states of sleep and wakefulness are also controlled by endogenous oscillators entrained to external zeitgebers. Both within and between state rhythmicities appear disrupted in narcolepsy where the normally monophasic relationship of sleep and wakefulness becomes polyphasic. This apparent dissociation of sleep wakefulness rhythms in narcolepsy has led to the suggestion that the pathophysiology of narcolepsy may reflect an underlying dysfunction of circadian organisation. This circadian dysfunction could reflect either a free running endogenous oscillation leading to internal desynchronisation of body rhythms or alternatively the possible weakening of regulatory mechanisms allowing the intrusion of 90 minute oscillatory rhythms into the sleep wake cycle.

Measures of rhythmicity in core body temperature have been used as a measure of the patency of the endogenous circadian pacemaker (Refinetti & Menaker, 1992). Several studies have assessed core body temperature patterns in narcolepsy (Dantz, Edgar & Dement, 1994; Mosko, Holowach & Sassin, 1983; Pollak & Wagner, 1994) and although Mosko et al. (1983) reported a higher mean temperature coupled to an earlier occurrence of the circadian low for narcoleptics, these findings have not been replicated in subsequent studies which found circadian temperature oscillations similar in narcoleptics and controls. Pollak and Wagner (1994) suggest that this "finding is evidence against an abnormality of circadian

pacemaker function...." (p. 66). An interesting secondary finding of the Pollack and Wagner (1994) study was that narcoleptic sleep attacks were preceded by decrements in body temperature, a finding that implies that naps in narcolepsy, even when involuntary, are associated with the physiological changes that accompany sleep onset in non pathologically sleepy subjects.

Although the findings on core body temperature indicate that circadian systems seem to be fundamentally intact in narcolepsy, Wever (1985) proposed that the disorder may represent a weakening of circadian cycles allowing for more dominant expression of ultradian sleep wake rhythms. Wever (1985) suggests the intrusion of sleep into wakefulness may reflect the lack of inhibition of the REM and NREM periodicity of night during wakefulness. An implication of this theory is that both daytime sleep episodes and REM episodes should demonstrate some phase relationship consistent with an ultradian periodicity. Several studies provide some support for this model. Bixler et al. (1986) assessed the nocturnal patterns of sleep and wakefulness in narcoleptic patients and concluded that periods of nocturnal wakefulness were distributed in a regular oscillating manner, which mimicked the periodicity of daytime vigilance described in normal subjects. Schulz (1985) and De Koninck, Quera Salva, Besset and Billiard (1986) further demonstrated that REM sleep episodes during the day occurred at intervals similar to night time REM periodicities. These 90-120 minute ultradian oscillations for narcoleptics were not demonstrated by Broughton et al. (1988b) in their ambulatory recording of narcoleptic sleep wake patterns. Rather Broughton et al. (1988b) found that all major circadian and circasemidian rhythms identified in normal sleepers were maintained in narcolepsy, a position which he maintains in a more recent review of the chronobiological aspects of narcolepsy (Broughton & Mullington, 1994).

Lavie (1991a) evaluated REM periodicity in narcolepsy under an ultrashort 7/13 minute sleep wake cycle again demonstrating an 80 minute cyclicity in REM suggesting that for narcoleptic subjects the REM oscillator remains activated during wakefulness. Lavie (1991a) argues, however, that the diurnal activation of REM in narcolepsy may represent a process independent from diurnal fluctuations in baseline arousal or sleepiness.

On the basis of current evidence, the aetiology of narcolepsy does not appear to be fundamentally chronobiological. Tafti, Rondouin, Besset and Billiard (1992) and Besset, Tafti, Nobile and Billiard, (1994) even argue for increased sensitivity of narcoleptics to homeostatic regulatory mechanisms. Despite the patency of endogenous homeostatic mechanisms in narcolepsy the intrinsic dysfunction of sleep wake mechanisms in the disorder appear to result secondarily in changes to the normal rhythmicity of sleep and wakefulness.

Diagnosis of Narcolepsy

Primary Diagnostic Criteria

Diagnosis of narcolepsy according to the ICSD criteria (ICSD, 1990) necessitates either (a) EDS or sudden muscle weakness accompanied by sleep laboratory indices, or, (b) the presence of sleep attacks and unequivocal cataplexy. Despite these specified criteria several dilemmas emerge in the literature in relation to appropriate diagnostic criteria. Of primary significance is the relative importance of clinical symptoms, particularly cataplexy, and sleep laboratory indices as major diagnostic criteria.

Rosenthal et al. (1990) would argue that cataplexy is not a necessary symptom for diagnosis and that rather the presence of sleep onset REM periods (SOREMs) in addition to excessive daytime sleepiness is sufficient for the diagnosis of narcolepsy. Others would question the use of the MSLT and emphasise the primary role of cataplexy as a diagnostic

criterion. Honda (1988) questions the sensitivity of the MSLT for narcolepsy and suggest a preferential emphasis on clinical features with a history of cataplexy being used as a necessary condition for diagnosis. There is an obvious appeal in this clinical approach as sleep laboratory testing is a complex and expensive testing procedure with limited accessibility for patients.

Kales et al. (1987a) compared the diagnostic value of SOREM's and shortened sleep latency in narcolepsy and found that SOREM's had a higher diagnostic sensitivity (78%) than sleep latency (68%) though the specificities of the two tests were similar, 88% and 90% respectively. Despite this validation of the use of nap recordings Kales et al. (1987a) suggest that they have limited usefulness in subjects presenting with clear histories of cataplexy and they should only be used in situations of equivocal presentation of cataplexy. Martinez-Arizala and McCarty (1987) support this position arguing that the MSLT becomes most useful in the diagnosis of EDS patients with no auxiliary symptoms of narcolepsy.

Moscovitch, Patinen and Guilleminault (1993) and Guilleminault, Mignot and Partinen, (1994) compared the validity of cataplexy and SOREMP's using MSLT as determinants of narcolepsy and found that the best determinant of narcolepsy was a combination of a history of cataplexy combined with two or more SOREMPs, however, two or more SOREMPs is a poorer discriminator of narcolepsy than an unequivocal history of cataplexy. The value of cataplexy as a diagnostic component in the assessment of narcolepsy is also emphasised by Dyken, Yamada, Lin-Dyken, Seaba and Yeh (1996).

One obvious problem, however, with the use of cataplexy as a primary diagnostic indicator is that only 70% of subjects with narcolepsy experience the symptom of cataplexy (Kales & Kales, 1974). This raises the question of whether sub-types of narcolepsy may exist with qualitatively different symptomologies - e.g. those characterised by waking features such

as cataplexy and those restricted to the waking characteristic of excessive daytime sleepiness? In particular the characteristics of narcolepsy without cataplexy that discriminate narcolepsy from disorders of idiopathic hypersomnia remain to be identified (Aldrich, 1996).

The symptomatic presentation of subjects with narcolepsy is clearly a heterogeneous one. Perhaps that heterogeneity reflects several distinct subclassifications of the disorder yet to be identified? Or perhaps it represents quantitatively different levels of diagnostic severity? It is interesting to note that despite the classification of severities of narcolepsy within the ICSD (1990) criteria none of the research literature utilises this classification system.

Secondary Diagnostic Criteria

In addition to clinical presentation and sleep laboratory indices several other tests for narcolepsy have been discussed in the literature these include genetic and ophthalmic testing.

HLA testing Original reports of HLA prevalence rates amongst narcoleptics suggested that 100% of narcoleptics tested positive for HLA-DR2 (Neely, Rosenberg, Spire, Antel, Arnason, 1987). This finding led to substantial interest in the development of a genetic screening test for the disorder. The subsequent identification however of DR2 negative narcoleptics and the fact that 24 - 28% of non narcoleptics in both European and Canadian populations test HLA-DR2 positive (Moscovitch, Partinen & Guilleminault, 1993), has led to the use of the test as diagnostic aid rather than definitive criterion.

An overview of current knowledge in relation to the genetic aspects of narcolepsy will be reviewed in detail later in this chapter.

Ophthalmic testing Narcolepsy appears to be associated with a number of ocular symptoms that may be used as diagnostic indicators of narcolepsy (Norman & Dyer, 1987). Ophthalmic complaints of subjects subsequently diagnosed with narcolepsy include blurred

vision, diplopia, tired or burning eyes. The usefulness of ophthalmic signs as a diagnostic indicator for the disorder is demonstrated by an evaluation of 405 subjects with narcolepsy of whom 14% were actually diagnosed through presentation to an opthamology department (Norman & Dyer, 1987).

In addition to the general finding of ophthalmic complaints in many subjects with narcolepsy, the disorder also appears to be associated with changes in pupillometric indices. Whilst normal alertness is associated with minimal variation in pupil diameter, subjects with narcolepsy demonstrate a sinusoidal variability in pupil diameter. Confirmation of the increased oscillations in pupillary diameter for narcoleptics compared to controls were achieved by Newman and Broughton (1991). However no other pupillary indices such as baseline pupil diameter or pupillary orienting response were found to discriminate between groups. Newman and Broughton (1991) suggest that part of this lack of sensitivity for pupillometric assessments may reflect the methodological difficulties associated with this measure. Dyer and Eisenberg (1982) suggest that pupillography be considered as an adjunct to clinical history diagnosis.

Additional diagnostic strategies for diagnosis of narcolepsy that have been investigated include P-300 evoked potentials, though Broughton, Aguirre and Dunham (1988a) suggest that in comparison to MSLT measures the use of evoked potential amplitudes were far less powerful diagnostic discriminators of narcolepsy.

Differential Diagnoses of Narcolepsy

A variety of disorders may present with persistent and excessive daytime sleepiness, these include insufficient sleep, sleep apnea, idiopathic hypersomnolence, periodic leg movements during sleep, drugs or alcohol, circadian rhythm disorders and affective disorders

such as depression (Moldofsky, 1992). Douglass, Hays, Pazderka and Russell (1991) report on five patients diagnosed with schizophrenia that were actually narcoleptic subjects with prominent hallucinatory symptoms. While treatment with antipsychotic drugs was ineffectual, patients responded to stimulant therapy. Narcolepsy may be also be misdiagnosed as hypothyroidism, hypoglycaemia, epilepsy (Manfredi, Vgontzas & Kales, 1989) or paroxysmal myoplegia (Roth, 1978). Aldrich (1996) suggests that features of narcolepsy, particularly for narcoleptics without cataplectic symptoms, are often evident in other disorders of excessive sleepiness and more stringent diagnostic criteria are necessary to discriminate between narcolepsy and idiopathic hypersomnia. Bruck and Parkes (1996) provide an overview of comparative features of narcolepsy and idiopathic insomnia suggesting that both the frequency of nocturnal awakenings and the change in severity of excessive daytime sleepiness over time may discriminate between the disorders.

Epidemiology of Narcolepsy

Prevalence

Estimates of the prevalence of narcolepsy vary and seem to differ significantly across cultural groups (Aldrich,1990; Aldrich, 1992). Hublin, Patinen, Kaprio, Koskenvuo and Guilleminault (1994a) and Hublin et al. (1994d) provide a review of prevalence studies. Countries such as Israel report the disorder as being extremely rare, estimating a prevalence as low as 1:435,000, whilst Japanese figures suggest that the disorder may affect up to 1:600 individuals. Prevalence figures are estimated at up to 1:1500 for the caucasian Americans but decrease to 1:5000 for black Americans. It is argued that these differences evident in the prevalence of narcolepsy reflect cultural variations in the frequency of occurrence of the DR2 antigen (Hublin, Partinen & Koskimies, 1991). The significance of this association will be

discussed in the section of this chapter which evaluates the genetic aetiology of narcolepsy. The accuracy of prevalence reports must however be treated with caution as to date the diagnosis of narcolepsy has been confounded by (a) the sensitivity and specificity of diagnostic procedures, (b) the economic availability of the often sophisticated diagnostic equipment and (c) the lack of knowledge about narcolepsy within the medical profession.

Gender Distribution

Narcolepsy effects equal numbers of males and females (Aldrich, 1992). Early reports of the increased frequency of the disorder amongst men has been explained as a consequence of either the misdiagnosis of sleep apneics (which is more frequent in the male population) as narcoleptics (Aldrich, 1990), or as a reflection of the changing social roles of men and women. Previously men had increased employment demands and therefore inappropriate sleepiness was more conspicuous and treated more seriously than for women (Roth, 1978). This explanation appears ratified by my personal communications with many older narcoleptic women who describe their doctors as dismissing their reports of excessive sleepiness as trivial or simply linked to early parenting responsibilities and therefore not significant enough for further evaluation. Even following diagnosis, women report significantly less support than men in living with the disorder (Merritt, Cohen, Mercer & Keegan, 1993).

Psychosocial Implications

The first major evaluation of the psychosocial implications of living with narcolepsy was carried out in 1981 by Broughton et al. (also reported in Broughton, 1992a,b). In a survey of 180 narcoleptics across North America, Europe and Asia, narcolepsy was reported

to have negative effects on a wide range of psychosocial factors. Educational and occupational opportunities were seen to be significantly reduced for narcoleptics compared to controls and for many of the narcoleptics, subjective impairments in memory function were seen as the causative factor for job difficulties. Both the frequency and severity of accidents, whilst driving, at home, or at work were significantly increased for narcoleptics. Psychological wellbeing was significantly impaired for narcoleptics, with over 50% of respondents reporting depression of which 24.6% experienced recurrent suicidal thoughts. Reports of sexual dysfunction, defined as impotence or decreased libido, were also significantly increased amongst the narcoleptic subjects. These life effects appeared to be consistent across cultural groups (Broughton et al. 1983; Broughton & Broughton, 1994) and have been replicated in more recent studies across the diverse areas of self esteem (Cohen, Ferrans & Smith, 1992b), reported accidents (Cohen, Ferrans & Eshler, 1992a; Broughton & Broughton, 1994; Findley, et al., 1995), male sexual dysfunction (Karacan et al. 1992), depression (Merritt, Cohen & Smith, 1992a), parenting tasks (Nehring & Cohen, 1994) and global quality of life issues (Alaia, 1992; Ferrans, Cohen & Smith, 1991 & 1992). Broughton and Broughton (1994) provide a further review of these diverse and debilitating psychosocial implications adding that for adolescent narcoleptics specific issues of diminished school performance, concerns of mental disorder, and possible social withdrawal, to hide excessive somnolence, or the possibility of cataplexy, result in significantly diminished self esteem for adolescents with narcolepsy.

McMahon, Walsh, Sexton and Smitson (1982) describe narcolepsy as a "severely disabling condition" (p. 85) on the basis of their research into the life effects of the disorder which concluded that in the areas of social, physiological, emotional and family needs, subjects with narcolepsy appeared deficient even when compared to people from other

disability groups. Mayer, Pollmacher, Meier-Ewert, and Schulz, (1993) suggest that the disorder should be identified with a minimum degree of impairment of 50% but for cases associated with drug resistant cataplexy the level of impairment rises to approximately 80%. Kales, Vella-Bueno and Kales (1987b) also report on the pervasive psychosocial effects of narcolepsy across interpersonal, vocational, educational and familial life areas. More detailed psychological profiles of narcoleptics were obtained by Kales et al. (1982) who tested 50 narcoleptic adults using the Minnesota Multiphasic Personality Inventory (MMPI), the Symptom Checklist - 90, the Bender Gestalt and several projective psychological tests. Findings indicated significantly increased psychopathology amongst narcoleptics compared to controls. Personality profiles of narcoleptics indicated a lack of emotional expressiveness and increased scores for anxiety and negative self image. Psychosocial attitudes to the disorder resulted in elevated interpersonal sensitivity for narcoleptic patients. Kales et al. (1982) concluded, however, that the psychopathology of narcolepsy occurs as a consequence of the disorder rather than a causative component. Factors consequential to the disorder and leading to psychosocial maladjustment may reflect either generic adjustment issues of living with a chronic disorder or issues specific to living with narcolepsy. Further support for psychopathology occurring as a reactive response to narcolepsy is provided by Kales and Kales (1987) who compared MMPI profiles between narcoleptic and other sleep disordered subjects and found similar levels of elevation between all sleep disordered groups. Similarly, Stepanski et al. (1990) compared MMPI profiles for narcoleptics to matched controls with EDS. Again no significant differences were found between the groups, suggesting that the negative psychosocial aspects of narcolepsy are not specific to narcolepsy, but reflect a more generalised response to disorders of excessive daytime sleepiness. Comparisons of quality of

life issues between narcoleptics and idiopathic hypersomniacs also demonstrated that the issues remained comparable across disorders of hypersomnia (Broughton, 1992b).

If the negative psychosocial aspects of narcolepsy emerge as a response to the disorder then it would be predicted that positive support systems should counter these negative effects. Interestingly, a study by Alaia (1992) examining the relationship between perceived levels of social support for narcoleptics and subsequent psychosocial adjustment have found no correlation between these factors. Alaia (1992) interprets this finding as an indicator that narcoleptics underestimate social support mechanisms, believing that outsiders are incapable of comprehending the implications of living with narcolepsy.

Aetiology of Narcolepsy

Whilst there is no complete understanding of the aetiology of narcolepsy it has long been recognised that the disorder is associated with a genetic component. Positive family histories of the disorder have been established with familial rates of occurrence being approximately 1:5, that is an investigation of 5 patients with narcolepsy would reveal 1 relative of the 5 also presenting with narcolepsy (Hublin, Partinen, & Koskimies, 1991).

Comparatively recent advances in cellular immunology have begun to unravel the complex genetic background to the disorder. Since the demonstration, in the early 1960's, of a link between the major histocompatibility complex (MHC) genotype and susceptibility to viral infection there has been a rapid development in associations between the MHC and propensity for disease, with the majority of linked disorders being characterised as autoimmune disorders (Guilleminault et al., 1988). The human MHC is located on the short arm of chromosome six and the human leukocyte antigen (HLA) is genetically coded through approximately four million base pairs in this MHC region. On the basis of both structure and

biological function HLA antigens are grouped into two categories - class I includes HLA-A,B C antigens and class 11 the HLA-D, DR, DQ, DP antigens (Powis & Trowsdale, 1991.)

Parkes and Lock (1989) state that by 1988 HLA data on over 500 narcoleptics had been reported and that 99% of all subjects tested were both DR2 and DQw1 positive compared to frequencies of approximately 22% and 54% respectively in the general population (Billiard et al., 1988). This high association between HLA-DR2 and narcolepsy appears maintained across diverse cultural samples (Honda & Juji, 1988; Pollack, Gideoni, Peled, & Lavie, 1988) and is the strongest known link between any disease and an HLA factor (Honda & Juji, 1988). Despite this significant association the genetic penetrance is low (Billiard et al., 1994b) with only about 0.2% of DR2 positive individuals developing narcolepsy (Parkes & Lock, 1989). Hence some genetic factor appears as a necessary but not sufficient condition for the development of narcolepsy. Honda (1988) suggests that additional genetic and/or environmental factors may be necessary as precipitants to the development of narcolepsy. Orellana, Villemin, Tafti and Billiard (1991) evaluated perceived environmental triggers in 100 narcoleptic patients and found that 20% of subjects cited changes in sleep wake schedule, 18% psychological stress factors, 5% pregnancy and 3% infectious disease as causative factors in the disorder. Similar environmental triggers were identified by Orellana et al. (1994) in their retrospective analyses of life events in the year preceding the onset of narcolepsy. Additional cited environmental triggers include mercury poisoning (Nahmias & Karetzky, 1989), closed head injury (Lankford, Wellman & O'Hara, 1994; Francisco & Ivanhoe, 1996) and brain radiotherapy (Appelbaum & Spire, 1991). A review of incidents of narcolepsy occurring as secondary to underlying neurological disorders, described as symptomatic narcolepsies, is provided by Autret, Lucas, Henry-Lebras and de Toffol (1994) and recent developments in brain imaging techniques have, in addition,

identified pontine lesions (Plazzi et al., 1996), hypothalmic tumours (Servan, et al. 1995) and arteriovenous malformations of the diencephalon leading to narcoleptic symptomology (Clavelou,et al., 1995).

The reports of monozygotic twins discordant for narcolepsy provides additional support for the role of environmental factors in the development of narcolepsy (Montplaisir & Poirier, 1987; Albert, Andreas-Zeitz, Keller, Roth & Schulz, 1988; Guilleminault, Mignot & Grumet, 1989; Honda & Matsuki, 1990; Pollmacher et al., 1990; Sforza & Lugaresi, 1993, and Partinen, Hublin, Kaprio, Koskenvuo, & Guilleminault, 1994). Recent evaluations of the relative roles of genetic and environmental factors in the aetiology of narcolepsy suggest, however, that the symptom of daytime sleepiness may be more dependent on genetic factors whilst the onset of cataplexy based symptoms may be more susceptible to environmental components (Kaprio, Hublin, Partinen and Heikkila, 1996). Billiard et al., (1994) further propose that some tentative evidence exists for an X linked inheritance mode.

The mechanisms of association between HLA and the disease process are discussed by Powis and Trowsdale (1991) and appear to be associated with autoimmune dysfunction. Despite the occasional reports of the coexistence of narcolepsy and the autoimmune disorder multiple sclerosis (e.g. Younger, Pedley & Thorpy, 1991; Autret et al. 1994) there appears no evidence to support an immune mediated pathogenesis for narcolepsy. Biochemical analyses of cerebrospinal (Fredrikson, Carlander, Billiard & Link, 1990) and serum fluids (Rubin, Hajdukovich & Mitler, 1988) from narcoleptic patients fail to identify any biochemical markers of autoimmune disease. Mignot, Tafti, Dement and Grumet, (1995) provide a review of the evidence surrounding the suggestion of autoimmune dysfunction in narcolepsy and whilst these authors acknowledge the failure of research to identify any evidence of linked

autoimmune disorder they argue that the connection may involve an, as yet undefined, association between immune function and general mechanisms of sleep generation.

Another explanation for the apparent lack of association between autoimmune dysfunction and the prevalence of HLA-DR2 in narcolepsy is provided by Parkes and Lock (1989) who suggest that the relationship between HLA DR2/DQw1 may be a spurious one with the genetic factor being a "linked non - HLA gene ... the genetic product being a neurotransmitter receptor involved in sleep wake systems" (Parkes & Lock, 1989, p. 106). The possible existence of a predisposing gene for narcolepsy secondarily linked to the HLA system could also provide a feasible explanation for the occurrence of narcolepsy in HLA-DR2 negative subjects (Rubin, Hajdukovich & Mitler, 1988; Guilleminault, Mignot & Grumet 1989; Neely, 1989; Mignot et al., 1994)). Mignot et al. (1994) suggesting that more specific genetic markers such as DQB1*0602 and DQA1*0102 may provide a more accurate predictor of narcolepsy across diverse ethnic groups. Alternatively the absence of HLA - DR2 amongst subjects with a clinical diagnosis of narcolepsy may indicate a disorder that mimics the symptomatology of narcolepsy but that has a separate pathogenesis (Ditta, George & Singh, 1992). This perhaps highlights the potential difficulty of both the definition of narcolepsy and the differential diagnoses of narcolepsy from other disorders of excessive daytime sleepiness (Matsuki, Honda & Juji, 1987). The strong association between narcolepsy and HLA-DR2 provides, however, a useful clinical tool for estimating familial risk factor for developing narcolepsy (Kramer, Dinner, Braun, Zachary & Teresi, 1987), for confirmatory diagnoses of narcolepsy in the absence of clear cataplexy (Rosenthal et al., 1991) and in facilitating the differential diagnosis of narcolepsy from other disorders of excessive sleepiness (Staner, Bouillon, Andrien, Dupont & Mendlewicz, 1991).

The Neurobiology of Narcolepsy

Current theoretical models of narcolepsy suggest that the disorder is neither a primary disorder of arousal nor a specific disorder of REM mechanisms. Rather it appears to represent a dysfunction of state lability with the development of inappropriate and diffuse boundaries between sleep and wakefulness states. It is clear that mechanisms of sleep and wakefulness are, in part, neurochemically regulated and hence attempts to decipher the sleep wakefulness dysfunction in narcolepsy have focussed on the investigation of differential abnormalities of neurotransmitters and their metabolites amongst narcoleptic subjects. Smith and Cohen (1988b) provide a summary of proposed biochemical dysfunction in narcolepsy stating that "... symptoms could be accounted for by a systematic neurotransmitter dysfunction primarily stemming from problems of dopamine release and a dynamic imbalance between dopaminergic and cholinergic systems in the central nervous system" (Smith & Cohen, 1988b, p. 230).

The principle course of narcolepsy involves the development of EDS prior to the onset of cataplectic symptoms (Scrima, 1991). This sequential emergence of NREM and REM based symptomology coupled to the differential effectiveness of medications for the two symptoms groups led investigators to propose that aspects of NREM and REM dysfunction in narcolepsy are modulated by different neurochemical mechanisms. Specifically, dopamine (DA) abnormalities have been linked with arousal (NREM) dysfunction whilst aspects of REM dysfunction are associated with changes in cholinergic (ACh) function (Broughton, 1990).

Dopamine has been demonstrated to influence both the maintenance of wakefulness and waking states of physiological arousal (Gaillard, 1990). Analysis of human narcoleptic cerebrospinal fluid indicates lowered concentrations of both dopamine (Montplaisir et al.,

1982), and the dopamine metabolite homovanillic acid (Parkes et al., 1974). Reports on autopsied brains from three narcoleptic patients also show significantly decreased levels of the dopamine metabolite, DOPAC, together with marked increases in the number of dopamine receptors (+125%) in the caudate and putamen regions of the brain (Kish, 1988; Kish et al., 1992; Mamalak, 1992). Findings of the upregulation of select brain dopamine receptors were reported from additional autoradiography studies of five human narcoleptic brains (Aldrich, Hollingsworth & Penney, 1992). More recent SPECT (single positron emission computed tomography) and PET studies fail however to identify any increases in dopamine D2 receptors (Hublin, Launes, Nikkinen & Partinen, 1994; Rinne et al., 1995). The evidence for increased D2 receptor sites from autopsy findings need therefore to be treated with caution as the research is unable to determine whether the observed changes in DA metabolism were the cause of, or consequent to the narcoleptic syndrome. Narcoleptic medication, especially gammahydroxybutyrate, has also been shown to influence brain dopamine and acetylcholine concentrations, further confounding the implications of the autopsy reports (Kalra & Hart, 1992).

Smith and Cohen (1988b) theorise that the development of narcolepsy may be associated with an increased sensitivity in autoreceptor sites linked to dopaminergic cells. These sites are responsible for the negative feedback mechanisms controlling dopamine release. Supersensitivity of presynaptic autoreceptor cells, which could develop as a consequence of either chronically low levels of dopamine or acute phases of dopamine restriction, could then result in diminished dopamine release. Smith and Cohen (1988b) further propose that once sensitised autoreceptor cells may begin to oscillate independently of dopamine levels leading to highly labile and unregulated release of dopamine with consequent lability in arousal and wakefulness.

Shiromani and Gillin (1987) provide a comprehensive review of the empirical evidence to support the association between cholinergic factors and the normal mechanisms of REM sleep. Although research has failed to identify the specific mechanisms of cholinergic dysfunction in narcolepsy there has been substantial support for this association (Sandyk, 1989; Broughton, 1990; Aldrich, 1991; Aldrich, 1993; Reid et al., 1994; Aldrich et al., 1994). Smith and Cohen (1988b) suggest that it is more constructive to view narcolepsy as a disorder of the "whole brain" moderated in part by the imbalance of key neurotransmitters. From this global perspective they formulate a possible model of narcolepsy as a disorder of "abnormal forebrain regulation of state changes" (Smith & Cohen, 1988b, p. 239) underscored by dysfunctional synergism between ACh and DA. Mamelak (1992) also suggests that narcolepsy may represent a dysfunction of the reciprocal interaction between monoaminergic and cholinergic mechanisms such that genetically induced increases in the levels of serotonin and noradrenaline may lead to inhibition of cholinergic mechanisms resulting in their sensitisation and the subsequent instability of REM functions. It is clear that explanations of the neurobiological factors associated with narcolepsy are as yet only speculative. Serotonin (Montplaisir & Godbout, 1989), adenosine (Marczynski, 1989), noradrenaline (Aldrich et al., 1994), and even the endogenous opiods (Sandyk, Bamford & Labadie, 1988) have all been proposed as agents in the disorder. Recent sophisticated developments in brain imaging techniques are also providing new insights into the abnormal pathophysiology of narcolepsy with SPECT analyses identifying characteristic changes in regional cerebral blood flow. The significance of these findings are, however, as yet not understood (Shettar et al., 1994).

Treatment of Narcolepsy

Pharmacological Interventions

As the pathogenesis of narcolepsy is not yet fully understood, treatment of the disorder is directed primarily at symptom relief coupled with psychosocial support. The extensive variability in both symptom presentation and symptom severity between narcoleptic sufferers means that treatment plans need to be highly individualised and for many narcoleptics finding the most effective treatment strategy may involve a period of experimentation with both treatment agents and dosages (Culebras, 1992; Gelb et al., 1994). The principal medications for the control of excessive daytime sleepiness and sleep attacks are the central nervous system stimulants which act at synaptic levels to influence the release, uptake and blockage of monaminergic systems. Methylphenidate acts primarily on dopaminergic systems (Seiden, Sabol & Ricaurte, 1993), whilst amphetamines have increased specificity for adrenergic and serotonergic systems (Manfredi & Kales, 1987). The major stimulants and their maximum recommended dosages are listed by Guilleminault (1989) as dextroamphetamine (Dexamphetamine) < 40mg/day; methylphenidate (Ritalin) < 60mg/day; mazidol (Sanorex) < 5mg/day and pemoline (Cylert) < 150mg/day). Manfredi and Kales (1987) and Parkes (1994) provide neuropharmacological reviews of pharmacological treatment agents in narcolepsy and Mitler, Aldrich, Koob and Zarcone (1994) evaluate the response of narcoleptic subjects to stimulant medications. Across all studies 65-85% of subjects experienced improvements in daytime sleepiness. Extracting from these drug efficacy studies the reports that utilised objective MSLT and MWT measures of sleepiness, Mitler et al. (1994) indexed the degree to which various stimulant medications 'normalised' daytime functioning amongst patients and found that methamphetamine produced the highest normalising factor. Dextroamphetamine and methylphenidate were found to be only slightly

less effective (ASDA, 1994). The normalising effects of methamphetamine appear to be dose dependent (Mitler, 1994) with doses of 40-60mg normalising narcoleptic sleep latencies and performance on the Steer Clear driving task (Mitler, Hajdukovic & Erman, 1993).

The use of stimulant medication, particularly amphetamines, as a long term treatment strategy for narcolepsy remains controversial and many of the issues are reviewed in a series of papers by Guilleminault (1993), Parkes and Dahlitz (1993), and Mitler, Erman and Hajdukovic (1993). Major themes to emerge from these articles include the issue of what should be the major outcome measure of treatment for subjects with narcolepsy? Therapeutic dosages of stimulants may improve, but not fully normalise, daytime sleepiness (Mitler, 1994) but dosages necessary to eliminate sleepiness increase the likelihood of adverse side effects such as nervousness, jitteriness, perspiration, decreased appetite (Phillips, 1983) and the development of drug tolerance and demonstrated cardiovascular problems (Guilleminault, 1993). The debate is not resolved. Parkes and Dahlitz (1993) advocate the aim of "... achieving less than ideal alertness but with few or no side effects rather than to have a fully alert but bad tempered, hyperactive, sweaty and hypertensive narcoleptic ....." (Parkes & Dahlitz, 1993, p. 203). Mitler et al. (1993) suggest a more aggressive approach to treatment with the therapeutic goal of "... total elimination of the symptom (EDS)" (Mitler et al., 1993). Schumacher, Merritt, and Cohen (1993) evaluated perceptions of 700 narcoleptic patients as to the effectiveness of their current medication and found that large proportions of respondents were still experiencing symptoms, including EDS, at a moderate to frequent level. These results could suggest that medication for many narcoleptics fails to achieve symptom relief and Schumacher et al. (1993) question whether those subjects reporting relief potentially represent subjects using medication at higher than recommended dosages. Alternatively, as demonstrated by Rogers, Aldrich and Caruso (1994a), subjective reports by

narcoleptic subjects of symptom relief following treatment may not match objective sleepiness measures.

The American Sleep Disorders Association (ASDA, 1994) provide clinical guidelines for the use of stimulant medication in narcolepsy and these guidelines provide a framework for current treatment and continued debate on appropriate strategies for treatment of daytime sleepiness in narcolepsy.

Stimulant medications, effective in limiting excessive daytime sleepiness and sleep attacks, have little influence on the REM based symptoms of cataplexy, sleep paralysis and hallucinations. Treatment of these symptoms is best achieved through the use of the tricyclic antidepressants, which appear to act through the blocking of serotonin uptake (Thorpy & Goswami, 1990). The major drugs and maximal dosages are listed by Guilleminault (1989) as protriptyline (Vivactil), < 20mg/day; imipramine (Tofranil), < 200mg/day; clomipramine (Anafril), < 200mg/day; desipramine, < 200mg/day ; viloxazine, < 200mg/day, and fluoxetine, < 60mg/day. Possible side effects of these drugs include dry mouth, constipation, urine retention and impotence (Phillips, 1983). Problems of tolerance may also interfere with prolonged use of anticataplectic medication and withdrawal from medication may lead to a spontaneous rebound of cataplectic symptoms (Scharf, Fletcher & Jennings, 1988).

Research continues to evaluate the effectiveness of other medications in the treatment of narcolepsy : clonidine (Salin-Pascual, Fuente & Guardiola, 1985); L-tyrosine (Mouret et al., 1988; Elwes et al., 1989 & Roufs, 1990), gamma-hydroxybutyrate (Scrima, Hartman, Johnson & Hiller, 1989; Scrima, Johnson & Hiller, 1991; Kalra & Hart, 1992 and Lammers et al., 1993), triazolam (Thorpy, Snyder, Aloe, Ledereich & Starz, 1992), bromocriptine (Boivin, Montplaisir, & Lambert, 1993), selegiline (Hublin, Partinen,

Heinonen, Puukka & Salmi, 1994; Reinish, MacFarlane, Sandor & Shapiro, 1995) and yohimbine (Wooten, 1993; Poceta, Hadjukovic, & Mitler, 1994).

Since 1986 clinical trials in Europe have investigated the use of modafinil, a central alpha 1 adrenergic agonist, as a treatment for narcolepsy. The medication appears to improve daytime sleepiness without effecting night time sleep (Besset, Carlander, Tafti & Billiard, 1993; Billiard et al., 1994a). Patients using modafinil report that the quality of wakefulness is more "natural" than that achieved with amphetamines and that there are minimal tolerance or side effect problems (Laffont, Mayer & Minz, 1994; Mignot, 1994). Reports of the effectiveness of modafinil on cataplexy remain ambiguous (Bastuji & Jouvet, 1988; Boivin, Montplaisir, Petit, Lambert & Lubin, 1993).

Non Pharmacological Interventions

Several studies have examined the efficacy of naps as a treatment strategy for excessive daytime sleepiness in narcolepsy. Naps have been shown to have an alerting effect for narcoleptics and to be more refreshing for narcoleptics than for subjects suffering other disorders of daytime sleepiness (Roehrs et al., 1984). The relationship between nap duration and alertness appears to be nonlinear for narcoleptic subjects. Roehrs et al. (1985) compared sleep latencies for narcoleptics and other EDS patients following naps of both 15 and 30 minute duration. For the 15 minute nap condition narcoleptics demonstrated a shorter sleep latency compared to the EDS group but following the 30 minute nap condition EDS patients demonstrated a shorter sleep latency than the narcoleptics. Roehrs et al. (1985) suggest that these findings may indicate that narcoleptics never achieve full alertness irrespective of nap duration, or, alternatively, that napping may serve a different role for narcoleptics compared to other EDS patients. Naps may not have a recuperative function in narcolepsy but rather a

"discharge function" necessary to restore CNS capacity.

Godbout and Montplaisir (1986) compared the effect of naps on a four choice reaction time measure for narcoleptic and control subjects. On days where subjects were allowed to nap, narcoleptic performance was normalised, and Godbout and Montplaisir (1986) conclude that scheduled naps may have important applications in the treatment of narcolepsy potentially decreasing the need for stimulant medications.

Rogers and Aldrich (1993) evaluated the effectiveness of nap therapy as an adjunct to medication in the treatment of daytime sleepiness for narcoleptic patients. Sixteen narcoleptic patients took three regularly scheduled 15-minute naps during the day, over a period of one month, the effects of naps on daytime alertness being measured using objective maintenance of wakefulness test (MWT) measures in addition to sleep log data and subjective assessments on the Narcolepsy Symptom Status Questionnaire. MWT measures indicated improved ability for some subjects to stay awake following the nap treatment though the frequency of self report daytime naps and subjective symptom severity remained unchanged. These findings of the Rogers and Aldrich (1993) study raise the questions of both the relationship between objective and subjective assessments of symptom severity in narcolepsy and the relationship between napping and sleepiness or ability to maintain wakefulness in this clinical population. Mullington and Broughton (1994) also argue that the recuperative power of a nap may be moderated by the propensity for the post nap period to be associated with sleep inertia. For some nap periods the subsequent inertia effect may extend over a period as long as 20 minutes and appears to be most pronounced following SWS nap episodes but diminishes with increased REM based nap infrastructures.

Garma and Marchand (1994) review the literature investigating non pharmacological treatments of narcolepsy including the use of nap therapy, the possibility of

utilising dietary factors in the control of sleepiness, and the role of psychosocial support in treatment interventions. Treatment of the disorder, they argue, must be focussed on multimodal interventions or as described by Broughton and Broughton (1994) "once a diagnosis of narcolepsy is made, the prescription pad cannot be the end of intervention" (p.S48).

Summary

Narcolepsy is a chronic disorder that presents as abnormal manifestations of REM and NREM sleep, and dysregulation of the control mechanisms maintaining the states of sleep and wakefulness. Whilst the aetiology of the disorder is not as yet fully understood, it appears to involve abnormalities of the neurotransmitter mechanisms which control sleep and wakefulness. The propensity to develop the disorder may be genetically predetermined, though as yet unexplained triggers appear necessary for the expression of this genetic predisposition. Treatment of the disorder focuses on symptom control with stimulant medication controlling the EDS symptoms, and tricyclic antidepressants controlling REM based cataplexy. The disorder is associated with significant psychosocial impairment, though it is unclear to what extent this reflects dysfunction central to the disorder, or occurs as a consequence of secondary factors. The investigation of narcolepsy raises many questions regarding the nature of sleep and wakefulness that relate not only to an understanding of the pathogenesis of the disorder itself, but also to the nature of sleep and wakefulness in non pathologically sleepy individuals.

CHAPTER 3

Sleepiness and Performance

The physiology of sleep is a very complicated subject, and any theory that has yet to be advanced is open to many objections, some of them hard to meet. The same is true even to a still greater extent as regards the phenomenon of attention and mental activity, and every attempt at explanation only opens up new questions that still remain for solution (Journal of the American Medical Association, 1895, as cited in Journal of the American Medical Association, 1995, p.198).

Attentional versus Cognitive Theories of the Influence of Sleepiness on Performance

Experimental investigations of the relationship between sleep deprivation and performance have been undertaken since the late 1800s and although the literature confirms that for a variety of tasks sleepiness leads to performance decrements, the underlying process of impairment is yet to be understood.

Two major theoretical positions emerge within the literature to explain the observed relationship between sleepiness and performance. Dinges and Kribbs (1991) provide a review of the literature on sleepiness and performance and conclude that performance decrements occur as a consequence of sleepiness diminishing the resources, in particular arousal resources, that a subject can apply to the task, "attentional deficits have long been recognised to be the common cognitive thread of sleep loss effects" (Dinges & Kribbs, 1991, p.120). In contrast to this exclusively attentional paradigm is the hypothesis that the effects of sleep deprivation on performance may be influenced by sleep deprivation leading to fundamental changes in sensory-cognitive capacity (Horne, 1988a; Horne, 1988b; Mikulincer, Babkoff &

Caspy, 1989; Wimmer, Hoffmann, Bonato, & Moffitt, 1992). Norman and Bobrow (1975) utilise the terms "resource limiting" to describe the attentional decline model and "data limiting" to describe the cognitive deficit model. Wimmer et al. (1992) define the issue as one of deciding whether cognition following extended sleep loss changes qualitatively or quantitatively. Horne (1988a) restates the problem as deciding between the influence of motivation and cerebral impairment. Declining resources are seen by Horne (1988a) as synonymous with an increasing behavioural drive to sleep that occurs independently of any physiological sleep function. Some performance decrements should therefore be counteracted by the application of compensatory effort. Conversely Horne (1988a) suggests that data limiting factors imply that sleep performs a restorative function for the brain and therefore sleep is necessary to maintain performance. Sleep deprivation therefore potentially leads to cerebral impairment or decreased nervous system capacity. Horne (1988a) emphasises that here impairment refers to "a reversible state, analogous to the impairment and recovery of muscle after exercise" (Horne, 1988a, p.46). The fundamental dilemma is then whether sleepiness induced performance decrements occur as a consequence of sleepiness leading to a "disinclination" to perform or to an "inability" to perform.

Within either of these theoretical paradigms - attentional versus cerebral impairment, further issues arise. An explanation of performance degradation in terms of attentional decrement raises the question of the process of attentional decline. One possibility is that performance decrements occur primarily as a consequence of errors of omission. This absence of response is attributed to the occurrence of lapses in attention. This proposal was first formulated by researchers at the Walter Reed Army Institute of Research and was labelled the "Walter Reed Lapse Hypothesis" (Johnson, 1982). The basic tenet of the theory is that sleep loss leads to intermittent response omissions for both mental and motor tasks.

These lapses are proposed to occur against a stable arousal background and therefore performance following sleep deprivation is marked by an unevenness in response factors rather than a gradual decrement. Broadbent (1955) summarises this lapse hypothesis suggesting,

> Crudely speaking, a man is not like a child's mechanical toy which goes slower as it runs down. Nor is he like a car engine which continues normally until its fuel is exhausted and then stops dead. He is like a motor which after much use misfires, runs normally for awhile, then falters again and so on (p.2).

Kjellberg (1977 a,b,c) supports the notion of sleep deprivation influencing resource limiting or attentional factors but questions the adequacy of the lapse hypothesis as an explanatory model. Rather Kjellberg (1977 a,b,c) suggests that sleep deprivation alters the way the individual responds to and interacts with the environment. He argues that if dearousal occurs as a consequence of sleep deprivation, then lapses represent the end point of the dearousal continuum and performance decrements occur not only at the point of lapsing but also as a consequence of these declining arousal levels which are presumed to lead to attentional deficits.

Similarly little is understood of the processes which could mediate cerebral impairment explanations of the relationship between sleep deprivation and performance. One current line of research is that cognitive deficits associated with sleep deprivation may be mediated through alterations in central nervous system catecholaminergic neurotransmission. McCann et al. (1992) demonstrated that the use of catecholamine synthesis inhibitors act as a synergist with sleep deprivation to lead to severe cognitive impairments on a variety of performance tasks. McCann et al. (1992) suggest that these findings of the role of

catecholamines in sleepiness induced performance effects are supported by the work of Wu et al. (1991) who used Positron Emission Tomography (PET) analyses to investigate neurochemical changes associated with sleep deprivation. Wu et al. (1991) demonstrated decreased basal ganglia glucose metabolism following 32 hours of sleep deprivation and McCann et al. (1992) suggest that previous metabolic links have been demonstrated between decreased glucose and catecholamine activity rates.

The rest of this chapter will review the experimental research on sleepiness and performance in non clinical populations to evaluate the possible roles, and mechanisms of action, of attentional versus cognitive models of sleepiness induced performance decline. Chapter 4 will focus specifically on the relevant literature in pathologically sleepy populations to better understand the relationship between sleepiness and performance in narcoleptic subjects.

The majority of relevant experimental work in the area of sleepiness and performance was carried out between the 1930's and early 1970's, and the present evaluation of the literature reflects that historical bias. Since that period of intense interest in sleepiness and performance, there have been few theoretical developments, with the more recent studies either consolidating early findings or focussing on more applied issues of sleepiness and performance, for example, the impact of sleepiness on military capabilities (Rosekind et al. 1994), or on the functional impairment of doctors undertaking hospital residency (Leung & Becker, 1992).

The focus of this chapter will be on an examination of the influence of sleepiness, induced through sleep manipulations, on performance. Chapter 1 has discussed the phenomenon of sleepiness and it is evident that substantial variability in sleepiness also occurs as a consequence of circadian fluctuations. The influence of circadian arousal rhythms on

performance has been widely investigated but the importance of these circadian factors are secondary to the major focus of this thesis and in the context of this thesis impact primarily on methodological factors i.e. circadian effects, if not controlled for, will confound sleepiness induced changes in performance (Babkoff, Caspy, Mikulincer & Sing, 1991). Because of the tangential nature of circadian performance rhythms to the study reported in this thesis the relevant literature will not be reviewed here and the reader is referred to Colquhoun (1982) for a review of research in this area.

Quantitative Changes to Sleep: The Influence on Performance

Sleep Deprivation

The earliest reported studies examining the relationship between sleep deprivation and performance in human subjects were undertaken by Patrick and Gilbert in 1896. Three subjects were kept awake for 90 hours and tested every 6 hours using a battery of tests which included reaction and discrimination time, vigilance, muscle fatigue and memory tasks. The nature of recovery sleep was also examined in one subject. These early studies highlighted many effects of sleep deprivation that have remained relevant to the literature over the past 100 years. These effects include the existence of a circadian rhythm in sleepiness and performance that appears superimposed over the performance decline that occurs as a consequence of sleep deprivation, the occurrence throughout the deprivation period of visual hallucinations associated with uncontrollable naps, the presence of mental "lapses" which interfered with attentional processes, the differential sensitivity of tasks and subjects to performance decrements and the increased depth of recovery sleep which represented approximately 25% of total sleep time lost.

The finding of Patrick and Gilbert (1896) of performance lapses during sleep deprivation gained increased significance following the work of Bills (1931). Bills (1931) working on the effects of fatigue on performance, noted that continuous and monotonous tasks were characterised by performance blocks. Blocks were characterised as response pauses equivalent to the time of two or more average response periods. It is interesting that even in these seminal studies the influence of both task duration and stimulus monotony were noted in relation to performance decrements. Bills (1931) noting that blocks increased with fatigue, and that errors occurred in conjunction with blocks, concluded that blocks provided the subjects with an opportunity for rest and compensated for the effects of fatigue. Warren & Clark (1937) evaluated blocking within a sleep deprivation paradigm and were able to demonstrate that the average percentage of blocks occurring during addition and subtraction tasks increased from 9.2% for initial trials to 23.5% following 40 hours of sleep deprivation. In 1949 Bjerner reexamined the concept of blocks or lapses and demonstrated that lapses during an auditory serial reaction task were consistently associated with the disappearance of EEG alpha rhythms. Williams, Granda, Jones, Lubin, and Armington (1962) examined the relationship between EEG frequency and reaction times during sleep deprivation and found that EEG frequencies recorded in the 1 second period prior to, and following the signal response, could be used to predict reaction time. This correlation between performance and electrophysiological parameters strengthened with prolonged periods of sleep deprivation, and following 50 hours of sleep deprivation a correlation as high as - 0.7 was recorded.

The interest in comparing performance measures with EEG spectral analyses remains a contemporary one and the development of more sophisticated EEG measurement procedures has resulted in increased sensitivity of analyses. Makeig and Inlow (1993), whilst not working within a sleep deprivation paradigm, were able to demonstrate that performance

fluctuations in vigilance measures were predicted by fluctuations in EEG power spectra. Error rates were highly positively correlated with EEG power below 6-7 Hz and highly negatively correlated with power around 10 Hz. Despite the finding of some interpersonal variability in the strength of relationship between electrophysiological and performance parameters (Williams et al., 1962; Makeig & Inlow, 1993) the consistent finding of performance errors associated with sleep EEG parameters has focussed attention on the potential for sleepiness to lead to performance decrements as a consequence of microsleeps or lapses intruding into waking states.

An additional finding of the Warren and Clark (1937) study was that despite increased blocking with prolonged sleep deprivation neither modal nor mean response rates changed significantly. A similar unevenness of response had been reported by Bills (1931) who observed that performance levels returned to baseline between omissions. These overall findings of performance fluctuations associated with diminished alpha recordings support the principal of the lapse hypothesis, that sleepiness induced performance decrements occur as a consequence of microsleeps being interspersed across normal performance parameters. In 1959 Williams, Lubin and Goodnow undertook a major study to differentiate between lapsing versus incremental decline models of sleepiness and performance. Williams et al. (1959) developed a protocol where they categorised tasks as experimenter (E) or subject (S) paced. S paced tasks allow the subject to control the rate of stimulus presentation whilst the presentation of E paced tasks were not under the subject's control. This experimental protocol allowed Williams et al. (1959) to develop and test performance predictions consistent with both the lapsing and gradual decrement hypotheses of arousal. They argued that for S paced reaction time tasks the lapse hypothesis would predict that the presence of a lapse coincident with a stimulus presentation would lead to a response delay and therefore

impairment would be reflected as either a change in speed or number of completed tasks. As sleep loss continues the frequency of lapses should increase and therefore the reaction time distribution should become more positively skewed. Alternatively, if sleep loss leads to a gradual decline in performance, as opposed to lapses, then results should demonstrate a gradual increment in reaction times across the deprivation period. This prediction of Williams et al. (1959) was based on the assumption that if the lapse hypothesis was not valid the relationship between sleepiness and performance could be defined by a linear model of decline. For more complex S paced cognitive tasks Williams et al. (1959) argued that the lapse hypothesis would predict that performance accuracy should be less sensitive to sleep loss than performance speed i.e. the occurrence of lapses will simply delay responses and performance capability will be unaffected by sleep loss. Alternatively a gradual decrement in performance capacity should be reflected in both speed and accuracy measures. Williams et al. (1959) found that for all S paced tasks, results supported the predictions of the lapse hypothesis, with sleep loss leading to changes in speed but not accuracy of performance. For E paced tasks the rate of presentation is controlled by the experimenter and therefore for both vigilance and complex tasks the lapse hypothesis would predict impairments in response accuracy. Response errors should be primarily errors of omission where the co occurrence of a lapse with a signal or a task leads to a failure of the subject to respond within the critical time period. Results supported this prediction and Williams et al. (1959) argue that their overall findings provide substantial support for the lapse hypothesis as an explanatory model of performance decrements associated with sleep deprivation.

In line with the findings of Bjerner (1949), Williams et al. (1959) were able to demonstrate that the occurrence of errors of omission, presumed to be reflecting lapses, were consistently associated with lowered alpha activity. In addition alpha activity demonstrated a

general decline over the sleep loss period. Lisper and Kjellberg (1972) suggest that the findings of the Williams et al. (1959) study were limited by the data analysis which examined the relationship between sleep deprivation and overall performance but failed to assess potential interactions between sleep deprivation and time on task. Using a 10 minute reaction time task Lisper and Kjellberg (1972) demonstrated a gradual increase in reaction times across task duration with even the shortest reaction times appearing sensitive to sleep deprivation. The reported gradual decrement in performance with each reaction time task provides support for an underlying mechanism of a progressive decline in arousal with time on task. Sleep deprivation may accentuate this decrement or as Lisper and Kjellberg (1972) suggest "might be as simple as adding a constant to a more basic process" (p. 290). Similar results were also recently demonstrated by Lorenzo, Ramos, Arce, Guevara and Corsi-Cabrera (1995) who evaluated the effect of up to 40 hours of sleep deprivation on reaction time and associated EEG activity. Lorenzo et al. (1995) were able to demonstrate a positive correlation between reaction time and both length of deprivation ($r = 0.85$), and theta EEG activity ($r = 0.53$). In addition however the number of omissions or lapses in performance were found to increase significantly with increased deprivation.

Attentional resources seem to significantly impact on performance following sleep deprivation, with sleep deprivation appearing to lead to both gradual performance decrements and performance omissions. Performance omissions may occur either at the end point of the arousal continuum or superimposed across the incremental decline process, demonstrating an increased frequency with decreasing arousal states.

One finding of the Williams et al. (1959) study that was inconsistent with the predictions of an attentional deficit model of sleep deprivation effects related to the E paced information learning task. This task which assessed both immediate and delayed recall in

sleep deprived subjects found that for periods of sleep deprivation beyond 50 hours delayed recall becomes significantly poorer than immediate recall. The lapse hypothesis would predict that as sleep loss increased so too would the number of lapses and therefore measures of both immediate and delayed recall should decline as subjects "miss" more stimulus items. The finding of a discrepancy between immediate and delayed recall with extended sleep loss indicates that some process additional to lapsing must be interfering with memory storage.

A sleep deprivation study conducted by Williams, Gieseking and Lubin (1966) further demonstrated impairments in immediate recall tasks that were not explicable in terms of an attentional based model of sleep deprivation. Despite adequate registration of stimuli, significant decrements in immediate recall tasks occurred. Deficits were attributed to the inadequate transfer of material from sensory to short term stores.

Elkin and Murray (1974) used a probe recognition memory task to examine both the acquisition and retention of material under conditions of sleep deprivation. Their findings indicated that both the initial perception of material and the postpresentation rehearsal of material were reduced following sleep deprivation. The authors suggest that these findings are consistent with sleep loss depleting attentional resources "leading to misperception and a failure to rehearse adequately material presented for memorisation" (p. 192). Polzella (1975), using a similar task to Elkin and Murray (1974), also demonstrated a significant impairment in memory function though he concluded that these results could be interpreted from either an attentional or cognitive paradigm with deficits reflecting either lapsing, resulting in inefficient intake of stimulus material, or decreased cognitive processing capabilities secondary to diminished arousal resources.

In an attempt to differentiate between deficits of stimulus input (attentional model) as opposed to stimulus processing (cognitive model) Dinges, Kribbs, Bates, and Carlin (1993)

developed a probe recall memory task where subjects were presented with a list of four word pairs for 30 seconds. Two of the word pairs comprised related words e.g. money-dollar, and two were non related pairs, e.g. inch-society. Recall of word pairs was tested following both one and two nights of sleep deprivation. Dinges et al. (1993) found significant effects for even one night of sleep loss and this effect increased over the second night. Of primary importance however was the finding that related words were recalled at a significantly higher rate than unrelated words. As the task required only 30 seconds to complete it is unlikely that these differences in recall reflect differential stimulus input for the two word classes and the findings are more aptly explained by sleep loss influencing the ability to process the more complex cognitive material.

Despite the difficulties of differentiating between explanatory models the findings from the memory research literature appear to be inconsistent with a strictly attentional based model of sleepiness and performance interactions and provide some support for sensory cognitive deficits associated with sleep deprivation.

As previously discussed the Warren and Clark (1937) study demonstrated that performance lapses or blocks increased over the deprivation period to reach a maximum of 23% following 40 hours of sleep deprivation. An additional finding however was that the final performance trials were associated with fewer performance blocks, perhaps reflecting increased motivation of subjects towards the end of the task. This end of task spurt in performance is frequently noted in both the performance and sleep deprivation literature and provides support for the theory that performance decrements represent, at least in part, decreased motivation of subjects to attend to the task. The failure of these end of task values to reach baseline levels may suggest that motivation was simply not sufficient to counteract

the increasing effects of sleeplessness or alternatively may suggest that a process secondary to attention is limiting the performance capability of sleep deprived subjects.

Horne and Pettitt (1985) attempted to differentiate between attentional versus cognitive impairment explanations by offering sleep deprived subjects substantial monetary rewards for performance. Two groups of subjects were sleep deprived over a 72 hour period. Every 6 hours subjects were tested using the Wilkinson Auditory Vigilance Task (WAVT) and all subjects, including a third non sleep deprived control group, were encouraged to perform at their optimum. One of the sleep deprivation groups were offered substantial monetary rewards for correct identification of targets and target errors were fined. As the deprivation period increased the incentives were also increased. Findings demonstrated that for deprivation periods up to 36 hours the use of incentives was sufficient to counteract the effects of sleep deprivation and detection performance scores for this group matched those of the control group. However by the second night of sleep deprivation incentives were unable to compensate for the effects of sleeplessness and detection scores for the incentives group fell to the level of the no incentive sleep deprived group. These findings suggest that performance decrements associated with low to moderate levels of sleepiness can be counteracted by the application of incentives which appear to reestablish baseline arousal levels within sleep deprived subjects. However, beyond a critical level of sleepiness, incentives seem no longer effective. Horne (1988a) interprets this as evidence that sleep deprivation eventually produces some fundamental cerebral "impairment".

An alternative explanation to the findings of Horne and Pettitt (1985) study is that monetary incentives are just not powerful enough to overcome more severe levels of sleeplessness but that if motivational factors could be increased sufficiently they would

continue to counter the effects of sleeplessness and therefore demonstrate that only resource factors influence performance.

Dinges, Kribbs, Steinberg, and Powell (1992) evaluated sleep deprived subjects' perceptions of their motivation to perform a series of cognitive tasks. Over a period of 64 hours of sleep deprivation subjects were tested every 2 hours on a 20 minute performance battery. Following the performance tasks subjects were asked to rate their performance, the effort they had expended on the tasks and whether they felt they could have done better if they had tried harder. As sleepiness increased, subjects felt they performed more poorly and compensatory effort increased, but subjects reported being unable to try any harder. This data suggests that performance decrements following sleepiness cannot always be compensated for by increased motivational factors and rather potentially reflect a diminished capacity to perform which is independent of volitional control.

Horne (1988b) argues that one reason that cognitive based performance decrements are difficult to demonstrate is that experimental procedures usually involve simple processing tasks such as vigilance measures. These tasks, whilst sensitive to attentional components of sleep deprivation, do not provide a high enough cognitive load to demonstrate cognitive change. Horne (1988b) reevaluated the motivational and cerebral impairment explanations of sleepiness effects by comparing subjects sleep deprived for 32 hours and control subjects on a series of short, stimulating, divergent thinking tasks which required complex thinking skills. Monetary rewards were also used in an attempt to counteract decreased motivation occurring as a consequence of sleep deprivation. Whilst interpretation of the study findings were confounded by the influence of practice effects, cognitive impairment was demonstrated for all divergent thinking tasks. The experimental protocol incorporated one simple, or

convergent, cognitive task and, in contrast to the divergent tasks, this simple task remained unaffected by sleep loss.

Wimmer et al. (1992) expanded on this work by Horne (1988b), evaluating the influence of sleep deprivation on divergent thinking processes for 12 male students following one night of sleep deprivation. Whilst not all tasks demonstrated statistically significant changes following sleep deprivation performance trends were in the direction anticipated by Horne (1988a,b). The control group demonstrated performance increments on the second testing session, as a consequence of practice effects, but performance for the experimental group declined following sleep deprivation. Wimmer et al. (1992) concluded that the observed deficits in performance following sleep deprivation occur as a consequence of sleepiness altering fundamental cognitive capacity and that sleep serves a cognitive restitution role.

Horne (1988a) suggests that if, as hypothesised, sleep deprivation ultimately leads to performance decrements because of cerebral impairment then more challenging tasks would be expected to accelerate this effect as they would be placing greater demands on processing capacity, whilst vigilance tasks with their low cognitive demands should be more resistant to sleepiness effects. The experimental evidence relevant to the relationship between task complexity and sensitivity is, however, contradictory. Wilkinson (1964) was able to demonstrate that complex, exciting tasks such as simulated battle tasks are resistant to performance decrements even after 60 hours of sleep deprivation. Alternatively Lisper and Kjellberg (1972) report findings which demonstrate that increasing the complexity of a task increases its sensitivity to sleep deprivation. More recently Foo et al., 1994, and How et al. 1994, provided support for the findings of Lisper (1972) demonstrating that tasks requiring

cognitive and perceptive skills are more susceptible to the effects of sleep deprivation than routine tasks.

It is possible to reconcile these apparently discrepant findings if task complexity is seen to impact not only on processing or cerebral demands but also on attentional resources, particularly motivation and fatigue. Increased task complexity could, as in Wilkinson's (1964) battle game, make the task more stimulating and lead to increased subject motivation and therefore decreased sensitivity to sleep deprivation. A signal detection task is, however, a repetitive intrinsically uninteresting task and increased complexity (i.e. increased signal rates) may lead to increased fatigue and sensitivity to sleep deprivation. A test of the cerebral impairment hypothesis for sleep deprivation would therefore require an assessment of performance decrements with increasing task load but maintenance of motivational factors.

This raises the more general problem of inter task comparisons in sleep deprivation research. This methodology is used almost exclusively within the literature but because of the multivariate nature of performance tests it is difficult to identify the differential sensitivity of task components e.g. stimulus modality, stimulus presentation or response criteria, to the effects of sleepiness. Babkoff, Mikulincer, Caspy, Kempinski and Sing (1988) suggest that analysis of performance sensitivity to sleep loss necessitates an intra task paradigm where one dimension of a task is manipulated against a stable task background. Using this methodology Babkoff et al. (1988) investigated the effects of sleepiness induced performance changes on increasing memory task load. Results suggest that general performance, measured as a percentage of letters scanned, was independent of task difficulty. Accuracy did, however, vary as a function of task load, with increased task loads most sensitive to levels of sleep deprivation. Signal detection analysis of the results was used to differentiate between the effects of motivation and discriminability on observed decrements. Findings support the

hypothesis that sleep deprivation affects fundamental information processing mechanisms with motivation unaffected by task load or sleep deprivation and discriminability decreasing as a function of task load. These conclusions from signal detection analysis need to be treated with caution as Naitoh (1983) suggests that the presence of performance lapses can decrease discriminability scores. Despite the controversial use of a signal detection analysis the overall findings of Babkoff et al. (1988) of diminished accuracy with increased task load, despite stable performance measures, provide support for sleep deprivation affecting functional capability. It is important to note, however, that increasing task load in the Babkoff et al. (1988) study may represent a differential task load to the studies reported by Horne (1988b) and Wimmer et al. (1992). Cognitive demands may increase in terms of load or complexity and the two may be affected differentially by sleep loss.

All of the experimental procedures discussed so far have utilised an intermittent testing schedule where testing occurs at only discrete intervals over the deprivation period. Angus and Heslegrave (1985) suggest that this type of methodology leads to underestimates of the effects of sleep deprivation on performance. They argue that the availability of breaks between test schedules may allow subjects to draw on unused resources to enhance subsequent test performance. Short test schedules also allow for increased motivational influences on performance outcomes as motivation is closely linked to time on task. Intermittent schedules also provide a limited quantity of data for analysis therefore restricting the validity of the findings. To overcome these potential problems Angus and Heslegrave (1985) suggest that performance testing should occur within a continuous performance paradigm. Angus and Heslegrave (1985) interspersed a variety of cognitive tasks into a continuous (54 hour) high demand work situation. The results for the cognitive performance tasks indicated a significant decline in performance over time with decrements due to

decreased number of responses over time as opposed to decreased performance accuracy. This pattern of results may reflect the use by Angus and Heslegrave (1985) of a self paced methodology where performance speed is sacrificed for performance accuracy. The authors suggest that comparison of performance decrements for continuous versus intermittent schedules demonstrates the increased sensitivity of the former schedule to sleepiness effects. For example previous intermittent schedules e.g. Opstad, Ekanger, Nummestad and Raabe (1978), have suggested that performance levels may be maintained to 90% of baseline following 90 hours of sleep deprivation whereas Angus & Heslegrave (1985) demonstrated a performance drop to 43% of baseline during the second night of deprivation. Such inter study comparisons need however to be treated with caution due to the diversity of methodological factors which may impact on performance sensitivity.

Sleep Reduction

The majority of studies examining the effects of sleepiness on performance have investigated performance changes following periods of total sleep deprivation. Investigations of the effects of partial sleep deprivation on performance appear less frequently in the literature despite the increased applied relevance of such research. For pathologically sleepy individuals, for example, sleepiness occurs as a consequence of reduced or fragmented nocturnal sleep patterns, while, for nonpathological populations, lifestyle or occupational demands may lead to conditions of partial sleep loss.

As with total sleep deprivation studies the findings of performance effects following partial sleep deprivation are contradictory and difficult to analyse. Some of the methodological issues that lead to difficulties of comparative analyses are common to the previously reviewed sleep deprivation literature and include factors such as the variability in

performance tasks and the general absence of control groups to assess practice effects. In addition to these generic issues, sleep reduction studies are further confounded by the range of methodologies used to induce sleep reduction. Researchers refer to acute or chronic paradigms, to short or long term reduction studies and to the singular or cumulative effects of sleep reduction. The use of this terminology appears to be subjectively defined with no clear definitions in the literature to differentiate these protocols. Similarly extensive variability exists between studies in the number of hours of sleep reduction and the general failure of studies to acknowledge the high intersubject variability in habitual sleep length (Jones & Oswald, 1968; Meddis, Pearson & Langford, 1973). Hamilton, Wilkinson and Edwards (1972) argue that to control for this intersubject variability sleep reduction needs to be reported as a ratio of deprivation to baseline sleep levels. The published research fails to address this issue generally reporting deprivation protocols in terms of absolute hours rather than ratios of sleep reduction. Another limitation of sleep reduction research is that the reduction of total sleep hours potentially leads to systematic changes in subsequent sleep architecture and it becomes difficult to differentiate, performance effects, attributable to total numbers of hours slept from changes consequent to structural changes in sleep.

Despite these difficulties associated with sleep reduction methodologies the following section will review the literature on sleep reduction and attempt to evaluate the relevance of this research to this chapter's general focus of the impact of non pathological sleepiness on performance.

Wilkinson, Edwards and Haines (1966) investigated the influence of 2 nights of 1, 2, 3, 4, or 5 hours of deprivation on performance and found that performance remained unaffected until sleep was reduced to 3 hours for vigilance tasks or less than 2 hours for addition tasks. Similar results were reported by Hamilton, Wilkinson & Edwards, 1972) who

compared the effects of 4 consecutive nights of 7.5, 6, or 4 hours of sleep, on an auditory signal detection task, an addition task and a running digit span task. Performance decrements occurred for both the signal detection and speed of addition tasks when sleep was reduced to 4 hours. Hamilton et al. (1972) suggest that for the signal detection task sleep loss does not decrease task sensitivity but rather decreases the ability of subjects to increase their performance over the testing period. When subjects maintained 6 or 7 hours of sleep each night they demonstrated an increase in signal detections over the test period whilst no increase in sensitivity was noted when subjects were allocated to the 4 hour sleep regime. Significant interactions were evident between day of testing and performance decrements suggesting that the effects of sleep loss are cumulative.

A further finding of the Hamilton et al. (1972) study was that for tests of running digit span an inverse effect of sleep reduction on performance was noted. For the first 3 days of sleep reduction subjects experiencing 4 hours of night time sleep performed more efficiently than the subjects allocated to the 6 or 7.5 hour regimes. Hamilton et al. (1972) explain this finding by suggesting that sleep reduction increases the time that material remains in acoustic storage, that is under conditions of low arousal trace decay times may be increased resulting in diminished processing rates and the subsequent increased accessibility of the stimulus materials. This prediction is supported by the research which demonstrates the interaction between arousal and memory function. Specifically it has been demonstrated that low arousal increases the efficiency of short term memory and high arousal, whilst enhancing long term memory, diminishes the efficiency of short term memory (Folkard & Monk, 1980). These findings are explained as a consequence of the impact of arousal on processing strategies. Low arousal is seen to support the maintenance processing necessary for short term storage whilst high arousal facilitates the elaborative processing necessary for the

transfer of material to long term storage (Oakhill, 1986). These findings of the interrelationship between memory and arousal further confound the analysis of the sleepiness and performance interaction, as it seems that at least moderate decreases in arousal can lead to performance increments for short term memory. Sleepiness may therefore not always be associated with performance decline.

Both Wilkinson et al. (1966) and Hamilton et al. (1972) utilised a reduction protocol where the number of hours of sleep was reduced from the first night of testing. This 'acute' deprivation protocol is contrasted with the work of Herscovitch and Broughton (1981) who reduced subjects' total sleep time across a 5 night period to achieve an overall 40% reduction in total sleep time with a final average of 4.6 hours per night. Using this more gradual methodology significant performance deficits were noted for both vigilance and reaction time tasks.

Johnson and Macleod (1973) also utilised a gradual deprivation methodology where two subjects reduced their total sleep time to 4 hours over a 5 month period. Performance decrements were evident for both subjects when total sleep time reached between 5.5 and 4 hours of sleep. In contrast, Friedmann et al. (1977) studied 8 subjects over 18 months, reducing sleep down to between 4.5 and 5.5 hours per night. No significant effects on performance measures were noted despite subjects' subjective reports of diminished performance efficiency and increasing subjective fatigue.

Horne and Wilkinson (1985) suggest that the inability of some studies to demonstrate performance deficits following sleep reduction may be due to the failure of experiments to utilise control groups and therefore eliminate the potential for practice effects to counter performance decrements. Horne and Wilkinson (1985) further argue that performance tasks of short duration which are frequently used in sleep reduction studies may

not be sensitive to the effects of sleep reduction. To overcome these potential methodological problems Horne and Wilkinson (1985) compared the daytime sleepiness and prolonged vigilance performance of 6 young adults who gradually reduced their night time sleep to 6 hours per night with 6 control subjects. No significant differences were noted in performance between the two groups with both groups displaying a similar increase in hit rate over the six week test period. This increased performance was attributed to practice effects. MSLT measurement of daytime sleepiness over the test period demonstrated decreased latencies to sleep onset for both sleep reduction and control groups. This unexpected finding is presumed to reflect an increase in familiarity with the test procedure rather than any significant change in baseline sleepiness. Subjective assessments of overall daytime sleepiness also failed to demonstrate any significant differences between experimental and control groups. In summary the Horne and Wilkinson (1985) study reduced sleep to an average of 6 hours per night and their findings suggest that this level of sleep reduction has no effect on the propensity to sleep as measured by the MSLT or SSS, on vigilance performance, or the sensitivity to practice effects.

Evidence from the sleep reduction literature seems to support the notion that under certain circumstances sleep reduction influences subsequent performance measures. Cognitive performance appears, however, to be protected against minor fluctuations in sleep quantity as performance decrements appear mainly when sleep is reduced to less than approximately 6 hours (Wilkinson et al., 1966; Hamilton et al., 1972; Johnson & Macleod, 1973; Herscovitch & Broughton, 1981) The absence of effect, in the reported studies, at sleep regimes of greater than 6 hours per night is consistent with Horne's (1991) proposition that sleep has both core and optional components.

Specifically Horne (1991) argues that sleep can be divided into two components - core sleep represents the first 3 to 4 sleep cycles (equivalent to between 4.5 and 6 hours of sleep) and is predominantly comprised of slow wave sleep with some brief REM periods. The remaining sleep period represents optional sleep and is comprised primarily of stage 2 and REM sleep periods. According to Horne's (1991) theory, core sleep is essential for restitution of the cerebrum and therefore levels of sleep deprivation that intrude into core sleep time result in cerebral impairment and the subsequent modification of recovery sleep structure to compensate this deprivation. Conversely intrusions into optional sleep time appear to have no effects on cerebral functioning and do not need to be compensated for in recovery sleep. Inadequate optional sleep may result in behavioural changes to information processing capacity such as diminished motivation to perform, but intrusions into core sleepiness, Horne (1991) believes, impacts on the data limiting or cognitive capacity of subjects to respond. The potential relationship between Horne's (1991) model of core and optional sleep, and the impact of sleepiness on performance will be reviewed further in the summary section of this chapter.

Changes to the Timing or Continuity of Sleep: The Influence on Performance

Sleep Fragmentation

The investigation of the relationship between sleepiness and performance has focussed on the impact of total sleep time on subsequent performance measures. The findings of Taub and Berger (1973, 1976) suggest, however, that a 3 hour advance or delay in sleep onset has similar detrimental effects on performance and mood to 3 hours of sleep deprivation. Such findings raise the general question of whether the observed relationship

between sleepiness and performance is determined by the total number of hours of sleep or the circadian distribution of sleep.

Sleep restriction studies typically limit total sleep time by delaying the time of sleep onset. One advantage of this methodology is that it allows for stable awakening times and therefore limits the potential for circadian variability to influence subsequent performance measures. The implication of this methodology is, however, that sleep reduction differentially limits sleep from sleep stages 1 and 2. Tilley and Wilkinson (1984) investigated the differential effects of sleep reduction from either the first or second half of the night on subsequent performance measures. Both reduction paradigms led to performance decrements and no differential effects were noted for time of night. These findings support the conclusions of Johnson (1982) who suggests that the desynchrony of physiological rhythms impacts on subsequent behavioural measures.

Bonnet (1985a, 1986, 1987, 1989) in a series of studies has examined the impact of sleep disruption on subsequent daytime performance. Interest in sleep disruption effects emerge from the findings of repetitive arousing stimuli disrupting sleep continuity in both pathological sleep disorders (narcolepsy, sleep apnea, periodic limb movement) and in changing sleep profiles associated with the process of normal ageing. In the earliest study (Bonnet, 1985a), subjects were awoken after every minute of EEG defined sleep for two consecutive nights. Despite this excessive fragmentation of sleep, total sleep time was decreased by only one hour per night. Performance scores following disruption were equivalent to scores obtained after 40 - 60 hours of total sleep loss. These findings led Bonnet (1985a) to propose that sleep continuity rather than total sleep time best predicted the role of sleep in cognitive performance. Further investigations of the impact of the frequency and placement of sleep disruption on performance (Bonnet, 1986 & 1989) supported this

sleep continuity theory. Increased rates of fragmentation were found to be associated with increased performance decrements and Bonnet (1989) suggests that periods of between 20 - 40 minutes of consolidated sleep appear necessary for maintenance of baseline performance levels. This time period, Bonnet (1986) suggests, may be linked to the time necessary for effective protein synthesis, a concept associated with the biochemistry of information processing. Roehrs, Merlotti, Petrucelli, Stepanski and Roth (1994) failed, however, to demonstrate any performance decrements on a divided attention task following sleep fragmentation although few details of the performance trials are provided. Fragmentation schedules have also been shown to be correlated with increased sleepiness on both subjective (Bonnet 1985a, 1989) and objective (Carskadon, Brown and Dement, 1982; Bonnet, 1986; Schweitzer, Stuckey & Walsh, 1993) sleepiness measures.

As discussed in Chapter 2, night time sleep patterns in narcolepsy are characterised by fragmented REM sleep periods. Therefore the relationship between REM sleep fragmentation and performance is of particular relevance to this study. Of added significance is the suggestion that REM sleep may serve some critical role in information processing (for a review of studies see Dujardin, Guerrien & Leconte, 1990) and therefore disruption of REM sleep may have added implications for performance measures. Bonnet (1989) was unable to identify a relationship between sleep stage composition and performance decrements though he acknowledges that small subject numbers limited the statistical validity of his findings. Johnson, Naitoh, Moses and Lubin (1974) investigated whether prior deprivation of REM or stage 4 sleep increased the effects of subsequent total sleep deprivation on performance. They found that although prior selective deprivation protocols influenced the architecture of subsequent recovery sleep, total sleep time rather than sleep composition was the prime determinant of subsequent performance outcomes. This finding has been replicated more

recently by Glovinsky et al. (1990) who compared the effects on performance between fragmentation of Stage 2 or REM sleep periods. No relationship was noted by Glovinsky et al. (1990) between performance outcomes and sleep composition, suggesting that sleep quantity, and/or continuity, may have a more significant impact on sleepiness induced performance decrements than sleep composition.

It remains to be tested whether, the pathological fragmentation of REM sleep is associated with performance decrements for narcoleptic subjects.

Proposed Model of the Interaction between Sleepiness and Performance

The above literature review has examined the relationship between experimentally induced sleepiness and performance. It is evident that an analysis of this relationship is very complex and confounded by the diversity of procedural and analytic methodologies described in the literature. An analysis of the diverse methodologies provides insight, however, into the multitude of factors which impact on the relationship between sleepiness and performance. This summary will attempt to integrate some of these factors into a theoretical model of the relationship between sleepiness and performance (see Figure 4) in non clinical subjects. This model, which is based on Horne's theoretical paradigm, has been proposed by the thesis author to serve as a basis for the exploration of the relationship between the sleepiness and performance in narcoleptic subjects and this applied analysis of the model will be discussed in Chapter 5.

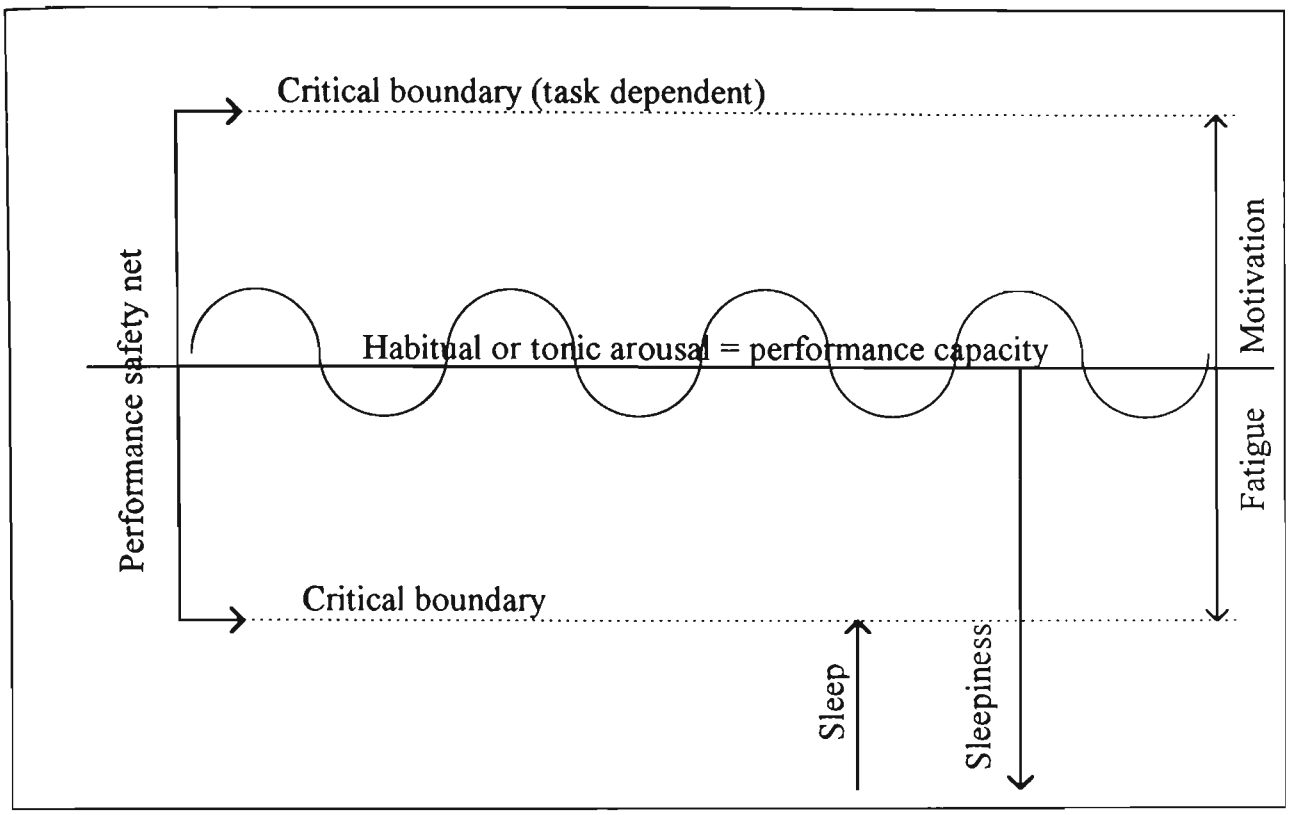

Figure 4 Proposed synthesis of attentional and cognitive models of performance.

Figure 4 suggests that in the absence of sleep manipulations information processing occurs from an habitual or tonic arousal level. This tonic arousal level, which fluctuates with a circadian rhythmicity, determines working attentional resources and appears to be influenced by aspects of individual difference e.g. personality factors of introversion and extroversion (Broadbent, 1971). This tonic arousal level can be either heightened or lowered by factors such as motivation or fatigue. Sleep deprivation appears to increase levels of sleepiness and therefore lower the baseline tonic arousal level. The specific relationship between factors such as motivation, fatigue and sleepiness has not yet been defined, but it would appear that the interaction of fatigue and sleepiness is nonlinear in nature with sleepiness potentially increasing the rate of decrement associated with fatigue. Despite the sensitivity of arousal to the factors of motivation, fatigue and sleepiness, the system seems to have a built in compensatory mechanism which operates as a safety net, such that small

fluctuations in any of these arousal factors have minimal effects on performance. The impact of changes in arousal on performance is not only a function of habitual arousal resources but will be determined by the nature of the performance task or more specifically by the arousal demands of the underlying cognitive process. Cognitive processes differ in their level of cognitive demand and for the successful completion of a particular task it is proposed that some critical arousal threshold is required. Complex convergent processing tasks require higher arousal resources than simple tasks. The observation of performance decrements is therefore contingent on arousal resources falling below the critical threshold of processing resources necessary for any individual task. Whilst task variables will alter the threshold of necessary arousal resources there appear to be critical limits where arousal resources are either too high or too low to allow for efficient processing. In the case of sleepiness, Horne (1991) suggests that optional sleep provides the required safety net, but once sleepiness intrudes into core sleep time then the increased decrements in performance that occur are reversed only by restorative sleep. Baseline arousal levels are therefore set by the intrinsic factors of circadian periodicity, and sleep need, and extrinsic parameters such as motivation or fatigue. Performance outcomes are a function of the relationship between these baseline arousal levels and task dependent cognitive load. If, however, the baseline arousal level falls below the critical arousal boundary for a particular task then attentional factors are no longer able to compensate for the decline in baseline arousal and cognitive deficits emerge. At this point cognitive deficits can be reversed only by restorative sleep.

CHAPTER 4

Sleepiness and Cognitive Performance in Narcolepsy

"Patients [with narcolepsy] complain that thinking is an effort; they cannot concentrate, and they forget easily" (Levin, 1942, p. 674).

Rationale for the Evaluation of the Interaction Between Sleepiness and Cognitive Performance in Subjects with Narcolepsy

This section will highlight the theoretical rationale behind the major focus of this thesis, which is an evaluation of the interaction between sleepiness and performance for subjects with narcolepsy. This rationale emerges from three distinct areas of the literature:

(a) The comparative literature on the relationship between non pathological sleepiness and performance,

(b) The subjective reports of diminished cognitive function by subjects with narcolepsy,

(c) The potential dual role of REM sleep in both cognition and the pathophysiology of narcolepsy.

(a) Findings from Non Pathologically Sleepy Populations

Chapter 3 has reviewed the literature on sleepiness and performance in non clinical subjects and whilst the physiological factors that mediate this relationship have yet to be defined there is substantial empirical support for the thesis that sleepiness influences performance over a wide range of cognitive tasks. Narcolepsy is a disorder characterised by a pervasive and excessive daytime sleepiness and it is therefore

reasonable to question the relationship between this pathological sleepiness and performance measures. To date there has been limited research into this relationship and one aim of this thesis is therefore to expand on the current literature in this area.

(b) Subjective Reports of Diminished Cognitive Function by Subjects with Narcolepsy

A second argument for examining the relationship between sleepiness and performance in narcolepsy is that survey research into the life effects of narcolepsy consistently report that subjective memory problems are of significant concern to narcoleptic subjects. For example Broughton and Ghanem (1976) undertook a study to assess the psychosocial consequences of narcolepsy on the life of the patient. They found that 48.8% of respondents to their questionnaire answered that their memory had deteriorated since the onset of narcolepsy. Within this subject group 71.4% stated that the narcolepsy affected recall of recent events, 19% remote events and 1% all memory functions. Similar findings were reported by Broughton et al. (1981), who in a cross cultural study of the socio-economic effects of the disorder, found that 48.9% noted memory problems as occurring following the onset of the symptoms of narcolepsy and respondents consistently attributed these cognitive problems directly to the disorder. As in the Broughton and Ghanem (1976) study the majority of patients surveyed by Broughton et al. (1981) reported that memory for recent events was most significantly affected. Smith, Merritt and Cohen (1992) in a more recent survey of 700 narcoleptics found 38% reported moderate or severe memory problems, 39% had problems with forgetfulness, 40% with concentration and 26% with general learning. Smith, Merritt and Cohen (1992) summarise this self report data stating "the evidence for self-perceived cognitive impairment in narcoleptic persons is consistent and compelling" (p. 103).

Aguirre, Broughton and Stuss (1985) emphasise the potential significance of these subjective reports of memory dysfunction with the observation that the frequency of self reports of memory dysfunction amongst narcoleptic subjects is equivalent to reports of the diagnostic symptoms of either sleep paralysis or hypnagogic hallucinations. The subjective experience of memory dysfunction appears then as a major characteristic of narcolepsy.

It is recognised that the relationship between subjective perceptions of cognitive functioning and subsequent objective cognitive performance remains contentious for any clinical population (Brown, Dodrill, Clark & Zynch, 1991; Niederehe & Yoder, 1989) and Chapter 10 of this thesis will directly address the issue of metacognitive functioning for subjects with narcolepsy. The frequency, however, of subjective reporting of memory dysfunction amongst subjects with narcolepsy provides a strong rationale for an empirical evaluation of cognitive function in this clinical population.

(c) The Potential Dual Role of REM Sleep in Both Cognition and the Pathophysiology of Narcolepsy

A third argument for an analysis of cognitive function in narcolepsy is the potential dual role of REM sleep in the pathophysiology of narcolepsy and the neurophysiology of cognition. Whilst the aetiology of narcolepsy is yet to be understood, one explanation of the disorder is that it represents a fundamental imbalance between REM and NREM activity, such that dissociative REM episodes intrude into the waking state (Mamelak, 1992). Regardless of whether REM abnormalities occur as cause or effect in this disorder it is nonetheless true that narcoleptics experience pathological manifestations of REM sleep function during both sleep and waking states. Cohen (1979) suggests that the major role of REM sleep is in the reorganisation and

restoration of brain processes that mediate the flow and structure of information. An analysis of the neurophysiological structure of REM sleep suggests that REM sleep is a sleep state characterised by high levels of cerebral activation (Steriade, 1989). Comparative studies of auditory arousal thresholds across sleep stages further indicate that central nervous system (CNS) sensitivity during REM and stage 2 sleep more closely approximate reactivity during waking than during stages 3 and 4 (Cohen, 1979). Enhanced synaptic excitability during REM and waking compared to NREM sleep states has been confirmed using electrical recordings of single cell synaptic transmission frequencies (Steriade, 1989).

REM sleep is therefore a state of high CNS activation and excitation paradoxically located in a behavioural state of sleep. As increased CNS activity during waking is associated with increased mentation (Posner, Petersen, Fox & Raichle, 1988), theorists have suggested that the increased activation of REM sleep is functionally similar to waking mentation states and that the principal role of REM sleep is one of information processing (Cohen, 1979). Dujardin, Guerrien and Leconte (1990) review the literature evaluating the role of REM sleep in cognition and conclude that despite the many methodological problems associated with validating this consolidation hypothesis there seems to be general support for REM sleep providing "a critical period for information processing ..." (Dujardin et al., 1989, p. 1275). As narcolepsy is a disorder characterised by REM sleep dysfunction the potential implications of the consolidation hypothesis for cognitive functioning in subjects with narcolepsy need to be assessed.

Studies of nocturnal sleep patterns in subjects with narcolepsy demonstrate the disruption and fragmentation of narcoleptic REM sleep episodes (Montplaisir et al., 1978). This finding of fragmented REM periods may have implications for memory

consolidation in narcolepsy. Smith (1985) suggests that brief periods of REM sleep, which she describes as REM windows, appear critical for information processing. Fragmentation of the REM sleep state may then selectively disrupt these critical periods.

REM sleep is not a homogenous neurophysiological event but is identified by the temporal convergence of specific phasic or microstructural events occurring against a stable referential background of tonic or macrostructural activity. Tonic features of REM sleep include EEG activation, EMG suppression and brain temperature elevation. Phasic events which are characteristic of, but not exclusive to the REM sleep stage, include REMs, Middle Ear Motor Activity (MEMAs) cardiorespiratory changes and PGO spikes (Carskadon & Dement, 1989). It is perhaps necessary that these distinct neuroanatomical components of the REM process must be viewed independently in any assessment of the functional relevance of the REM state.

Tafti, Olivet and Billiard (1991) compared the architecture of REM sleep between subjects with narcolepsy and controls. In support of the earlier studies by Montplaisir et al. (1978) the amount of REM sleep as a percentage of total sleep time was not found to vary between narcoleptic and control groups. However more detailed comparative analyses of macro and micro structural components of REM in narcoleptic and control groups demonstrated differences in phasic events between the groups, with narcoleptics demonstrating a significant increase in phasic events. Price and Kremen (1980) demonstrated that periods of tonic REM activity were associated with increased CNS activation and behavioural responsivity compared to phasic REM periods. The increased periods of phasic REM activity demonstrated in narcoleptic subjects may therefore interfere with the periods of tonic activity and these tonic periods may represent the critical periods for information processing.

As REM sleep is possibly an active component of information processing, and REM pathology is associated with narcolepsy, this provides an additional rationale for this thesis' evaluation of information processing in narcolepsy.

Scrima (1982) utilised 10 narcoleptic subjects in an experiment designed to test the role of REM sleep in information processing. Recall of information following isolated nap periods of REM sleep in the narcoleptic subjects was found to be superior to recall following periods of NREM sleep, which in turn was significantly better than recall following periods of wakefulness. The possible implications of REM dysfunction on information processing in narcolepsy cannot, however, be evaluated from the Scrima (1982) study due to the lack of a control group to assess decrements in overall recall performance occurring potentially as a consequence of interference effects.

Review of the Literature Evaluating Cognitive Functioning in Subjects with Narcolepsy

This section will review the published literature evaluating both general cognitive functioning, and applied memory performance, in subjects with narcolepsy. A summary of these studies is provided in Table 1.

Comparative analyses of the literature in this area is confounded, in part, by the use of interchanging terminologies between studies. This terminology has been defined in the glossary of this thesis and the reader is referred to this section.

General Cognitive Functioning in Narcolepsy

The first empirical attempts to evaluate the relationship between narcoleptic sleepiness and performance were undertaken by Valley and Broughton in the early 1980's. Ten subjects with narcolepsy and ten control subjects were compared on four performance tasks, the Wilkinson Auditory Vigilance Task (WAVT), 4-choice serial

reaction time, paced auditory serial addition (PASAT) and digit span. Sleepiness for subjects with narcolepsy was measured using both subjective (SSS) and objective, EEG and Auditory Evoked Potential (AEP) criteria. Aspects of this study were reported across three papers, Valley and Broughton (1981); Broughton, Low, Valley, Da Costa and Liddiard (1982) and Valley and Broughton (1983). [Text continues on Page 96 following Table 1.]

Table 1

Studies of Performance Measures in Narcolepsy

STUDY	YEAR	SUBJECTS	AROUSAL MEASURE	PERFORMANCE TASKS	PERFORMANCE DECREMENT	STUDY CONCLUSION
Valley & Broughton	1981					
Broughton, Low, Valley, Da Costa, Liddiard	1982	10N 10C	SSS EEG AEP	4 WAVT CRT --- PASAT Digit Span	Yes --- No	Demonstrated high lability of narcoleptic wakefulness and associated susceptibilty of vigilance tasks to arousal fluctuation.
Valley & Broughton	1983					
Aguirre, Broughton & Stuss	1985	10N 10C	Observational/ Behavioural	Digit Span: Knox Cube Recurring Figures Visual Reproduction Paired Associates Logical Memory	No	No organic cognitive deficit - performance deficits secondary to arousal fluctuation.
Levander & Sachs	1985	20N 28C 15 Anxiety Disorder C 14 Psychosomatic Disorder C	Skin Conductance Heart Rate Finger Tremor	CFF - Method of limits --- CFF - 3 Alternative forced choice --- 2 CRT --- Krakau Visual Acuity	Yes --- Yes --- No --- No	Narcoleptics experience a disturbance of time resolution of stimulus input - unrelated to arousal levels.

Table 1 Continued

STUDY	YEAR	SUBJECTS	AROUSAL MEASURE	PERFORMANCE TASKS	PERFORMANCE DECREMENT	STUDY CONCLUSION
Godbout & Montplaisir	1986	10N 8C	Nap/No Nap Conditions	10 min 4 CRT with naps --- 10m min 4 CRT No naps	No --- Yes	Naps normalise performance for narcoleptics.
Ollo, Squires, Pass, Walsleben, Baker, Gujavarty	1987	10N Composed to normative data	ERP	Weschler Memory California Verbal Learning Trailmaking Test Symbol Digit Modalities --- Auditory oddball task	Low performance compared to normative data --- Yes	Significantly, decreased P300 amplitudes indicate decreased attentional capacity or stimulus evaluation (unrelated to arousal level)
Henry, Hart, Kwentus, Sicola	1988	8N	On/Off Protriptyline Medication	Logical Memory Digit Span Benton Auditory Vigilance Continuous Performance --- Sternberg Memory Frequency Estimation	No --- Yes off medic.	Considerable variability exists in both cognitive functioning and the effect of medication on information processing in narcolepsy.

Table 1 Continued

STUDY	YEAR	SUBJECTS	AROUSAL MEASURE	PERFORMANCE TASKS	PERFORMANCE DECREMENT	STUDY CONCLUSION
Rogers, Rosenberg	1990	30N 30C	EEG	Weschler Memory RAVLT Rey Complex Figure List of Letters Symbol Digits Modalities	No	No relationship exists between subjective experience of memory dysfunction and objective test performance.
Pollak, Wagner, Moline, Monk	1992	6N 9C	VAS EEG	Serial Search Verbal Reasoning Pegboard	No apart from mild acuracy decrement	No differences in performance between narcoleptics and controls when narcoleptics allowed to nap under free running conditions.
Smith, Merritt, Cohen	1992	24N 24C	VAS Ocular Symptoms	Stroop Word Lists	Relationship high ocular symptoms decreased	Cognitive impairment in narcolepsy may be related to depression.
Henry, Satz & Heilbronner	1993	10N 10C	Temperature	Word Lists --- Signal detection Motor speed --- Sternberg	Yes --- No --- Yes	No evidence for time of day effects on performance. No relationship betwen arousal and peformance. Deficits may be explained by perceptual encoding deficit.
Greenbaltt, Campbell, Pollak, Moliner	1993	6N 6C	VAS EEG	Continuous Performance	Yes	Narcoleptics demonstrate deficits on both focussed and sustained attention.

Table 1 Continued

STUDY	YEAR	SUBJECTS	AROUSAL MEASURE	PERFORMANCE TASKS	PERFORMANCE DECREMENT	STUDY CONCLUSION
Mercer,Merritt, Keegan, Hale, Myerson	1994	13N 11C	-	Letter Matching Mental Rotation Visual Search Abstract Matching	No	No evidence to support a perceptual encoding deficit hypothesis for narcolepsy.

KEY TO ABBREVIATIONS

AEP - Auditory Evoked Potential
C - Control
CFF - Critical Flicker Fusion
CRT - Choice Reaction time
EEG - Electroencephalogram
N - Narcoleptic
PASAT - Paced Auditory serial Addition task
RT - Reaction time
SSS - Stanford Sleepiness Scale
WAVT - Wilkinson Auditory Vigilance Task

A fundamental question emerging from the 1980's research into sleepiness and performance for non pathological sleepers was the evaluation of Bjerner's lapse - microsleep hypothesis as an adequate model for explaining performance decrements associated with sleepiness in non clinical populations. Valley and Broughton (1983) adopted this theme from the contemporary sleep literature and evaluated the sufficiency of the lapse microsleep hypothesis in explaining the observed performance decrements in narcolepsy. Vigilance performance was assessed for narcoleptic subjects using the WAVT. The number of correct responses and false positive responses were scored across the 60 minute task. The scoring of EEG arousal measures were adjusted to provide a more sensitive measure of arousal. Waking and stage 2 sleep were classified according to standard criteria but stage 1 sleep was reclassified as stage 1A or stage 1B on the basis, in part, of the relative percentages of alpha and theta rhythms across the scored epoch. Four stages of physiological vigilance were therefore defined. An analysis of the wakefulness pattern across the 60 minute task indicates that narcoleptic subjects spent significantly less time in wakefulness and demonstrated significantly increased state lability in comparison to the control group. Further analysis of the relationship between signal response and physiological state demonstrated an overall decline in response rates between wakefulness and stage 2 sleep. For narcoleptics both the hit rate, defined as the number of hits in proportion to total signals, and the hit response rate, defined as the number of hits in proportion to total responses, were significantly lowered in wakefulness compared to controls and this decreased "waking" performance was seen to reflect the fragmentary nature of narcoleptic wakefulness. Periods of sustained wakefulness, defined as 13 seconds of EEG wakefulness prior to the signal, were associated with hit and hit response rates for narcoleptic subjects that did not differ

significantly from control rates. For narcoleptic subjects periods of fragmented wakefulness defined as 3 seconds of wakefulness immediately prior to the signal but preceded by 10 seconds of reduced EEG vigilance were, however, associated with significantly diminished performance on the vigilance task. Valley and Broughton (1983) argue that the finding of equivalent response rates between narcoleptics and controls during sustained wakefulness, associated with the decreased performance efficacy of the narcoleptic group during fragmented wakefulness suggests that for narcoleptic subjects performance deficits cannot be explained by the lapse microsleep hypothesis. It appears that in narcolepsy, as in non clinically sleepy populations, performance efficiency appears to decline gradually with decreased physiological arousal and lapses reflect the end point of this arousal continuum.

The Valley and Broughton (1983) study highlights both the lability of wakefulness for narcoleptic subjects as well as the sensitivity of performance measures to minimal changes in vigilance levels. Three seconds of wakefulness preceded by another 10 seconds of clear wakefulness resulted in vigilance performance measures that did not differ significantly from controls. When, however, the signal was preceded by 3 seconds of wakefulness that followed as little as 10 seconds of decreased vigilance, the performance of narcoleptic subjects was significantly decreased. This pattern of a highly labile arousal state and the potential high sensitivity of particular cognitive tasks to arousal fluctuations underscores the fundamental problem of evaluating the impact of sleepiness on performance for narcoleptic subjects. Valley and Broughton (1983) adopted a research methodology that allowed for analysis of performance change over periods as brief as several seconds. Using this methodology decrements in vigilance performance were established.

In 1986 Godbout and Montplaisir attempted to further evaluate the relationship between sleepiness and performance in narcoleptic subjects by assessing performance on a four choice reaction time task (4CH). Performance measures were determined under conditions where narcoleptics were permitted to nap and under no napping conditions. As naps have a recuperative value for narcoleptic subjects (Roehrs et al., 1984), Godbout and Montplaisir (1986) predicted that napping conditions should lead to improved task performance. This prediction was supported. The performance of narcoleptic subjects on days without naps was significantly poorer than for control narcoleptics who did nap, both on the measures of reaction time and the number of response gaps. Response gaps were measured as reaction time latencies of greater than 1 second. Interestingly the percentage of errors was not significantly different between nap and no nap groups suggesting that the performance deficit, resulting from sleepiness, related to speed rather than accuracy of response. This suggests that narcoleptics may compensate for sleepiness by increasing their response time, and this increase in response time may reflect more centralised cognitive impairment which results in diminished rates of information processing. On days where narcoleptic subjects were allowed to nap, their performance on the reaction time task was not significantly different from controls. Godbout and Montplaisir (1986) suggest that this demonstrates that 'naps tend to 'normalise' performance of narcoleptic subjects' (Godbout & Montplaisir, 1986, p. 203).

In line with the findings of Valley and Broughton (1981, 1983), Godbout and Montplaisir (1986) identified significant changes in vigilance performance for subjects with narcolepsy across relatively brief time periods. Godbout and Montplaisir (1986) found that performance decrements for narcoleptic subjects, on days without naps, were more prominent during the second half of the ten minute testing session. It cannot be

determined from the study whether this performance decline was linearly related to increasing levels of sleepiness. In addition to performance change associated with sleepiness the observed decrements may represent increased state lability, boredom with the tasks, or general fatigue.

Whilst a significant difference in RT performance between "no nap narcoleptics" and controls was reported in the Godbout and Montplaisir (1986) study, a previous study by Levander and Sachs (1985) failed to demonstrate a significant difference in reaction time performance between narcoleptic and control subjects. One possible explanation for these discrepant results is that the Levander and Sachs (1985) task was a two choice RT task of 4 minute duration whereas Godbout and Montplaisir (1986) utilised a 4 choice task over a 10 minute duration. As identified previously an examination of the Godbout and Montplaisir (1986) task indicates that a significant difference in task performance between narcoleptics and controls was evident only for the second half of the 10 minute task, which was presumed to represent a period of increased sleepiness. Comparison of the two studies is also complicated by the differing cognitive demands of the two performance tasks. A four choice reaction time task incorporates a memory factor not relevant to two choice reaction time tests. This additional cognitive load for the Godbout and Montplaisir (1986) study may have accelerated either the sleepiness or fatigue decrement.

Whilst Levander and Sachs (1985) found no impairment for narcoleptics on RT or visual acuity, as measured by the Krakau Visual Acuity Test, a significant impairment was noted for narcoleptic subjects on the vigilance measure of Critical Flicker Fusion (CFF). The use of central stimulants appeared to selectively normalise this vigilance measure. Levander and Sachs (1984) state that the testing procedure did not induce

drowsiness or microsleeps in the narcoleptic subjects and therefore the finding of decreased vigilance performance, unrelated to decreased visual acuity, reaction time measures, or induced sleepiness, suggests that narcolepsy may be associated with a disturbance of central processing capacity, specifically affecting the time resolution of the stimulus input. This suggestion by Levander and Sachs (1985) of a central disturbance in the information processing capacity of narcoleptic subjects is the first challenge to the position first espoused by Valley and Broughton (1981) and repeated consistently in the literature that performance decrements in narcolepsy are secondary to the effects of sleepiness and that narcoleptics do not have any "inherent problems of information processing" (Valley & Broughton, 1981, p. 138).

Levander and Sachs (1985) suggest that this diminished central processing capacity occurs as a consequence of lowered tonic or habitual arousal levels in narcolepsy. In support of this proposal Levander and Sachs (1985) measured cortical and autonomic function in narcoleptic subjects using Skin Conductance Levels (SCL) and demonstrated that narcoleptics had decreased SCL compared to controls. In addition narcoleptic subjects demonstrated a marked tendency to decreases in short term phasic arousal (attentional input) during prolonged testing sessions. The Levander and Sachs (1985) study therefore predicts a model of information processing where performance decrements in narcolepsy may result from a combination of diminished tonic arousal levels coupled with either a decreased capacity for phasic arousal or a sleepiness induced accelerated decline of effortful or phasic arousal states. It is interesting however that the CFF findings of Levander and Sachs (1985) were not supported by the more recent work of Schulz and Wilde-Frenz (1993) who demonstrated that, whilst performance variability on the CFF was greater for narcoleptic subjects than controls, the

peak performance scores, were not significantly different. This finding of equivalent peak performance capacity between narcoleptics and controls arguing against a model of diminished tonic arousal in narcolepsy.

The suggestion of Levander and Sachs (1985) that narcoleptics may have diminished capacity for performance on tasks requiring attentional input is supported however by the event related potential (ERP) measures obtained by Ollo et al. (1987). ERP amplitude measures, which are seen to reflect effortful attentional responses, were significantly decreased in narcoleptics compared to controls during tasks requiring effortful processing. However Ollo et al. (1987) suggest that tonic arousal states for narcoleptics are not significantly different than for controls. P300 latency and amplitude measures were within normal limits under non effortful arousal conditions.

Applied Memory Functioning in Narcolepsy

Four studies have attempted an objective evaluation of the subjective experience of narcoleptic subjects of diminished memory function. The first study to be reported in the literature was published in 1985. In this study Aguirre, Broughton and Stuss (1985) compared ten diagnosed narcoleptics with ten matched controls. All narcoleptic subjects chosen for inclusion had complained of memory difficulties to a degree which was intrusive on their everyday lives. The test procedure required each subject to complete a 7 item memory battery which included digit span, knox cube, recurring figures and paired associates tests. The tests were chosen to investigate both short and long term memory functions as well as potential modality (material and sensory) specifications of memory processes. Testing procedures involved narcoleptics both on medication and following withdrawal of medication. Analysis of results demonstrated no significant differences

between subject and control groups for all seven memory tests. Aguirre et al. (1985) suggest that whilst no organic impairment of memory function appears to exist, memory impairment in narcolepsy may well be secondary to impaired alertness and they recommend that future memory investigations of this group must focus on the interaction of memory and arousal. Similar results were achieved by Rogers (1987) who compared narcoleptics immediate and delayed recall as well as testing verbal and visual memory. No significant differences were found between narcoleptic and control groups. Subjective reports of memory problems in narcolepsy were, therefore, again presumed secondary to difficulties maintaining attention rather than to organic impairments of memory function.

Rogers and Rosenberg (1990) utilised a research design similar to that of Aguirre et al. (1985) and Rogers (1987). Narcoleptic and control subjects were given a battery of neuropsychological tests to determine whether memory scores differed significantly between groups. Results were consistent with those of previous studies with no significant differences demonstrated between subject and control groups. Objective memory scores further appeared unrelated to subjective memory assessments within the narcoleptic group.

In line with Aguirre et al. (1985), Rogers and Rosenberg (1990) reported that almost all subjects maintained full wakefulness throughout the testing period. Of the five subjects reported to experience drowsiness, only three were narcoleptic, which raises the possibility of fatigue affecting both narcoleptic and control groups. Rogers and Rosenberg (1990) conclude that there is no evidence of memory impairment in this clinical population.

Smith, Merritt and Cohen (1992) tested 24 narcoleptic subjects using a range of neuropsychological tests aimed at assessing global cognitive functioning in addition to memory processes. Results suggested that, despite self rated difficulties in memory and concentration being higher for the narcoleptic group, these differences did not transfer to performance differences in memory and concentration between the groups.

The failure of the previous studies to demonstrate impairments in memory function appears at odds with the Levander and Sachs (1985) finding of lowered tonic arousal and potentially diminished vigilance performance in narcoleptic subjects. Henry, Hart, Kwentus and Sicola (1988) suggest that this discrepancy arises because of the nature of the performance tasks tested. Specifically, Henry et al. (1988) argue that there is a need to differentiate between automatic tasks, such as vigilance tasks, that rely on tonic arousal states and effortful tasks which require active attentional capacity. Henry et al. (1988) suggest that memory tasks require significant effort and are therefore dependent on attentional resources which are synonymous with phasic arousal capacity.

If the findings of the Levander and Sachs (1985) study are to be ratified it is expected that automatic tasks would be impaired in narcolepsy but that effortful tasks should not initially be affected but performance decline on effortful tasks requiring phasic input should be faster for narcoleptic than non narcoleptic subjects. Henry et al. (1988) attempted to compare vigilance, effortful memory, and non effortful memory performance tasks for narcoleptic subjects and to assess the impact of Protriptyline, which is a tricyclic antidepressant with psychomotor stimulant properties (Kaplan, Sadock & Grebb, 1994), on these performance measures. Effortful memory was evaluated using the Sternberg memory scanning procedure. This task involves subjects being given 1, 2 or 4 digits to remember and then probe digits are presented and subjects

need to decide whether the probe digit belongs or does not belong to the digit set being held in memory. The task therefore measures response times as a function of cognitive load. Non effortful memory processes were evaluated using a frequency of occurrence task, where following the reading of word lists subjects are read a word and asked to estimate the frequency with which the word occurred in the original list. Vigilance was assessed using an auditory vigilance measure. The results are difficult to evaluate. Protriptyline failed to influence vigilance measures though non effortful memory tasks demonstrated significant improvement with stimulant medication. As both vigilance and non effortful encoding tasks are presumed to reflect tonic arousal states the observed discrepancy in stimulant effectiveness is difficult to reconcile. Henry et al. (1988) suggest that the variability in vigilance response data may have limited the significance of the effects of medication and recommends further evaluation of this finding.

Of particular interest in the study were the results of the Sternberg task which measures response times as a function of cognitive load and is therefore considered an effortful task dependent on phasic arousal. Whilst Protriptyline resulted in a decrease in response latency for the task it did not influence the relationship between increasing cognitive load and subsequent central processing times. These findings suggest that effortful tasks dependent on phasic arousal capacity are either not diminished in narcolepsy, or not influenced by Protriptyline.

Henry, Satz and Heilbronner (1993) reevaluated the comparative performance of narcoleptic and control subjects on the Sternberg task. Whilst no significant difference existed between narcoleptics and controls subjects in the ability to manage increasing task loads the narcoleptic subjects demonstrated significantly increased response latencies compared to controls i.e. whilst the *absolute* response latency was greater for

narcoleptic subjects the *rate of increase* of central processing speed remained comparable between groups. Henry et al. (1993) suggest that these findings argue for the decreased ability of narcoleptic subjects to encode stimulus materials (tonic arousal) but to retain equivalent central processing rates (phasic arousal) to control subjects. Henry et al. (1993) describe this as a perceptual - encoding deficit.

Several studies have investigated the perceptual encoding hypothesis as an explanation of cognitive deficits in narcolepsy and the findings remain inconclusive. Mercer, Merritt, Keegan, Hale and Myerson (1994) compared the efficiency of stimulus input processes between narcoleptic and control groups and found no significant differences between groups. In contrast Greenblatt, Campbell, Pollak and Moline (1993) utilising a visual vigilance task found that narcoleptic subjects had fewer hits and significantly longer reaction times than controls and the use of the CNS stimulant dexamphetamine increased response hits. These findings support for the theory that cognitive deficits in narcolepsy are underscored by some decrement in tonic arousal states which interferes with the rate of encoding of stimulus materials.

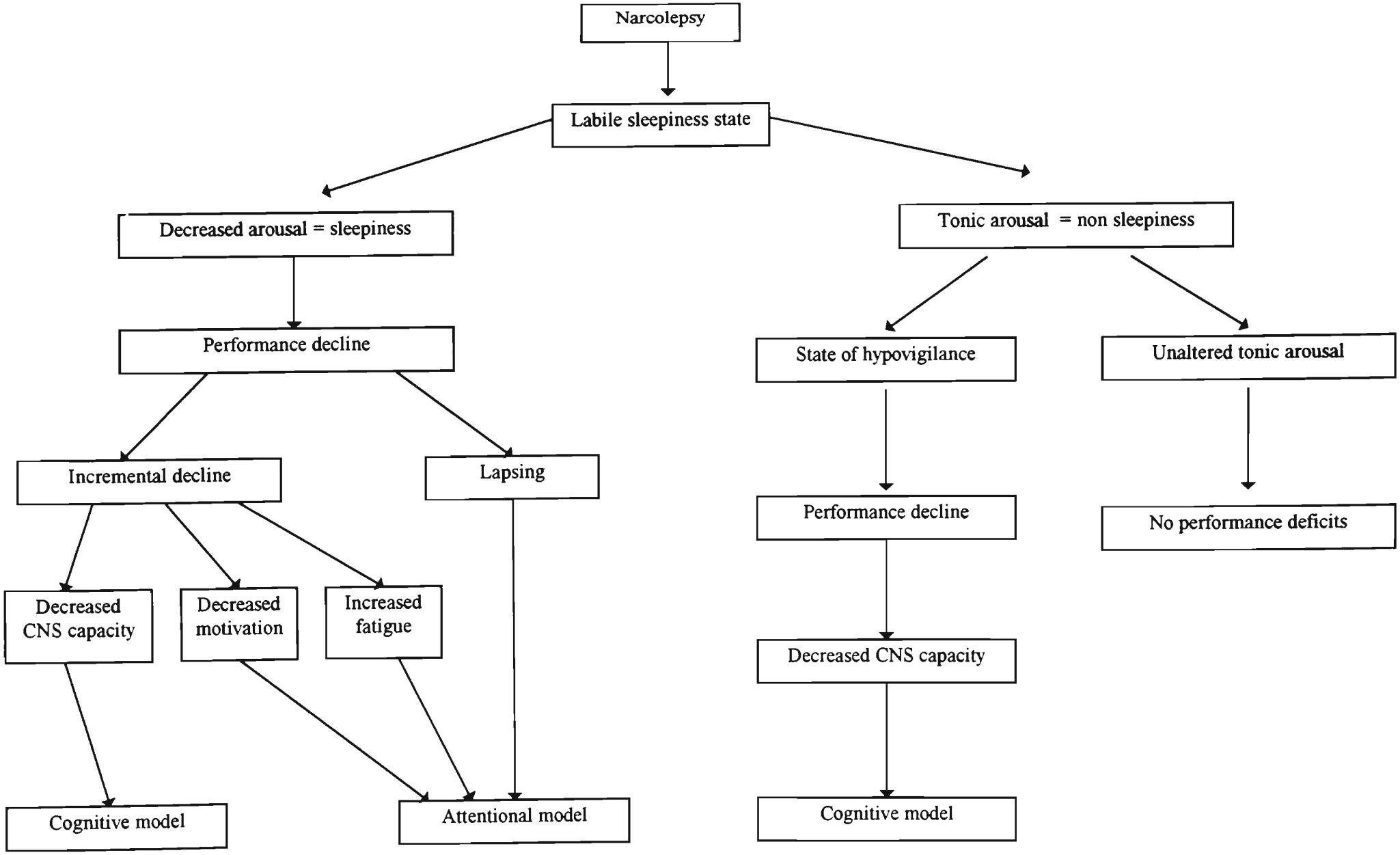

Figure 5 Summary of potential aspects of performance in narcolepsy

Summary of Potential Factors Associated with Performance Measures in Narcolepsy

In summary there appears to be no conclusive understanding of the impact of narcolepsy on cognitive function. Figure 5 outlines several theoretical positions that emerge from the previous literature review and it is interesting to note that many of these theoretical positions mirror the issues that were explored in Chapter 3 for the analysis of the relationship between sleepiness and performance in non pathologically sleepy subjects.

Whilst some of the narcolepsy literature indicates that the disorder may be associated with a central hypoarousal syndrome, resulting in impaired tonic arousal, other reports contradict this proposal, and demonstrate no impairment on measures such as vigilance and reaction time which reflect tonic arousal capacity. If narcolepsy is not associated with diminished tonic arousal systems then it is possible that periods of sleepiness impact on performance for these subjects in just the same way that sleepiness impacts on performance in non clinical groups. If sleepiness does lead to performance decrements in narcolepsy then the nature of this decrement needs to be evaluated. Are decrements the result of lapsing or do they occur as a consequence of a gradual decline in arousal between alertness and sleep? Within a model of arousal decline it then becomes necessary to evaluate whether this decline occurs as a function of diminished CNS capacity (cognitive model) or alternatively does it reflect decreased attentional capacity (attentional model) associated with sleepiness? Additional issues that remain uninvestigated include the interaction between attentional capacity (phasic arousal) and the factors of motivation, fatigue or boredom on cognitive function in narcolepsy. Chapter 5 of this thesis will locate these issues, relevant to the sleepiness performance

interaction in narcolepsy, into a theoretical framework which allows for the development of testable models of these issues.

In addition to developing appropriate models of the theoretical aspects of cognitive functioning in narcolepsy, new methodological procedures need to be devised to facilitate testing of these theoretical positions. Research has failed to adequately address the issue of the relationship between sleepiness and performance in narcolepsy, as reports of the assessment of cognitive function in narcolepsy consistently focus on subjects under high arousal conditions. To understand the impact of narcolepsy on cognitive function it seems imperative therefore to create a methodology, with high external validity, which allows for assessment of functioning whilst subjects with narcolepsy are sleepy. Chapter 6 of this thesis will discuss the methodology devised by the thesis author to allow for expression of both sleepy and non sleepy states for subjects with narcolepsy.

CHAPTER 5

Theoretical Resume and Rationale for Study One[1]

Introduction

In the one hundred years since Patrick and Gilbert (1896) reported on performance decrements associated with experimentally induced sleepiness in non clinical subjects, there has been extensive interest in the physiological processes mediating the relationship between sleepiness and cognitive dysfunction. The first major theoretical model to develop will be referred to as the attentional model. This model developed initially from the work of Broadbent on the relationship between arousal and performance (Broadbent, 1971). Broadbent proposed that performance was dependent on the interaction between two arousal systems (Figure 6). A lower arousal mechanism representing a tonic or passive arousal system is responsible for the performance of well established cognitive tasks. Altered efficiency of the lower mechanism, due to factors such as sleeplessness or psychophysiological noise, is not immediately apparent as an upper arousal mechanism acts to compensate for changes in the lower mechanism establishing a homeostatic performance loop.

According to Broadbent the lower arousal mechanism is determined by endogenous personality (introversion and extroversion) and circadian factors. The upper mechanism is activated by the interaction between external performance actors such as the nature of the task and internal motivational factors.

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[1] [1]Aspects of this study have been published in the Journal of Sleep Research. Refer Appendix 1.

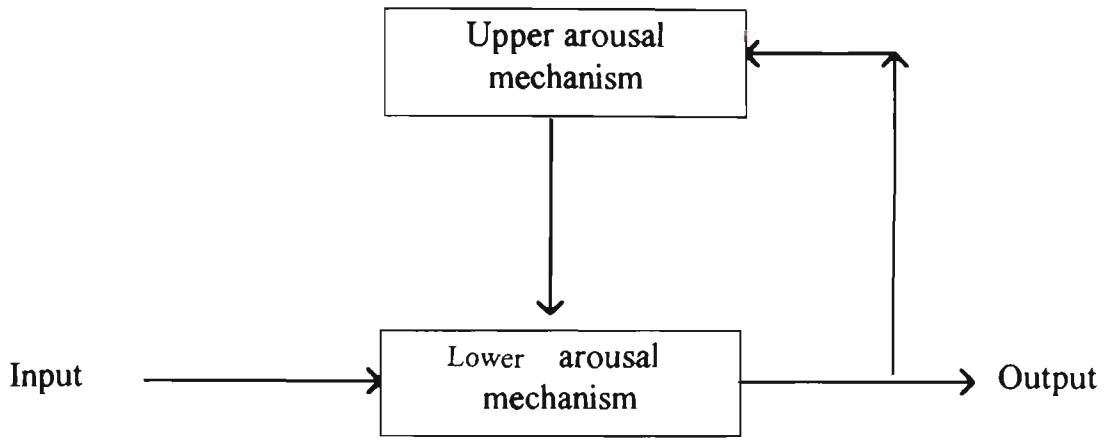


Figure 6 Broadbent's homeostatic performance loop (Broadbent, 1971, p. 446)

The components of the Broadbent model that provide a foundation for the evaluation of the more general relationship between sleepiness and performance include the existence of a tonic or habitual arousal state determined by endogenous factors and the existence of a phasic or compensatory mechanism which functions to adjust for sleepiness induced changes in tonic arousal. The major implication of this model, which is supported by theorists such as Kjellberg, (1977 a,b,c) and Meddis (1982), is that performance decrements that occur as a consequence of sleepiness are reversible by the application of increased compensatory processing. This increase in effortful processing could be seen as synonymous with the application of attentional resources.

An assumption of this model proposed by Broadbent (1971) is that there is a linear relationship between cognitive load and cognitive effort and therefore increases in task difficulty can usually be compensated for by additional attentional resources. More recent conceptualisations of cognition demonstrate however that cognitive demands vary on a number of qualitative dimensions and that increasing cognitive load may not simply reflect increased need for compensatory attention but may reflect the capacity to utilise different processing mechanisms (Matlin, 1994). For example, simple cognitive tasks are identified by

a sequence of procedural steps, whereas complex tasks are not an additive mechanism of increasing the number of processing steps but rather require the implementation of a complex set of underlying rules. Convergent tasks utilise well defined rules to achieve a single solution whereas divergent tasks involve working towards an acceptable outcome within a framework of knowledge. Similarly algorithmic processes involve sequencing steps to achieve an outcome whereas a heuristic approach to problem solving involves strategies being generated from a conceptual knowledge base. Complex, divergent and algorithmic tasks therefore require the application of cognitive skills that are qualitatively different from more structured cognitive processes (Colley & Beech, 1989).

Theorists such as Horne (1988a) would argue that sleep deprivation, that intrudes into core sleep, leads to fundamental changes in processing capacity, particularly for more complex cognitive tasks and that these changes are only reversed, not by increased effort, but by restorative sleep processes.

> Therefore, during sleep loss, part of the behavioural and psychological changes could be due to cerebral impairment.....*this cerebral impairment is not to be viewed as brain damage, but as a reversible state , analogous to the impairment and recovery of muscle after exercise*. However, unlike exercise recovery, which takes place during the physical rest of wakefulness, this cerebral restitution can only take place during sleep (Horne, 1988a, p. 46).

Horne (1988a) does not discard the demonstrated role of attentional processes in performance but suggests an integrative model between attentional and cognitive factors. Horne (1988a) retains the attentional framework of a fundamentally homeostatic system where certain sleepiness induced changes in performance can in part be compensated for by

active or phasic attentional resources. Horne (1988a) however extends the attentional model by proposing the existence of a critical sleepiness boundary beyond which performance decrements are reversible only by restorative sleep. The location of this critical boundary is task dependent and sensitive to qualitatively more complex processing demands. The fundamental components of Horne's model have been presented in Figure 4 (refer Chapter 3).

As narcolepsy is a disorder characterised by excessive and pervasive daytime sleepiness there is considerable face validity to the suggestion that this sleepiness would lead to observable decrements in performance, in just the same way as sleepiness leads to performance decrements in normal populations. Subjective reports from narcoleptic subjects support this prediction (see previous chapter) and since the early 1980's there have been several studies that have attempted to demonstrate the relationship between sleepiness and performance for narcoleptic subjects (these studies have been reviewed in the previous chapter). The findings surrounding these studies, reflect the same theoretical dilemma that pervades the general sleep deprivation literature - are performance decrements in narcolepsy explained by attentional or cognitive mechanisms? Aguirre et al. (1985), Ollo et al. (1987), and Rogers and Rosenberg (1990), would argue that performance decrements in narcolepsy have no organic base, but occur as a consequence of diminished attentional resources, that are secondary to narcoleptic sleepiness. Performance decrements can therefore be compensated for by increased attentional effort. This attentional model is supported by the finding that narcoleptics perform as effectively as controls in stimulating test environments (Aguirre et al., 1985; Rogers and Rosenberg 1990) but demonstrate performance decrements for repetitive and monotonous tasks, such as vigilance tasks, where there is minimal motivation to apply compensatory effort (Valley and Broughton, 1983). The diminished performance of narcoleptics on vigilance tasks, can however, be explained within an alternative paradigm. On

the basis of psychophysiological data Levander and Sachs (1985) suggest that narcoleptics may have a decreased tonic or habitual arousal state. Automatic tasks, such as vigilance tasks, that tap into tonic arousal capacity, would then demonstrate performance decrements in comparison to controls. Additional support for this model comes from the findings of Henry et al. (1988), and Henry et al. (1993), who demonstrated that unmedicated narcoleptics had significantly increased response latencies on the Sternberg scanning task, suggesting a deficit in perceptual encoding capacity, consistent with diminished tonic arousal levels.

Theoretical Models

The above introduction has raised a series of theoretical questions relating to the relationship between sleepiness and performance for narcolepsy subjects. If these issues are located within the theoretical framework adapted from the work of Horne (1988a) three possible theoretical models exist. The critical features of these models and their implications for performance are described below.

Model A (Figure 7). No differences exist between narcoleptic and control subjects in relation to the influence of sleepiness on performance.

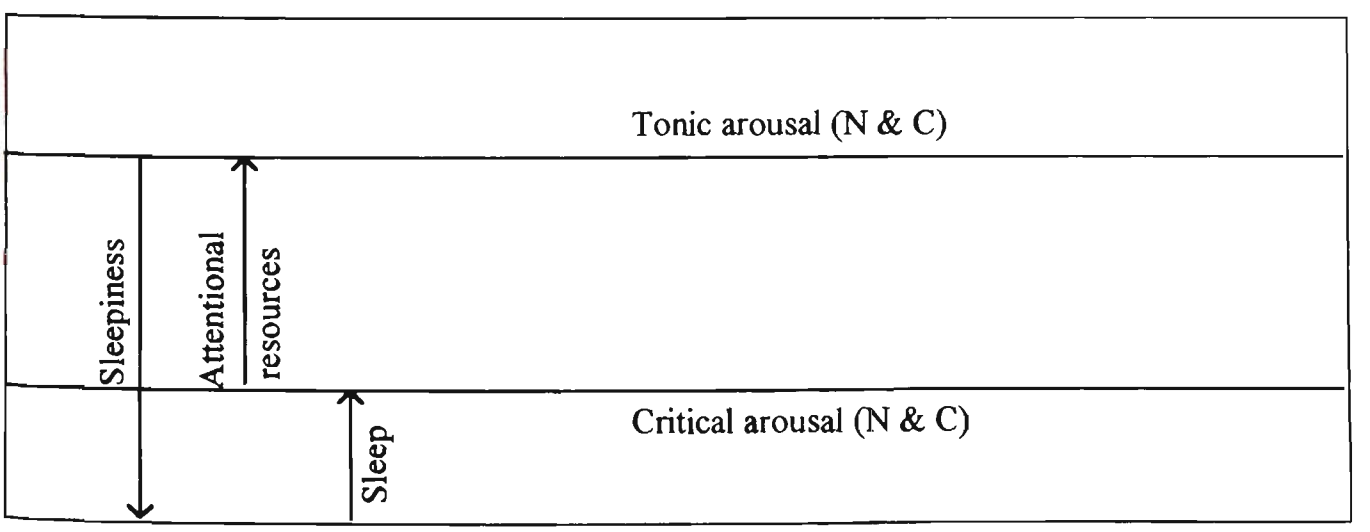


Figure 7 Model A: No difference model.(N = narcoleptic, C = control)

Model A proposes that no differences exist in the relationship between sleepiness and performance between narcoleptic and control subjects. Reports, for subjects with narcolepsy, of impairments on routine cognitive tasks occur as a function of diminished attentional resources that sleepy subjects apply to a task and these sleepiness effects can be compensated for by increased attentional effort. The experimental implications of this model would be (a) at high arousal narcolepsy subjects should perform as effectively as controls on tasks tapping tonic arousal capacity, (b) that performance decrements associated with sleepiness for subjects with narcolepsy should occur at a similar rate to decrements for sleepy controls, (c) that compensatory effort can restore sleepiness induced performance decrements to baseline levels at a similar rate for subjects with narcolepsy and controls, and (d) at some critical level of sleepiness decrements on complex performance tasks will only be reversed by compensatory sleep mechanisms.

Model B (Figure 8). Narcolepsy is associated with diminished tonic arousal levels.

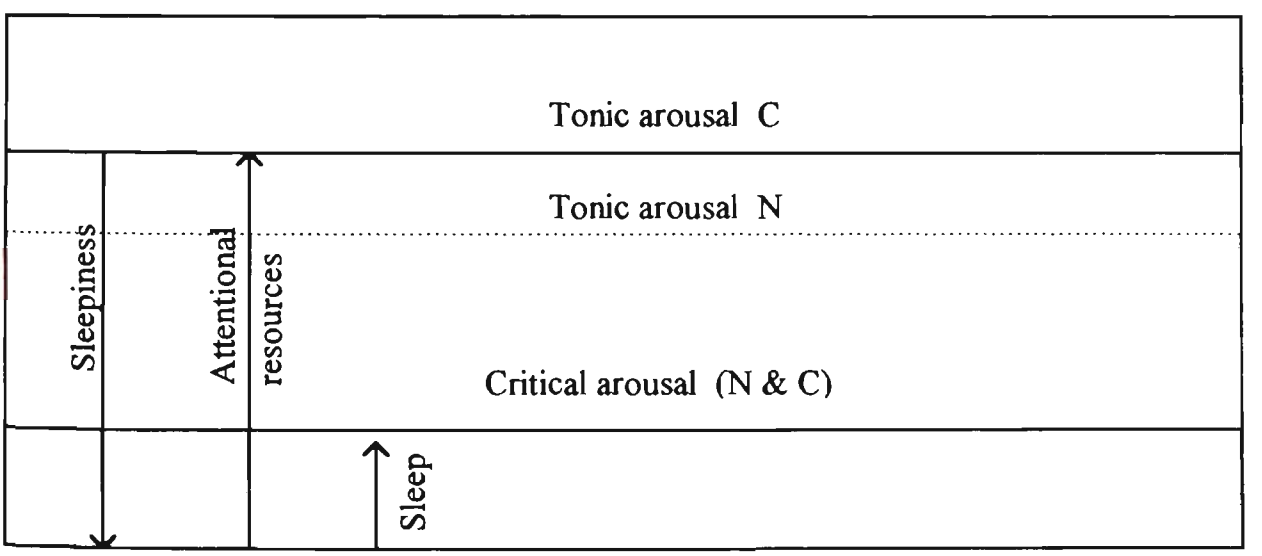


Figure 8 Model B: Decreased tonic arousal for subjects with narcolepsy.

This model proposes that narcolepsy is associated with a diminished tonic arousal state as a consequence of altered physiological factors. The major implication of this model is

that even at high arousal subjects with narcolepsy will have significantly reduced capacity on automatic performance tasks. A secondary implication of a diminished tonic arousal state is that sleepiness for narcolepsy subjects will lead to performance decrements falling below the critical processing boundary more rapidly than for controls.

Model C (Figure 9). Narcolepsy is associated with decreased phasic arousal capacity.

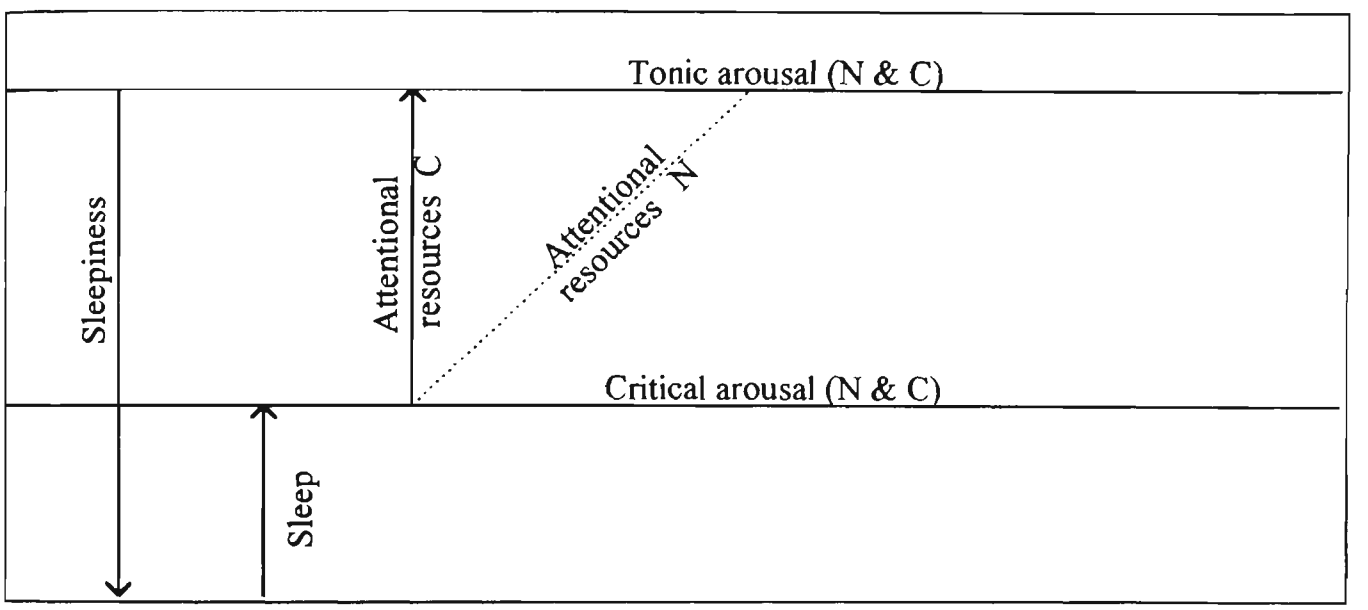


Figure 9 Model C: Decreased phasic arousal for subjects with narcolepsy.

Model C proposes that whilst tonic arousal states are unaltered between narcoleptic and control subjects, narcoleptic subjects have diminished capacity for, or ability to sustain phasic arousal, and therefore sleepiness induced performance decrements are not compensated for as efficiently by narcoleptic subjects as controls.

A methodological confound to many of the studies evaluating the relationship between sleepiness and performance in narcolepsy is that narcoleptics are clearly able to contain their sleepiness for brief testing periods and often fail to demonstrate any behavioural signs of sleepiness during testing sessions (Aguirre et al., 1985; Henry et al., 1993). Previous evaluations of the relationship between performance and sleepiness in narcolepsy have

operationalised sleepiness through either electrophysiological definitions such as electroencephalography (Valley & Broughton 1983; Rogers & Rosenberg 1990; Pollack et al., 1992) and evoked potential measures (Broughton et al., 1982; Ollo et al., 1987), or behavioural (Aguirre et al., 1985), or physiological parameters (Levander & Sachs, 1985; Henry et al., 1993). It is difficult to establish whether the often very brief changes in narcolepsy arousal states identified by these measures reflect the day to day experience of sleepiness for narcoleptics. Researchers have therefore questioned the external validity of laboratory based performance findings for this clinical population (Rogers & Rosenberg, 1990; Rogers & Aldrich, 1993).

Study Aims

The present study aimed to establish a test protocol which allowed cognitive testing of narcolepsy subjects under stable states of sleepiness and non sleepiness, and to evaluate the effect of sleepiness on performance for narcolepsy subjects across a range of automatic, attentional and complex cognitive tasks. Comparison of performance measures between narcolepsy subjects and controls across this range of performance tasks should provide a more detailed understanding of the relationship between sleepiness and performance in this clinical population and potentially allow for an explanation of this relationship within a theoretical paradigm. The models presented in this chapter provide a theoretical framework for this analysis.

As most aspects of this study are exploratory in nature no relevant literature base exists to allow the development of specific research hypotheses. Rather the analysis is directed by the specific experimental questions that are outlined in Chapter 7.

CHAPTER 6

Methodology for Study One

Sixteen subjects, eight narcolepsy subjects and eight controls, participated in the study. Subjects with narcolepsy were recruited from the Australian Narcolepsy Association (Narcolepsy and Overwhelming Daytime Sleep Society - NODDS). The group maintains a research register and subjects were recruited, initially by mail from the register. All narcolepsy subjects had specialist diagnosis of narcolepsy and met the International Classification of Sleep Disorders (ICSD, 1990) criteria of excessive daytime sleepiness with the presence of recurrent daytime naps and unequivocal cataplexy. The testing protocol did not allow for confirmatory MSLT measures to be recorded on the day of testing as accurate polysomnographic interpretations require that patients be (a) free of stimulant medications for 15 days prior to testing, and that (b) sleep wake schedules are standardised for at least seven days prior to testing (ICSD, 1990). The commitment and time required by participants to meet these criteria and undertake MSLT measures needed to be weighed against the availability of volunteer subjects and their adherence to the experimental protocol. As (a) confirmatory MSLT recordings are considered necessary only when there is an ambiguous clinical profile with an equivocal history of cataplexy (Kales et al., 1987a), and (b) MSLT measures are not a mandatory ICSD criteria for diagnosis (ICSD, 1990), MSLT measures were not utilised in the current study. As all subjects selected for the current study had unequivocal clinical histories of cataplexy the absence of MSLT recordings was not seen as resulting in ambiguity in the subject population's diagnostic status.

The group of narcolepsy subjects comprised seven females and one male subject. The age of the narcoleptic subjects ranged from 28 to 72 years with a mean age of 53 years

(SD = 12.5). Intelligence scores of narcoleptics were determined using the K- Bit Brief Intelligence Scale (Kaufman & Kaufman, 1990) and scores ranged from 93 to 123 with a mean score of 102 (SD = 11.3). Of the eight narcoleptic subjects six were taking stimulant medication: dexamphetamine (subjects N1, N3, N5), methylphenidate (N2, N7), and mazidol (N8). Additional medications included anafranil (N1), insulin (N8), and angina medication (N6). (The subject numbers (e.g. N1) correspond to narcoleptic participants in the first study. An overview of subject details is provided in Table 2). As central nervous system (CNS) stimulant medication interferes with both arousal and cognitive performance measures, subjects were requested to withdraw from stimulants a minimum of 18 hours prior to testing. The criteria of a minimum of 18 hours withdrawal provided a compromise aimed at minimising both the potential effects of stimulant confounds and the level of disruption to subjects' daily functioning. Thorpy and Goswami (1990) report that dexamphetamines have a 3-4 hour effectiveness, and methylphenidate a 4-6 hour effectiveness. Mazidol has a 8-10 hour effectiveness (Skidmore-Roth, 1995). For the purposes of this study the minimal 18 hour withdrawal period is assumed to provide a sufficient withdrawal period such that mazidol was no longer exerting a stimulant effect.

Any residual effects of stimulant medication were not considered to effect the validity of the study as the emphasis of the analysis relates to within subject changes in performance in a repeated measures pre and post nap experimental design. Measures of baseline arousal, free of any effects of medication, were therefore not critical to the study. Additional, non stimulant medications, were continued throughout the test period.

Control subjects were selected from acquaintances of the experimenter and individually matched with narcoleptic subjects on the variables of gender, age (within an arbitrarily defined seven year range), and IQ (within the 95% IQ confidence interval of the

narcolepsy subject). These three variables have been demonstrated to influence test performance on a range of cognitive tasks (gender - Seward & Seward, 1980; age - Charness, 1985; intelligence - Spreen and Strauss, 1991). Educational status has also been demonstrated to affect performance measures (Spreen & Strauss, 1991) but it was not included as a matching variable in this study as narcolepsy has been demonstrated to significantly impair educational opportunities (Kales et al., 1982). Control subjects were screened to exclude subjects reporting night time sleep disruptions, daytime sleepiness or depression. One of the control subjects (C6) was on medication for angina at the time of testing and this medication was continued over the test period.

A summary table of subject characteristics is provided in Table 2.

Table 2

Characteristics of Narcolepsy and Control Subjects for Study One

Subject	Gender	Age	IQ (95% CI)	Stimulant medication
Narcoleptic				
1	F	56	123 +/- 4	Amphetamine
2	F	49	93 +/- 6	Methylphenidate
3	F	52	104 +/- 6	Amphetamine
4	F	28	93 +/- 6	Amphetamine
5	F	62	93 +/- 4	-
6	M	72	115 +/- 4	-
7	F	52	99 +/- 6	Methylphenidate
8	F	53	96 +/- 6	Mazidol
Control				
1	F	53	125 +/- 4	-
2	F	45	102 +/- 6	-
3	F	45	95 +/- 5	-
4	F	28	97 +/- 6	-
5	F	61	87 +/- 4	-
6	M	75	120 +/- 4	-
7	F	52	98 +/- 6	-
8	F	52	93 +/- 4	-

Ethical Considerations

Consent to undertake the study was obtained from the Victoria University Human Ethics Committee. Prior to participation in the experiment the experimental protocol was discussed with all subjects and participants signed a consent form. Subjects were aware that they were free to withdraw at any stage from the experiment and that their individual data would remain confidential. Although subjects with narcolepsy were advised to check with their doctor prior to stimulant withdrawal the demedication from stimulants of subjects with narcolepsy was not considered to pose any significant risk to the participants. Subjects with narcolepsy frequently vary their own stimulant medication regime to fit with occupational or social demands. As one subject commented "... if I have nothing special to do I don't bother taking the pills, I just have a few extra naps". The principal side effect of stimulant withdrawal is the potential risks associated with the resultant excessive sleepiness. Because of this risk all subjects were transported to and from the testing venue and were carefully monitored over the testing period.

Criteria for Selection of Performance Tasks

Performance tasks were selected to test automatic, attentional and complex cognitive functioning. The theoretical categorisation of tasks is difficult with no precise criteria for selection. Whilst new brain imaging techniques, such as positron emission tomography (PET), are able to gauge cognitive effort as a function of changes in regional cerebral blood flow, the estimation of cognitive load as a function of task characteristics remains imprecise. There seem, however, to be several criteria that differentiate automatic from attentional tasks. Schneider and Shiffrin (1977) utilised the terminology of automatic versus controlled processing. Automatic tasks being characterised as easy, highly familiar

functions that require no cognitive effort and therefore can operate in parallel with other tasks. Tasks requiring controlled processing involve unfamiliar or difficult stimuli, necessitating effortful and serial processing of tasks (Schneider & Shiffrin, 1977). More recently Treisman (1988) has redefined this distinction as one between preattentive processing and focussed attention, with the major discriminator between categories being the level of consciousness or awareness of cognition. Preattentive tasks requiring no consciousness or awareness in contrast to the attention to stimuli that characterises focussed attention tasks. Matlin (1994) suggests that even with discriminating criteria for automatic and attentional tasks, in practice tasks vary along a continuum between these pivotal extremes. Similarly tasks requiring attention vary continuously as a function of both cognitive load and cognitive complexity. Whilst tasks have been selected for inclusion in the present study on the basis of literature definitions, face validity, and relatively clear differences in cognitive effort between categories, the differentiation of automatic, attentional, and complex cognitive tasks does remain in part arbitrary.

A second factor influencing task selection was task duration. Task duration was seen to potential confound results with increased time on task increasing the potential for fatigue to affect performance. Also as narcolepsy is associated with constant fluctuation in arousal levels researchers have demonstrated that even relatively brief performance tasks can be confounded by *within* task changes in arousal level (Godbout & Montplaisir, 1986). To minimise these effects of fatigue and fluctuating arousal, brief performance tasks were selected where possible.

Finally task selection was influenced by the potential for task practice effects to confound the results. Tasks were selected that were reported in the literature to either have

minimal associated practice effects, to have scoring protocols that compensated for practice, or had published alternate versions that minimised the effects of practice.

The central features of each task and outcome variables utilised in the study are outlined in Table 3. Detailed descriptions of the tasks are presented in the following section.

Table 3

Summary of Performance Tasks for Study 1

TASK	CLASSIFICATION	CENTRAL FEATURES	OUTCOME MEASURES	PRESENTATION
Physical match	Automatic	Identification of physical similarity of stimulus letters	Response Latency	Subject paced
Reaction time	Automatic	Discrimination of randomly presented stimulus figures	Response Latency	Experimenter paced
Stroop dots	Automatic	Colour identification	Response latency and accuracy	Subject paced
D2 concentration endurance task	Attentional	Serial search task for target stimuli embedded in distracting stimuli	Total correct Fatigue/Performance fluctuations. Error type	Experimenter paced
Digit symbol substitution	Attentional	Coding task	Total Correct	Experimenter paced
Rey auditory verbal learning task	Attentional	Word list serial learning task	Short term memory Long term memory	Experimenter paced
Complex reasoning	Complex	Matching visual and semantic descriptors	Response latency	Subject paced
PASAT	Complex	Serial addition task	Total correct. Total correct as a function of time on task.	Experimenter paced
Semantic match	Complex	Identification of semantic similarity of stimulus figures	Response latency	Subject paced
Stroop colours	Complex	Naming of stimulus colour with interfering colour name stimulus	Response latency and accuracy	Subject paced
Word fluency	Complex	Word generation	Total number generated	Experimenter paced

Performance Tasks

Rey Auditory- Verbal Learning Task (RAVLT)

Test features The RAVLT is a brief serial learning task which assesses a wide range of memory functions (Spreen & Strauss, 1991). The test has been demonstrated to be sensitive to changes in memory function across both clinical (Mungas, 1983) and non clinical samples (Mitrushina, Satz, Chervinsky & D'Elia, 1991). As repeated testing using the RAVLT has been demonstrated to result in significant practice effects (Crawford, Stewart & Moore, 1989), parallel versions of the RAVLT have been developed. Alternate form reliability is high (Ryan, Geisser, Randall & Georgemiller, 1986) and no significant practice effects are evident on retesting with alternate test versions (Spreen & Strauss 1991). This experiment utilised the Crawford, Stewart and Moore (1989) version as an alternate test form to the RAVLT. The decision to locate the RAVLT in the attentional, rather than complex processing category, is based on the work of Rogers and Rosenberg (1990) who argue that a potential explanation of the failure of research protocols to identify memory impairments in narcolepsy occurs as a consequence of the use of standardised memory tasks. Rogers and Rosenberg (1990) suggest that tasks, such as the RAVLT, tap into already well established skills, such as rote learning of word lists, and are not therefore dependent on higher order creative and divergent cognitive processing.

Outcome measures This study utilised the RAVLT to derive the dependent attentional measures of immediate and long term memory function.

Stroop Colour and Word Test

Test features The Stroop colour word interference task (Stroop, 1935), provides a measure of cognitive flexibility or the ability of the subject to shift their perceptual set in response to changing task characteristics (Lezak, 1983). The task has been used for both

clinical (Dodrill, 1978) and nonclinical (Dyer, 1973) populations and several formats of the task have been developed (e.g. Talland, 1965; Golden 1978). The task comprises three levels of cognitive difficulty but for the study reported in this thesis the test utilised only two of the three task components. The first level of the task comprises a card with a series of 24 coloured dots (blue, green, yellow and red) and the subject is required to name the colour of the dots as quickly as possible. This colour recognition and identification task reflects an automatic processing skill. The second stimulus card represents the colour - word task. In this condition colour words are written on the display card in incongruent coloured ink, for example the word 'green' may be written in yellow. Subjects are required to name the colour the word is written in and ignore the word itself. The increased response latency for the colour - word condition, provides a measure of the subject's cognitive flexibility in suppressing an automatic response and utilising a new response strategy.

Outcome measures Performance, measured in seconds, on the Stroop dots condition provided a measure of automatic processing speed, whilst times for the colour-word condition were considered a measure of complex processing speed. The difference in speed between conditions, provides an index of performance latency under increasing cognitive load.

Digit Symbol

Test features The digit symbol task is a subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R). The task comprises 100 numerals between one and nine. A template is provided with the task where each numeral is matched with a specified symbol e.g. the number one is represented by a vertical slash "-". The subject is required to substitute

each numeral for the appropriate symbol across a limited time span. The first seven numerals are used as practice items to ensure the subject understands the task.

Lezak (1983) describes the digit symbol task as a sensitive measure of sustained attention, visuomotor coordination and response speed. The task is categorised in this study as an attentional task.

Outcome measures The score represents the total number of correctly coded numbers within the 90 second time frame.

Paced Auditory Serial Addition Test

Test features This serial addition task was originally developed by Gronwell and Sampson (1974) to provide a measure of sustained attention and speed of information processing. The test is presented on audio tape. The examiner reads out 60 pairs of randomised digits at a predetermined rate and the subject needs to add each digit to the digit immediately preceding it, for example if the examiner read out 1,4,7,9, the subject would respond 5,11,16.

> The test requires subjects to comprehend the auditory input, respond verbally, inhibit encoding of one's own response while attending to the next stimulus in the series, and perform at an externally determined pace. (Spreen & Strauss, 1991, p. 143).

Each subsequent trial increases the rate of digit presentation with the entire task comprising four trial runs at rates of 2.4, 2.0, 1.6 and 1.2 seconds. Significant practice effects are associated with the first presentation of the PASAT but subsequent to this initial trial practice effects appear minimal (Gronwall, 1977). To minimise the effect of practice all subjects in this experiment were given several practice trials prior to the test presentation and

performance scores were recorded only for the second experimental trial at the 2.0 second pacing. The two faster pacings were not included in the experimental design as some subjects did not achieve a performance score above 20 on the 2.0 second pacing. This minimal performance criterion is necessary for presentation of all four trials (Spreen & Strauss, 1991).

Outcome measures The number of correct responses on the second performance trial were recorded and utilised as a complex performance measure. The task also provided a measure of fatigue with the number of performance errors being totalled for each block of five responses, providing a measure of performance change with time on task.

Complex Reasoning Task

Test features This computer based task measures the reaction time of subjects to a series of semantic descriptors relating to a visual image. The subject is presented with a visual display of a star '*' and a plus symbol '+'. The image is either presented with the star located above or below the plus sign. Once the subject has understood the spatial relationship between the two symbols a semantic description of the visual display is provided and the time taken for the subject to identify whether the descriptor is a true or false description of the previous visual image is recorded. Task difficulty is manipulated by changing the semantic complexity of the referent statements. For example if the initial visual image shows the '*' above the '+' the semantic descriptor could be

i) The true affirmative sentence (Star above plus).

ii) The false affirmative sentence (Plus above the star)

iii) The true negative sentence (Plus is not above the star)

iv) The false negative sentence (Star is not above the plus)

Levy, Fischler and Griggs (1979) suggest that these sentences represent differentially complex semantic descriptors as the inclusion of prepositional mismatches and semantic negations increase the cognitive processing demands of the task. As the original visual presentation has two variants i.e. the star above the plus, or the star below the plus, there are eight possible combinations of picture and sentence relations. These eight variants are presented randomly across sixty four trials and the reaction times for responses to each trial recorded. The task is not dependent on computer literacy as response timing does not commence until the semantic descriptor is displayed and the subject is then required to only press a True or False key. A single experimental run takes approximately 10 minutes.

Outcome measures Mean reaction times in milliseconds (msecs) were reported for the eight trial variants. Only correct responses were scored by the computer program. To simplify the analysis the data was then compressed into two categories which were classified as simple and complex task measures. The simple tasks incorporated the mean reaction time (msec) score for all affirmative sentence statements. The complex tasks represent mean reaction time (msec) score for all negative sentence structures. Only performance scores for the complex reasoning trials were utilised in this study. Levy, Fischler and Griggs (1979) suggest that initial trials are confounded by significant practice effects, however as the task involves 64 trials and levels of complexity are randomly dispersed between trials the effect of practice does not significantly interfere with the final outcome measure.

Pattern Interpretation: Physical and Semantic Match

Test features This computer based program developed by Levy, Fischler and Griggs (1979), replicates an experiment devised originally by Posner and Mitchell (1967), to evaluate response times for increasingly complex levels of cognitive processing. Two letters

of the alphabet, e.g. Aa or AB, are displayed on the screen under two trial conditions, which are referred to as physical and semantic match conditions. Under the physical match condition subjects are asked to respond, by pressing a computer key, to whether the two letters are physically identical (same) or physically dissimilar (different), e.g. AA would be "same" and Aa would be "different". Under the semantic match condition subjects are asked to respond "same" if the letters have the same name, or "different" if the letters have different names, e.g. Aa or aa would be "same" and ab would be "different". Each response condition has 64 stimulus presentations and takes approximately five minutes to complete. Posner and Mitchell (1967) argue that the physical match condition represents an automatic response time whilst the semantic match condition requires the subject to describe the stimulus, search for a matching representation in memory and then produce the relevant name. Latencies for response are measured in milliseconds. Practice effects were minimised by subjects responding to trial runs until they felt familiar with the task requirements.

Outcome measures For this study the response latency under the physical match condition was used as a dependent variable for the category of automatic tasks. Response latency for the semantic match condition was scored as a dependent variable under the category of complex tasks.

D2 Concentration Endurance Test

Test Features

The D2 concentration endurance test is a cancellation task where subjects are required to visually scan rows of letters which have embedded randomly dispersed target stimuli. For this task the target stimulus was the letter "d" printed with two slashes around the figure.

The task comprises fourteen rows of 47 letters and subjects are given 20 seconds to scan each row for target stimuli. The subject places a slash across identified target stimuli.

Outcome measures For the purposes of this study several outcome measures, described by Spreen and Strauss (1991), were derived from the D2. The total number of items scanned minus the number of incorrectly scanned items provided a measure of scanning speed. A measure of performance fluctuation was derived from the difference between the score for the row with the highest number of correctly scanned items minus the lowest number of correctly scanned items. A fatigue score was calculated by the difference between the total number of correctly scanned items across the first four rows minus the total of correctly scanned items across the last four rows. As errors on the task could occur as either errors of omission where subjects miss correct target items or errors of addition where subjects identify incorrect target items the D2 also provided a measure of the nature of performance errors. The sum of omission and addition errors providing a measure of the total number of errors. Lezak (1983) suggests that visual cancellation tasks provide a sensitive measure of the ability for sustained attention and this task is therefore classified in the current study as an attentional task.

Reaction Time

Test features Reaction time tasks have been used extensively in neuropsychological testing to provide a measure of the time from stimulus onset to the initiation of a behavioural response (Welford, 1980). Simple reaction time tasks involve a single stimulus and response whereas choice reaction time tasks incorporate several stimulus figures and the task involves discriminating between stimuli prior to the behavioural response. The task utilised in this experiment was a choice reaction time task where triangular or square figures were randomly displayed on a computer screen and subjects were asked to identify the shape displayed by

pressing a predetermined computer key. The mode of presentation of the stimulus figures was preprogrammed to provide fifteen stimulus figure presentations separated by randomised interstimulus intervals. The stimulus figures were presented in reverse order which meant that the stimulus figure was always presented on the alternate side of the computer screen to the computer key nominated to identify the particular stimulus figure. Subjects completed several practice trials on the task to minimise the subsequent practice effect. Each task then involved three separate presentations of the fifteen stimulus figures. All response times were recorded and displayed by the computer.

Reaction time measures have been used extensively in the literature on performance decrements associated with sleepiness (Bonnet, 1986; Bonnet, 1989; Herscovitch & Broughton, 1981; Lorenzo et al., 1995) and have also been used in the applied literature evaluating performance decrements in narcolepsy (Broughton, et al. 1982; Godbout & Montplaisir, 1986; Levander & Sachs, 1985; Valley & Broughton, 1981).

Outcome measures The reaction time task of figure identification is described as an automatic processing task requiring minimal attentional capacity (Welford, 1980) and was therefore included in the current study within the automatic task category. The task measure was the mean response time calculated across the 45 stimulus presentations.

Word Fluency

Test features The word fluency task requires subjects to generate as many words as possible that begin with a letter nominated by the experimenter. The subject has a one minute interval for each of the three letters nominated. For one trial the letters P, R, and W, were used and the alternate trial utilised F, A, and S. The presentation of letters was counterbalanced across trials to compensate for any possible variance in difficulty. Proper

nouns and derivates of previously used words (e.g. eat - eating) were not included in the scoring.

PET studies have demonstrated the role of frontal lobes in this word generation task (Parks et al., 1988) and the task has been demonstrated to be sensitive to lesions within the frontal lobes (Miceli, Caltagirone, Gainotti, Masullo & Silveri, 1981). Horne (1992) argues that tests dependent on frontal lobe functioning are more "cerebrally demanding" and provide more sensitive measures of sleepiness than routine convergent thinking tasks. Word fluency tasks have demonstrated deficits after only one night of total sleep deprivation (Horne, 1988b).

Outcome measures The task is scored as the total number of admissible words generated for the three letters. The ability to generate language, as measured in the word fluency task, has been classified for this study, as a complex reasoning task.

Procedure for Narcoleptic Subjects

Testing was carried out at the Victoria University Sleep Laboratory. The laboratory is a two bedroom temperature controlled facility shielded from the external environment. Important features of the testing schedule include:

Overnight Sleep Laboratory Monitoring

All narcoleptic subjects were required to attend the sleep laboratory on the night prior to testing. The decision to bring narcoleptic subjects into the laboratory the evening prior to testing allowed the study (a) to adhere to common sleep testing protocols where subjects are generally monitored the night prior to testing, (b) to ensure that the timing of the

testing schedule (refer Figure 10) could be closely monitored, and (c) maximise the similarity of environmental conditions for subjects prior to commencing the testing schedule.

Whilst subjects were free to self select their time of going to bed all subjects were woken on the day of testing at 7.30am. Subjects were then allowed to shower, dress, and have breakfast prior to the first testing session at 8.30am. This schedule resulted in subjects' first test session occurring approximately 1 hour after waking but that hour was associated with significant activity by the subjects and no behavioural signs of sleepiness were observed by the experimenter across this period. Evaluation of subjective sleepiness measures for this first testing session also failed to identify any significant difference in this mean high arousal testing condition in comparison to subsequent post nap evaluations of arousal.

Subjects' overnight sleep was monitored using a Grass polysomnograph, calibrated in line with standard criteria. Twelve electrodes were attached to the subject including four EEG placements, four EOG placements, three EMG placements and a ground electrode, giving a modified montage of the 10-20 electrode placement system (Guilleminault, 1982). The electrodes were not removed until after the completion of the daily testing schedule to allow for possible monitoring of nap periods.

Manipulation and Assessment of Arousal

A central aim of this study was to maximise external validity by creating a testing environment that allowed for the expression of both high (HA) and low arousal (LA) states amongst narcoleptic subjects (refer Figure 10). As naps have been shown to have a have a refreshing effect on narcoleptic subjects (Roehrs et al., 1984) conditions of high arousal were achieved by the use of naps throughout the testing day. In line with published research

(Roehrs et al., 1985) twenty minute naps were scheduled prior to each of the HA testing sessions. Following the nap a refractory period of 5 minutes was allowed prior to testing.

Low arousal conditions were established by the use of both temporal and environmental factors. Baseline sleepiness levels in narcoleptics potentially recur within 30 minutes of a nap (Roehrs et al., 1986). However to increase the potential for low arousal conditions, the current study utilised a period of one hour following a nap period to re establish a low arousal testing condition. The period prior to low arousal testing was structured in line with the protocol demonstrated by Volk et al. (1984) to provide an environment facilitating low arousal conditions. The initial 30 minutes of the low arousal induction involved subjects having free quiet time. Subjects used this time to read or glance at magazines. They were not allowed to interact with the experimenter during this period but were observed to ensure that no naps occurred. If subjects demonstrated any behavioural signs of sleep or they were aroused by the experimenter. For the thirty minutes immediately prior to LA testing subjects completed the Wilkinson Auditory Vigilance Task (WAVT) which has been demonstrated to be a sleep inducing task for narcoleptic subjects (Valley & Broughton, 1981). The WAVT is a thirty minute task which involves subjects listening to a series of auditory tones of 55 millisecond duration. These tones are presented, via an amplifier, every two seconds, and occur against a background of 85 decibels of white noise. Twenty signal tones of 375 millisecond duration are randomly dispersed throughout the thirty minute test period. Subjects are instructed to press a key when they hear a signal tone. The task is automatically scored for the number of correct positive or false positive signal tones to be identified. Prior to commencing the task the subjects were given the following standard instruction.

During the following task you will hear beeps at regular intervals. Occasionally, at random, a beep will be of slightly shorter duration than the others, when you hear a shorter beep press the button immediately. If you fall asleep during the task I will wake you. Remember the short beeps will only happen occasionally and at random.

The subjects were given a five minute trial WAVT to ensure they understood the procedure and following the trial the thirty minute task was undertaken. Initially it was expected that the experimenter would score the task but several subjects became anxious about the scoring and this anxiety potentially interfered with the sleep inducing properties of the task. It was therefore decided to advise subjects that their scores were not incorporated in the general testing procedure.

Observation of subjects during the WAVT again controlled for subjects falling asleep. The restriction of stimulant medication for a minimum of 18 hours prior to testing further facilitated the expression of the low arousal state.

The efficacy of the arousal fluctuation needs to be inferred by the strength of the manipulation and the extent to which the testing schedule reflected theoretical and experimental knowledge relating to arousal fluctuation in narcolepsy. VAS measures were used to gain a subjective assessment of the efficacy of the arousal fluctuation. The VAS scale was a 100mm line with pivotal extremes marked with the SSS anchors of "feeling active and vital; alert; wide awake" which represented the maximum high arousal point of the scale and "almost in reverie; sleep onset soon; lost struggle to remain awake" representing the minimum arousal condition. Subjects were asked prior to all testing sessions (low and high arousal conditions) to mark their subjective level of sleepiness at some point along the line.

One criticism of the use of subjective sleepiness ratings is that they have diminished validity for subjects with excessive daytime sleepiness. Dement et al. (1978) suggest that this

diminished validity may occur as a consequence of chronically sleepy subjects losing an appropriate frame of reference by which to measure their sleepiness. This potential limitation of subjective rating scales is not however seen to invalidate the findings of the present study where the effectiveness of the arousal fluctuation was evaluated as a consequence of subjects' estimations of *change* in their sleepiness state rather than an absolute estimate of sleepiness.

HA = high arousal
LA = low arousal
VAS = Visual Analogue Scale

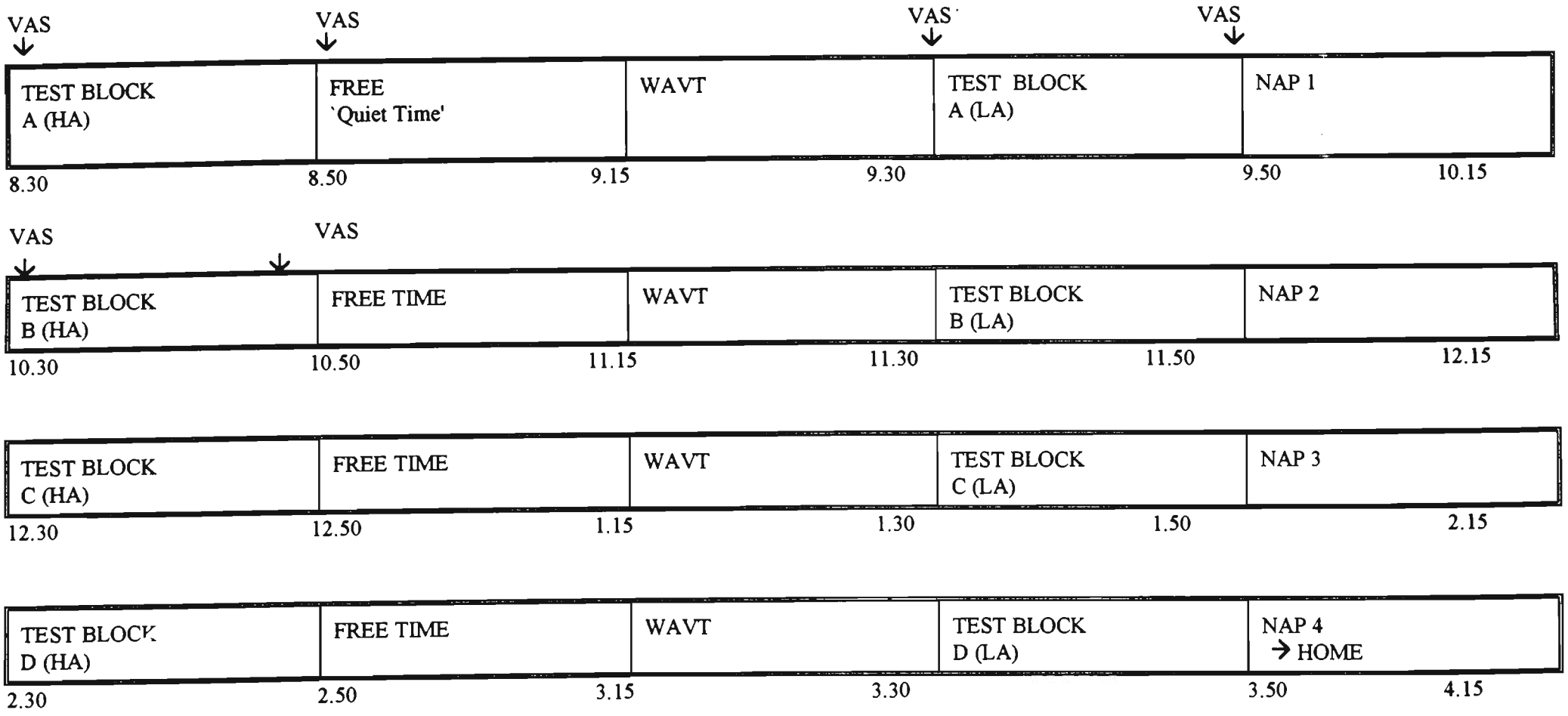


Figure 10 Testing schedule for narcoleptic subjects in study one.

Experimental Design

A repeated measures, or within subject design, was selected for this experiment. The independent variable of arousal was manipulated, as described in the previous section, so that the eight narcoleptic subjects completed each cognitive task twice i.e. under both low and high arousal conditions. The advantage of this within subject design is that in a clinical disorder such as narcolepsy there is extensive between subject variance in symptomology. As a major between subject variant is baseline arousal levels and, as the independent variable in this study is arousal, the use of a within subject design provides a means of estimating arousal treatment effects that are not confounded by between subject arousal variability. Using a within subject design, variations in subject arousal, extraneous to the experimental arousal manipulation, may still occur as a consequence of factors such as motivation or fatigue - "a subject is not the 'same' individual on successive tasks" (Keppel, 1991, p. 334) and therefore the experimental design has been adapted to minimise the potential for these extraneous arousal effects to influence task performance. The potential limitations of this within subject design are discussed more fully in Chapter 11 of this thesis.

Whilst a repeated measures design has the advantage of eliminating between subject variability it has the major disadvantage of the potential for practice effects to occur. These systematic changes in subject performance, that occur as a consequence of repeated testing, may be either (a) positive, resulting in enhanced test performance, due to factors such as familiarity with test procedures or content or (b) negative, leading to diminished performance as a consequence of factors such as fatigue or boredom (Keppel, 1991). There are two methodological strategies for controlling the influence of practice effects on the outcome variable. The first procedure involves the use of a counterbalanced design where treatment conditions are ordered so that each arousal condition occurs with equal frequency for each

testing position i.e. half the subjects would undergo testing with the low arousal condition being followed by the high arousal condition and the other half of the subject group would have a reverse experimental order of high arousal then low arousal testing. This technique assumes that practice effects are spread evenly over treatment conditions (Keppel, 1991).

A second technique for controlling practice effects is to estimate the size of the practice effect using a control group and then to subtract this practice factor from the overall effect. By measuring and subtracting the practice effect an estimate can then be made of the residual treatment effect (May & Kline, 1987). This study has used this second strategy to estimate the size of the practice effect. All narcoleptic subjects performed a series of tasks and each task was performed first under a manipulated low arousal (LA) condition and then under a manipulated high arousal (HA) condition.

The rationale and limitations of this experimental design are discussed fully in Chapter 9.

Procedure for Control Subjects

The procedure for recruitment of control subjects is reported in the subject section of this chapter and the demographic characteristics of the control group are listed in Table 2. To minimise the possibility of circadian factors impacting on performance measures, control subjects followed the same testing protocol as narcoleptic subjects (Figure 10). Control subjects were requested to wake at 7.30am. and to be ready for testing by 8.30am. Testing of control subjects was carried out in the subjects' home to ensure that the timing of the testing schedule was adhered to.

As no attempts were made to manipulate the arousal condition for control subjects the WAVT was not utilised with the control group. No structure was imposed on control

subjects' use of time between testing sessions, except that no naps were permitted across the day. Control subjects demonstrated no behavioural signs of sleepiness across the testing sessions though this observation was not quantified in the present study.

CHAPTER 7

Results for Study One

Rationale for methodology of data analyses

An overview of the narcolepsy literature indicates that experimental investigations of this clinical population typically involve small subject groups. This reflects perhaps the difficulties of recruiting adult narcoleptic subjects whose diagnostic profiles meet the ICSD (1990) criteria. Table 1 (refer Chapter 4) lists the published studies of performance measures in narcolepsy and the median number of narcoleptic subjects utilised in these experimental protocols is ten. With such small sample groups assumptions of statistical normality are difficult to demonstrate. However for this clinical group the published literature consistently utilises parametric statistics for the analysis of experimental data. This reflects, perhaps, the unstated assumption that the experimental data is representative of a normally distributed population of narcoleptic subjects. This presumption of the representative nature of the sample data is difficult to validate as the demographics of the population of narcoleptic subjects are not clearly defined. This difficulty of achieving experimental representativeness for chronic illnesses, which may have multifaceted presentations, has also been reported by Robinson (1988).

The experimental protocol reported in this chapter utilised eight subjects with narcolepsy and eight control subjects and, in line with the literature in the field, will utilise parametric analyses.

Identification of subject groups

The four experimental groups will be identified in this analysis section using the following abbreviations, C1 = control subjects at the first testing session, C2 = control subjects at the repeat testing session, LAN = subjects with narcolepsy tested under manipulated low arousal conditions. This represents the first test session for these subjects. HAN = subjects with narcolepsy tested under high arousal conditions, representing the second testing session for these subjects. Analyses involving comparison of C1 and LAN measures both represent the first testing session and are therefore considered free of the effects of practice. Comparison of HAN and C2 conditions represent the second testing session for both subject groups and practice effects are therefore considered equated between groups. This assumption of the equivalence of practice effects between the narcoleptic and control groups will be addressed in the discussion section in Chapter 9.

Organisation of experimental data

The results have been organised to address the research questions listed below. These questions emerge from the theoretical literature relating to the relationship between sleepiness and performance. The questions are also structured to allow for an analysis of the various models of sleepiness and performance in subjects with narcolepsy that are presented in Chapter 5.

1) Has the experimental manipulation of arousal for subjects with narcolepsy led to significant differences in arousal between the manipulated low and high arousal conditions?

2) When subjects with narcolepsy move between low and high arousal conditions what degree of performance change is associated with this arousal change?

3) How do high and low arousal conditions for subjects with narcolepsy compare in relation to

   (i) The influence of fatigue on performance

   (ii) The stability of performance measures

   (iii) The nature of performance errors for both experimenter and subject paced performance tasks

   (iv) The capacity for phasic arousal

4) Can performance tasks be used to discriminate between narcoleptic and control groups or more specifically

   (i) As automatic tasks have been shown to reflect tonic or habitual arousal states (refer Chapter 5) do the automatic tasks selected for this study discriminate between HAN and C2 subjects?

   (ii) Do attentional or complex thinking tasks discriminate between narcoleptic subjects at low arousal and controls?

These issues are presented as research questions rather than hypotheses as there are no published studies which have manipulated arousal conditions to evaluate the sleepiness and performance interaction in narcolepsy. The study is therefore exploratory in nature.

Results

SPSS for Windows was used for all data analyses. Where multiple analyses have been undertaken the alpha criterion has been adjusted from .05 using the Bonferroni adjustment.

Summary statistics

Table 4 provides summary statistics for all variables measured in Study one.

Table 4

Summary Statistics of Performance Variables in Study One
(see text for abbreviations)

Variable		C1	C2	LAN	HAN
Complex	$\overline{X}$	562.25	588	850.50	651.12
reasoning	SD	236.08	286.05	351.55	234.68
Digit	$\overline{X}$	41.25	47.37	49.50	54.25
symbol	SD	11.13	13.43	4.17	5.12
D2 fatigue	$\overline{X}$	-12.75	7.12	-3.62	14.62
	SD	11.62	10.72	26.76	17.76
D2	$\overline{X}$	13.25	11.25	16.12	12.37
fluctuation	SD	5.01	3.37	4.64	3.42
D2 errors	$\overline{X}$	19	22.12	40.88	40.50
	SD	13.18	14.59	60.05	42.90
D2 total	$\overline{X}$	444.62	495.75	400.87	492.25
	SD	48.26	28.84	44.35	20.09
LTM	$\overline{X}$	8.75	8	8.62	8
	SD	4.28	4.28	4	4.57
PASAT	$\overline{X}$	30.12	32.37	19.12	34.88
	SD	6.42	6.83	10.33	7.55
Physical match	$\overline{X}$	89.75	71.25	90.50	67.13
	SD	19.88	14.33	22.65	8.87
Reaction time	$\overline{X}$	.74	.56	.71	.57
	SD	.43	.16	.17	.11
Semantic match	$\overline{X}$	78.37	73.62	105.63	80.50
	SD	17.23	12.48	27.21	11.34
STM	$\overline{X}$	5.87	6.37	6.12	6
	SD	1.55	2.07	2.10	1.51
Stroop Colours	$\overline{X}$	33.23	25.76	34.14	27.40
	SD	9.74	6.52	11.16	7.74
Stroop dots	$\overline{X}$	13.71	13.04	15.00	13.07
	SD	1.91	2.35	1.45	2.35
Word fluency	$\overline{X}$	42.37	47.87	33.12	42.12
	SD	20.13	15.77	8.58	10.87

1) Manipulation of arousal

As an index of the degree of arousal change associated with the experimental manipulation of arousal conditions each narcolepsy subject was asked to complete the VAS sleepiness rating on eight occasions. The VAS scale required subjects to assess their

subjective sleepiness level by indicating on a 100mm scale their sleepiness rating between anchor points of minimal and maximum alertness (full details of the scale have been described in Chapter 6). Four of these ratings represented manipulated low arousal conditions (LAN) and four manipulated high arousal (HAN) conditions. Of the possible 64 ratings, 52 were completed by subjects, with the missing data equally distributed between arousal conditions. The manipulation was demonstrated to create a highly significant change in arousal conditions. For the low arousal manipulation the mean M arousal rating was 27.35, and the standard deviation SD = 19.62, and for the manipulated high arousal condition the mean arousal rating was M = 74.73, SD = 17.55. A dependent t-test analysis of these findings demonstrated a significant difference between arousal conditions, $t(25) = 12.13$, $p=.000$.

2) Arousal fluctuation and performance measures

Descriptive analysis of the impact of sleepiness on performance across all performance tasks

Mean performance scores for narcolepsy and control subjects, across all performance tasks, are presented in Table 5. Visual analyses of descriptive statistics displayed in Table 5 indicate that with repeated testing of control subjects (comparing columns A and B) mean scores for ten of the twelve performance measures demonstrated an increment on the second testing session (column C). The percentage change in performance scores between the two control testing sessions, ranged from 5 to 24 % (column C), and Table 5 provides an estimate of the level of practice associated with repeated testing. For two tasks, long term memory and complex reasoning, the second control testing session was associated with performance decrements.

Table 5

Mean Performance Scores and Percentage Change for Practice and Sleepiness Effects Across all Performance Tasks

	A (Mean) Cont 1	B (Mean) Cont 2	C Practice Effect%	D (Mean) LA Narc	E (Mean) HA Narc	F Arousal + Prac Effect %	G (F-C) Arousal Effect %
Automatic							
Reaction time (sec)	0.74	0.56	24	0.71	0.57	20	-
Stroop dots (sec)	13.71	13.04	5	15	13.07	13	8
Physical match (msec)	89.75	71.25	21	90.5	67.13	26	5
Attentional							
Digit symbol (tota;)	41.25	47.37	15	49.5	54.25	10	-
D2	444.62	495.75	9	400.87	492	23	14
Short term memory (total)	5.87	6.37	9	6.12	6	-2	-
Long term memory (total)	8.75	8	-9	8.62	8	-7	-
Complex							
Word fluency (total)	42.37	47.87	13	33.12	42.12	27	14
PASAT (total)	30.12	32.37	7	19.12	34.87	82	75
Stroop colours (sec)	33.20	25.67	23	34.14	27.4	20	-
Complex reasoning (msec)	562.25	588	-5	850.5	651.12	23	28
Semantic match (msec)	78.37	73.62	6	105.62	80.5	24	18

For tasks with time (msecs/secs) as the outcome measure the percentage change score for practice (C) is derived from the percentage difference of A-B, and the percentage change score associated with practice ✦ sleepiness (F) is derived as a percentage difference of D-E. Where total number of times correct (total) is the outcome variable the procedure is reversed, and the effect of practice (C) is derived from the percentage change B-A, and the percentage change associated with practice ✦ sleepiness (F) is derived from the percentage difference E-D. Residual percentage sleepiness effect (G) always represents F-C.

HAN conditions led to increments in performance for all tasks except both memory tasks, which demonstrated a small performance decline under high arousal conditions (compare columns D and E). The percentage increment in performance scores for narcolepsy subjects between low and high arousal conditions (column F) provides an estimate of the cumulative effects of both practice and arousal change. Column G represents the residual increment in performance for narcolepsy subjects, between low and high arousal conditions following the removal of practice effects.

Of the twelve initial tasks completed by subjects with narcolepsy, seven demonstrate some performance increment, free of practice, between low and high arousal testing conditions. Specifically the percentage change due to arousal fluctuation ranges from 75 % to 5% with the complex tasks of the PASAT, complex reasoning, semantic match and word fluency demonstrating the greatest sensitivity to arousal fluctuation with percentage increments at high arousal of 75, 28, 18 and 14 percent respectively. The D2 attentional task also demonstrated a 14 % increment under the high arousal condition and the automatic tasks of physical match and Stroop dots demonstrated residual arousal effects of 5% and 8% percent respectively.

3) Characteristics of performance under high and low arousal conditions for subjects with narcolepsy

3(i) Comparative performance on automatic tasks between narcolepsy subjects at high arousal and controls

To determine whether subjects with narcolepsy differed from control subjects on tasks tapping automatic processing, a discriminant function analysis was performance using the three automatic tasks as potential predictors of membership between the two groups. Predictors were therefore the automatic tasks of reaction time, Stroop dots, and visual match.

Groups were narcolepsy subjects, under the high arousal condition, and controls. For both groups, scores represented performance measures at the second testing session, and practice effects were therefore considered equated between groups.

The calculated discriminant function was not statistically significant with a $\underline{x}^2$ (3) = 0.25, $\underline{p}$ >.05. Thus the tasks tapping automatic processing do not discriminate between control subjects and narcoleptics at high arousal.

3(ii) Comparative performance on attentional and complex tasks between narcolepsy subjects at low arousal and controls

To evaluate the tasks most sensitive to sleepiness for subjects with narcolepsy, a stepwise discriminant function analysis was performed using the attentional and complex performance tasks as potential predictors of the grouping variables of narcolepsy subjects at low arousal, and control subjects at the first testing session. For both groups performance scores represented the first testing session and were therefore free of practice effects. To meet the criterion of discriminant analysis, that the number of predictor variables be less than the group sample size (Tabachnick & Fidell, 1989), the variables of STM and LTM were excluded from the discriminant analysis, as they demonstrated no clear residual arousal effect (Table 5). The predictor variables included in the analysis were digit symbol, word fluency, PASAT, Stroop colours, complex reasoning and semantic match. The calculated discriminant function was highly significant with $\underline{x}^2$ (3) = 18.36, $\underline{p}$ = .0004. The function accurately classified group membership for 100% of cases. The structure matrix of correlations between predictors and the discriminant function suggests that the best predictors for distinguishing between low arousal narcolepsy subjects and controls were the complex tasks of PASAT (-.47635) and semantic matching (.46395). Narcolepsy subjects at low arousal have decreased performance on the PASAT ($\underline{M}$ = 19.12) compared to controls ($\underline{M}$ =

30.12) and took significantly longer to complete the semantic matching task (M = 105.62 seconds) than controls (M = 78.37 seconds).

4) Comparative performance characteristics under low and high arousal conditions for subjects with narcolepsy

4(i) The impact of fatigue on performance

The previous section has demonstrated that the most powerful discriminator between narcolepsy subjects at low arousal and controls is the PASAT task, a complex experimenter paced processing task. The measure of PASAT performance utilised in the above analysis is the total number of correct responses by subjects across a performance trial. One performance trial for the PASAT involves 60 stimulus items, presented at two second intervals, with each interval recording a correct or incorrect response from the subject. The data therefore allows for the evaluation of the number of performance errors committed across time. The evaluation of changes in cognitive performance as a function of time on task represents a measure of fatigue (Dinges & Kribbs, 1991). To compare the influence of fatigue on performance between narcoleptic subjects and controls the PASAT raw data was regrouped into 12 time blocks. This decision to identify 12 response blocks (each block incorporating five discrete responses and therefore a time period of 10 seconds) was modelled on the early work of Valley and Broughton (1983) who, using a vigilance task, identified performance change in subjects with narcolepsy over such brief time periods.

The mean number of performance errors across the 12 blocks for the four experimental conditions are provided in Table 6. To investigate the trend in performance across time the number of cumulative errors for each experimental group was also calculated and the data included in Table 6.

Table 6

Mean Number of Performance Errors and Cumulative Frequency (cf) Error Rates for the PASAT

		Block number*											
		1	2	3	4	5	6	7	8	9	10	11	12
LAN	$\overline{X}$	2.5	3.5	3	3.5	3.25	3.62	3.75	4.12	3.5	3.12	3.62	3.5
	cf	20	48	72	100	126	155	185	218	246	271	300	328
HAN	$\overline{X}$	0.71	1.85	1.42	2.14	0.71	2.42	2.14	1.14	1.42	1.14	2.14	1.42
	cf	13	27	42	54	72	90	107	127	145	161	186	204
C1	$\overline{X}$	1.12	2.25	2.25	3.12	2.12	3	2.37	3.62	2.5	2.75	2.75	2.62
	cf	9	27	45	70	87	111	130	159	178	200	222	243
C2	$\overline{X}$	0.75	1	1.12	1.37	2	1.5	1.12	1.5	2	1.5	1.87	1.87
	cf	6	14	31	52	69	89	110	132	154	177	196	217

* A block represents 5 discrete responses

The cumulative error data from Table 6 was plotted to identify comparative error rates on the PASAT across time between LAN and C1 subjects (Figure 11) and HAN and C2 subjects (Figure 12).

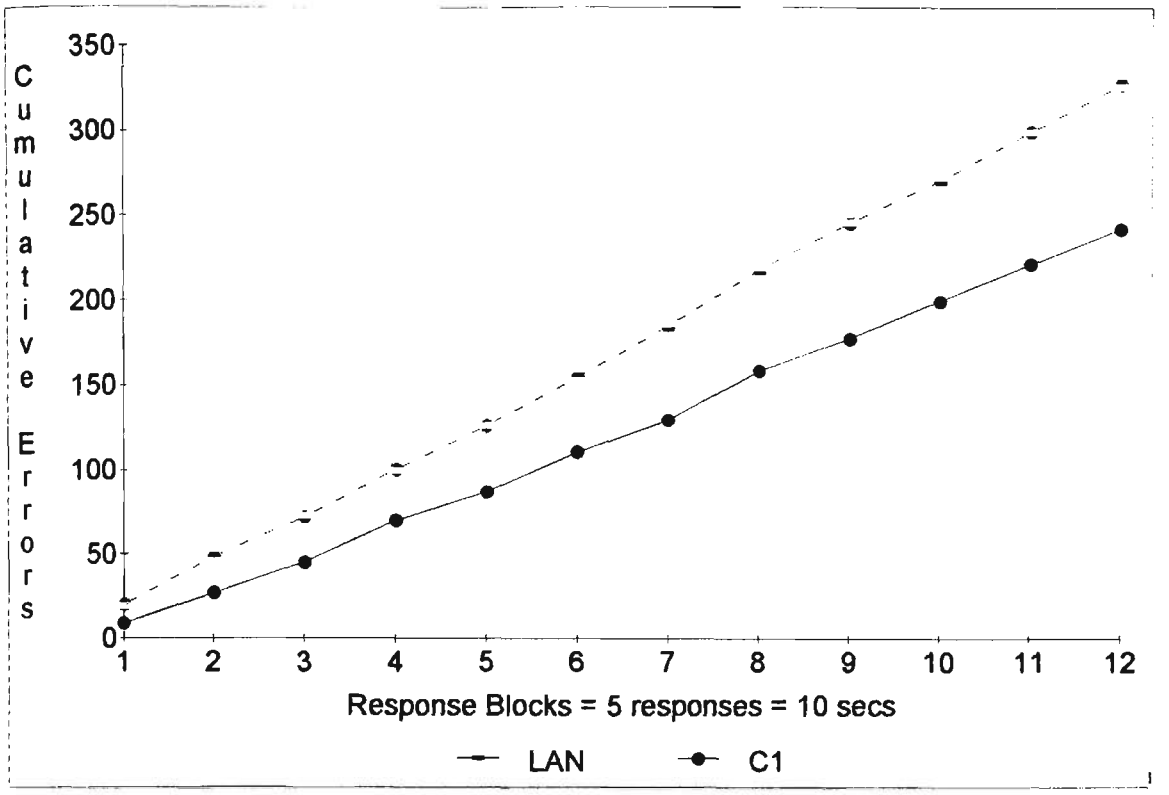


Figure 11. Cumulative errors of LAN and C1 subjects

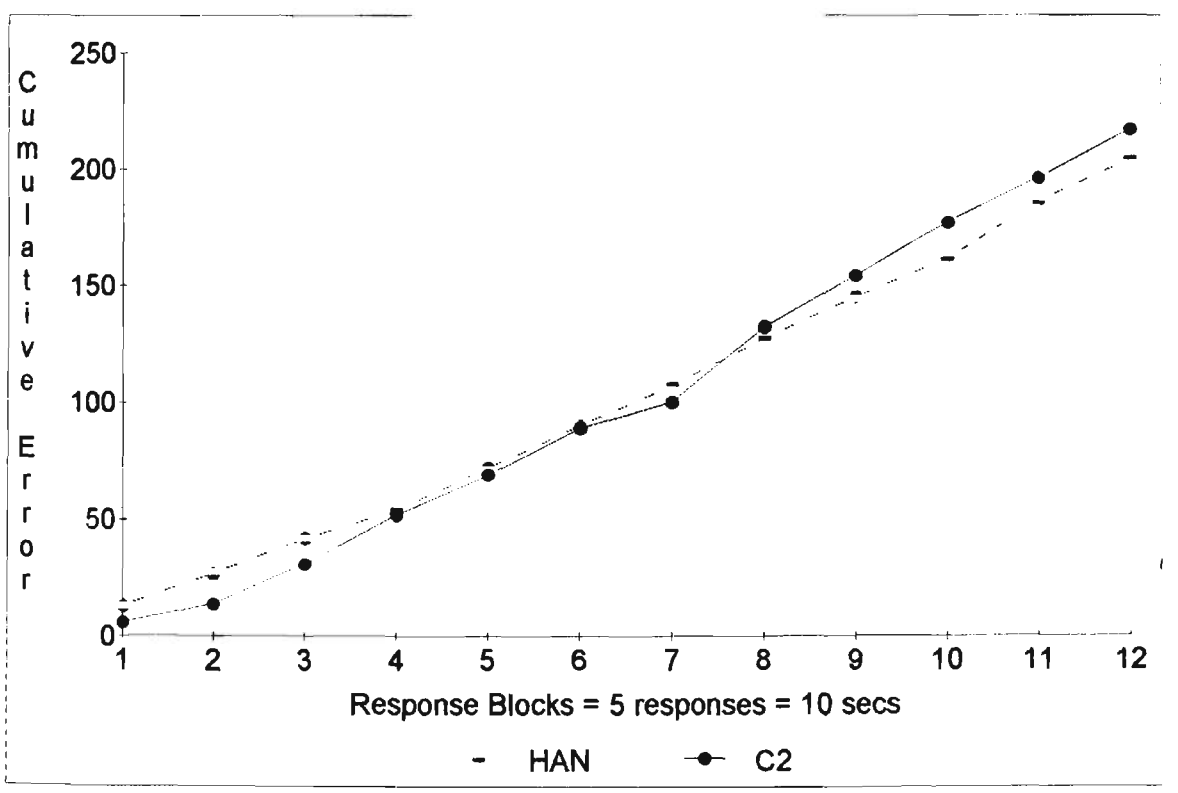


Figure 12. Cumulative errors of HAN and C2 subjects

Visual analysis of the data presented in Figures 11 and 12 identifies approximately linear relationships for all experimental groups. This linear trend indicates a constant relationship between time on task and the number of performance errors, suggesting that for the twelve time blocks in this brief two minute task, the increase in error rate remained constant across time. No fatigue effects appear therefore to impact on PASAT performance for any of the experimental groups.

The identification of linear relationships between the variables of the number of performance errors and response blocks allows for the t-test comparison of these variables between LAN and C1 subjects, and HAN and C2 subjects. The mean number of performance errors per time block for LAN subjects equals 3.41 (SD = .41) and for C1 subjects equals 2.54 (SD = .62). T-test analysis of the significance of these mean differences identifies a highly significant effect, $t(11) = 8.35$, $p = .000$. No significant difference, however, is noted between mean performance errors for the HAN ($M = 2.13$, $SD = .44$) and C2 ($M = 2.25$, $SD = .68$) groups; $t(11) = -0.63$, $p = .54$. These results, taken together with the visual analysis of Figures 11 and 12, indicate that a significant yet constant difference in the number of performance errors for each time block exists between LAN subjects and their comparative C1 group. In other words the performance decrement in narcoleptics remains stable and low arousal does not increase the *rate of performance decline* relative to control subjects across the PASAT performance task.

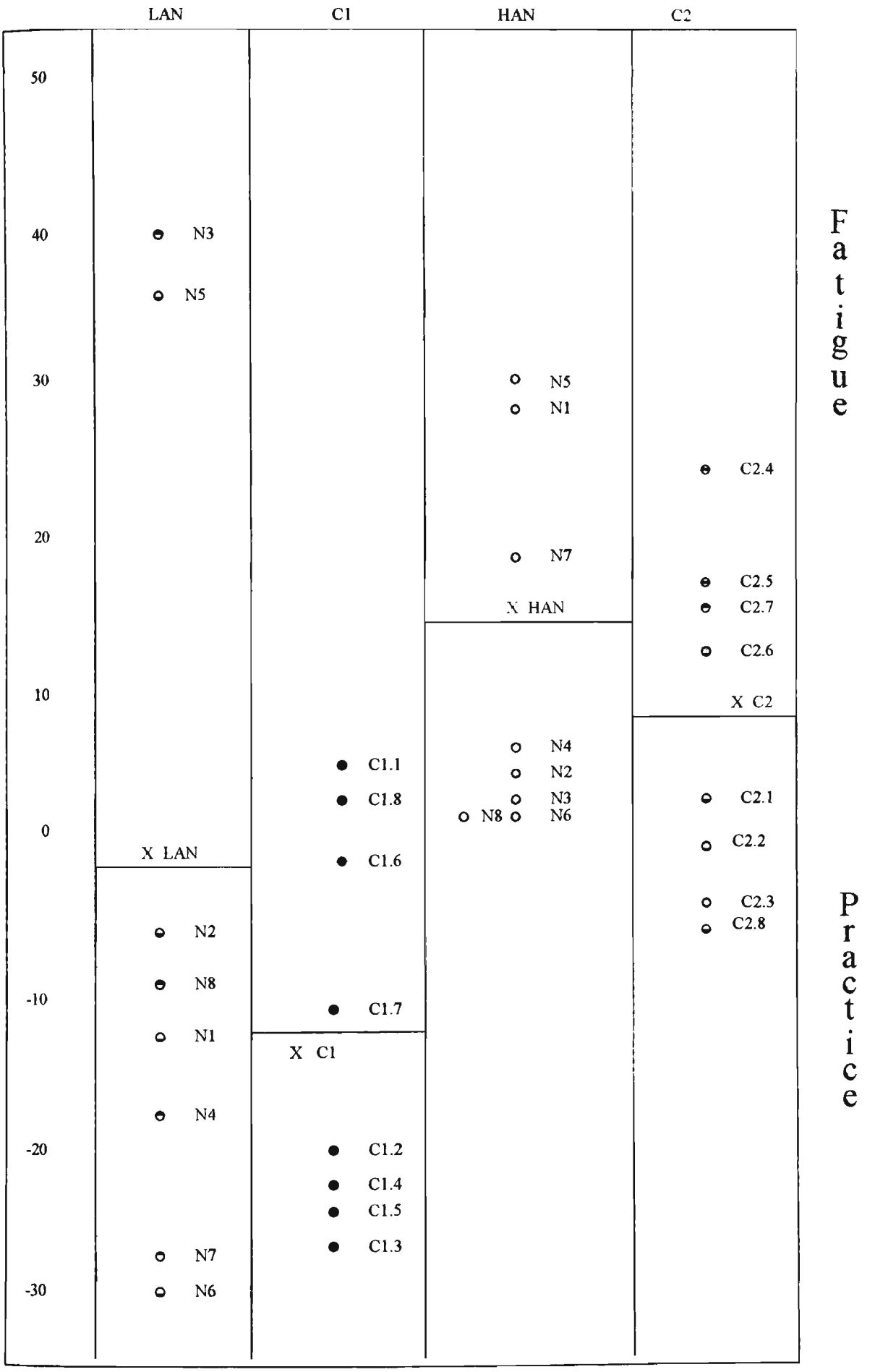
The measure of fatigue as defined by the cumulative error rate on the PASAT task represents a fatigue measure across a complex processing task. The D2 concentration endurance task, which represents an attentional processing task, also incorporates a fatigue score. The D2 task requires the identification of critical stimulus figures embedded in a series of distractor figures. Fourteen trials of the task are completed by each subject, with a limited

time period for each trial (refer Chapter 6 for full details of the task). The total number of items scanned and the number of performance errors across each trial are calculated. The fatigue score, (described in Chapter 6) represents the difference between the total number of correctly scanned items across the first four trials (T1) minus the number of correctly scanned items across the last four experimental trials (T2) (Spreen and Strauss, 1991). Positive difference scores, indicating a higher score for total correct across the first four trials in comparison to the last four trials, suggest fatigue across the task. Negative difference scores represent a performance increment across the task.

Table 4 provides the mean and standard deviation D2 fatigue scores for the four experimental groups. Visual analysis of this data indicates that both LAN and C1 subject groups demonstrated a practice effect across the D2 task (negative mean fatigue scores) whilst the HAN and C2 groups both experienced a fatigue effect (positive mean fatigue scores). Dependent t-test analyses of the difference in mean fatigue scores between experimental groups, at each testing session, demonstrate no significant effects for fatigue. For HAN subjects $\underline{M}$ = 14.62, $\underline{SD}$ = 17.76 and for C2 subjects $\underline{M}$ = 7.12, $\underline{SD}$ = 10.72 [$\underline{t}(7)$ = - 1.05, $\underline{p}$=.33]. For LAN subjects $\underline{M}$ = - 3.62, $\underline{SD}$ = 26.76 and for C1 subjects $\underline{M}$ = - 12.75, $\underline{SD}$ = 11.62 [$\underline{t}(7)$ = -.73, $\underline{p}$ = .49].

The finding of no significant difference in D2 fatigue measures between LAN and C1 subjects is an unexpected finding in view of the apparently large differences in mean fatigue measures (LAN $\underline{M}$ = - 3.62 cf C1 $\underline{M}$ = - 12.75. Note - negative fatigue scores represent practice effects i.e. controls demonstrated an apparently higher mean practice score than low arousal narcoleptics). Visual analysis of the descriptive statistics for the D2 fatigue measure presented in Table 4 indicates that for the LAN group the mean fatigue score has an apparently large standard deviation score ($\underline{SD}$ = 26.76) in comparison to both the HAN

standard deviation (SD = 17.76) and the C1 (SD = 11.62) and C2 (SD = 10.72) measures. To clarify the source of this variability, as indexed by the standard deviation measures, all individual data points for the fatigue measure were plotted for the four experimental groups. This data is presented in Figure 13.


LAN
C1
HAN
C2
50
40
30
20
10
0
-10
-20
-30
N3
N5
N2
N8
N1
N4
N7
N6
X LAN
C1.1
C1.8
C1.6
C1.7
X C1
C1.2
C1.4
C1.5
C1.3
N5
N1
N7
X HAN
N4
N2
N3
N8
N6
C2.4
C2.5
C2.7
C2.6
X C2
C2.1
C2.2
C2.3
C2.8
Fatigue
Practice

Visual analysis of the individual fatigue measures plotted in Figure 13 demonstrates that the high standard deviation score associated with the low arousal fatigue measure occurs as a consequence of the extreme scores for subjects N3 and N5. The effect of these extreme scores is to skew the LAN fatigue measure in a negative direction and therefore increase the mean LAN score. Without these two extreme scores the LAN fatigue measure would more closely approximate the C1 fatigue mean suggesting that the group trend for LAN subjects on the D2 fatigue factor is similar to the fatigue measure for the C1 comparison group. It is difficult to explain the extreme scores observed in the low arousal condition for subjects N3 and N5, though analysis of these subjects' low arousal VAS scores (the VAS scale range is 0 - 100) scale range indicate that both N3 and N5 have mean low arousal scores (N3 = 9.0; N5 = 8.9) that fall well below the group LAN mean of 27.35. Subjects N3 and N5 therefore considered themselves sleepier following the low arousal manipulation than the LAN reference group and this increase in perceived sleepiness may account for the observed increase in fatigue measures for these subjects on the D2 task.

4(ii) The comparative stability of performance for subjects with narcolepsy under low and high arousal conditions

To compare performance stability for subjects with narcolepsy under conditions of low and high arousal performance fluctuation was measured using the D2 concentration endurance task. The task incorporates a fluctuation score which is calculated as the difference between the highest trial score and the lowest trial score across the fourteen performance trials for each subject. The mean D2 fluctuation scores (as provided in Table 4) across the four experimental conditions are: HAN: $\underline{M}$ = 12.37, $\underline{SD}$ = 3.42; C2: $\underline{M}$ = 11.25, $\underline{SD}$ = 3.37; LAN: $\underline{M}$ = 16.12, $\underline{SD}$ = 4.63; C1: $\underline{M}$ = 13.25, $\underline{SD}$ = 5.00. Dependent t-test analysis of the difference in mean fluctuation scores between LAN and HAN conditions for

subjects with narcolepsy identifies a highly significant within subject effect $t(7) = -4.36$, $p = .003$. However dependent t-test analysis of the difference in mean fluctuation scores between C1 and C2 conditions indicates no significant within subject effect, $t(7) = 0.86$, $p = .416$.

The lack of a significant difference between fluctuation scores for the control conditions suggests that across the first task presentation control (C1) subjects reached their performance threshold and that the second exposure for controls (C2) to the task was not subject to performance variability i.e. practice on the D2 task does not significantly affect performance variability. The observed difference in mean fluctuation scores between arousal conditions for subjects with narcolepsy therefore suggests that the factor of arousal influences the fluctuation measure, with a significantly greater degree of performance fluctuation under low arousal conditions compared to the high arousal condition.

In line with the results of the Godbout and Montplaisir study (1986) it would be reasonable to predict that, for subjects at low arousal, performance variability would increase with increased task duration and therefore variability measures for long duration tasks would be greater than variability measures for tasks of short duration. To evaluate this prediction covariance matrices were created for the four experimental groups (C1, C2, LAN and HAN) for both short (reaction time, PASAT, Stroop colours, digit symbol) and long duration tasks (complex reasoning, simple reasoning, semantic match, and physical match). To test the hypotheses of common covariance matrices between C1 and C2 for short and long duration tasks, and LAN and HAN for both short and long duration tasks, the Box MC^{-1} statistic was calculated for each of the comparisons. This statistic is provided as a measure of the equality of covariance matrices in Morrison (1976) who reports that the calculated measure MC^{-1}, which when used as a test of variability, varies as a chi square distribution and the significance

of this statistic is therefore measured against the critical chi squared value. For this data set the critical chi value for alpha set at 0.01 with 10 degrees of freedom is equal to 23.2.

Calculated MC^{-1} values for each of the four comparative matrices are presented in Table 7.

Table 7

MC^{-1} Values Comparing Performance Variability for Long and Short Duration Tasks

	C1 Vs C2	LAN Vs HAN
Long duration tasks	13.90 ns	11.29 ns
Short duration tasks	9.56 ns	25.14 $p<0.01$

The statistics presented in Table 7 demonstrate that repeat testing for control subjects was not associated with any significant difference in performance variability for either the short or long duration performance tasks i.e. practice on these tasks does not influence performance variability. In contrast to the predicted result the transition between low and high arousal conditions was not associated with any significant difference in performance variability for the long duration tasks. For tasks of short duration, however, a significant difference in variability was demonstrated between low arousal and high arousal conditions. The absence of a significant effect between control (C1 and C2) variability across these short duration tasks suggests that this difference in variability occurs as a function of the arousal manipulation.

In order to determine whether HAN or LAN conditions were associated with the increase in variability the relevant standard deviation scores were examined. These scores are provided in Table 8.

Table 8

SD Scores for Short Duration Tasks

	Digit symbol (total)	PASAT (total)	Reaction time (secs)	Stroop colours (secs)
LAN	4.17	10.33	0.17	11.16
HAN	5.12	7.55	0.11	7.74
HAN < LAN	No	Yes	Yes	Yes

Visual analysis of these scores indicates that for three of the four short duration tasks conditions of low arousal were associated with increased performance variability. The statistical significance of this visual trend has been validated using the covariance matrices reported in Table 7.

4(iii) The comparative nature of performance errors between high and low arousal conditions across both subject and experimenter paced tasks.

Performance tasks can be classified as either subject paced (where the subject is able to determine the time taken to respond to the stimulus item) or experimenter paced (where a predetermined period exists between presentation of stimulus items and the subject is therefore required to respond within a limited time frame). Performance errors can also be classified as either errors of omission where subjects simply fail to respond to the stimulus item or errors of commission where subjects provide an incorrect response to the item. For subject paced tasks respondents are able to decide between the performance outcomes of speed or accuracy. Experimenter paced tasks do not allow subjects to compensate for increased task demands by extending the time on task and therefore forced errors may be either of omission or commission.

Subject paced performance tasks

The Stroop task is a subject paced performance task which comprises two performance trials with each trial involving an increased cognitive load (refer Chapter 6 for full details of the task). The task therefore provides an opportunity to evaluate the performance strategies utilised by the experimental groups in response to increasing cognitive load across trials.

No performance errors occurred across the experimental task for any of the subject groups. Where errors in response occurred, all subjects corrected their answer before continuing with the next response. Clearly, for this brief performance task, all subjects maximised their response accuracy, even under conditions of low arousal, in preference to maintaining response speed.

Experimenter paced performance tasks

The D2 concentration endurance task was analysed to evaluate the nature of performance errors for an experimenter paced performance task. Scoring of the task allows for the calculation of the total number of items scanned within a specified time and the evaluation of performance errors as either errors of omission (miss) or errors of commission (false positives). Table 9 provides a summary of these measures for the four task conditions.

Table 9

Descriptive Statistics and T-test Comparisons on D2 Error Types

					Dependent t-test analyses (df = 7)			
	C1	C2	LAN	HAN	(C1 Vs C2)	(LAN Vs HAN)	(C1 Vs LAN)	(C2 Vs HAN)
$\overline{X}$ D2 total scanned	463.62	517.87	441.75	545.25	t = -4.79 p = .002	t = 6.68 p = .00	t = 0.73 ns	t = -1.46 ns
$\overline{X}$ D2 omission errors	17.75	19.87	37.25	39.62				
$\overline{X}$ D2 false positives	1.25	2.25	3.62	0.87				
$\overline{X}$ E% percentage errors[1]	4.06	4.20	8	7				
					Wilcoxon signed rank test			
Median E%	3.7	4.15	2.7	3	z = -0.84 ns	z = -1.12 ns		
ns								

[1] $E\% = \frac{100 \times E \text{ (total no of errors}}{TS \text{ (total no scanned)}}$

Dependent t-test analyses of the difference in total number of items scanned demonstrates that for both control and narcoleptic subjects the second trial of the D2 task (C2 and HAN) was associated with a significant increase in the total number of items scanned in relation to the first task trial (C1 and LAN). The significance of the increased number of items scanned by subjects with narcolepsy under high arousal conditions therefore remains confounded by the strength of the practice effect. No significant difference in number of items scanned was noted however between the LAN and C1 subjects indicating that even at low arousal subjects with narcolepsy are able to maintain their processing speed for brief attentional tasks.

Visual analysis of the summary data relating to the nature of performance errors (Table 9) indicates a clear trend for both narcoleptic and control subjects to miss correct target stimuli (omission errors) rather than to identify false positive items. Whilst omission errors appear highly inflated for narcoleptic subjects (LAN $\underline{M}$ = 37.25; HAN $\underline{M}$ = 39.62) compared to controls (C1 $\underline{M}$ = 17.75; C2 $\underline{M}$ = 19.87) this mean score for narcoleptic subjects is negatively skewed, once again, as a consequence of extreme scores occurring for individual narcoleptic subjects. The extreme scores for the narcoleptic subjects appear attributable to the performance of subject N6. Similarly for identification of false positive errors subject N6 again distorts the data set with 28 false positive errors. Only one other false positive score occurs across all LAN subjects. Because of the existence of extreme scores within the data set Table 9 also provides the calculated median error rates for the four experimental groups and visual interpretation of these median scores suggests minimal differences between number of errors across the four experimental groups. The analysis of potential statistically significant differences between number of errors under the four subject conditions was evaluated using the Wilcoxon signed rank test. This non parametric analog of the dependent t - test evaluates group differences as a function of data rankings and therefore remains independent of the

mean statistic. Using the Wilcoxon, no significant differences occurred in the total number of performance errors between either C1 and C2 ($\underline{Z}$ = -.84, ns) or LAN and HAN subjects ($\underline{Z}$ = - 1.12, ns).

4(iv) The comparative capacity for phasic arousal under manipulated conditions of high and low arousal.

To determine whether narcoleptic subjects at low or high arousal differ from control subjects in their ability to respond to increasing cognitive load, performance was compared between narcoleptic and control subjects across two conditions of the Stroop task. Chapter 6 provides a detailed analysis of the Stroop task which for this study consisted of two levels of cognitive load. Stroop dots representing an automatic task and Stroop colours a complex processing task. The difference in response time between the colour and dots (colour - dots) conditions will be used in this analysis as a measure of the difference in response latency between automatic and complex processing demands.

The Stroop task is dependent on colour identification and as one of the narcoleptic subjects (N6) was colour blind the data analysis excluded this subject and their matched control (C6). Table 10 presents the mean performance scores for the Stroop dots and colour conditions in addition to the change in response times for all subject groups between the two cognitive load conditions.

Table 10

Comparative Measures of Phasic Arousal Associated with Increasing Cognitive Load

					Dependent t-test analyses (df = 6)			
	C1	C2	LAN	HAN	(C1 Vs C2)	(LAN Vs HAN)	(C1 Vs LAN)	(C2 Vs HAN)
$\overline{X}$ dots	13.71	13.04	15.0	13.07				
$\overline{X}$ colours	33.20	25.67	34.14	27.4				
$\overline{X}$ colours-dots	19.50	12.62	19.14	14.32	t = .09 ns	t = -2.54 p = 0.04	t = 2.52 p = 0.04	t = -0.048 ns

Dependent t-test analyses of the mean change scores across experimental conditions demonstrates no significant effect at the 0.01 level of significance (using Bonferroni's adjustment criterion) indicating that under conditions of low arousal subjects with narcolepsy are able to increase their processing capacity at a similar rate to control subjects to meet the demands of increased cognitive load. It is, however, relevant to note that significance may have been achieved with a larger experimental group.

Summary

This chapter has presented the findings associated with the impact of the manipulation of arousal on cognitive functioning in narcolepsy. An analysis of the theoretical aspects of these findings, and their relationship with the current literature on the impact of sleepiness on performance for narcoleptic subjects, will be addressed in Chapter 9. Chapter 8 of this thesis will replicate aspects of the methodology of this first study to evaluate the comparative impact of 32 hours of sleep deprivation on performance for non pathological sleepers. The thesis author has chosen to combine the discussion of the results of these two experimental chapters to highlight both the commonalities and differences between the impact of sleepiness on performance for pathologically sleepy narcoleptic subjects and non pathologically sleepy subjects whose sleepiness is secondary to sleep deprivation. A discussion of the methodological issues relevant to all experimental procedures utilised in this thesis will be addressed in Chapter 11.

CHAPTER 8

Study Two

Introduction

Chapter 5 of this thesis provided a theoretical framework for the analysis of the relationship between sleepiness and performance for subjects with narcolepsy. Based on an adaptation of the theoretical model of sleepiness proposed by Horne (1988a), specific aspects of sleepiness for subjects with narcolepsy were investigated. In particular, Study 1 evaluated the effect of the manipulation of narcoleptic sleepiness levels on performance across a range of cognitive tasks, estimating the percentage impact of sleepiness induced changes on performance levels, and evaluating the cognitive nature of performance tasks most sensitive to this sleepiness effect. Study 1 also investigated additional aspects of cognitive function for subjects with narcolepsy that were potentially affected by sleepiness. These included the nature of performance errors associated with sleepiness, the impact of fatigue on performance, the capacity for phasic arousal under conditions of induced sleepiness, and the comparative stability of performance measures between low and high arousal conditions.

An interesting question to emerge from this characterisation of sleepiness induced cognitive changes for subjects with narcolepsy is the extent to which these changes reflect sleepiness induced cognitive changes in sleep deprived controls. Are the observed performance decrements associated with narcoleptic sleepiness specific to narcolepsy or do they reflect more general aspects of performance change associated with daytime sleepiness? As narcolepsy is described as a condition of excessive daytime sleepiness, the observed changes in performance may vary only quantitatively from those experienced by sleep

deprived non narcoleptic subjects. Alternatively secondary aspects of narcolepsy may lead to a qualitatively different relationship between sleepiness and performance in this clinical group.

Comparative analyses of performance outcomes in sleep deprivation research are confounded by a multitude of methodological factors (refer Chapter 3), with perhaps the most complex confound being the differential sensitivity of particular performance tasks to sleep deprivation. Aspects of task duration, neuropsychological complexity and intrinsic interest have been cited as impacting on performance outcomes (Johnson, 1982). Chapter 3 of this thesis has introduced these factors as limiting comparative analyses of sleep deprivation research and Chapter 11 will reexamine these factors in more detail. The implication, however, of this differential task sensitivity for the current study is that analyses of the findings from the narcolepsy research cannot be clearly compared with the published sleep deprivation research. To provide a comparative analysis of sleepiness induced performance deficits between narcoleptic and sleep deprived controls the current study therefore utilised selected performance tasks from Study 1.

The principal methodological aim of this study is consequently to induce a level of sleepiness in normal sleepers that equates with the level of sleepiness of narcoleptic subjects in the previous study. If a matched level of sleepiness can be induced in controls by sleep deprivation, then this study aims to evaluate the implications of this sleepiness on cognitive performance. Specifically this study will utilise the cognitive tasks demonstrated in the previous study to be most sensitive to narcoleptic sleepiness across the three cognitive domains of automatic, attentional and complex processing tasks (refer Table 5).

In addition, the comparative impact of a twenty minute nap for narcoleptic and sleep deprived controls can be evaluated to determine the impact of this nap period on both arousal and cognitive factors.

Method

Subjects

Sixteen subjects participated in the study responding to advertisements placed around the Victoria University campus. Eight subjects undertook the sleep deprivation component of the study and eight subjects acted as controls. Despite the payment of $50.00 for participation in the sleep deprivation component of the study, recruitment of subjects was extremely difficult. To increase both the external validity of the study and the compatibility of this study with the previously reported narcoleptic subject group the experimenter aimed to recruit an experimental group that was not comprised of typically young (18-21 year old) undergraduate students. Advertisements for participants therefore targeted mature age students. Control subjects were matched to the sleep deprived subjects using the same criteria as described in study 1, i.e. matching variables were age (within an arbitrarily defined seven year range), IQ (within a 95% confidence interval as measured with the K-Bit brief intelligence task) and gender. Neither sleep deprivation or control subjects reported any sleeping difficulties, nor were they on any medications at the time of the study. The demographics of the final subject groups are described in Table 11.

Table 11

Characteristics of Sleep Deprivation and Control Subjects

Subject	Gender	Age	IQ
Sleep Deprivation			
1	F	39	83+/-6
2	F	30	90+/-6
3	F	34	80+/-6
4	M	40	121+/-6
5	F	26	127+/-6
6	F	26	122+/-6
7	F	26	108+/-6
8	M	23	106+/-6
Control			
1	F	41	90+/-6
2	F	29	96+/-6
3	F	39	82+/-6
4	M	47	115+/-6
5	F	33	121+/-6
6	F	23	116+/-6
7	F	23	98+/-6
8	M	22	108+/-6

Ethical Considerations

Consent to undertake the study was obtained from the Victoria University Human Ethics Committee. Prior to participation the experimental protocol was explained to all subjects and they signed a consent form. Because of the nature of the study, all sleep deprived subjects were carefully monitored over the duration of the experiment and were driven home at the conclusion of the experiment.

Performance Tasks

Performance tasks for the sleep deprivation study were selected from the task battery utilised in experiment 1. The tasks most sensitive to arousal manipulation for each of the three cognitive categories of automatic, attentional and complex tasks were incorporated in the current study. These tasks were the Stroop dots task, the D2 concentration endurance task and the PASAT (refer Table 5). As the Stroop dots is a component of the overall

Stroop task the entire task was utilised in the current study. Full details of these tasks are provided in Chapter 6.

Experimental Design

Duration of sleep deprivation

Reported sleep deprivation studies incorporate a diverse range of methodologies with periods of deprivation ranging between 24 and 264 hours (Babkoff, Caspy, Mikulincer and Sing, 1991). As no estimates exist in the literature of the quantitative relationship between narcoleptic sleepiness and sleepiness secondary to sleep deprivation in normal sleepers the duration of sleep deprivation induced in the current study was selected on theoretical grounds. For this thesis the theoretical aspects of the evaluation of sleepiness and performance have been grounded primarily in the work of Horne (1988a). At some critical level of sleep deprivation, Horne argues, decrements secondary to sleep deprivation cannot be reversed by increased attentional effort but are contingent on sleep as a restorative process. The previous chapter on sleepiness and performance in narcolepsy demonstrated clear performance decrements for complex processing tasks under low arousal conditions and the aim of the current study was therefore to create a "matched" sleep deprivation environment to evaluate the comparative effects of sleepiness on performance for non pathologically sleepy subjects.

Horne (1988a) investigated the impact of sleep deprivation for normal sleepers on the capacity to perform complex thinking tasks and demonstrated that a period of 32 hours without sleep resulted in significant impairments in complex thinking tasks. This minimal period of 32 hours was therefore seen as an appropriate matching period for sleep deprived subjects.

Pilot study

Initially it was intended to arbitrarily extend the study protocol beyond the 32 hours identified by Horne (1988a) to a 36 hour deprivation period. Subjects were to be woken at 6am of day 1 of the study and it was felt that the protocol could be extended to 6pm on day 2 of the study. An initial pilot study (n=2) utilised this 36 hour deprivation period. Following the 36 hour deprivation period, pilot subjects were tested on the three performance tasks and then allowed to sleep for 20 minutes prior to repetition of the tasks. The pilot study indicated, however, that subjects were unable to sleep at 6pm even following the 36 hour deprivation period. The early evening has been demonstrated to be associated with a period of minimal sleep propensity (Borbély, 1982; Lavie, 1986) and this circadian barrier to sleepiness appeared, in the pilot study, to override the sleepiness induced through 36 hours of sleep deprivation. As extending the deprivation period beyond this circadian barrier could potentially result in diminished subject compliance (which presents as a major difficulty in sleep deprivation research) the circadian confound was overcome by decreasing the deprivation duration back to the 32 hours demonstrated by Horne (1988a) to be sensitive to complex cognitive function.

This 32 hour deprivation period resulted in performance testing falling at 2pm, a time consistently reported in the circadian and ultradian literature as associated with a "window" enhancing sleep initiation (Borbély, 1982; Lavie, 1986).

Procedure

Sleep deprivation subjects were woken by telephone at 6am on day one of the study. They were instructed to remain awake for that day and to abstain from alcohol, nicotine and caffeinated drinks across the duration of the day. Apart from these restrictions subjects were

free to engage in normal activities across that day. At 8pm on day one of the study sleep deprivation subjects reported to the sleep laboratory at Victoria University. Subjects were tested in pairs. Overnight the subjects were free to engage in any activities they chose which included personal work, playing computer games or watching videos. The subjects remained in the laboratory area overnight and the following morning, to allow for observation by the experimenter and ensure that no naps occurred.

At approximately 2pm on day 2 of the study subjects were tested on the three performance tasks of Stroop, D2 concentration endurance and PASAT. The testing protocol took approximately twenty minutes which provided a matched testing duration to that of the narcoleptic subjects in study 1. Matching the duration of testing to the previous study was required to eliminate the possibility of differential fatigue effects confounding the comparison of findings between studies 1 and 2. To overcome the additional potential confound of order or carryover effects influencing performance outcomes for Study 2, the order of presentation of the three tasks was randomised.

Following this initial testing session subjects were given the opportunity to sleep. The sleep period was monitored using the polysomnograph and subjects were awoken after 20 minutes of EEG defined sleep. All subjects were able to sleep during this period with time in bed ranging from approximately 25 to 45 minutes. Two subjects declined permission for the polysomnograph and they were permitted a 30 minute opportunity to sleep with wrist actigraphs attached. The occurrence of sleep during this period was validated retrospectively with the actigraph measures and subjective reports by the subjects.

Following the nap, in line with the protocol utilised in study 1, subjects were given a five minute refractory period prior to recording VAS measures and repeat cognitive testing.

Again test order was randomised and an alternate version of the Stroop task was utilised. Following this second test period subjects were transported home.

In addition to the cognitive performance testing sessions described above subjects completed the VAS subjective sleepiness measure every hour from 11pm on day 1 to 2pm on day 2, and then again at between 3pm and 4pm following the twenty minute nap period (full details of the VAS were reported in Chapter 6).

Baseline performance measures across the three tasks were recorded at a third testing session scheduled between three and five days post the deprivation period. The timing of this baseline measure was matched to the prenap measure (i.e. baseline testing occurred between 2-3pm) to minimise circadian confounds.

Control subjects for the study also completed the three tasks at three testing sessions. Again to minimise circadian confounds the first test session for control subjects was undertaken at 2pm and repeated thirty to sixty minutes later. The third testing session was completed, as for the sleep deprived subjects, between three and five days later. To match potential controls with sleep deprived subjects on IQ, the K - Bit scale was completed prior to the first testing session.

Results

SPSS for Windows was used for all analyses. Where multiple analyses have been undertaken the alpha criterion has been adjusted from .05 using the Bonferroni adjustment.

Nomenclature and Abbreviations

Both sleep deprived and control subjects undertook three testing sessions. These sessions will be identified using the following abbreviations in the results section.

PreN: Pre nap - this testing session represents pre nap scores for the subjects following 32 hours of sleep deprivation.

PostN: Post nap - this testing session represents the scores for the sleep deprived subject group following their 20 minute nap.

B: Baseline - the scores for the sleep deprived subjects recorded 3-5 days post the deprivation study.

C1: Control 1 - testing session one for the control group.

C2: Control 2 - testing session two for the control group measured 30 to 60 minutes post the C1 session.

C3: Control 3 - testing session three for the control group measured 3-5 days post the C2 session.

Arousal Manipulation and Measures

As with the arousal manipulation for the narcoleptic subjects (described in study 1), the sleep deprivation period in the current study aimed to establish a low arousal testing condition. The initial VAS subjective sleepiness measure (recorded at 11pm) for the current study will be identified as the high arousal sleep deprivation measure (*SDHA*) and the prenap condition following 32 hours of sleep deprivation will be identified as the low arousal sleep deprivation period (*SDLA*). These testing conditions are compared to the high (*HAN*) and low (*LAN*) arousal manipulations for the narcoleptic subjects.

Figure 14 provides a visual analysis of the distribution of mean VAS arousal scores across the deprivation period. A measure of post nap arousal was also recorded and the mean post nap arousal measure is also displayed.

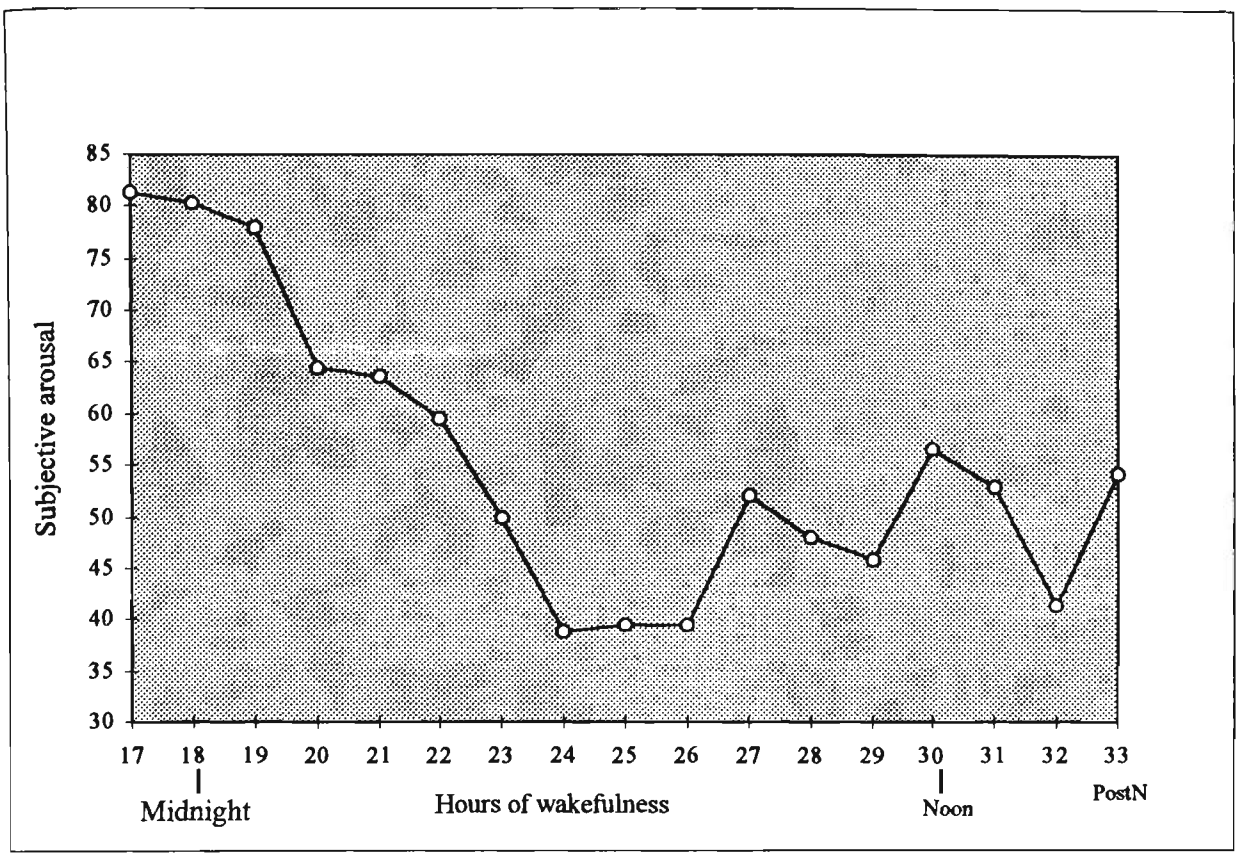


Figure 14 Mean subjective arousal measures across the sleep deprivation period.

Visual analysis of the data provided in Figure 14 suggests that for these subjects a gradual decrement in subjective arousal occurred across the night, stabilising at the lowest point between 6am and 8am of the second day. Subsequently between the hours of 8am to 12 midday on this second day an increment in arousal occurred which dropped, as theoretically predicted, across the post lunch period between 12 midday and 2pm.

Figure 15 demonstrates the comparative change in low to high VAS arousal measures for both narcoleptic and sleep deprived subjects.

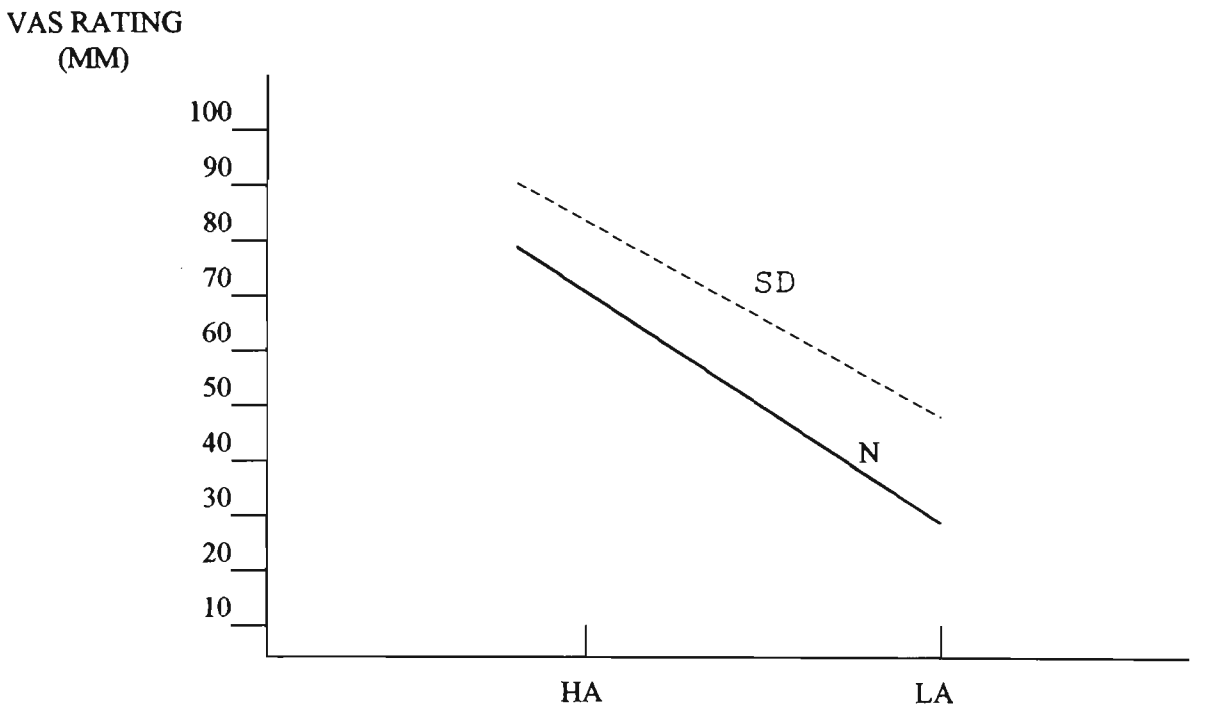


Figure 15 Comparative high to low VAS arousal change for narcoleptic (N) subjects (Study 1) and sleep deprived (SD) subjects (Study 2).

Whilst baseline cognitive testing occurred between 3 and 5 days following the sleep deprivation protocol this study utilised the 11pm VAS rating for subjects as the comparative high arousal sleepiness rating. This decision to utilise the 11pm VAS rating prior to the sleep deprivation manipulation as the high arousal VAS rating rather than a subsequent rating associated with baseline testing 3 - 5 days later was based on the following considerations:

(a) The emphasis for Study 1 was not on absolute scale values but rather on the efficacy of the manipulation in facilitating a significant change in arousal. As the manipulation of the sleep deprived subjects also focussed on changing arousal levels this change was measured pre (11pm/day 1) and post (2pm/day 2) the deprivation methodology.

(b) The continuous monitoring of subjective sleepiness states across the deprivation period was seen to increase the face validity of the subjects' frame of reference in

relation to their subjective monitoring of arousal states between the 11pm and 2pm ratings. In addition, post-hoc visual analyses of sleepiness levels across the deprivation period (see Figure 14) indicates that the 11pm initial rating was clearly the maximum arousal point for the study with a mean arousal rating of 81.37 across the 100mm scale.

Furthermore, if this 11pm rating underestimates the baseline sleepiness level, then conclusions relevant to the interaction between sleep deprivation and performance would be subject to type 2 rather than type 1 errors. Use of this measure as the high arousal (baseline) sleepiness rating was therefore seen as a conservative estimate of high arousal subjective sleepiness.

Table 12 provides the means, standard deviations, and t-test analyses of the significance of both the sleep deprivation arousal manipulations in the current study, and the comparative analysis of this study with the narcoleptic subjects' manipulation utilised in study 1. T-test comparisons also evaluate the significance of the change in arousal for sleep deprived subjects from the pre to post nap condition.

Table 12

Analyses of Comparative Arousal Manipulations both Within the Sleep Deprivation Protocol and between the Sleep Deprivation and Narcoleptic Protocols
(Arousal Key SDHA = Sleep Deprivation High Arousal , SDLA = Sleep Deprivation Low Arousal, HAN = High Arousal Narcolepsy, LAN = Low Arousal Narcolepsy)

Comparative arousal conditions					
	Condition 1 Vs	Condition 2	t	df	p
	SDHA	SDLA	dependent		
$\overline{X}$	81.37	41.25	4.83	7	.002
SD	16.92	27.84			
	SDHA	HAN	independent		
$\overline{X}$	81.37	74.73	-.94	32	.352
SD	11.92	17.54			
	SDLA	LAN	independent		
$\overline{X}$	41.25	27.34	-1.59	32	.123
SD	27.84	19.62			
	SDLA	SD Post N	dependent	7	.355
$\overline{X}$	41.25	54.12	-.99		
SD	27.84	30.09			
	SDHA-SDLA	HAN-LAN	independent	32	.893
$\overline{X}$	40.12	47.38	.87		
SD	23.49	19.92			

Four major findings emerge from this analysis (a) across the deprivation period (SDHA Vs SDLA) a significant decrease in subjective arousal ratings occurred (this result remains significant at the Bonferroni adjusted alpha level of 0.01); (b) comparison of data from study 1 indicates that both high and low arousal ratings for narcoleptics demonstrate no significant difference in sleepiness ratings between matched high (SDHA Vs HAN) and low (SDLA Vs LAN) arousal ratings for sleep deprivation subjects; (c) comparative evaluation of the change in arousal conditions for narcoleptic and sleep deprived subjects (HAN-LAN Vs SDHA-SDLA) further indicates no significant difference in induced sleepiness levels between

the subject groups, and (d) no significant difference exists in sleepiness ratings measured pre and post nap (SDLA Vs SDPostN) for sleep deprived subjects.

In summary the sleep deprivation manipulation resulted in a significant decrease in subjective arousal ratings and this arousal decrement is statistically equivalent to the arousal decrement experienced by the narcoleptic subjects. However, for the sleep deprivation subjects the 20 minute nap led to no significant change in arousal measures compared to the significant increase in arousal ratings subsequent to the nap for narcoleptic subjects (refer Chapter 7).

Impact of 32 hours of Sleep Deprivation on Performance

The analysis of arousal manipulations has demonstrated that the sleep deprivation protocol resulted in a significant decrease in arousal conditions and that this decrement was comparable, in both absolute, and differential rating terms, to the manipulations in the narcoleptic subject group. This analysis aims to evaluate the impact of this arousal decrement for sleep deprived subjects on selected performance tasks. The performance tasks were the Stroop dots, the D2 concentration endurance task and the PASAT. Descriptive statistics for the three testing sessions of PreN, PostN, and Baseline are provided in the following Table.

Table 13

Summary Statistics of Cognitive Tasks for Sleep Deprived Subjects

Variable		PreN	PostN	B	C1	C2	C3
Stroop Dots							
(secs)	$\overline{X}$	14.88	13.19	12.50	13.70	12.56	12.60
	SD	4.33	1.73	2.41	2.35	2.14	2.04
D2							
(total correct)	$\overline{X}$	464.37	496.38	547.63	520.38	577.63	590.75
	SD	66.24	80.80	70.71	55.56	42.66	36.98
Stroop Colours							
(secs)	$\overline{X}$	23.82	22.31	19.34	24.10	19.15	19.98
	SD	6.26	4.94	3.64	3.00	2.81	1.88
PASAT							
(total correct)	$\overline{X}$	32.50	37.12	39.50	36.38	41.38	43.25
	SD	9.18	9.33	10.89	8.72	5.71	7.92

As sleep deprived subjects undertook three testing sessions (PreN, PostN and B), the change in performance scores potentially include both practice and arousal effects. To control for the practice effect this study again utilised the methodology reported by May and Kline (1987), where measures of change associated with repeated testing are subtracted from overall change parameters and residual performance effects are attributed to arousal. This strategy, which compensates for the effects of practice, was also utilised in Study 1. Potential limitations of this methodology will be discussed in Chapter 9.

To compare the impact of sleep deprivation on performance across the selected tasks PreN scores were compared to baseline measures. As the baseline measure is the third testing session the percentage level of practice was evaluated using the mean percentage difference for each task between the C1 and C3 conditions. For the Stroop task where the outcome measure is scored as a time variable the percentage practice effect was added to the B performance score. For the D2 and PASAT tasks where the outcome variable is the number of correct responses the estimated change due to practice was subtracted from the B

performance score. Table 14 provides a summary of mean performance scores for the PreN and adjusted baseline measures. In addition the table identifies the significance level for comparison of the PreN and adjusted B levels.

Table 14

Analyses of Potential Performance Change due to Sleep Deprivation

Task		Pre N	B	C3-C1 % Practice	Adjusted B	Dependent t-test t(df = 7)	p
Stroop dots	$\overline{X}$	14.87	12.50		13.68		
	SD	4.33	2.41	8	2.31	-.64	.540
Stroop colour	$\overline{X}$	23.81	19.34		23.38		
	SD	6.24	3.64	17	4.56	-.41	.697
D2 Total	$\overline{X}$	464.37	547.63		484.93		
	SD	66.24	70.71	13.5	64.68	1.04	.333
PASAT	$\overline{X}$	32.50	39.50		33.65		
	SD	9.18	10.89	18	9.81	.38	.713

Table 14 demonstrates that, after adjustment of the baseline performance measure to account for practice effects, there is no significant difference in performance for any of the measured cognitive tasks between the PreN and baseline conditions.

Table 15 provides a similar analysis of performance change between the PreN and PostN conditions. This analysis is included for the sake of completeness but, theoretically, no change in performance is predicted as the PreN/PostN manipulation was not associated with a significant change in subjective arousal ratings. A secondary reason for not predicted any performance change between PreN and PostN conditions is that the absence of effect between adjusted baseline and PreN conditions (refer Table 14) suggests that both conditions are associated with optimum performance. PostN conditions would therefore not be expected to yield greater than optimum performance. In addition, the inclusion of a refractory period in the methodology should compensate for any major sleep inertia effects

and therefore PostN conditions would not be expected to demonstrate a reduced performance compared to PreN conditions.

As in the previous analysis the PostN score was adjusted to compensate for practice with the percentage practice score identified as the difference between the C2 and C1 conditions.

Table 15

Analyses of Performance Change between Pre and Post Nap Conditions

Task		PreN	PostN	C2-C1 % Practice	Adjusted Post N	Dependent t-test t(df = 7)	p
Stroop dots	$\overline{X}$	14.87	13.19		14.37		
	SD	4.33	1.73	8	1.65	-.3	.775
Stroop colour	$\overline{X}$	23.81	22.31		24.38		
	SD	6.26	4.94	20	9.84	-.23	.826
D2 Total	$\overline{X}$	464.37	496.38		445.29		
	SD	66.24	80.80	11	76.72	-.77	.466
PASAT	$\overline{X}$	32.50	37.12		32.57		
	SD	9.18	9.33	14	8.45	.03	.978

Table 15 demonstrates that after adjustment of the PostN condition to compensate for practice effects there is no significant difference in mean performance scores between the PreN and PostN conditions.

Results Summary

The 32 hour sleep deprivation manipulation led to a significant decrease in arousal conditions that statistically matched the level of sleepiness across both absolute and differential ratings for the narcoleptic subjects reported in study 1. However, unlike the arousal manipulation for the narcoleptic subjects this arousal change for sleep deprived subjects was not associated with significant decrements on any of the selected performance tasks. Furthermore the nap period of 20 minutes sleep did not lead to any significant

increment in arousal conditions for the sleep deprived subjects and there were no associated changes in performance across the pre and post nap manipulation. The implications of these sleep deprivation findings and their relationship to the reported findings in Study 1 will be discussed in the following chapter.

CHAPTER 9

Theoretical Discussion of Studies One and Two

Research Questions

Chapters 7 and 8 identified specific research questions that would be addressed in the analyses of experimental results of the relationship between sleepiness and performance for both narcoleptic (Chapter 7) and sleep deprived (Chapter 8) subjects. Chapter 7 argued that as this work is largely exploratory, no literature base exists to convert these research questions into specific hypotheses. This discussion section will therefore focus on the research questions identified in Chapter 7 but will combine the findings from studies 1 and 2, resulting in a review of the following four issues:

i) Discussion of the impact of the arousal manipulation on sleepiness for narcoleptic subjects and a comparison of this induced sleepiness with the effects on arousal for normal sleepers consequent to 32 hours of sleep deprivation. As a secondary evaluation the recuperative impact, on arousal, of a twenty minute nap, for both narcoleptic and sleep deprived controls, will be discussed.

ii) The comparative impact of these induced low arousal states for narcoleptic and sleep deprived subjects on performance across automatic, attentional and complex cognitive domains will be discussed and the subsequent impact of the nap period on performance change evaluated.

iii) Aspects of the nature of sleepiness in narcolepsy will be described in an attempt to provide a characterisation of sleepiness in this clinical population. In particular

aspects of fatigue, performance stability, performance errors and the capacity for phasic arousal will be evaluated.

iv) Finally, this chapter will evaluate the implications of the observed sleepiness and performance interactions for both narcoleptic subjects and sleep deprived controls within the theoretical model of sleepiness proposed by Horne (1988b).

The focus of this discussion chapter is therefore on an evaluation of the theoretical issues relevant to the results of studies 1 and 2. Chapter 10 will include a discussion of the findings from study 3 which involved a metacognitive analysis of memory performance in narcolepsy. Chapter 11 will integrate the findings from the three studies in addition to providing a more general discussion of methodological factors relevant to this thesis.

The Manipulation of Arousal

Study 1: Narcolepsy

Study 1 aimed to explore the impact of sleepiness on performance for subjects with narcolepsy in an experimental setting that allowed for the expression of the behavioural states of sleepiness and non sleepiness. Low arousal conditions were induced by both withdrawing subjects from stimulant medication, if applicable, and exposing them to an environment that has been demonstrated experimentally to increase sleepiness. Naps were used to induce high arousal conditions.

Visual analogue scale ratings of sleepiness levels under these manipulated high and low arousal conditions demonstrate a highly significant change in subjective sleepiness between conditions suggesting that the experimental manipulation was successful. As described in Chapter 6, problems of validity associated with the use of subjective sleepiness

measures are not seen as limiting the validity of this finding as the impact of the manipulation is measured as a consequence, not of absolute measures, but of *difference* scores between low and high arousal conditions. Similarly the use of change scores neutralises the possible impact of residual effects of stimulant medication on arousal.

The capacity of the current study to repeatedly induce sleepiness across the day demonstrates the susceptibility of unmedicated narcoleptics' arousal state to environmental factors. One of the fundamental problems in performance testing has been the capacity of narcoleptic subjects to retain full alertness in stimulating test environments (e.g. Aguirre, Broughton & Stuss, 1985). Volk, Schulz and Yassouridis (1990) have further shown the sensitivity of narcoleptic arousal states to environmental influences demonstrating that confining narcoleptic patients to bed increases the amount of daytime sleep by a factor of 2 to 3 times that of narcoleptics who sit at a table across the day. Besset, Tafti, Nobile and Billiard (1994) reiterate this sensitivity of narcoleptic sleepiness to environmental factors suggesting "narcoleptic subjects appear more sensitive to environmental conditions than normal sleepers" (p. S32).

The finding in the current study of significantly increased subjective arousal for narcoleptics following the 20 minute nap period also provides support for the work of Roehrs et al. (1984, 1985) who suggest that naps as short as fifteen minutes duration have an alerting effect for narcoleptics.

Whilst the current study achieved the primary aim of inducing manipulated low and high arousal states for narcoleptic subjects the degree to which these manipulated states reflect the everyday experience of narcoleptic subjects remains to be tested. It has been demonstrated that although night time sleep patterns for narcoleptic subjects remain relatively stable between laboratory and home based recording environments (Broughton et al., 1988b),

laboratory based assessments may be less accurate predictors of daytime sleepiness patterns. These findings by Broughton et al. (1988b) demonstrate quantitative changes in sleepiness for subjects monitored in ambulatory settings, with non laboratory based measures identifying decreases in daytime sleepiness in comparison to laboratory based assessments. In addition to changes in the *amount* of daytime sleepiness associated with laboratory measures it also remains to be defined whether, for narcoleptic subjects, the sleepiness induced through environmental manipulations, including the withdrawal from stimulant medication, represents the same qualitative sleepiness as that experienced in naturalistic environments. Another way of conceptualising this question is to ask whether the mechanisms generating sleepiness for narcoleptic subjects in the current laboratory setting are the same as those generating sleepiness in naturalistic settings? If, as Lavie (1991a) argues, the experience of daytime sleepiness in narcolepsy occurs as a consequence of diurnal activation of the REM oscillator, then perhaps the expression of this oscillatory mechanism is facilitated by diminished environmental stimuli. Non stimulating environments, such as that described in the current study, may therefore result in increases to the amount of daytime sleep. The ability of environmental factors to mask or facilitate expression of ultradian rhythms has certainly been argued in relation to the expression of daytime alertness rhythms in non pathological sleepy individuals (Kleitman 1963; Lavie & Scherson, 1981; Lavie & Zomer, 1984; Wever, 1985; Lavie 1986; Mavjee & Horne, 1994) and therefore it seems reasonable to propose that similar factors may impact on the expression of narcoleptic sleepiness patterns. The identification, however, of factors generating narcoleptic sleepiness in both naturalistic and laboratory based settings remains to be resolved and therefore the comparative nature of the sleepiness between settings also remains to be defined.

Therefore whilst this study therefore provides an experimental analysis of performance change associated with experimental manipulations of sleepiness for narcoleptic subjects, the extrapolation of the current findings to non laboratory based 'sleepy narcoleptic environments' needs to be validated by replications of the research protocol within naturalistic environments.

Study 2: Sleep Deprivation

To create a level of sleepiness amongst normal sleepers that matched the sleepiness level achieved under the low arousal manipulation for narcoleptic subjects, a sleep deprivation period of 32 hours was utilised. Whilst this period of sleep deprivation did not lead to as 'sleepy' a mean rating as that experienced by the narcoleptic subjects, statistically there was no significant difference between mean scores. For the purposes of this study therefore the sleep deprivation and narcoleptic subjects were considered equated for the low arousal condition.

Whilst the previous section has argued that the reported inability of narcoleptic subjects to make accurate assessments of their own sleepiness levels (Browman & Mitler, 1988) has not invalidated the evaluation of change scores between manipulated high and low arousal states, the comparison of sleepiness levels between narcoleptic and sleep deprived controls may be confounded by this factor. Periods of sleep deprivation for normal sleepers seem to be matched by appropriate increments in subjective sleepiness ratings (Carskadon & Dement, 1981; Babkoff, Caspy & Mikulincer, 1991; Gillberg, Kecklund, & Åkerstedt, 1994) but as pathologically sleepy individuals are reported to underestimate their sleepiness levels (Browman & Mitler, 1988) it may be that whilst no significant difference in low arousal was noted in the current study the potential underestimation of narcoleptic sleepiness levels may have masked a significant differential in actual sleepiness levels between the narcoleptic and

sleep deprived groups. This potential difference in validity of the VAS scale between subject groups is however difficult to assess, or control for, as subjective sleepiness measures have limited convergent validity with objective sleepiness measures for either pathologically sleepy or sleep deprived normal sleepers and therefore issues of construct validity for subjective sleepiness remain unresolved.

The Impact of Napping on Arousal

For narcoleptic subjects the twenty minute nap period was associated with a significant increase in subjective arousal ratings, this contrasts with the finding that the nap period for the sleep deprived control subjects was not associated with any significant change in arousal conditions. As levels of subjective sleepiness measured pre nap are equated between narcoleptic and sleep deprived subjects this outcome of the nap period on arousal for sleep deprived subjects contrasts significantly with the subjective recuperative nature of naps for narcoleptic subjects.

Whilst a comparative analysis of napping behaviour is beyond the focus and scope of this thesis (for a comprehensive review of aspects of both normal and pathological napping the reader is referred to Dinges & Broughton, 1989) it is evident that significant aspects of nap behaviour may vary between narcoleptic and sleep deprived normal sleepers and aspects of these differences may result in differences between groups in relation to their recuperative power. Of particular relevance to the current study is that naps for normal sleepers were induced by a period of sleep deprivation and, according to Borbély's (1982) sleep wake model, this extended period of prior wakefulness would predict increased pressure in the nap period for slow wave sleep. The twenty minute nap duration may not fully dissipate this SWS pressure. In contrast it has been shown that the architecture of naps for narcoleptic subjects

are not influenced by extended wakefulness and subsequent nap periods result in a recuperative effect for subjects.

An analysis of factors differentiating napping between narcoleptic and sleep deprived subjects is further confounded by the difficulties associated with discriminating between naps and sleep attacks for narcoleptic subjects. For non pathologically sleepy subjects Dinges and Broughton (1989) suggest that a nap is defined in relation to the comparative duration of the daytime sleep episode in relation to the major nocturnal sleep period. Hence naps were defined as any sleep period that had a duration of less than 50% of the major nocturnal sleep episode. This definition appears inappropriate when examining daytime sleep episodes for subjects with narcolepsy as it fails to discriminate between episodes of daytime sleep that are initiated with volitional intent or that appear as irresistible intrusions of sleep into wakefulness. Within the literature the former is described as a nap whilst the latter is termed a sleep attack though no clear definitional parameters exist to discriminate between these sleep episodes.

Despite the difficulties of the differentiation of naps and sleep attacks in narcolepsy, daytime sleep episodes for narcoleptic subjects generally result in the re establishment of arousal, and this finding, which is replicated in the current study, appears in contrast to the non recuperative function of the twenty minute nap for the sleep deprived control subjects.

The following section will examine the implications on performance, of these arousal differences, at both pre and post nap testing conditions, for narcoleptic and sleep deprived control subjects.

The Implications of Arousal Manipulation on Performance

Controlling for Practice Effects

To evaluate the impact of arousal on performance narcoleptic subjects were tested on performance tasks both preceding and subsequent to a nap period. An inevitable confound of this experimental design was that the second (post nap) testing session was potentially confounded by practice effects. To control for these practice effects repeat testing of control subjects on performance tasks was used to estimate the degree of practice, which was then subtracted from the overall change in performance between low and high arousal conditions, with the assumption that any residual effects for the narcoleptic subjects represented performance change due to arousal. This methodology, which was based on the work of May and Kline (1987), assumes that the factors of sleepiness and practice can be combined in an additive model. This assumption may not represent the relationship between these components of performance change. For example an interactive model may exist resulting in a synergistic relationship that cannot be unravelled in this simplistic additive way. However until research can identify the relationship between factors that potentially impact on this sleepiness and performance interaction

> the treatment of the practice and experimental effects as additive is justified - an interactive model may work well, but would gain little from the extra complexity, and would make applied studies like this one impracticable (May & Kline, 1987, p. 453).

A second methodological difficulty with this experimental design was the assumption that the degree of practice identified with the control subjects represents an appropriate assessment of practice for the narcoleptic participants. The effects of practice are

dependent on the extent of task learning associated with the first testing session. If sleepiness results in a performance decrement, then for the narcoleptic subjects, the first exposure to the tasks may have been associated with decreased task learning and therefore a diminished practice effect in relation to the control subjects. Utilising the practice effect for controls, as an estimate of practice for the narcoleptics, therefore potentially overestimates the practice for narcoleptics. Residual performance effects for narcoleptics, attributed to arousal change, are therefore more robust and susceptible to type 2 rather than type 1 errors.

A third methodological issue associated with the experimental design presented in study 1 is that whilst the order of presentation of all tasks was counterbalanced, using a Latin square design, there was no counterbalancing of the low and high arousal sequence of task presentation. The non utilisation a counterbalanced arousal protocol was deliberate. The major aim of this study was to provide an evaluation of the impact of sleepiness on performance, the low arousal measure for narcoleptic subjects was always the first testing session and was therefore free of the confound of potential practice effects. The difficulties of assessing the extent of practice have been discussed and as this confound may vary depending on whether the first testing session represented a high or low arousal condition it was decided not to introduce a potential inconsistency that may arise through counterbalancing.

Study 1: Narcolepsy

For the narcolepsy subjects in study one the experimentally induced sleepiness was associated with performance decrement across a range of tasks. Comparison of both the within subject effects for narcolepsy subjects of the transition between low and high arousal states, and the between subject effects of low arousal for narcolepsy subjects compared to controls, indicate that complex cognitive tasks are the most sensitive to arousal change for

this clinical population. This finding supports the conclusions of Rogers and Rosenberg (1990) that the consistent failure of research to demonstrate sleepiness associated performance decrements for narcolepsy subjects may be partly explained by the use of standardised tests which are insensitive to higher order cognitive functioning. In the current study the most sensitive measure of sleepiness for narcolepsy subjects was the PASAT. This task measures central information processing capacity and requires the subjects to respond verbally to an externally paced auditory addition task and simultaneously inhibit the automatic encoding of their response and direct their attentional resources to the next incoming stimulus (Spreen & Strauss, 1991). As the task is experimenter paced, subjects cannot compensate for sleepiness by increasing the processing and response time. The divided attention and central processing demands of the task may reflect everyday experiences of competing cognitive demands, and sleepiness in narcolepsy may interfere with the capacity to respond to this cognitive load. Newcombe and Ratcliff (1979) argue that laboratory testing of cognitive capacity is potentially limited by the failure of standardised tests to reflect real life cognitive demands where stimuli are continuous and demand multiple responses. The sensitivity of the PASAT to low arousal may reflect the ability of this task to replicate more realistically the complexity of cognitive functioning in naturalistic settings and may be a more sensitive indicator of the difficulties narcoleptics describe in everyday cognitive functioning.

One paradoxical finding of the first study was that despite the consistent self reports of memory dysfunction amongst subjects with narcolepsy (Broughton and Ghanwem, 1976; Smith et al. 1992) no decrements in either short or long term memory performance were noted. This discrepancy between subjective reports and objective findings of memory function for subjects with narcolepsy has been noted in several studies (Aguirre, et al. 1985; Rogers, 1987; Rogers and Rosenberg, 1990; Smith et al. 1992). The lack of effect in the

current study could arise from either of the following i) sleepiness may not be associated with memory performance decrement for narcoleptic subjects and the subjective reporting of memory decrements relates to inaccurate perceptions of memory functioning or ii) laboratory based memory tasks have limited external validity in relation to everyday memory processes. Study 3 will evaluate subjective experiences of memory dysfunction in narcolepsy, using a metamemory instrument. Nevertheless the findings of study 1 provide tentative support for the second alternative. The PASAT certainly has a high memory component as subjects are required to retain information in short term storage whilst performing other cognitive tasks. The PASAT performance decrement therefore possibly represents a decrement also in short term memory functioning (narcoleptic subjects typically report short term memory as being most affected e.g. Broughton & Ghanem, 1976). Standardised memory tests isolate the memory component from other cognitive demands but naturalistic environments seldom utilise discrete memory processes, hence the 'real world' perception of memory functioning may be better represented by tasks such as the PASAT than formalised memory tests.

Another difficulty in evaluating memory change as a function of arousal is that the relationship between memory and arousal has been shown to be a complex one with arousal differentially affecting short and long term memory (Folkard, Monk, Bradbury & Rosenthal, 1977). This differential effect may be mediated by qualitative changes in the nature of the processing strategies. Short term memory is enhanced by low arousal and impeded by high arousal. Conversely, long term memory is enhanced under high arousal conditions yet impeded by low arousal states (Folkard, 1979). The interaction of sleepiness and memory performance is therefore complex and the general assumption that sleepiness will lead to memory performance deficits underestimates this complexity.

It is interesting that the current study did not identify any attentional tasks as discriminators between low and high arousal situations. The evaluation of the sleepiness and performance interaction in narcolepsy frequently concludes that performance decrements may be secondary to diminished attentional capacity associated with narcoleptic sleepiness. For example

> It is therefore concluded that patients with narcolepsy - cataplexy, in fact do not have a true organic deficit of memory capabilities. The latter are considered to be due to problems in sustaining full alertness in everyday life situations (Aguirre, Broughton & Stuss, 1985 p. 22).

The findings of the current study indicate that even in situations where attentional capacity either remains unaffected, or can be compensated for (as evidenced by the lack of performance decrement on attentional tasks) tasks requiring high levels of cognitive function demonstrate performance deficits that remain reversible only as a consequence of a sleep episode. This finding of cognitive dysfunction in narcolepsy provides some support for the theoretical position of Horne (1988a) that for complex processing tasks sleepiness may lead to fundamental changes in processing capacity that are reversed only by restorative sleep.

It has been postulated that narcolepsy may represent a generalised state of hypoarousal (Lurkin, 1984). A summary of the physiological evidence for this position is presented by Henry, Hart, Kwentus and Sicola (1988). One implication of this hypoarousal hypothesis is that lowered tonic arousal will be reflected by decrements for narcoleptic subjects on automatic processing tasks. To evaluate this hypothesis study 1 compared performance for high arousal narcoleptic subjects to controls on a series of automatic processing tasks. None of the automatic performance tasks were found to discriminate

between narcoleptic and control subjects suggesting that at high arousal narcoleptics perform as effectively as controls on tasks of automatic function. In line with the conclusions of Aguirre et al. (1985), Ollo et al. (1987), and Rogers and Rosenberg (1990), this finding suggests that the capacity to perform automatic tasks for narcoleptic subjects is not restricted by fundamental physiological factors, or tonic arousal levels. Where performance tasks require minimal processing capacity, subjects with narcolepsy appear able to compensate for sleepiness effects with increased attentional resources. However, as task complexity increases, sleepiness has a more pervasive influence on performance and decrements may be reversed only by restorative sleep.

One methodological problem with the evaluation of tonic arousal as a function of automatic performance capability is that whilst this study selected tasks, such as reaction time, that have been identified within the literature as tapping automatic cognitive processes it is difficult to validate that these tasks remain unaffected by attention. It would seem that the very process of laboratory experimentation directs subjects' cognitive resources to a particular task and therefore the assumption that these 'automatic' tasks remain independent of attentional resources is difficult to validate. It remains again necessary to validate these experimental findings within naturalistic environments.

Study 2: Sleep Deprivation

In contrast to the performance decrements observed under low arousal conditions for narcoleptic subjects the sleepiness induced for non pathologically sleepy subjects was not associated with any significant change in performance in relation to baseline performance measures, i.e. the automatic, attentional and complex processing tasks utilised in study 2

demonstrated no significant decrement as a consequence of the 32 hour sleep deprivation manipulation.

One potential explanation for this lack of effect is that the sleep deprivation period of 32 hours was too short to impact on performance measures. Horne (1988b), however, has demonstrated that a period of 32 hours led to significant impairments in complex processing tasks and Foo et al. (1994) report that after 30 hours of sleep deprivation performance decrements were noted for tasks requiring cognitive and perceptive skills. Similarly Wimmer et al. (1992) identified performance decrements for divergent thinking tasks as a consequence of one night of sleep deprivation. The difficulty in replicating performance outcomes for sleep deprivation research underscores the entire literature relating to sleepiness and performance interactions and highlights the difficulties of research in this area. Chapter 11 will overview methodological factors associated with sleep deprivation research but it appears that aspects of task nature, sleepiness and testing environments all impact on outcome measures. As levels of induced sleepiness in the current study have been matched with the Horne (1988b), Wimmer et al. (1992) and Foo et al. (1994) protocols it would seem that either intertask or methodological factors led to the observed differences. Horne (1988b) argues that tasks associated with complex processing functions will demonstrate increased sensitivity to sleepiness effects yet the critical factors that identify complex cognitive processing remain to be defined. Because of the difficulties of identifying critical task factors susceptible to sleepiness the current study utilised the same complex performance measure (PASAT) for both narcoleptic and sleep deprivation subjects. The differential impact of sleepiness on performance between subject groups therefore cannot be explained as a function of task differences. As noted previously the observed performance differences between low arousal narcoleptic and sleep deprived subjects may be explained as a

consequence of differences in sleepiness ratings that were not identified by the VAS ratings. If, however, VAS sleepiness ratings are considered valid measures of sleepiness, then the absence of a significant difference between these ratings for the subject groups suggests that sleepiness differentially affects the processing of complex material for sleep deprived and narcoleptic subjects. Sleep deprived subjects appear able to compensate for sleepiness, even for the processing of complex material, and therefore demonstrate no performance decrements. In contrast the performance decrements consequent to sleepiness experienced by narcoleptic subjects appear not to be reversed by compensatory effort but dependent on sleep as a restorative process i.e. it is only post nap that observed performance decrements are reversed for narcoleptic subjects.

Another explanation for the observed differences in complex task performance measures is that sleepiness does not differentially affect the capacity to perform but rather affects the motivation to perform. Hence normal sleepers, when sleep deprived, may be willing to increase cognitive effort to deal with more complex performance tasks whilst sleepiness for narcoleptic subjects may interfere with this motivation to perform. This dilemma reflects a fundamental issue of sleep deprivation research - does sleepiness lead to diminished ability to perform (cognitive model) or simply a diminished willingness to perform (attentional model)? In the current study there was no cognitive decrement following 32 hours of sleep deprivation for normal sleepers. The observed decrement for narcoleptic subjects may then reflect either cognitive or attentional deficits. Failure of the attentional tasks utilised in studies 1 and 2 to demonstrate sleepiness induced performance decrements argues that for both low arousal narcoleptic, and sleep deprived normal sleepers, the sleepiness manipulation did not alter the capacity for attentional resources. This finding, coupled to the finding of significantly reduced performance capacity on the complex

performance tasks for narcoleptic subjects, supports the position that narcoleptic sleepiness is associated with changes in cognitive processing capacity unrelated to performance motivation.

The Characterisation of Narcoleptic Sleepiness

Study 1 manipulated sleepiness to provide a low arousal testing condition for narcoleptic subjects. In addition to this manipulation the performance tasks utilised allowed for an evaluation of the effects of fatigue, performance stability, the nature of performance errors, and the capacity for phasic arousal under conditions of low arousal. As the sleep deprivation condition was not associated with performance decrement the impact of sleepiness on these parameters could not be assessed for this subject group.

Fatigue

Evaluation of the impact of fatigue (resulting from time on task) on performance under low arousal conditions is limited by the methodological problem that fatigue is presumed to confound the analysis of sleepiness induced effects (Johnson, 1982). As yet there is no understanding of the interrelationship between these variables and therefore experimental protocols are utilised which minimise the potential for fatigue confound effects by either limiting task duration or changing of attentional resources to novel tasks. Study 1 deliberately focussed on short duration performance tasks to evaluate sleepiness effects. Fatigue can therefore only be evaluated in this study across these brief duration tasks.

Two discrete performance measures were utilised to evaluate the impact of fatigue on performance. The first measure evaluated fatigue effects associated with the PASAT task. No significant difference in fatigue scores occurred between low arousal narcoleptic and

control subjects. This finding suggests that for this complex processing task the capacity of narcoleptic subjects to maintain cognitive effort, even under conditions of low arousal, does not decline as a function of time on task. This conclusion needs to be modified, however, by the acknowledgment that this fatigue measure spanned a very brief (2 minute) time span and therefore has perhaps limited external validity in relation to the everyday continuous demands on cognitive function.

The D2 concentration endurance task also incorporates a fatigue score and again no significant differences in fatigue measures between low arousal narcoleptics and control subjects were observed. The analysis of this fatigue data in Chapter 7 indicates, however, that considerable inter subject variability in fatigue data was noted and the potential implications of this inter subject performance variability will be discussed in Chapter 11. As the performance literature for narcoleptic subjects typically evaluates performance under high arousal conditions, no comparative research, of the interrelationship between sleepiness and fatigue is available for this clinical group.

Performance Stability

Whilst the previous discussion of fatigue effects suggests that intersubject differences may affect the degree of fatigue associated with performance outcomes, the literature on performance outcomes for narcoleptic subjects has frequently argued that performance measures are characterised by high intrasubject performance variability.

The concept of performance lability is central to theoretical aspects of sleepiness and performance interactions which have been extensively reviewed in Chapter 3. High performance lability provides support for the lapse hypothesis, where the impact of sleepiness on performance is seen to be primarily one of a 'hit or miss' outcome with sleepiness affecting

performance outcomes by causing subjects, possibly as a consequence of microsleeps, to 'miss' stimulus items. According to the lapse hypothesis the capacity to respond to stimulus items is not limited by sleepiness and therefore 'hits' are characterised by correct responses. This lapse hypothesis is contrasted with an attentional model of sleepiness and performance interaction that argues for sleepiness leading to incremental declines in performance capacity.

The current study utilised a performance fluctuation measure from the D2 concentration endurance task to assess the impact of sleepiness on performance stability. A significant increase in performance fluctuation was noted for narcoleptic subjects between low and high arousal conditions with increased lability under sleepy testing conditions. The findings from the D2 fatigue analysis presented in the previous section indicate that performance decrements for low arousal narcoleptic subjects do not occur as a consequence of fatigue effects leading to a gradual decrement in task performance. The finding of increased performance fluctuation for sleepy narcoleptic subjects that is therefore unrelated to fatigue decrements suggests that attentional capacity for subjects with narcolepsy is less stable under conditions of low arousal leading to a generalised increase in attentional variability. This finding of sleepiness induced performance lability for narcoleptic subjects has been noted in several studies. Valley and Broughton (1983) demonstrated that although periods of sustained wakefulness (defined as > 13 seconds of EEG defined wakefulness) were not associated with performance decrements for narcoleptic subjects on the WAVT, sleepiness and the associated lability of wakefulness, led to decrements for narcoleptic subjects on both hit and hit response rates. Valley and Broughton (1983) argue, however, that the lapse hypothesis does not fully account for performance decrements associated with narcoleptic sleepiness

> Previous suggestions that deficits also occur at higher levels of vigilance ... were confirmed and elucidated. The presence of deficits during wakefulness and Stage 1A while the narcoleptics were still able to respond is evidence that performance efficiency decreases gradually. Both lapses (omissions) and false positives increasingly replace detected signals before the ability to respond is totally abolished and lapses become the sole characteristic of the performance deficit (Valley & Broughton, 1983, p. 248)

This conclusion of Valley and Broughton (1983) is supported by the present study where performance at low arousal for narcoleptics was characterised by both increased performance fluctuation (as measured by the D2 fluctuation score) and decrements in response accuracy (as measured by the PASAT task). The decrease in response accuracy was unrelated to fatigue which argues for an essentially sleepiness induced performance decrement.

In an attempt to determine the pattern of performance fluctuation as a function of time on task, the current study compared performance variability between arbitrarily defined long and short performance tasks. Short performance tasks appeared most susceptible to performance variability, a finding which suggests that the application of cognitive effort under conditions of low arousal is initially characterised by high performance lability that stabilises with increased time on task. This interpretation is consistent with an effect noted by Valley and Broughton (1983)

> In the present study, the continuous fluctuating pattern in which amounts of each stage remained constant across the task (as did performance), implies that narcoleptics quickly reach a nadir of decline which they are able to maintain without

falling into overt sleep, but above which they are unable to rise to sustain full wakefulness (Valley & Broughton, 1983, p. 248).

Performance Errors

The literature relating to the relationship between sleepiness and performance in sleep deprived subjects suggests that sleepiness provides subjects with two response strategies. Under subject paced task conditions, where individuals can extend the response time, sleepy subjects can choose to maintain performance accuracy by increasing response latency, or can ignore performance accuracy to maintain performance speed. Analysis of low arousal performance for narcoleptics on the Stroop task indicates that, in this subject paced protocol, sleepy narcoleptic subjects elect to decrease processing speed to maintain response accuracy. This strategy is also frequently observed in general sleep deprivation studies. It remains to be evaluated whether this increased processing time, subsequent to sleepiness, relates to increased time necessary for cognitive processing of stimulus material or increased latencies for the initial registration of stimulus materials.

The D2 task provides an experimenter paced performance task. Under these conditions subjects are unable to manipulate processing time and therefore are forced into errors of omission or commission, i.e. they select to miss items or respond within the available processing time, possibly leading to decreases in performance accuracy. In the current study the analysis of median error rates on the D2 between narcoleptic high and low arousal conditions, and between repeat control testing protocols, demonstrated no significant difference in overall error rates. Therefore, despite the observation that for all subjects the trend was to increase errors of omission rather than commission for experimenter paced tasks, no significant difference in error rates was demonstrated between groups.

Phasic Arousal

Levander and Sachs (1985) suggest that the sleepiness and performance interaction in narcolepsy may be characterised by narcoleptic subjects experiencing a decrease in phasic arousal capacity such that over short duration performance tasks they are unable to increase their cognitive effort in response to increasing task demands. The work by Ollo et al. (1987) supports this suggestion with the demonstration of decreased ERP amplitude measures for narcoleptics associated with increasing cognitive load.

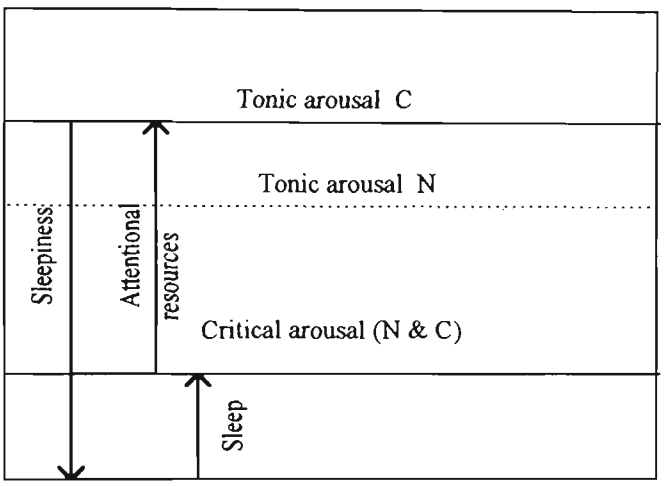
To evaluate the potential of narcoleptic subjects to respond to increasing cognitive demands the current study compared the change in response latencies for subjects responding to the two levels of the Stroop performance task. The difference in latency times (complex - automatic) providing a measure of the ability of narcoleptic subjects to adapt to this increasing load. Statistical comparisons were made between low arousal narcoleptics and control subjects to determine whether low arousal significantly increased the difference in response latencies associated with the shift to a more complex task. No significant effects on latency were noted for the low arousal condition compared to controls suggesting that over brief time intervals attentional resources can be increased by narcoleptic subjects to deal with increasing cognitive loads and that the rate of increase is comparable to that demonstrated by control subjects.

Implications of the Study Findings for the Sleepiness and Performance Interaction Models.

Chapter 5 provided an overview of potential models of the interaction between sleepiness and performance. These models, are reproduced in this section to clarify this theoretical discussion.

Processing of Automatic Tasks

The first component of the theoretical model to be evaluated is the capacity of narcoleptic subjects, under conditions of high arousal, to respond to automatic processing demands. The capacity for automatic processing represents a measure of tonic or habitual arousal. Model B (Chapter 5) represented the position of decreased tonic arousal in narcolepsy and this model is replicated here to facilitate the discussion.



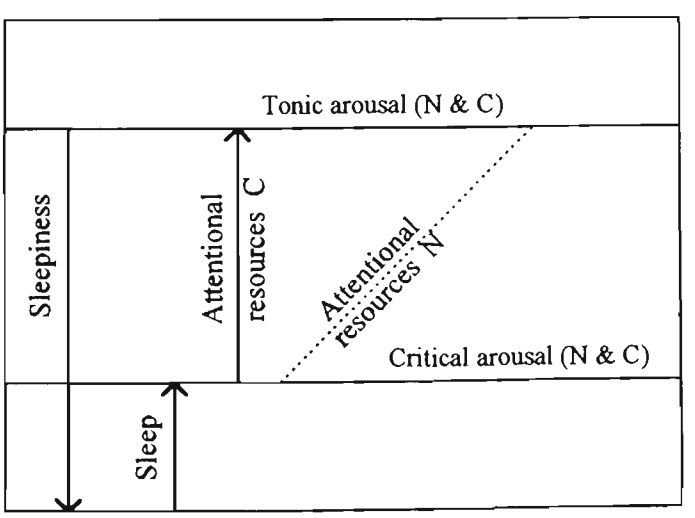
Two major theoretical positions emerge in the literature, Levander and Sachs (1985), Henry et al. (1988), Greenblatt et al. (1993) and Henry and Henry et al. (1993) would argue that narcolepsy is a disorder of hypoarousal characterised by deficits in tonic arousal. In opposition to this position Aguirre et al, (1985), Ollo et al. (1987) and Rogers and Rosenberg (1990) argue that no organic arousal differences exist between narcoleptic and control subjects and differences reflect the impact of sleepiness on performance. This latter position can be supported by both physiological and performance data. Ollo et al. (1987) cite ERP data as evidence of the patency of automatic arousal mechanisms in narcolepsy and this position is strengthened by the demonstration of the maintenance of temperature rhythms in this clinical population (Dantz et al, 1994; Pollack & Wagner, 1994). Performance data also

demonstrates that under conditions of full wakefulness narcoleptics perform as efficiently as controls on vigilance testing measures (Valley and Broughton, 1983).

The findings of the present study support the position that narcolepsy is not associated with decrements in tonic arousal, as discriminate analyses failed to identify any significant performance differences between high arousal narcoleptics and control subjects on tasks tapping automatic information processing. These findings lead to the rejection of Model B as an explanatory model of performance decrements in narcolepsy.

Processing of Attentional Tasks

A second issue to emerge from the theoretical models of sleepiness and performance is the comparative impact of sleepiness on attentional capacity for narcoleptic and control subjects. The ability to increase cognitive effort in response to task characteristics provides a measure of phasic arousal. The concept of fatigue is perhaps the reverse of phasic arousal or attentional capacity, representing decreased attentional effort associated with increasing time on task. This position of decreased phasic arousal in narcolepsy is presented by Model C (Chapter 5) which is replicated below.

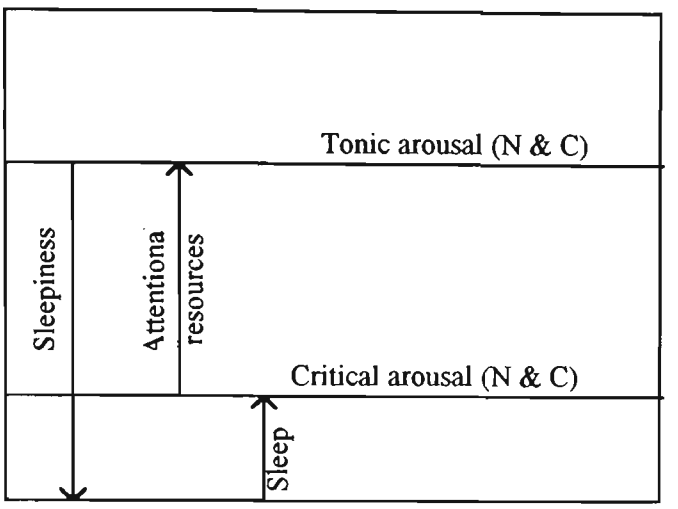


The first important finding of the present study was that for attentional tasks no significant performance decrement was noted between narcoleptic subjects at low arousal and controls. This finding suggests that for tasks requiring attentional resources narcoleptics are able to increase their attentional focus and compensate for narcoleptic sleepiness increasing performance capacity back to baseline levels (phasic arousal). In addition, results of Study 1 suggest that performance decline as a function of time on task (fatigue) appears not to be accelerated for narcoleptic subjects, at least over brief performance trials. This finding of attentional resources counteracting sleepiness effects is an interesting one. This attentional capacity is evident in much of the performance literature for narcolepsy where no decrements are observed between narcoleptic and control performance measures and this lack of effect is attributed to the observation that narcoleptics perform as effectively as controls in stimulating test environments (Aguirre et al., 1995; Rogers and Rosenberg, 1990). It is evident that the ability to sustain attentional effort, to overcome both sleepiness and performance decline, is quite powerful in narcoleptic subjects, where testing protocols of up to two hours e.g. Aguirre et al. (1985) fail to identify any performance decrements or observational signs of sleepiness.

Processing of Complex Tasks

Model A (replicated on the following page) provides a theoretical paradigm for investigating the relationship between sleepiness and complex processing tasks. According to Horne (1988a) task complexity interacts with sleepiness to predict performance decrements. Increases in either levels of sleepiness or task complexity may lead to performance capacity falling below a critical boundary where performance decrements are reversed only by restorative sleep. Less significant levels of sleepiness or less complex processing demands

may lead to decrements in performance capacity that remain above critical limits and therefore are potentially reversed by attentional effort.



Although narcoleptic sleepiness was not associated with performance decline on attentional tasks there was a significant decrement in performance capacity for narcoleptic subjects in response to the complex processing PASAT and semantic match task. Whilst 32 hour sleep deprived control subjects appeared able to compensate for their sleepiness, demonstrating no significant difference on PASAT scores compared to non sleepy controls, sleepy narcoleptic subjects appeared unable to adequately increase cognitive effort and their performance on the PASAT and semantic match task was significantly different from matched control subjects. This lack of decrement for sleep deprived subjects indicates that, in relation to the theoretical model adapted from Horne (1988a), performance on selected complex tasks remains located above the critical boundary where sleepiness induced performance decrements are reversed by attentional processes Conversely for sleepy narcoleptic subjects, sleepiness induced performance decrements appear to fall below the critical boundary i.e. they are not reversed by attentional effort, but are compensated for by the 20 minute nap period. These effects are demonstrated in Figure 16.

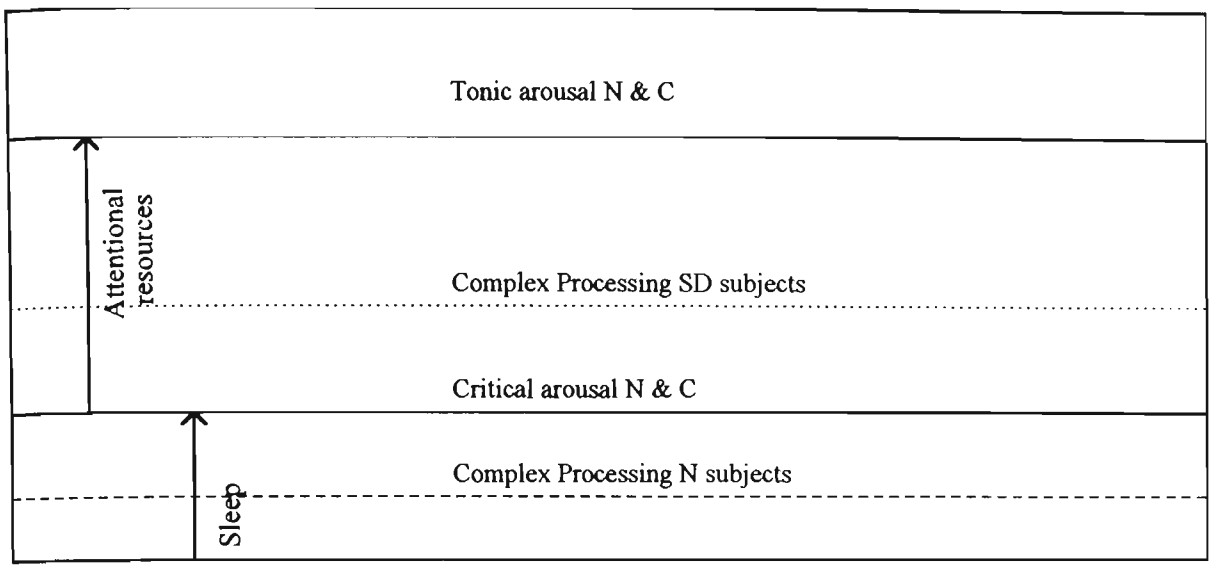


Figure 16 Differential effects of the interaction between sleepiness and complex processing for narcoleptic (N) and sleep deprived (SD) controls.

This differential inter relationship between sleepiness and performance for the two sleepy experimental groups may have several explanations. As mentioned in the arousal section of this discussion chapter, sleepiness for narcoleptics may have been quantitatively more severe than sleepiness for the sleep deprived controls and the use of the VAS measure may not have identified these differences. If this explanation is correct then the decrements on complex processing tasks for narcoleptic subjects could have occurred as a function of the increased sleepiness for this population, leading to a lower arousal level than for sleep deprived controls. An interesting consequence of this explanation is that the one hour environmental manipulation of sleepiness for the narcoleptic subjects resulted in a level of sleepiness that exceeded the effect of 32 hours of sleep deprivation for control subjects!

If however quantitative levels of sleepiness between narcoleptic and sleep deprived controls were adequately measured by the VAS task then the observed difference in ability to process complex material may reflect qualitatively different sleepiness states between the two subject groups. Chapter 1 of this thesis has argued that sleepiness may vary on both

quantitative and qualitative dimensions. As daytime sleep episodes for narcoleptic and sleep deprived subjects typically demonstrate significant structural differences it is possible that the nature of the preceding sleepiness states may also differ and these differences may impact on information processing systems.

Summary

The findings from the present study suggest that narcolepsy is not a state of hypovigilance and therefore under non sleepy conditions narcoleptics do not demonstrate impairements in cognitive function.

For most tasks tapping attentional resources both sleep deprived and sleepy narcoleptic subjects were able to utilise attentional resources to overcome the potential impact of sleepiness on performance. The performance decrements on attentional tasks found in Study 1 (D2 task) are explained as indicating that sleepiness potentially reduces subjects' willingness to process information rather than reducing their cognitive capacity (i.e. an attentional model). Previous chapters within this thesis have indicated that within an attentional model, the nature of performance deficits can further be explained either as a consequence of lapsing, where decreased attentional resources lead to subjects missing stimulus items, or as a function of the incremental decline in arousal resources which sleepy subjects apply to the task (refer Figure 5, Chapter 4). The significantly increased variability of performance, unrelated to fatigue effects, for sleepy narcoleptic subjects provides some tentative support for the lapse hypothesis. However, despite the finding of increased variability in performance for sleepy narcoleptic subjects, this variability was not significant enough to translate into decreased mean performance scores on attentional tasks for sleepy narcoleptics compared to controls. This lack of overall effect for attentional tasks may well

have occurred as a consequence of both the small subject numbers and the stringent significance levels utilised in this study, leading to difficulties achieving statistical significance.

On complex processing tasks the sleepy narcoleptic subjects in the current study appeared unable to compensate for the effects of sleepiness using attentional resources, suggesting that performance decrements on complex tasks for narcoleptics are explained within a cognitive paradigm, with decrements representing an inability to respond rather than an unwillingness to do so. Where other studies have found performance decrements in sleep deprived subjects, it is suggested that these are explained by attentional models This difference in response capabilities for complex processing tasks between sleep deprived and narcoleptic subjects raises the question of the differential nature of the sleepiness between these subject groups and the impact of this sleepiness on CNS function. Additional findings from this study which underscore the question of the differential nature of sleepiness between narcoleptic and sleep deprived controls include the differential impact of the subsequent sleep episodes for sleep deprived and narcoleptic subjects on both arousal and performance parameters.

A one hour manipulation of environmental factors leads to a significant decrement on subjective sleepiness measures for narcoleptic subjects - this sleepiness appears to not affect tasks tapping attentional resources but leads to diminished capacity for processing of complex cognitive material. Short sleep episodes (20 minutes) for narcoleptics lead to the re establishment of both baseline arousal levels and complex processing capacity. Thirty two hours of sleep deprivation leads to statistically equivalent subjective sleepiness for non pathological sleepers. This sleepiness, however, has no impact on subjects' capacity for complex cognitive processing. Brief periods of sleep fail to reverse the reported arousal decrement.

It remains for further research to identify the qualitative factors that discriminate these sleepiness states.

CHAPTER 10

Metamemory in Narcolepsy

Introduction

The Concept of Metamemory

Chapter 4 has evaluated the research on cognitive functioning in narcolepsy. One paradox to emerge from this literature is the lack of association between subjective and objective memory performance in this clinical population. Whilst subjects with narcolepsy consistently report on diminished memory function, which they attribute to the disorder, research has been unable to identify any memory impairment for narcoleptics in comparison to control subjects.

Recently there have been substantial changes in the way that cognitive scientists conceptualise subjective experiences of memory ability with one significant change being the development of the concept of metamemory (Flavell & Wellman, 1977). Metamemory can be defined as

> ... one's knowledge, perceptions, and beliefs about the functioning, development, and capacities of (1) one's own memory, and (2) the human memory system. It includes knowledge perceptions, and beliefs about the demand characteristics of particular tasks or situations, the availability and employability of relevant strategies and aids, and of the memory-relevant characteristics of the persons themselves (Dixon, Hertzog & Hultsch, 1986, p. 166).

This chapter will evaluate the subjective experiences of narcoleptic subjects of diminished memory function using a metamemory instrument.

Dimensions of Metamemory

Hertzog, Hultsch, and Dixon (1989) suggest that Bandura's work on self efficacy provides a useful framework in which to conceptualise metamemory as it provides a distinction between the constructs of memory knowledge and memory beliefs. Bandura (1989) writes that whilst much emphasis has been placed on an analysis of the knowledge and skills necessary for efficient cognitive functioning, the effective utilisation of these skills requires a "resilient sense of efficacy" (p. 733). Similarly Markus and Wurf (1987) propose that self efficacy is a dynamic structure that mediates the efficiency of all intrapersonal processes including information processing. At the simplest level then, metamemory relates to an understanding of how one's memory actually works (knowledge), coupled to an assessment of an individual's confidence to utilise their memory most effectively (beliefs).

Research into metamemory has tended to differentially emphasise the knowledge dimension. Such an evaluation of metamemory as primarily knowledge based provides a potential explanatory framework for age related changes in memory function. For example developmental changes in memory task performance can be explained as a function of changing awareness of strategies of encoding and retrieval. Childrens' increasing memory efficiency reflecting a growing awareness of these strategies (Flavell and Wellman, 1977). Conversely poor memory performance, perhaps associated with ageing, could occur as a consequence of inappropriate use of memory systems, a perspective described (but not supported) by Light (1991) as the production deficiency hypothesis. An implication of this emphasis on metamemory as a knowledge based system is that deficits in memory functioning can be reversed by memory training. Supporting research exists for this position, for example Murphy, Schmitt, Caruso and Sanders (1987) demonstrated that the use of explicit instructions on memory strategies resulted in improved memory performance.

Whilst an understanding of knowledge based aspects of memory functioning is clearly a necessary condition for efficient memory processing it is not a sufficient condition.

An understanding of the relationship between an individual's belief system and subsequent memory function has recently assumed a significant role in the memory research literature. Perceptions of memory function are considered to be based more on a generalised and stable theory of 'self' and the way that the 'self' usually operates in the world than on factual evaluation of memory processes (Sehulster, 1981). This belief system is presumed to be organised in a hierarchical manner with individuals holding both global and localised beliefs, such that they identify a usual response mode e.g. I am not good at names, but also hold beliefs that are limited more contextually, eg. I always have trouble remembering student names at the beginning of a semester (Hertzog, Dixon and Hultsch, 1990). A review of the literature evaluating the two metacognitive paradigms of knowledge and beliefs is beyond the scope of this project but the reader is referred to an extensive review by Hertzog, Dixon and Hultsch (1990).

Of primary relevance to the current study is, however, the finding that there is often a lack of association between subjective memory appraisals and subsequent memory function, with correlations in the order of .2 to .3 (Hultsch et al. 1988). The unreliability of self report indices of memory function is evident amongst both clinical (Beatty & Monson 1991) and non clinical (Brown, Dodrill, Clark & Zych, 1991) subject groups. Hertzog, Hultsch and Dixon (1989) suggest that this poor association between perceptions of cognitive function and objective performance measures may occur as a consequence of individuals developing distorted belief systems. Individuals may construct a belief system about their memory function that is not based on factual incidents of memory functioning but rather emerges as secondary to a more global perception of performance which individuals then use

retrospectively to provide a performance estimate. Factors which distort self schemata therefore lead to inaccurate self estimates of performance.

One example of distorted self schemata interfering with subjective memory appraisals is the relationship between subjective and objective memory functioning in depressed subjects, where subjective impressions of memory dysfunction have minimal relationship with subsequent memory functioning (West, Boatwright & Schleser, 1984; O'Hara, Hinrichs, Kohout, Wallace, & Lemke, 1986). Niederehe and Yoder (1989) evaluated metamemory factors in depressed adults who reported generalised memory problems. Reports of memory problems by depressed subjects were characteristically more global than those of control subjects who gave nonspecific reports of generalised memory dysfunction, particularly for more recent events. Results of the metamemory analysis indicated that depression was not associated with decreased knowledge about memory function or less usage of mnemonic strategies, nor did depressed individuals hold different perceptions to controls regarding the personal significance of memory. Niederehe and Yoder (1989) suggest that these findings support the notion that depressed individuals make subjective appraisals of diminished memory function based on global perceptions rather than specific incidents of behaviour and that negative global perceptions may be understood within a learned helplessness model of depression. This potential association between affective disorder and reported memory dysfunction, which is unrelated to actual memory performance, may have important implications for assessment of memory dysfunction in narcoleptic subjects where up to 50% of individuals report depressive symptomology (Broughton et al., 1981). Hence self report measures of memory dysfunction by narcoleptics may well reflect negative belief schemata rather than accurate reports of previous memory performance. Additionally, the substantial psychosocial disruption for narcoleptics in areas

such as educational and work opportunities (Broughton et al., 1981) may lead to the development of negative self evaluations of cognitive capacity across a range of domains and, from the paradigm of the role of belief systems in memory function, it is these negative evaluations that form the basis for subjective assessments of performance capability.

Metamemory Scales

Whilst the two parameters of knowledge and belief systems form the fundamental dimensions of metamemory the construct has been developed to subsume a range of associated factors. Hultsch, Hertzog, Dixon, and Davidson (1988) propose four dimensions (a) memory knowledge (b) memory monitoring, reflecting self knowledge about the way one uses their memory, (c) memory self efficacy and (d) memory related affect, which identifies affective states of anxiety or depression associated with the use of memory. Several other subscales have been incorporated in metamemory measurement scales. Two frequently used metamemory scales being the Memory Functioning Questionnaire (MFQ) by Gilewski, Zelinski, Schaie, and Thompson, (1983) and the Metamemory in Adulthood (MIA) Questionnaire developed by Dixon and Hultsch (1983b). Full copies of the two instruments are provided in Gilewski and Zelinski (1988) and Dixon, Hultsch, and Hertzog (1988). The MFQ (Gilewski and Zelinski, 1988) comprises 64 items across seven scales: general rating of memory, retrospective functioning, frequency of forgetting, frequency of forgetting when reading, remembering past events , seriousness of forgetting and mnemonics usage. Factor analysis of the items suggesting three primary factors - general frequency of forgetting, seriousness and retrospective functioning. Subjects rate their responses to items on a seven point Likert scale with higher ratings representing more positive memory perceptions. The MIA scale identifies eight subscales of strategy, task, capacity, change, anxiety, achievement,

activity and locus. The activity subscale being subsequently deleted from the instrument for psychometric reasons (Hultsch et al., 1988).

Both the MIA and MFQ scales have been used and reported on extensively in the literature. Experimental references relevant to the MFQ include, Gilewski, Zelinski and Schaie, (1990) and Brown, Clark, Dodrill, & Zych, (1991). For examples of the use of the MIA refer to Davidson, Dixon, and Hultsch (1991); Dixon and Hultsch (1983a); Dixon, Hertzog and Hultsch, (1986) and Luszcz, (1993).

Several studies have investigated the construct validity of metacognition and in particular have attempted to identify its fundamental dimensions. Hertzog, Dixon & Hultsch (1990) argue that one difficulty associated with validation of metacognition is that there are no identifiable outcome measures to be used as reference criteria. As metacognition, by definition, has only a limited relationship with either subsequent memory performance scores or predictions of performance outcomes, attempts at construct validation have centred on an evaluation of both the convergent and discriminant validity of metamemory instruments. Reports of convergent validity studies between the MIA and MFQ (Hertzog, Hultsch, & Dixon, 1988; Hertzog, Hultsch, & Dixon, 1989, and Hertzog, Dixon, & Hultsch, 1990) demonstrate a factor correlation of greater than .9 on the factors of 'capacity' from the MIA and 'frequency of forgetting' on the MFQ. For each questionnaire several other subscales were demonstrated to have factorial convergence with these principle measures. These principle convergent factors are therefore presumed to represent alternate measures of the memory self efficacy construct (Hertzog, Dixon & Hultsch 1990).

If the fundamental dimension of metamemory is self efficacy then it is necessary to evaluate whether this construct of cognitive self efficacy differs from more global and well validated self esteem measures. Similarly the observed relationship between metamemory

scales and affective dysfunction suggests the possibility of a common latent variable. Discriminant factor analysis of the MIA and MFQ scales with general self efficacy scales demonstrated that memory self efficacy is related to but statistically separate from general self efficacy measures (Hertzog, Dixon, & Hultsch, 1990). Discriminant analysis of metamemory scales suggests that only the MIA anxiety subscale is significantly related to personality, locus of control and affective state measures (Hultsch, et al 1988).

Conclusion

Metamemory appears to be a valid, multidimensional construct that principally measures an individual's knowledge about, and self efficacy for, memory function. The relationship between metamemory scales and predictive or actual memory performance is, however, often relatively weak. This lack of association may reflect the discrepancy between performance self efficacy and performance outcomes, and occur as a consequence of the complex processes by which individuals construct referent cognitive self schemata.

The MIA questionnaire was selected for use in the current study as the inclusion of affective subscales on the MIA, which are not incorporated in the MFQ, were seen as appropriate for this clinical group of subjects with narcolepsy, who are potentially at risk of affective dysfunction (Kales et al., 1982; Mosko et al., (1989) and Stepanski et al., 1990).

Study Aims

The aims of the present study are to

1. Explore the relationship between dimensions of metamemory and the three subject groups of (a) subjects with narcolepsy, (b) non narcoleptic subjects experiencing

excessive daytime sleepiness and (c) a control group of normal sleepers with no reported excessive daytime sleepiness.

2. Evaluate the within group patterns of metamemory amongst narcoleptic subjects.

As such analyses have not been previously reported there is no current evidence on which to base specific hypotheses. Consequently the study is largely exploratory in nature.

Method

Subjects

A total of 85 subjects responded to the MIA metamemory questionnaire. Issues of subject selection are detailed below. The distribution of subjects between the three comparative categories of subjects with narcolepsy, other disorders of excessive daytime sleepiness (EDS) and non sleepy controls is displayed in Table 16. The comparative distribution of the variables of age and gender are also displayed.

Table 16

Selected Demographics of Respondents to the MIA Questionnaire

		Narcoleptic	EDS	Control
Total = 85	n	33	23	29
Age	Mean	55.18	48.52	49.64
	S.D.	14.38	11.81	12.73
Gender	Male	15	14	11
(f)	Female	18	9	18

An analysis of the difference in mean age scores between categories using one way ANOVA indicated no significant difference between groups, $F(2,81) = 2.15$ ($p > .05$).

Similarly analysis of gender distribution differences between categories was evaluated using the phi coefficient and again there was no significant relationship between the variables of category and gender (Phi = 0.18). The three subject group were therefore considered equated on the variables of gender and age.

Subject selection

Subjects with narcolepsy

Initial contact with potential subjects with narcolepsy was made by mail. Names of subjects were taken from the Australian narcolepsy support group's (NODSS) contact list which included subjects from seven Australian states. (The contact list provides a subsample of the members of the organisation who are willing to provide telephone support for the disorder). Names were selected from this register rather than from the association's general mailing list as it was predicted that subjects on the contact register may be more motivated to respond to the questionnaire. One unforeseen consequence of this decision to utilise the contact list was that the final sample of subjects with narcolepsy represented an older subject group with a mean age of 55 years.

In addition to the MIA questionnaire subjects with narcolepsy were required to complete a form which detailed their demographics and aspects of the diagnosis, symptomology and management of narcolepsy.

Sixty one questionnaires were distributed and 42 were returned, giving a response rate of 69%. Many respondents wrote additional information to that requested appearing interested in the study and in narcolepsy research in general. A few respondents were critical of the questionnaire finding it repetitive but still completed the items.

Of the 42 returned questionnaires 33 subjects were then selected for inclusion in the study on the basis of several criteria. All selected subjects had specialist, or sleep laboratory diagnoses of narcolepsy and met the International Classification of Sleep Disorders' criteria of excessive daytime sleepiness and unequivocal cataplexy (ICSD, 1990). Cataplexy was assessed using the postural atonia scale (Parkes, 1994). One subject was excluded as she was only 13 years old and her mother had been the contact name (the MIA questionnaire has only been validated with adult populations). This final group of 33 subjects had a mean cataplexy rating of 275 (sd = 173), with a potential scale range of 0 to 1000, and 85% were using stimulant medication at the time of the study. The mean age of onset of symptoms of narcolepsy, as estimated by the respondents, was 23 years (SD = 9) and the mean age for diagnosis was 35 years (SD = 11).

Control subjects

Included with the questionnaire to the subjects from the narcolepsy contact register was a second questionnaire which they were asked to give to partner or friend, without narcolepsy, who considered themselves to be a normal sleeper. Thirty three questionnaires were returned by these control subjects. Four of these 33 were excluded from the analysis as they failed to complete the questionnaire or responded 'yes' to the screening question "do you suffer from daytime sleepiness?". The final 29 subjects comprised the study control group.

EDS subjects

The third subject group comprised 23 subjects with EDS not associated with narcolepsy. Subjects were recruited from the sleep disorders centre of Sentara Medical Centre, Virginia, U.S.A. and had presented to the centre for assessment of excessive daytime sleepiness. All subjects utilised had subsequent, confirmatory sleep laboratory diagnoses of sleep apnoea, though their inclusion in the current study was because of their subjective

assessment of excessive daytime sleepiness rather than apnea. The clinical histories and overnight sleep studies of these EDS subjects provided no suggestion of narcolepsy as evaluated by a sleep disorders clinician at Sentara.

Apparatus

The following section describes the seven dimensions of the MIA questionnaire, the range of possible scores for each dimension and a sample item from each subscale. The 108 items of the MIA are responded to with a five point multiple choice response, ranging either from "agree strongly" to "disagree strongly" or from "never" to "always". To avoid subjects developing a response set to the questionnaire a percentage of question were structured so that a reverse scoring procedure was used.

Achievement. For the achievement dimension the MIA comprises 16 items and the range of possible scores is 16 to 80, a higher score representing increased perceptions of the importance of a good memory. "It is very important that I am very accurate when remembering names of people".

Anxiety. The 14 item anxiety dimension has a potential range of scores from 14 to 70 with increased scores representing increased stress related to memory performance. "I do not get flustered when I am put on the spot to remember new things".

Capacity. The capacity dimension comprises 17 items with a potential score range of 17 to 85. Higher scores represent increased perceptions of performance capabilities on memory tasks. "I am good at remembering names".

Change. The change dimension is the largest scale of the MIA comprising 19 items with a score range of 19 to 95. For this dimension higher scores represent increased memory stability whilst lower scores indicate memory decline across time. "The older I get the harder it is to remember things clearly".

Locus. he locus subscale incorporates only 9 items and therefore has a potential range of 9 to 45. Low scores represent an external locus of control with higher scores moving towards internality. "Even if I work on it my memory ability will go downhill".

Strategy. The strategy scale has a score range of 18 to 90 with 18 questionnaire items. The scale evaluates the use of memory aids to enhance memory performance. Higher scores represent increased usage of memory strategies. "Do you write appointments on a calendar to help you remember them?".

Task. The final dimension of the MIA is the task subscale. This comprises 16 items with a score range of 16 to 80. This dimension measures knowledge of basic memory processes and an awareness of others memory capabilities. A higher score represents increased knowledge. "For most people, facts that are interesting are easier to remember than facts that are not".

Factor analyses of the MIA questionnaire identifies two higher order factors. The scales of strategy, task, achievement and anxiety loading onto the knowledge factor. The self efficacy factor is defined by the capacity, change, anxiety and locus subscales though the loadings of the change and locus subscales appeared age dependent (Hultsch et al. 1988).

Procedure

As noted previously subjects from the narcolepsy and control groups received the MIA questionnaire by mail. The questionnaire incorporates directions for completion and practice items. Completed questionnaires were returned by mail. The EDS group responded verbally to the questionnaire during their presentation for an overnight sleep study at the sleep disorders unit.

Data Analysis

MANOVA Analysis of MIA Data

To determine whether responses to the dimensions of the metamemory questionnaire varied as a function of the subject group a Multivariate Analysis of Variance (MANOVA) was computed using SPSS. MANOVA was considered as the appropriate statistic as the dependent variables, being factors within the general metamemory construct, were considered related. As there is no theoretical basis for ordering the dependent variables, univariate F statistics, rather than a stepdown analysis, were used to identify significant univariate relationships.

Several statistical assumptions underlie the use of MANOVA and prior to analysis these assumptions were checked.

Cell sizes: the data meets the requirement that there are more subjects in each cell than the number of dependent variables.

Univariate and Multivariate Normality: One statistical assumption to underlie the use of MANOVA is that the distribution of the univariate dependent variables is approximately normal (Tabachnick & Fidell, 1989). Normal Q-Q plots were used to assess the distribution of the dependent variables. All dependent variables show distributions

approximating the normal curve and this visual analysis is supported by the Lilliefors statistic which, for all dependent variables was greater than 0.2. Multivariate normality was evaluated as satisfactory using the Mahalanobis Distance statistic. Minor violations to normality were also considered compensated for by the size of the sample, as robustness of the MANOVA statistic is achieved where sample sizes of greater than 20 are achieved in each cell (Tabachnick & Fidell, 1989).

Linearity: Within cell scatterplots were used to identify the relationship between pairs of dependent variables. The data indicates satisfactory linear relationships between pairs of dependent variables.

Homogeneity of Variance - Covariance matrices: At the univariate level the assumption of homogeneity of variance-covariance is met with all dependent variables having non-significant Bartlett - box F values. Multivariate homogeneity of variance is also satisfactory with a nonsignificant Box's M value.

Multicollinearity and Singularity: Issues of multicollinearity and singularity were checked using the Log (determinant) of the correlation matrices. As this statistic exceeded the critical value the data was assumed to not be confounded by singularity or multicollinearity issues.

All assumptions necessary for the use of MANOVA were met by the metamemory data set.

Results

Within the MANOVA the independent variables were the three subject groups of narcolepsy, EDS and control respondents and the dependent variables were the seven subscales of the MIA questionnaire. Using the Wilk's criterion, the combined dependent

variables were significantly affected by subject grouping, $\underline{F}$ (14,152) = 2.13, $\underline{p}$ = .013. Univariate F statistics were used to identify significant univariate relationships. Table 17 provides an overview of both the summary statistics of the MIA dimensions and the univariate analysis.

Table 17

Summary Results of Univariate Analyses of MIA Dimensions

		ACHIEVEMENT	ANXIETY	CAPACITY	CHANGE	LOCUS	STRATEGY	TASK
NARCOLEPTICS (N)	$\overline{X}$	57.72	47.27	44.58	43.06	28.92	62.71	60.99
	SEM	1.20	1.82	1.88	1.69	1.02	1.88	1.07
CONTROLS (C)	$\overline{X}$	55.70	40.79	52.72	55.34	30.52	60.24	61.34
	SEM	1.41	1.88	2.01	2.35	1.05	2.24	1.59
EXCESSIVE DAYTIME SLEEPINESS (EDS) n = 23	$\overline{X}$	58.40	43.65	55.22	51	31.04	63.74	62.86
	SEM	1.60	1.95	2.15	2.55	1.16	2.57	1.25
UNIVARIATE ANOVA RESULT F (2,82)	F =	.99	3.22	7.90	9.15	1.07	.64	.51
	P =	.375	.045	.001	.000	.345	.531	.600
TUKEY B POST HOC TEST SIGNIFICANT DIFFERENCES		-	N>C	C>N EDS>N	C>N EDS>N	-	-	-

From the data presented in Table 17 the three significant univariate dimensions were the subscales of *anxiety*, *capacity*, and *change*. The remaining four dimensions *achieve*, *locus*, *strategy* and *task* were not significant. The significant univariate dependent variables were then analysed using the one way ANOVA procedure with post hoc Tukey-B tests used to identify significantly different groupings. For the variable of *anxiety* the mean anxiety rating for subjects with narcolepsy was significantly greater than the control group's anxiety rating. For the variable of *capacity* the mean scores for both the EDS and control group were significantly greater than the mean score for subjects with narcolepsy. A similar significance pattern was noted for the variable of *change* where the mean scores for EDS subjects and control subjects were found to be significantly greater than the mean score for the subjects with narcolepsy.

Comparison was also made of the higher order factors of the MIA scale described by Hultsch et al. (1988). Scores on the strategy, task, achievement and anxiety scales were summed to give a score representing *memory knowledge* and the variables of capacity, change, anxiety and locus were summed to define the *memory self efficacy* factor. Two, one way ANOVA analyses were then performed with the independent variables representing subject group i.e. subjects with narcolepsy, EDS and controls and the dependent variables of memory knowledge and memory self efficacy. For the *self esteem* factor a significant difference between subject groups was found $\underline{F}(2,82) = 7.49$, $\underline{p} = .001$. However for the *memory knowledge* factor no significant difference was found between subject groupings $\underline{F}(2,82) = 2.07$, $\underline{p} = .132$. Post hoc analysis using the Tukey's test identified that the subjects with narcolepsy had a significantly lower mean self esteem score ($\underline{M} = 163.7$) than both the control subjects ($\underline{M} = 180$) and the EDS ($\underline{M} = 180.9$) group.

Discussion

The results of the MANOVA analysis indicate that there is a significant difference between the three subject groups on the multivariate dimension of the MIA questionnaire. Univariate analyses identified three significant dimensions which contributed to the multivariate effect. Subjects with narcolepsy were found to have significantly greater mean scores on the *anxiety* dimension than control subjects. For the *capacity* dimension subjects with narcolepsy rated themselves significantly below both the control and EDS groups. A similar pattern to capacity was noted for the *change* factor where subjects with narcolepsy had significantly lower mean scores than both the control and EDS groups.

Analysis of differences between subject groups on the higher order factors of self efficacy and knowledge indicated a significantly lower *self esteem* score for subjects with narcolepsy compared to both the EDS and control subjects. However there was no significant differences between groups on the *knowledge* factor.

The dimension of anxiety loads into both the knowledge and self efficacy factors and represents an assessment of subjective feelings of stress associated with memory performance. Subjects with narcolepsy appear to be more anxious about their memory performance than control subjects. The observed mean anxiety rating for EDS subjects falls between the mean scores for subjects with narcolepsy and controls. Whilst this EDS anxiety rating is not significantly different from either of the groups of narcolepsy or control subjects the trend appears to be that the general influence of daytime sleepiness may be to increase anxiety in relation to memory performance. This relationship between sleepiness and performance anxiety may be heightened for subjects with narcolepsy either because of the increased sleepiness experienced by subjects with narcolepsy, compared to EDS subjects, or because other factors, specific to the experience of living with narcolepsy, may feed into this anxiety

dimension. There is minimal published literature evaluating the impact of pathological sleepiness on global anxiety. Stepanski, Markey, Zorick and Roth (1990) utilised the MMPI to compared emotional well being between narcoleptic, EDS and control groups. Both the narcoleptic and EDS subjects scored significantly higher on the anxiety dimension than the control groups. Similar findings were earlier reported by Kales et al. (1982) who noted elevations, compared to normative data, for subjects with narcolepsy on the psychasthenia or anxiety dimension of the MMPI. Anxiety therefore appears to be a psychological state associated with living with narcolepsy and the results of the current study suggest that this global anxiety may translate into aspects of memory performance anxiety.

On the MIA dimension of capacity subjects with narcolepsy rated themselves as significantly below both the EDS and control subjects. This dimension evaluates the subject's subjective assessment of their performance capacity for a range of memory tasks and subjects with narcolepsy are less confident of their abilities than either EDS or control subjects. This elevated experience of self doubt for subjects with narcolepsy is again reflected in analysis of elevations of the MMPI. Kales et al. (1982) suggest that MMPI profile patterns for subjects with narcolepsy suggest that "many of the patients appear to respond psychologically to their disorder with internalised distress, reduction of pleasure, confusion and self doubt, and a relatively negative self image" (p. 169). The literature pertaining to the psychosocial implications of living with narcolepsy, consistently reports that people with narcolepsy may withdraw emotionally, often as a precaution against cataplectic attacks. One consequence of this emotional guardedness and isolation from social contact, may be, as quoted by Broughton et al. (1981), that they " .. lack confidence. It makes life such a struggle" (p. 301). The capacity dimension of the MIA scale is perhaps the extension of that global self-doubt to performance capabilities in the applied area of memory function.

The findings on the dimension of change are interesting with subjects with narcolepsy scoring significantly below both EDS and control subjects. As indicated previously, elevated scores on the change dimension reflect increased stability of memory function as opposed to lower scores which reflect declining memory function. Thus subjects with narcolepsy appear to assess their memory as deteriorating across time. This perceived decline in memory function appears to be related to factors additional to age related changes as similar change scores were not evident for the age matched EDS and control groups. Studies into the life effects of narcolepsy consistently report diminishing memory abilities which subjects attribute to the onset of the disorder (Broughton et al., 1981). Findings from the locus subscale provide tentative support for the attribution of memory dysfunction to the development of narcolepsy. Whilst the difference in mean locus subscale scores between subjects with narcolepsy, EDS subjects and controls fail to reach statistical significance, they indicate a trend for narcoleptics to externalise the locus of control for their memory capabilities in relation to the more internal attributions of EDS and control subjects (see Table 17).

The cluster of dimensions of anxiety, capacity and change, all of which reached statistical significance for subjects with narcolepsy, represent, with the addition of the locus scale, the higher order factor of memory self efficacy. The remaining dimensions of task, strategy, achievement and anxiety represent the knowledge dimension. Apart from the repeated anxiety factor none of the knowledge dimensions reached statistical significance. This indicates an interesting picture of perceived memory function for subjects with narcolepsy. Knowledge subscales reflect an understanding of the way that memory processes work and how to utilise memory strategies to enhance memory function. Subjects with narcolepsy demonstrate no differences in this knowledge domain compared to control or

EDS groups. It is specifically in the area of self efficacy for memory performance that narcoleptics appear to have diminished capacity.

Cohen, Ferrans and Smith (1992) evaluated global self esteem for people with narcolepsy. The Rosenberg self-esteem scale was used to measure self esteem in a sample of 485 subjects with narcolepsy. Results indicate that self esteem measures for subjects with narcolepsy were significantly lower than scores for the general population and that, as the severity of the symptoms of narcolepsy, or the degree of psychosocial disruption increased, self esteem measures decreased. This finding of decrements in global self esteem for subjects with narcolepsy appears, in the current study, to translate to diminished self efficacy across the applied area of cognitive self efficacy.

As mentioned previously, a consequence of the subject selection process, was that the sample of subjects with narcolepsy had a mean age of approximately 55, and whilst the EDS and control subject groups were matched with this sample, the findings of diminished self efficacy for the subjects with narcolepsy may reflect a cohort effect for this sample. It is only recently with the development of sleep disorder clinics in Australia that a diagnosis of narcolepsy has been more readily obtained and the sample of subjects with narcolepsy in the current study had a mean period of 13 years between the onset of symptoms and diagnosis of narcolepsy. This extensive period prior to diagnosis may have resulted in the development of diminished self esteem in this subject group and therefore the findings from the present study may not be generalisable to all narcoleptic subjects. The results of this study therefore require validation across more diverse narcoleptic populations.

The results of the current study suggest that subjects with narcolepsy have equivalent knowledge of memory processes to control subjects. The perception of diminished memory function for subjects with narcolepsy (that is secondary to decreased self

efficacy for memory capabilities) may provide one explanation of the discrepancy in the literature between subjective and objective measures of memory function for people with narcolepsy. Study 1 of this thesis also provides an alternate, or potentially additional explanation for these subjective memory deficits. Subjects with narcolepsy may experience diminished memory function when sleepy, but this decrement has not been demonstrated by studies which have utilised "artificial" memory performance tasks, often in stimulating testing environments, where narcoleptic subjects remain fully alert. The results of study 1 suggest, however, that under conditions of induced sleepiness, where memory functions are embedded in more realistic complex processing tasks (such as the PASAT), then significant performance decrements can be demonstrated.

Chapter 11 will further discuss the argument of the thesis author that subjective impressions of memory dysfunction in narcolepsy are potentially explained by both (a) the diminished self esteem that narcoleptics develop, secondary to the experience of living with narcolepsy, and, (b) by the objective experiences of diminished cognitive function, secondary to the effects of sleepiness in narcolepsy.

CHAPTER 11

General Discussion

Overview

Chapters 5 to 8 have reported on the theoretical framework, the methodology, and results of studies one and two of this thesis. The focus of these studies was an evaluation of the impact of sleepiness on performance for subjects with narcolepsy (Chapters 5-7) and the subsequent comparison of these findings to the impact of 32 hours of sleep deprivation on performance for non pathologically sleepy subjects (Chapter 8). The theoretical implications of these studies have been discussed in Chapter 9. The results of the third study, an evaluation of metamemory processes for subjects with narcolepsy, have been discussed at the conclusion of Chapter 10.

This final discussion chapter will review the methodological issues associated with the evaluation of the relationship between sleepiness and performance in narcolepsy in addition to discussing more general aspects of the issues raised in this thesis.

Performance Measures as Indices of Daytime Sleepiness

Chapter 1 of this thesis reviewed the literature that has attempted to define and characterise the construct of daytime sleepiness. It is evident that relative to the parent states of sleep and wakefulness, sleepiness, as a psychophysiological state, has received relatively limited attention. Attempts to measure sleepiness have been confounded by the lack of convergent validity between instruments (Broughton, 1992c) a finding which has been explained as evidence for the multidimensional nature of the state (Broughton, 1992c). Accurate definition of the state of sleepiness therefore needs to encompass the integration of

these multidimensional components. The difficulties of defining daytime sleepiness for people with narcolepsy reflect this dilemma with minimal relationships reported between their subjective and objective measures of sleepiness (Browman & Mitler, 1988). This lack of congruence between measures has traditionally been explained as a consequence of subjects with narcolepsy providing inaccurate evaluations of their own state. It seems inappropriate, however, to argue that objective laboratory based assessments of sleepiness, such as the MSLT, should be used as criteria for the assessment of sleepiness symptoms without recognition of the experiences of the person living with the disorder, especially as there is evidence to suggest that, for subjects with narcolepsy, laboratory assessments of sleepiness, have limited external validity. Similarly the response of subjects to intervention strategies, such as stimulant medication, must incorporate a measure of the subject's own impression of increased functional capacity rather being entirely dependent on an objective measure of sleep latency. There is little value in *telling* people that their sleepiness is contained if their everyday experience of the impact of sleepiness on their lives remains unchanged.

Thayer (1978) would argue that subjective experiences are in fact the most accurate assessments of a psychophysiological state such as sleepiness, as the process of developing subjective evaluations involves the integration by the CNS of the multifaceted aspects of the state. So ultimately, Thayer suggests, how sleepy one feels may be a function of the integration of the physiological need to sleep, moderated by influences such as environmental and motivational factors.

A second potential strategy for measuring daytime sleepiness, which acknowledges the multidimensional aspects of the state, is to infer the severity of the state from the impact of sleepiness on functional capacity, as defined by performance measures. Neuropsychology certainly embraces the premise that changes to aspects of CNS functioning are mirrored by

measurable changes in performance capabilities. There is considerable face validity therefore to the suggestion that changes in performance capabilities provide a measure of sleepiness that has some external validity by acknowledging the impact of the disorder on everyday functional capacity. In fact the literature on non pathological sleepiness has been primarily driven by the need to assess the impact of sleepiness on performance. Gillberg, Kecklund and Akerstedt (1994) suggest that subjective sleepiness measures are in fact the only criteria that individuals can use to make decisions about their capacity to continue work. For people with narcolepsy, however, there has been limited attention to functional outcomes of sleepiness, in preference to an analysis of objective criteria for sleepiness. This lack of attention to performance outcomes seems to have occurred partly as a consequence of general methodological difficulties associated with performance testing, coupled to aspects of sleepiness that seem specific to narcolepsy, in particular perhaps the high lability of the sleepiness and its apparent sensitivity to extraneous factors.

Study one evaluated the impact of sleepiness on performance for subjects with narcolepsy and demonstrated that complex processing tasks such as the PASAT were highly significant discriminators between sleepy and non sleepy narcoleptic subjects. This affirmed that under conditions where sleepiness is expressed by narcoleptic subjects functional performance deficits can be demonstrated. Perhaps a practical implication of this finding is that future investigations of sleepiness in narcolepsy may make use of *change* in performance capacity as both a baseline measure of the level of narcoleptic sleepiness and the subsequent responsiveness of this sleepiness to treatment strategies.

Issues Re Utilisation of Performance Measures

Whilst the previous section has argued the theoretical advantages of utilising performance measures as indices of sleepiness there are substantial methodological problems associated with evaluating this interaction between sleepiness and performance. Johnson (1982) provides an overview of the extraneous variables that potentially impact on the general relationship between sleepiness and performance and this section will evaluate the impact of some of these variables on evaluating both the effects of sleepiness on performance and the use of performance as a measure of sleepiness for subjects with narcolepsy.

Fatigue

A primary factor associated with performance evaluations is the interactive relationship between sleepiness and fatigue. Whilst the term fatigue is constantly used in the performance literature, and frequently noted as a confounding factor in sleep deprivation research, the term, and its relationship with the concepts of, arousal, sleepiness, attention, vigilance and tiredness, remains ill defined. Welford (1980) defines fatigue as the performance decrement that occurs as a consequence of prolonged time on task, this effect being reversed by rest, or by the redirection of attention to a novel activity. Whether sleepiness interacts with fatigue as an additive function or whether a more complex exponential function exists between the variables is yet to be defined. Prior to the study reported in this thesis no literature existed on the impact of fatigue on performance measures for subjects with narcolepsy. Godbout and Montplaisir (1986) noted that across a ten minute reaction time task, deficits for the narcoleptic subjects, in comparison to controls, became more pronounced in the second half of the testing session, though the authors did not directly attributed this to the effect of fatigue. The current study evaluated the effects of fatigue on

performance across the brief (two minute) PASAT task and the five minute D2 concentration endurance task. Neither task demonstrated an increase in error rate across time for the sleepy narcoleptic subjects compared to controls, supporting the finding from the general sleep deprivation literature that fatigue effects can be controlled for by the utilisation of brief performance tasks.

Welford's (1980) definition of fatigue suggests that the propensity for fatigue to impact on performance appears to have a volitional component that reflects the degree of interest the subject retains in the task. Henry et al., (1993) utilised a one hour testing protocol for narcoleptic subjects but " the order of tests was changed within subjects and between sessions to control for fatigue effects " (p. 124). As with most attempts to compensate for fatigue effects within the experimental methodology there is no measurement strategy to evaluate the effectiveness of the manipulation, and to separate residual fatigue from sleepiness induced impairments. Johnson (1982) argues that perhaps at some critical level of sleep loss, fatigue effects become inseparable from sleepiness effects and it is meaningless to attempt to differentiate the causes of performance decrement.

Motivation

The possibility of limiting the effects of fatigue by providing opportunities for subjects to shift attention to novel tasks introduces the role of motivation in performance outcomes. A frequently reported finding in the literature on narcolepsy is that narcoleptics perform well on short, interesting cognitive tasks (Aguirre et al. 1985; Rogers & Rosenberg, 1990) but display performance deficits on monotonous tasks such as vigilance and reaction time tasks (Godbout & Montplaisir, 1986; Greenblatt, Campbell, Pollak & Moline, 1993;

Henry et al., 1988; Valley & Broughton, 1981). This capacity of subjects with narcolepsy for phasic arousal is noted by Aguirre et al., (1985) who suggest

> A final explanation, which we prefer has to do with the narcoleptics'... capacity to rally their resources and perform well when given a challenging task.... narcoleptics can perform normally on tasks which are relatively motivating ... whereas they show substantial impairment on more boring repetitive tasks (p. 21).

The quotation cited above suggests that for subjects with narcolepsy the capacity to overcome the effects of sleepiness, by increasing attentional effort, is influenced, in part, by task variables and these within task factors will be discussed below. The present study noted, however, that in addition to task factors, aspects of individual difference, not necessarily associated with narcolepsy, also influenced the extent to which subjects attempted to overcome the effects of sleepiness. For example subject N3 (study 1) at the start of the low arousal testing on the digit symbol substitution task stated "now let me get really comfortable so I can win this one". This motivational confound highlights perhaps the general difficulty of testing within an artificial, laboratory environment, and questions the external validity of these test outcomes for the everyday experience of cognitive functioning. Effects of motivation on performance are potentially artefacts of the laboratory testing protocol where attentional demands are focussed specifically by the experimenter. In non laboratory settings the responsibility to even select appropriate stimuli for attention remains with the subject, as does the ability to maintain or prioritise attention in the context of irrelevant stimuli. Norton (1970) has demonstrated that sleep loss interferes with this ability to screen out irrelevant stimuli and it is interesting therefore that the most sensitive measure for sleepiness effects in

narcolepsy was the PASAT, a task which assesses in part the ability to cope with competing cognitive demands.

Whilst no literature exists directly measuring the effects of motivation on performance for subjects with narcolepsy the findings from the general sleep deprivation literature suggest that critical limits of sleepiness exist, beyond which compensatory effort cannot overcome sleepiness effects (Dinges et al., 1992). Observation of narcoleptic subjects during testing sessions provide tentative support for the conclusion that critical limits also exist for subjects with narcolepsy. Subject N5 (study 1) when woken after a nap session reported she felt too "shaky" to attempt any tasks and needed more sleep. Subject N2 (study 1) needed urging under the low arousal condition to even attempt any tasks. Both subjects became angry at the experimenter when coaxed to continue with the tasks. This increase in negative affect for sleepy subjects has also been demonstrated in non pathologically sleepy subjects (Brendel et al., 1990). It remains unclear however how aspects of individual difference interact with levels of sleepiness to determine an individual's motivation to perform a task.

Task Variables

The sensitivity of performance tasks to levels of sleepiness appear to be partly determined by task characteristics, however, the relationship between task characteristics and sensitivity to sleepiness remains confounded. Several variables may impact on task characteristics including task duration (which has also been demonstrated to influence fatigue factors), task complexity and the intrinsic interest of the task (again potentially influencing motivational factors). Whilst brief monotonous tasks (such as reaction time or vigilance tasks) may limit the extraneous variables of motivation and fatigue and therefore increase the

sensitivity of the task to sleepiness effects, Horne (1991) argues that the cognitive skills measured by these laboratory tasks have a limited relationship with the complex processing tasks necessary for everyday functioning. Rogers and Rosenberg (1990) anticipated the concerns of Horne suggesting that the inability of laboratory studies to replicate performance deficits in subjects with narcolepsy may reflect the artificial nature of standard laboratory tests of cognitive skills such as memory functioning which test mundane learning skills rather than the skills of "spontaneity, creativity and flexibility" (p. 51) that characterise the everyday context of memory performance. The data presented in study one of this thesis certainly supports the contention that increased task complexity results in increased sensitivity to sleepiness effects. Complex tasks demonstrating an increased sensitivity to arousal despite the possibility that the more complex performance tasks may also increase the motivational incentive for subjects.

Whilst study 1 reported in this thesis was able to demonstrate the impact of sleepiness on performance for subjects with narcolepsy, the use of performance measures to index levels of sleepiness is confounded by factors such as fatigue, motivation, task variables and aspects of individual difference. Despite these confounds, which are intrinsic to all sleep deprivation research, the utilisation of performance as a measure of sleepiness in narcolepsy remains an area for future research, potentially providing a more functionally valid assessment of daytime sleepiness than objective sleepiness measures.

Methodological Problems for Within Subject Designs

The current study utilised a within subject design to evaluate the effect of sleepiness on cognitive performance for both narcoleptic and control subjects. In both studies one and two manipulations of the levels of subject sleepiness provided low and high arousal conditions

for evaluation of performance change as a function of arousal. Repeated testing of non sleepy control subjects was also used as a measure of practice associated with the performance tasks.

The major advantage of within subject designs are that they allow for the estimation of performance variability as a function of the experimental manipulation and are not confounded by differences due to between subject variability. As narcolepsy is associated with high intersubject variability in symptomology, including levels of daytime sleepiness (Aldrich, 1992) a within subject design was selected to minimise this extraneous arousal confound. Webb (1992) cautions, however, that the use of within subject difference scores (which are utilised extensively in the sleep deprivation literature) may be associated with several measurement problems. Specifically, he argues that (a) the measurement of change between time intervals is confounded by the fact that whilst change is often presumed to occur in a linear fashion it is more accurately described via an exponential function. Replication of experimental findings of change scores are therefore dependent on precise matching of time intervals as measurement at different phases of the exponential curve will result in significant differences between measures; (b) measurement of change scores may be confounded by mathematical dependencies in the data and dimensions of change may be inappropriately attributed to experimental manipulations rather than identified as secondary to this mathematical relationship. Similarly the tendency of initial extreme scores to regress toward the mean across repeated measures confounds the influence of the independent variable on measures of change; (c) difference scores are, according to Webb (1992), always less reliable than initial data scores and, as the reliability of the data measurement increases, the reliability score becomes so low that "residual difference scores have such low reliabilities that they cannot serve as effective dependent variables" (p. 161); (d) finally Webb (1992) argues that

across an experimental protocol changes secondary to the experimental manipulation invariably influence the dependent variable. Within a sleep deprivation protocol testing post the arousal manipulation may be confounded by extraneous variables such as fatigue, mood variability or motivational effects. The comparison of difference scores between experimental protocols is therefore confounded by the difficulty in replicating the conditions of the initial and end measures.

One issue that emerges specifically in relation to within subject measurement in narcolepsy is that whilst the within subject methodology is utilised to limit the between subject variability in arousal measures, arousal at any time for subjects with narcolepsy is unstable and therefore variability in arousal remains a significant measurement problem even using a within subject design. Valley and Broughton (1983) report that across a one hour vigilance task narcoleptic subjects demonstrated an average of 36 shifts between EEG defined arousal conditions in comparison to an average of 3.6 shifts for control subjects. Valley and Broughton (1983) were further able to identify performance change associated with arousal fluctuation across time intervals as brief as three seconds. Comparison of performance measures across five or ten minute performance tasks could therefore be subject to multiple within subject arousal fluctuations. The presumption, therefore, that manipulated conditions of high or low arousal represent a stable testing arousal condition for the narcoleptic subject must be treated with caution. It is also possible that the low and high arousal conditions vary for subjects with narcolepsy in relation to state stability Dinges and Kribbs (1991) suggest that state lability is the most predominate characteristic of sleepiness in non clinical subjects with an "increasing fluctuation between alertness, lowered vigilance, drowsiness and microsleeps, that results from the interplay of motivation to perform and a relentless pressure, for rapid transition from wake to sleep" (p.119). The results of study one reported in this

thesis certainly support the contention that for subjects with narcolepsy conditions of increased sleepiness are associated with increased lability of performance. Particular issues of experimental reliability therefore exist for evaluation of performance change associated with increased sleepiness for this experimental group as without continuous monitoring of arousal states, matched arousal conditions for study replication cannot be identified. Perhaps this performance lability associated with sleepiness provides partial explanation for the diverse findings of experimental studies that have attempted to evaluate cognitive function in narcolepsy (refer Table 1, Chapter 4).

Despite these cautionary notes on the limitations of within subject experimental designs the protocol still provides control over the additional confound of intersubject variability and appears therefore the most appropriate methodology currently available for an evaluation of the impact of sleepiness on performance.

Study one reported in this thesis categorised arousal for subjects with narcolepsy into the dichotomous states of low and high arousal and whilst this separation was validated by the subjective ratings of the participants, it fails to acknowledge that arousal is a labile state and the degree of lability increases with decreasing levels of arousal. The implications of this characterisation of sleepiness in narcolepsy to the theoretical perspectives of sleepiness have been discussed in Chapter 9.

Methodological Problems With the Use of Mean Performance Scores

Millar (1992) provides a substantial overview of the potential difficulties that develop as a consequence of utilising mean scores as performance outcomes. The failure to report on individual variability of performance may obscure the fact that significant differences exist between subjects in response to the experimental manipulation. Millar

(1992) highlights the potential dangers of ignoring or excluding from the data analysis extreme values, suggesting that in the field of clinical research the failure to evaluate the variance of scores about the mean may lead to the development of inappropriate general rules about the efficacy of particular treatment interventions. For example Millar (1992) notes that despite the general pharmacological rule of benzodiazepines impairing performance, evaluations of the efficacy of benzodiazepine treatment amongst highly anxious patients demonstrates that for this subgroup of patients treatment significantly improves memory performance.

Narcolepsy is associated with considerable variability in symptomology and as yet it remains unclear whether these differences reflect differences in the severity of the disorder or potentially represent qualitatively different subgroups of the disorder. Of central interest is the potential significance of the presence of cataplexy in the diagnosis of narcolepsy. Rosenthal et al. (1990) suggest that there has been a shift from clinical symptom based diagnoses of narcolepsy to polysomnographic criteria and this has resulted in two subgroups of narcoleptic patients - those with EDS and polysomnographic signs of narcolepsy but without cataplexy and those with clear clinical signs of EDS coupled to unequivocal cataplexy. Subjects with cataplexy appear to have increased levels of daytime sleepiness, increased nocturnal sleep disruption and increased REM symptomology in comparison to subjects with polysomnographic diagnoses of narcolepsy unassociated with cataplexy (Rosenthal et al., 1990). Moscovitch et al. (1993) and Guilleminault et al. (1994) have also tried to identify whether subgroups of narcoleptic subjects can be identified using the criteria of cataplexy versus MSLT measures. Whilst patients with cataplexy were the most homogenous group in terms of both polysomnographic and clinical variables, not all narcoleptic subjects (with cataplexy) met the diagnostic criterion of two or more SOREMPs.

As a diagnostic criterion the finding of two or more SOREMPs also results in false positive diagnoses of narcolepsy (Guillemiault et al., 1994).

Measures of narcoleptic performance in the current study have been evaluated on the basis of mean performance scores. For several analyses it was evident that extreme scores led to a skewed performance distribution with an associated shift of the mean performance score. Whilst statistically there are arguments for removing outliers from the analysis, attention to these outliers may well provide insights into the heterogeneity of the narcoleptic population. Future evaluations of performance measures in narcolepsy could therefore focus on potential performance differences as a function of presenting symptomology.

Narcolepsy as a Chronic Illness

Narcolepsy is an illness characterised by chronicity and often fluctuating symptomology. The experience of living with narcolepsy and its implications for psychosocial adjustment demonstrate similarities with the reports of the life experiences of other people living with disorders such as multiple sclerosis, chronic fatigue syndrome and lupus erythematosus, disorders which Donoghue and Siegel (1988) describe as invisible chronic illness (ICI). Donoghue and Siegal (1988) suggest that psychological consequences of living with ICI include self doubt, self dislike, uncertainty, interpersonal insecurity, loss of self esteem, guilt, and fear of mental illness. These feelings are often expressed by narcoleptic sufferers and reinforced by societal, professional and often familial scepticism about the "realness" of their disability. Many of the subjects who participated in the first study reported in this thesis described their early experiences of daytime sleepiness being attributed to laziness, and sleepiness in early adulthood as consequent to the normal tiredness associated with caring for children. Subject J. describes the onset of her sleepiness at about the age of

10 but no one took any notice until she was about 14 when she remembers being taken to the doctor who suggested she was just too fat and too lazy. J remembers feeling that "there were other fat kids at school who didn't fall asleep". J's self doubt is expressed in her statement that she feels angry at living with narcolepsy "angry that my mind is not strong enough to beat it" Subject K reports the worst aspect of the disorder as people's lack of acceptance "they basically believe it is just in my mind, I've given up trying to explain it to people it's not worth the effort". This lack of acceptance may extend to family members of the person with narcolepsy. One respondent to the metamemory questionnaire apologised for his wife not completing the control questionnaire writing "sorry but my wife - who largely believes that narcolepsy could be overcome with more discipline!! - got tired of trying to answer what she called ridiculous questions". The desperation experienced by many people with narcolepsy to find a solution to their sleepiness is illustrated by the reports of subject E. who provided a list of the treatments she has tried and said "...some have remembered this funny old woman and her persistent sleep problem and have referred her to some other poor unfortunate - others have led me on, taking my money with no difference felt". The lack of acceptance of the disorder has lead many people with narcolepsy to develop strategies to hide the disorder. Sleep attacks are reported to be managed by hiding in the toilets to get a few seconds sleep (subject J) and the fear of cataplexy has led people to become socially withdrawn - subject E reports that cataplexy occurs when she tries to "be smart and speak up---I know it or can do it --but cannot".

Despite the substantial literature that exists identifying the negative psychosocial implications of living with narcolepsy (Broughton, et al., 1981; Kales et al., 1982; McMahon, Walsh, Sexton & Smitson, 1982; Broughton et al., 1983; Krishnan et al., 1984; Alaia, 1992; Broughton, 1992; Cohen, Ferrans & Smith, 1992; Ferrans, Cohen & Smith, 1992; Cohen &

Mudro 1992; Merritt, Cohen & Smith, 1992; Karacan et al., 1992) no parallel literature base exists to evaluate the implications of adjustment to the disorder as a consequence of treatment strategies that incorporate attention to these psychosocial aspects. Goswami (1992) acknowledges the need for attention to the psychosocial aspects of the disorder with the need to incorporate a counselling service in the treatment of narcolepsy but no literature exists to report on the outcome of adjustment to the disorder as a consequence of psychosocial intervention strategies. This occurs despite the clear evidence in the literature that adaptation to the psychosocial dimensions of chronic illness directly effects the outcome of the illness (White, Richter & Fry, 1992).

Current investigations of narcolepsy reflect the predominance of a biomedical model of the disorder, which assumes that illness can be fully accounted for by biological factors (DiMattoe, 1991). The questions investigated in the narcolepsy literature reflect this biological orientation, evaluating the features of the disorder, its neurophysiology and the efficacy of pharmacological interventions in the treatment of the biological symptoms of narcolepsy. This emphasis on a medical model of narcolepsy has resulted in tensions existing in the literature between objective and subjective experiences of narcolepsy. The subject with narcolepsy may report subjective sleepiness but the failure of objective experimental indices of sleepiness to validate these subjective impressions has led researchers to conclude that the discrepancy reflects the inability of subjects with narcolepsy to evaluate their own sleepiness state. Such conclusions act to invalidate the experience of the person with narcolepsy. Engel (1977) argues that a paradox of the biomedical model is that treatment is only available for people whose illness can be validated by laboratory findings and the subjective experience of illness, or the *reality of illness in human experience*, becomes inconsequential. Engel (1977) contends that illness must be redefined within a biopsychosocial model which incorporates

physical, cultural, social and psychological components. Maximising adjustment to chronic illness therefore involves attention to all facets of the model and successful interventions are validated, not solely by laboratory indices, but by the subjective experience of improved functional status for the individual. For the person with narcolepsy improved scores on the MSLT are of little significance if their subjective experience of an inability to cope with daytime sleepiness remains unaltered. Perhaps the discrepancy that exists in the literature between subjective and objective experiences of narcolepsy emerge as a consequence of the failure of interventions to be provided within this biopsychosocial model of illness. Successful adjustment to this disabling illness can be enhanced by attention to the significant psychosocial issues which accompany the biological aspects of the disorder.

Conclusion

This thesis has attempted to evaluate the relationship between sleepiness and performance in narcolepsy. Narcolepsy is a disorder that is characterised by constantly fluctuating arousal states and perhaps it is this fluctuation of arousal, rather than the sleepiness itself, that makes both the exploration and understanding of sleepiness and performance interactions so complex in this clinical group. This thesis has demonstrated that under conditions of high arousal narcoleptics perform as efficiently as control subjects on tasks tapping a range of cognitive processes, suggesting that the disorder is not one of general hypoarousal. When it is possible to 'capture' narcoleptic sleepiness, however, this thesis suggests that sleepiness leads to significant decrements in complex processing tasks and these decrements appear to be unrelated to motivational or attentional factors, and, in the current study, were reversed only by restorative sleep. This finding of diminished cognitive

functioning associated with sleepiness provides support for the subjective experiences reported by narcoleptic subjects.

The symptom of daytime sleepiness, associated with fluctuating arousal, also has significant psychological implications for narcoleptic sufferers. Typically narcoleptic subjects report feelings of self doubt, diminished confidence and decreased self esteem as a consequence of living with the disorder. The experience of self doubt appears linked with the difficulties for families, friends and even health professionals in diagnosing, understanding and providing appropriate support for the sufferer. The psychological impact of this disorder is clearly demonstrated by the high prevalence of psychological disorder, particularly depression, within the narcoleptic population.

Psychological factors appear to also impact on the capacity of individuals to evaluate their own cognitive function. The metamemory analysis reported in this thesis demonstrated that it was decreased self efficacy for memory function rather than decreased memory knowledge, or capacity, that characterised narcoleptics' understanding of their memory function.

This thesis argues that the subjective experience of cognitive dysfunction for narcoleptic subjects is therefore consequent to both their objective experiences of actual dysfunction during periods of decreased arousal and their diminished confidence for memory functioning which is subsequent to the psychological impact of living with narcolepsy. These dual pathways to the subjective experience of cognitive dysfunction are demonstrated in Figure 17.

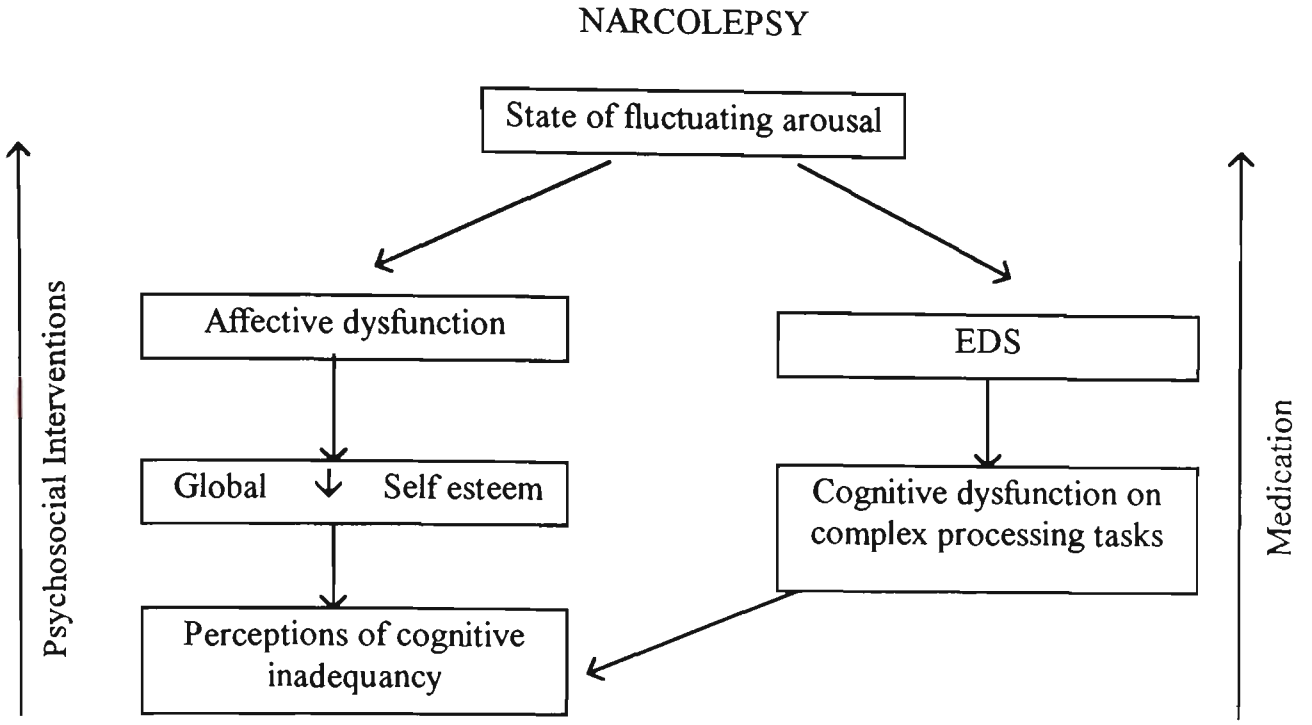


Figure 17 Integrative model of the physiological and psychological factors leading to perceptions of cognitive dysfunction in narcolepsy.

Interventions for subjects with narcolepsy therefore need to address both the physiological and psychological components of this experience of cognitive dysfunction. Use of stimulant medication decreases the symptom of daytime sleepiness and therefore potentially also decreases the objective experience of cognitive dysfunction that occurs consequent to sleepiness. Psychological interventions are also necessary, however, to both ratify the subjects' experience of actual cognitive dysfunction associated with the disorder, in addition to increasing global self esteem and confidence in relation to cognitive functioning. The need to attend to the subjective experiences of narcoleptics of cognitive dysfunction are highlighted by subject J. who stated :

"I often wonder how different my life might have been, if people had just believed me".

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APPENDIX 1

Journal Article

Hood, B.M., & Bruck, D. (1996). Sleepiness and performance in narcolepsy. Journal of Sleep Research, 5, 128-134.

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Sleepiness and performance in narcolepsy

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SUMMARY Previous attempts to investigate the relationship between sleepiness and performance for subjects with narcolepsy have been limited by both the ability of narcoleptic subjects to contain their sleepiness for brief testing periods and the potential lack of sensitivity of routine performance tasks to sleepiness induced changes. The present study developed a research protocol which allowed subjects with narcolepsy to express states of sleepiness and non sleepiness and to then compare the performance of subjects with narcolepsy to age, gender and IQ matched controls on tasks evaluating automatic, attentional and complex cognitive functioning. The results indicated that at high arousal subjects with narcolepsy performed as well as controls on automatic tasks suggesting that the capacity to perform for narcolepsy subjects is not restricted by physiological factors but is secondary to the effects of sleepiness. Comparison of both the within subject effects for narcolepsy subjects of the transition between high and low arousal states, and the between subject effects of low arousal for narcolepsy subjects compared to controls indicate that complex cognitive tasks are the most sensitive to arousal fluctuation. This study provides support for the subjective experiences of subjects with narcolepsy of diminished cognitive function associated with the disorder.

KEYWORDS induced sleepiness, narcolepsy, performance, sleep

INTRODUCTION

In the one hundred years since Patrick and Gilbert (1896) reported on performance decrements associated with experimentally induced sleepiness in non clinical subjects, there has been extensive interest in the physiological processes mediating the relationship between sleepiness and cognitive dysfunction. Two major theoretical models have evolved; attentional and cognitive. Proponents of the attentional model (Kjellberg 1977a,b,c; Meddis 1982) argue that performance decline, associated with sleepiness, occurs as a function of the diminished attentional factors that sleepy subjects apply to a task. The implication of this model is that sleep-induced performance decrements are reversible and contingent on behavioural resources, such as attention or motivation. In contrast, theorists supporting a cognitive model (Horne 1988) suggest that sleepiness leads to fundamental changes in sensory and cognitive processing capacity. These cognitive changes are not reversed by compensatory effort but are contingent on restorative sleep. Horne (1988) further combines the attentional and cognitive models proposing that performance decrements associated with sleepiness can initially be compensated for by increased attentional resources, but beyond some critical level of sleepiness, subsequent performance decrements are only reversed by restorative sleep. The tasks most dependent on restorative sleep are those that assess more complex cognitive function (Horne 1988).

Narcolepsy is a disorder characterized by excessive and pervasive daytime sleepiness and therefore there is considerable face validity to the suggestion that this sleepiness would lead to observable decrements in performance, in just the same way as sleepiness leads to performance decrements in normal populations. Subjective reports from narcoleptic subjects support this prediction with over 40% of narcoleptics reporting impaired memory function since the onset of the disorder (Broughton and Ghanem 1976).

Since the early 1980s there have been several studies that have attempted to demonstrate the relationship between sleepiness and performance for narcoleptic subjects (Broughton *et al.* 1982; Aguirre *et al.* 1985; Levander and Sachs 1985; Godbout and Montplaisir 1986; Ollo *et al.* 1987; Henry *et al.* 1988; Rogers and Rosenberg 1990; Pollack *et al.* 1992; Smith

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et al. 1992; Henry *et al.* 1993). The findings surrounding these studies, reflect the same theoretical dilemma that pervades the general sleep deprivation literature – are performance decrements in narcolepsy explained by attentional or cognitive mechanisms? Aguirre *et al.* (1985), Ollo *et al.* (1987), and Rogers and Rosenberg (1990), would argue that performance decrements in narcolepsy have no organic base, but occur as a consequence of diminished attentional resources, that are secondary to narcoleptic sleepiness. Performance decrements can therefore be compensated for by increased attentional effort. This attentional model is supported by the finding that narcoleptics perform as effectively as controls in stimulating test environments (Aguirre et al. 1985; Rogers and Rosenberg 1990), but demonstrate performance decrements for repetitive and monotonous tasks, such as vigilance tasks, where there is minimal motivation to apply compensatory effort (Valley and Broughton 1983). However, the diminished performance of narcoleptics on vigilance tasks could be explained within an alternative paradigm. On the basis of psychophysiological data Levander and Sachs (1985) suggest that narcoleptics may have a decreased tonic or habitual arousal state. Automatic tasks, such as vigilance tasks, that tap into tonic arousal capacity, would then demonstrate performance decrements in comparison to controls. Additional support for this model comes from the findings of Henry *et al.* (1988), and Henry *et al.* (1993), who demonstrated that unmedicated narcoleptics had significantly increased response latencies on the Sternberg scanning task, suggesting a deficit in perceptual encoding capacity, consistent with diminished tonic arousal levels.

A methodological confound to many of the studies evaluating subjective reports of performance decrements in narcolepsy is that narcoleptics are clearly able to contain their sleepiness for brief testing periods and often fail to demonstrate any behavioural signs of sleepiness during testing sessions (Aguirre *et al.* 1985; Henry *et al.* 1993). Previous evaluations of the relationship between performance and sleepiness in narcolepsy have operationalised sleepiness through either electrophysiological definitions such as electroencephalography (Valley and Broughton 1983; Rogers and Rosenberg 1990; Pollack *et al.* 1992) and evoked potential measures (Broughton *et al.* 1982; Ollo *et al.* 1987), or behavioural (Aguirre *et al.* 1985), or physiological parameters (Levander and Sachs 1985; Henry *et al.* 1993). It is difficult to establish whether the often very brief changes in narcolepsy arousal states identified by these measures reflect the day to day experience of sleepiness for narcoleptics, and researchers have therefore questioned the external validity of laboratory based performance findings for this clinical population (Rogers and Rosenberg 1990; Rogers and Aldrich 1993).

The present study aimed to establish a test protocol which allowed cognitive testing of narcolepsy subjects under stable states of sleepiness and non sleepiness, and to evaluate the effect of sleepiness on performance for narcolepsy subjects across a range of cognitive tasks.

Three specific research questions were addressed:

1 If changes in levels of sleepiness for narcolepsy subjects can be demonstrated experimentally, what is the impact of that sleepiness on performance for narcolepsy subjects?

2 If sleepiness for narcolepsy subjects is associated with performance decrements are attentional or complex processing tasks most sensitive to these sleepiness effects?; and

3 Under conditions of high arousal or non sleepiness do subjects with narcolepsy demonstrate diminished performance on tasks measuring tonic arousal capacity compared to controls?

METHOD

Subjects

Eight narcolepsy subjects participated in the experiment. All subjects had specialist diagnosis of narcolepsy and met the International Classification of Sleep Disorders (1990) criteria of excessive daytime sleepiness with the presence of recurrent daytime naps and unequivocal cataplexy. The group comprised seven females and one male subject. The age of the narcoleptic subjects ranged from 28 y to 72 y with a mean age of 53 y (SD = 12.5). IQ scores of narcoleptics were determined using the K-Bit Brief Intelligence Scale (Kaufman and Kaufman 1990) and scores ranged from 93 to 123 with a mean score of 102 (SD = 11.35). Of the eight narcolepsy subjects six were normally taking stimulant medication: Dexamphetamine (N1, N3, N5), Methylphenidate (N2, N7) and Mazidol (N8). As central nervous system stimulant medication interferes with both arousal, and cognitive performance measures, subjects were requested to withdraw from stimulants a minimum of 18 h prior to testing. This withdrawal period provided a compromise between minimizing both the effects of stimulant confounds and the level of disruption to subjects' daily functioning. All other medications, including tricyclic antidepressants, were continued throughout the test period. Any residual effects of medication were not considered to effect the validity of the study as the emphasis of the analysis relates to within subject changes in performance in a repeated measures, pre and post nap experimental design. Measures of baseline arousal, free of any effects of medication, were therefore not critical to the study.

Eight control subjects were selected from acquaintances of the experimenter and matched with narcoleptic subjects on the variables of gender, age (within an arbitrarily defined seven year range), and IQ (within the 95% IQ confidence interval of the narcoleptic subject). Although educational status has also been demonstrated to effect performance measures, it was not included as a matching variable in this study, as narcolepsy has been demonstrated to substantially impair educational attainment (Kales *et al.* 1982). Control subjects were screened to exclude subjects reporting nightime sleep disruptions, daytime sleepiness or depression. One control subject (C6) was on medication for angina at the time of testing and this medication was continued over the test period.

Apparatus and Procedure

Testing was carried out at the Victoria University Sleep Laboratory. The laboratory is a two-bedroom temperature-

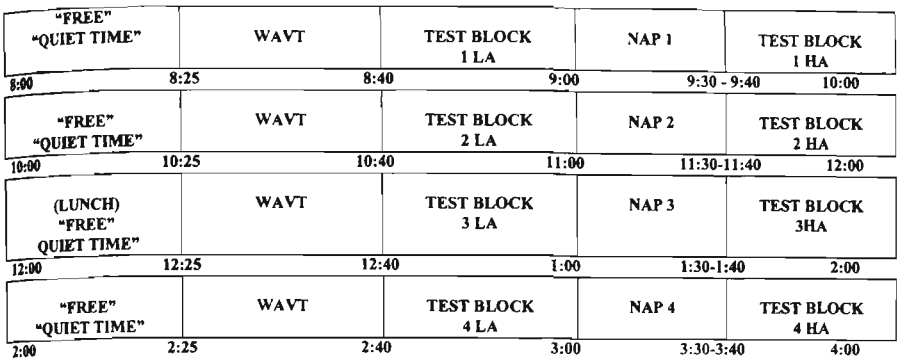

Figure 1. Schematic representation of testing schedule for subjects with narcolepsy. LA, low arousal, HA, high arousal.

controlled facility shielded from the external environment. Figure 1 provides an overview of the testing schedule.

Subjects attended the laboratory the night prior to testing and their overnight sleep was recorded, using standard recording measures (Rechtschaffen and Kales 1968). The testing day incorporated four testing sessions with each session being divided into a low arousal (LA) and high arousal (HA) condition. The period prior to low arousal testing was structured in line with the protocol demonstrated by Volk *et al.* (1984) to provide an environment facilitating low arousal conditions. The initial 25 min of the low arousal induction involved subjects having free quiet time. Subjects used this time to read or listen to music. For the 15 min immediately prior to LA testing subjects completed the WAVT task which has been demonstrated to be a sleep inducing task for narcoleptic subjects (Valley and Broughton 1983). Subjects were observed during this period and were wakened if any behavioural signs of sleepiness occurred. Following this manipulation subjects completed a 20 min LA test block. Testing sessions were limited to this period to minimize the effect of fatigue on performance scores. Directly following the testing period narcolepsy subjects were given the opportunity to nap for 30 min. The literature demonstrates that naps have an alerting effect on narcolepsy subjects (Roehrs *et al.* 1984) and that naps as short as 15 min may be as refreshing as more extended nap durations (Roehrs 1985). In line with the findings of Mullington and Broughton (1994) a refractory period was included, following the nap, and before HA testing, to allow narcolepsy subjects to achieve full alertness. The tasks previously presented in the LA test period were then repeated under HA conditions. This sequence of LA and HA manipulation for testing was repeated for four test blocks across the day, with tasks evenly distributed between testing sessions. To assess the effectiveness of the arousal manipulation, narcolepsy subjects completed a visual analogue scale (VAS) measure of subjective sleepiness prior to each test session. The scale line was 100 mm in length with anchor points of 0 mm = lost struggle to remain awake, and 100 mm = alert wide awake. Control subjects completed a similar testing protocol, but no attempts were made to manipulate their arousal condition so the WAVT was not utilized with the control group. No structure was imposed on control subjects' use of time between testing sessions, except that no naps were permitted across the day. Control subjects demonstrated no behavioural signs of sleepiness across testing sessions though this observation was not quantified in the present study.

Performance tasks

Tasks were selected on theoretical grounds to test automatic (reaction time, Stroop dots and physical match); attentional (digit symbol substitution, Rey Auditory Verbal Learning Task, D2 concentration endurance task), and complex cognitive functioning (word fluency, paced auditory serial addition task, complex semantic reasoning, Stroop colours and semantic matching). Where possible brief tasks were selected to minimize fatigue effects. Administration and scoring of the Stroop, digit symbol, Rey Auditory Verbal Learning task (RAVLT), word fluency, D2 concentration endurance task (D2), and the paced auditory serial addition task (PASAT) followed standard protocols recommended by Spreen and Strauss (1991). Repeat administrations of the Stroop, RAVLT and the word fluency task utilized published alternate versions. Additional tasks included a two choice reaction time measure and two computerized cognitive tasks that assessed the speed of visual and semantic processing and response latencies for simple and complex semantic reasoning tasks. Full details of these computerised cognitive tasks are given in Levy *et al.* (1979).

Test presentation

Since narcolepsy is associated with high intersubject variability in arousal a repeated-measures experimental design was used and all narcolepsy subjects completed the performance tasks under both low and high arousal conditions. To control for both order and differential carry over effects test presentation was counterbalanced using a digram balanced Latin square design (Wagenaar 1969). However, the sequence of arousal fluctuation was not counterbalanced, and all tasks were completed at low and then high arousal. This low arousal/high arousal order of testing was maintained to allow for direct, practice-free comparison of performance scores between low arousal narcoleptics and controls. For the comparison of high arousal scores of narcolepsy subjects compared to controls, performance for both subject groups, represented the second testing session, and practice effects were considered equated between groups.

Data analysis

All data were analysed using SPSSx. Discriminant function analyses were used to identify the tasks which were the most powerful discriminators between experimental groups.

RESULTS

Manipulation of arousal

Each narcolepsy subject was asked to complete the VAS sleepiness rating on eight occasions. Four of these ratings represented manipulated low arousal conditions and four manipulated high arousal conditions. Of the possible 64 ratings 52 were completed by subjects, with the missing data equally distributed between arousal conditions. For the low arousal manipulation the mean arousal rating was 27.35, SD = 19.62, and for the manipulated high arousal condition the mean arousal rating was 74.73, SD = 17.55. Dependent *t*-test analyses of these findings demonstrated a significant difference between arousal conditions, $t_{25} = 12.13$, $P = 0.000$.

Performance measures

(i) The impact of sleepiness on performance for narcolepsy subjects

Mean performance scores for narcolepsy and control subjects, across all performance tasks, are presented in Table 1.

Descriptive statistical analyses of the data in Table 1 indicate that with repeated testing of control subjects mean scores for 10 of the 12 performance measures demonstrated an increment on the second testing session. The percentage change in performance scores between the two testing sessions, ranged from five to 24 percent (column C), and provides an estimate of the level of practice associated with repeated testing. For two tasks, long-term memory and complex reasoning, the second control testing session was associated with performance decrements, possibly representing fatigue or interference effects. Repeated testing of subjects with narcolepsy under LA and HA conditions led to increments in performance at the second testing session for all tasks except both memory tasks, which demonstrated a performance decline under high arousal conditions. The percentage increment in performance scores for narcolepsy subjects between low and high arousal conditions (column F) provides an estimate of the cumulative effects of both practice and arousal change. Column G represents the residual increment in performance for narcolepsy subjects, between low and high arousal conditions following the removal of practice effects. Of the 12 initial tasks completed by the subjects with narcolepsy, seven demonstrate some performance increment, free of practice, between low and high arousal testing conditions. Specifically the percentage change due to arousal fluctuation ranges from five to 75 percentage with the complex tasks of word fluency, semantic match, complex reasoning, and the PASAT demonstrating the greatest sensitivity to arousal fluctuation with percentage increments at high arousal of 14, 18, 28 and 75%, respectively. The D2 attentional task also demonstrated a 14% increment under the high arousal condition and the automatic tasks of physical match and Stroop dots demonstrated residual arousal effects of five and eight percentage, respectively.

(ii) Comparative performance on attentional and complex tasks, between narcolepsy subjects at low arousal and controls

To evaluate the tasks most sensitive to sleepiness for subjects with narcolepsy a stepwise discriminant function analysis was performed using the attentional and complex performance tasks as predictors of the grouping variables of narcolepsy subjects at low arousal, and control subjects. For both groups performance scores represented the first testing session and were therefore free of practice effects. To meet the criterion of discriminant analysis that the number of predictor variables be less than the group sample size (Tabachnick and Fidell 1989), the variables of STM and LTM were excluded from the discriminant analysis, as they demonstrated no clear residual arousal effect (Table 1). The predictor variables included in the analysis were digit symbol, word fluency, PASAT, Stroop colours, complex reasoning and semantic match.

The calculated discriminant function was highly significant with a $\chi^2_3 = 18.36$, $P = 0.0004$. The function accurately classified group membership for 100% of cases. The structure matrix of correlations between predictors and the discriminant function suggests that the best predictors for distinguishing between low arousal narcolepsy subjects and controls are the complex tasks of PASAT (−0.47635) and semantic matching (0.46395). Narcolepsy subjects at low arousal have decreased performance on the PASAT (mean = 19.12, SD = 10.33) compared to controls (mean = 30.12, SD = 6.42) and took significantly longer to complete the semantic matching task (mean = 105.62, SD = 27.21) than controls (mean = 78.37, SD = 17.23).

(iii) Comparative performance on automatic tasks between narcolepsy subjects at high arousal and controls

A discriminant function analysis was performed using three tasks as predictors of membership between the two groups. Predictors were the automatic tasks of reaction time, stroop dots, and visual match. Groups were narcolepsy subjects, under the high arousal condition, and controls. For both groups, scores represented performance measures at the second testing session, and practice effects were therefore considered equated between groups.

The calculated discriminant function was not statistically significant with a $\chi^2_3 = 0.25$, $P > 0.05$. The tasks tapping automatic processing do not discriminate between control subjects and narcoleptics at high arousal.

DISCUSSION

The present study aimed to explore the impact of sleepiness on performance for subjects with narcolepsy in an experimental setting that allowed for the expression of behavioural states of

Table 1 Mean performance scores and percentage change for practice and sleepiness effects across all performance tasks.

	A	*B*	*C*	*D*	*E*	*F*	*G (F−C)*
	(Mean) Cont 1	*(Mean) Cont 2*	*Practice Effect %*	*(Mean) LA Narc*	*(Mean) HA Narc*	*Arousal+ Prac Effect %*	*Arousal Effect %*
Automatic							
Reaction time (s)	0.74	0.56	24	0.71	0.57	20	–
Stroop dots (s)	13.71	13.04	5	15	13.07	13	8
Physical match (msec)	89.75	71.25	21	90.5	67.13	26	5
Attentional							
Digit symbol (total)	41.25	47.37	15	49.5	54.25	10	–
D2	444.62	495.75	9	400.87	492	23	14
Short term memory (total)	5.87	6.37	9	6.12	6	−2	–
Lomg term memory (total)	8.75	8	−9	8.62	8	−7	–
Complex							
Word fluency (total)	42.37	47.87	13	33.12	42.12	27	14
PASAT (total)	30.12	32.37	7	19.12	34.87	82	75
Stroop colours (s)	33.20	25.67	23	34.14	27.4	20	–
Complex reasoning (msec)	562.25	588	−5	850.5	651.12	23	28
Semantic match (msec)	78.37	73.62	6	105.62	80.5	24	18

For tasks with time (msec s^{-1}) as the outcome measure the percentage change score for practice (C) is derived from the percentage difference of A–B, and the percentage change score associated with practice + sleepiness (F) is derived as a percentage difference of D–E. Where total number of items correct (total) is the outcome variable the procedure is reversed, and the effect of practice (C) is derived from the percentage change B–A, and the percentage change associated with practice + sleepiness (F) is derived from the percentage difference E–D. Residual percentage sleepiness effect (G) always represents F–C.

sleepiness and non sleepiness. Visual analogue scale ratings of sleepiness under the manipulated high and low arousal conditions demonstrated a highly significant change in subjective sleepiness between conditions indicating the effectiveness of the experimental manipulation. One criticism of the use of subjective sleepiness ratings is that they have diminished validity for subjects with excessive daytime sleepiness. Dement *et al.* (1978), suggest that this diminished validity may occur as a consequence of chronically sleepy subjects losing an appropriate frame of reference by which to measure their sleepiness state. This potential limitation of subjective rating scales is not, however, seen to invalidate the findings of the present study where the effectiveness of the arousal manipulation was evaluated as a consequence of subjects' estimations of *change* in their sleepiness state rather than an absolute estimate of sleepiness.

For the narcolepsy subjects in the current study this experimentally induced sleepiness was associated with performance change across a range of tasks. Comparison of both the within-subject effects for narcolepsy subjects, of the transition between high and low arousal states, and the between-subject effects of low arousal for narcolepsy subjects compared to controls, indicate that complex cognitive tasks are the most sensitive to arousal change for this clinical population. This finding provides support for the conclusions of Rogers and Rosenberg (1990) that the consistent failure of research to demonstrate sleepiness associated performance decrements for narcolepsy subjects may be partly explained by the use of standardized tests which are insensitive to higher order cognitive functioning. The most sensitive measure of sleepiness for narcolepsy subjects in the present study was the PASAT. This task measures central information processing capacity and requires subjects to respond verbally to an externally paced auditory addition task and simultaneously inhibit the automatic encoding of their response and direct their attentional resources to the next incoming stimulus (Spreen and Strauss 1991). As the task is externally paced subjects cannot compensate for sleepiness by increasing the processing and response time. The divided attention and central processing demands of the task may reflect everyday experiences of competing cognitive demands, and sleepiness in narcolepsy may interfere with the capacity to respond to this cognitive load. This finding may provide some objective support for the subjective impressions of some people with narcolepsy of diminished cognitive capacity. Performance on the PASAT has been shown to correlate with subjective ratings of cognitive impairment amongst other clinical groups (Gronwall 1976).

To determine whether narcolepsy is associated with diminished habitual or tonic arousal levels, non sleepy narcoleptic subjects were compared to controls on automatic

performance tasks. None of the automatic tasks were found to discriminate between narcoleptic and control subjects, suggesting that at high arousal narcoleptics perform as effectively as controls on tasks of automatic function. In line with the conclusions of Aguirre *et al.* (1985), Ollo *et al.* (1987), and Rogers and Rosenberg (1990), this finding suggests that the capacity to perform automatic tasks for narcolepsy subjects is not restricted by fundamental physiological factors, or tonic arousal levels, but is determined by the impact of sleepiness on cognition. Where performance tasks require minimal processing capacity subjects with narcolepsy appear able to compensate for sleepiness effects with increased attentional resources. However, as task complexity increases sleepiness has a more pervasive influence on performance and performance decrements appear to be reversed only by restorative sleep.

One paradoxical finding was that despite consistent self reports of memory dysfunction amongst subjects with narcolepsy (Broughton and Ghanem 1976; Smith *et al.* 1992) no significant residual effects for either short- or long-term memory performance were noted in the current study. This discrepancy between subjective reports and objective findings of memory function for subjects with narcolepsy has been noted in several studies by Aguirre *et al.* (1985), Rogers (1987), Rogers and Rosenberg (1990) and Smith *et al.* (1992). The lack of effect reported in the current study suggests that the discrepancy between subjective and objective memory performance may be unrelated to the effects of sleepiness, but potentially occur as a consequence of inaccurate subjective assessments of memory performance which subjects with narcolepsy develop, secondary to more global negative, cognitive self schemata.

The current study has been able to manipulate arousal states for subjects with narcolepsy and to demonstrate the nature of performance change associated with sleepiness for this clinical group. It remains to be tested whether these performance changes are specific to narcolepsy, or reflect more general aspects of performance change associated with daytime sleepiness. As narcolepsy is a condition of excessive daytime sleepiness the observed changes in performance may vary only quantitatively from those experienced by sleep deprived non-narcoleptic subjects or secondary aspects of narcolepsy may lead to a qualitatively different relationship between sleepiness and performance in this clinical group. Further research comparing subjects with narcolepsy to sleepy non-narcoleptic subjects is necessary to discriminate between these positions.

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