



VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

*Diurnal Actigraphy and Stimulant Efficacy in
Narcolepsy*

This is the Published version of the following publication

Bruck, Dorothy, Kennedy, Gerard, Cooper, Ameer and Apel, Sabine (2005)
Diurnal Actigraphy and Stimulant Efficacy in Narcolepsy. *Human
Psychopharmacology: Clinical and Experimental*, 20 (2). pp. 105-113. ISSN
0885-6222

The publisher's official version can be found at
<https://onlinelibrary.wiley.com/doi/abs/10.1002/hup.666>
Note that access to this version may require subscription.

Downloaded from VU Research Repository <https://vuir.vu.edu.au/299/>

Diurnal actigraphy and stimulant efficacy in narcolepsy

Dorothy Bruck*, Gerard A. Kennedy, Ameer Cooper and Sabine Apel

School of Psychology, Victoria University, PO Box 14428 Melbourne City MC 8001 Australia

Email: dorothy.bruck@vu.edu.au

Current Claim: The actigraphy variable of Immobility is sensitive enough to detect daytime stimulant treatment effects in narcolepsy.

SRO Category : Sleep Disorders – narcolepsy

Running Head: Narcolepsy treatment and actigraphy

ABSTRACT

The aim of this study was to determine whether wrist actigraphy could be used to assess the daytime effects of stimulant medication treatment in narcolepsy. Nine subjects with narcolepsy/cataplexy (medicated and unmedicated) were compared with matched control subjects. Data was collected over four days in the subjects' home. It was found that the actigraph variable of Immobility (mean duration of periods of no activity) could be used to successfully differentiate medicated and unmedicated phases, correctly classifying 89% of cases. Narcolepsy subjects differed from controls on Immobility both when medicated and unmedicated. During the unmedicated phase self-reported nap duration was longer and more naps (3.94 naps) were taken. However, the frequency of naps was still high when medicated (2.43 naps). During the unmedicated phase narcolepsy subjects reported more negative mood states (Profile of Mood States, POMS) than control subjects. However, with the exception of Vigor, scores on the individual mood factors were within the normal range. Total POMS scores were highly correlated with the actigraphic measure of Movement for both narcolepsy conditions as well as controls, with negative mood associated with less movement. It was concluded that the actigraphy variable of Immobility is sensitive enough to detect treatment effects. The relationship between mood and motor activity warrants further investigation in both clinical and non-clinical populations.

Key Words: narcolepsy, actigraphy, stimulants, motor activity, mood, diurnal

INTRODUCTION

In the absence of an objective, reliable, ecologically valid and cost effective method of quantifying the effects of stimulant medication on daytime functioning in narcolepsy, clinicians have relied heavily on individual patient's reports. Self-reports of sleepiness and diurnal function are currently the main parameters used to estimate of treatment effectiveness in clinical setting. However, individuals with narcolepsy often underestimate daytime sleep (Rogers et al., 1994) and have been hypothesised to lack an appropriate frame of reference for evaluating treatment efficacy (Mitler et al., 1993). In a study of 522 patients with narcolepsy (Sangal et al., 1999), estimates of sleep propensity [Epworth Sleepiness Scale, ESS; Johns, 1991)] were shown to remain unchanged despite objectively measured changes in sleep propensity in the laboratory (Maintenance of Wakefulness Test, MWT). Costly sleep laboratory based procedures such as the Multiple Sleep Latency Test (MSLT) and MWT provide inconsistent results in the evaluation of treatment efficacy of disorders of excessive sleepiness (Mitler et al., 1982, 1990, 1991, 1993). In addition, external validity is questionable due to confounding motivational and environmental factors inherent under laboratory conditions (Broughton et al., 1988; Roth et al., 1994). Thus, clinicians may not know how much to trust the patient's subjective perceptions of treatment efficacy or be guided by the objective laboratory procedures that may not necessarily reflect a patient's usual sleep propensity.

The American Sleep Disorders Association (ASDA, 1992) recommended that wrist actigraphy, being home-based, may be useful in conjunction with other measures to document the severity of sleep disorders. Similarly, others researchers (Stanley 2003, Sadeh 1995) have suggested that actigraphy is a potentially useful and cost-effective data collection tool that may be used to explore sleep-wake activity, monitor treatment processes and activity rhythms. To date, only a single study by Hajek et al.(1989) has used actigraphy to assess treatment effects in narcolepsy patients. This study found that a small group of narcolepsy subjects exposed to bright light showed no improvement in either objectively or subjectively measured symptoms.

Middelkoop et al. (1995) investigated the circadian distribution of activity in unmedicated narcolepsy and matched control subjects and found that during the day the actigraph variable of "mean duration of uninterrupted immobility" (hereafter called Immobility), successfully discriminated between narcolepsy and control subjects. It was concluded that higher Immobility values were most likely caused by intermittent episodes of sleep during the major wake period. However, the other variables of mean diurnal Activity level and Movement index did not differ significantly between experimental and control groups.

The main aim of this study was to determine whether wrist actigraphy variables may be useful in the assessment of the effects of stimulant medication treatment in narcolepsy. Therefore, motor activity measures related to daytime behaviour were compared in medicated and unmedicated narcolepsy subjects. Data from age- and sex- matched control subjects were also collected to (1) confirm Middelkoop et al.'s (1995) finding that actigraphy can discriminate between the daytime activity of narcolepsy and control subjects; and (2) determine to what extent stimulant medication brings measures of daytime function measures closer to levels reported by individuals without pathological sleepiness. Self-report measures of mood and sleep-wake behaviour were also collected in order to (1) determine possible subjective differences due to treatment; (2) compare self-report variables with actigraphy variables; and (3) investigate differences between unmedicated, medicated and control subjects. Data were collected over consecutive days and nights, but only the finding for diurnal behaviour are discussed here. The nocturnal data will be the subject of a subsequent paper.

METHOD

Subjects

Subjects in the narcolepsy group were six females (aged from 41 to 70, mean age = 57.3, SD = 9.9) and three males (aged 19 to 63, mean age = 39.6, SD = 22.1). The control subjects were age- and

sex- matched as closely as possible (within three years) to the narcolepsy subjects and consisted of six females (aged 42 to 71, mean age = 56.1, SD = 8.9) and three males (aged 19 to 65 years, mean = 41.0, SD = 23.1). All subjects in the narcolepsy group had previously been diagnosed by a medical specialist and displayed unambiguous cataplexy. Two subjects with narcolepsy were also being treated for sleep apnoea with Continuous Positive Airway Pressure (CPAP). During the unmedicated phase of the study, narcolepsy subjects were required to withdraw from all stimulant medication for a period of 60 hours before the first evening recording period. Thus, when the diurnal actigraphy commenced, the narcoleptic subjects had gone without stimulant medication for about 72 hours. Many people with narcolepsy report taking drug holidays when circumstances permit. Therefore, the drug-free period required in this study would not have necessarily been unusual for the subjects. Both the stimulants used by the patients have a relatively short half-life (10-12 hours for dexamphetamine and 2-3 hours for methylphenidate) and it is likely that at least 90% would have been excreted from the body within the pre-testing withdrawal phase. Parkes and Dahlitz (1993) suggest that the main rebound sleepiness lasts 2-3 days. While a longer withdrawal period would have been more desirable, the pool of potential subjects would have been smaller and compliance probably much less likely. Compliance with treatment withdrawal was confirmed at the beginning and end of the study period by the analysis of urine samples collected in the Victoria University Sleep Laboratory. Urine samples were subsequently analysed for stimulant medication metabolites by Australian Research Laboratories in Melbourne, Australia. These analyses showed that all subjects remained free of stimulant medication during the untreated phases of the study. All other regular medications were maintained during the study and no subjects were taking tranquillisers. During the medicated phase, all narcolepsy subjects took their normal daily dose of stimulant medication (Ritalin or Dexamphetamine). All day periods were spent in the subject's own home environment, while the narcolepsy subjects (but not the controls) slept in the Sleep Laboratory on Nights One and Four and left after breakfast. The narcolepsy subjects were recruited through local members of the Australian narcolepsy support group, (Narcolepsy and Overwhelming

Daytime Sleep Society, NODSS). The control subjects were all acquaintances of the authors and were all normal sleepers with no diagnosed chronic and/or serious medical conditions. Control and narcolepsy subjects were paid \$60 to cover any expenses incurred while participating in the study.

Actigraphy

Motor activity was continuously recorded using a Mini-Mitter 2000 Mini Logger wrist actigraph (Mini-Mitter Co., Inc., USA), worn on the nondominant arm, from the evening of Day One to the morning after Night Four (Middlekoop et al. (1995) used Gaehwiler Electronic wrist actigraphs, model CH-8634, Hombrechtikon, GDR). The accelerometer sensitivity of the Gaehwiler Electronic wrist actigraph used by Middelkoop et al., (1995) was $> 0.1g$ and that of the Mini-Mitter used in this study was $> 0.05g$. Three complete day periods were obtained (Days Two, Three and Four), sufficient to obtain a representative description of sleep-wake behaviour in narcolepsy (ASDA, 1992; Middelkoop et al 1995). Movements were recorded in 16-second bins. The motor activity measures reported by Middelkoop et al.(1995) were adapted and calculated across each selected period: [a] Activity = mean number of activity counts per 16 second epoch; [b] Movement = the percentage of epochs with an activity count > 0 across the entire period; and [c] Immobility = the mean duration in minutes of uninterrupted immobility (that is where activity = 0). Each diurnal period was selected using the Sleep Diary (see below) reports from "time finally awoke" to "time tried to go to sleep" for the main night's sleep. The actigraphy variables were computed from the raw data using software (NEWVUT). The NEWVUT software was designed to calculate the actigraph variables in the manner described by Middelkoop et al. (1995).

Questionnaires

During the day/evening each subject completed the following questionnaires: [a] Profile of Mood States (POMS)- a checklist of 65 items related to mood developed by McNair et al. (1981). Each item is rated on a 5-point Likert scale and the POMS Total score consists of the sum of scores from the negative subscales- Confusion/Bewilderment, Anger/Hostility, Tension/Anxiety, Fatigue and Depression. The positive subscale, Vigour, is not included in the total score. POMS ratings related

to the day just completed; [b] Epworth Sleepiness Scale (ESS) a measure of sleep propensity in a variety of situations with a score range from 0 to 24. This was adapted to relate to the day just completed rather than "in recent times"; [c] a Day Log to record daytime naps, medication, caffeine or alcohol intake and times of removal of the wrist actigraph (e.g. for showering); and [d] a Sleep Diary completed each morning by the subjects. The beginning and end points for each diurnal (i.e. wake) period of actigraphy were extracted from the diary.

Procedure

The narcolepsy subjects participated in two phases, unmedicated and medicated. Each phase consisted of a continuous four-day and four night period. The unmedicated phase was always conducted first (to reduce subject attrition). The procedures used in the study were approved by the Victoria University Human Experimentation Ethics Committee and informed consent was obtained from each subject. Urine samples were obtained on Nights One and Four, when the subjects attended the Sleep Laboratory. During the medicated phase subjects were requested to maintain their usual stimulant medication intake levels. If the usual level varied significantly from day to day, subjects were requested take their usual dose prescribed for maximum alertness. Subjects were instructed to maintain their normal 24-hour schedule (the sleep periods in the sleep laboratory were scheduled to fit with this) and engage in their normal daytime activities, but to moderate caffeine and alcohol intake. The scheduling of experimental days controlled for the possibility of different levels of activity on weekdays or weekends. For the narcolepsy subjects participation was either all on weekdays in both medicated or unmedicated phases, or included a weekend in both phases. Control subjects were yoked to the same schedule as matched narcolepsy subjects, thus including either weekend or weekdays.

Data Analysis

The times when the actigraph were not worn were extracted from the Day Log and these data were eliminated prior to data analysis. Given that the three groups (unmedicated narcolepsy, medicated narcolepsy and controls) were either individuals undergoing repeated testing or carefully matched

controls, repeated measures statistics were used. The main analysis was a MANOVA with repeated measures, conducted across the three groups, using five dependent variables as described below. In the event of an overall MANOVA being significant, univariate effects for dependent variables were explored. Where these were significant, planned contrasts were used to determine the nature of the between groups effects for the relevant variables. A significance level of 0.05 was set.

The dependent variables analysed were the actigraph variables of Activity, Movement and Immobility and the self-report variables of ESS, POMS Total, Nap Duration and Number of Naps. The control subject's data for both Nap Duration and Number of Naps did not meet the normal distribution assumption required for MANOVA (control nap data was zero), and therefore these variables were not included in the MANOVA comparing the medicated and unmedicated subjects and the control group. However, these data were analysed separately using paired sample *t*-Tests comparing only the medicated and unmedicated groups.

A stepwise discriminant function analysis using SPSS (2000, Version 10.0) default settings was conducted to determine which of the dependent variables (using all seven as described above) best discriminated between the medicated and unmedicated groups. The "leave-one-out" classification method was used. A second discriminant analysis considered only the four self-report variables.

Where a planned contrast showed a significant difference for POMS Total scores between medicated and unmedicated narcolepsy and control subjects, possible differences on each of the six POMS factors were also examined investigated using paired sample *t*-Tests.

In order to determine whether there was any relationship between the objective actigraph variables and the subjective self-report variables for the medicated and unmedicated narcolepsy and the control subjects a series of bivariate Pearson's correlations were calculated.

RESULTS

For the self-report variables, four diurnal periods were available (Days One to Four), while actigraphy data from three diurnal periods (Day Two to Four) were collected. MANOVA tests for the main effect of days were all non-significant within each group, so mean values for each variable across all the days available were calculated and used in the analyses. Using MANOVA, the five dependent variables as described above (three actigraph and two self-report variables) were compared. A significant overall group effect was found ($F(2,6) = 14.78, p = 0.005$). Planned contrasts were conducted between: (1) medicated and unmedicated narcolepsy phases; (2) control subjects and medicated narcolepsy subjects; and (3) control subjects and unmedicated narcolepsy subjects (Table 1).

Actigraphy

Table 1 shows that differences were found between the medicated and unmedicated narcolepsy subjects, and both medicated and unmedicated narcolepsy and control subjects for the actigraph variable of Immobility. Narcolepsy subjects, (particularly unmedicated) showed significantly longer periods of Immobility. The data for the individual narcolepsy subjects are shown in Figure 1. These data indicate that all narcolepsy subjects had much higher Immobility values when unmedicated compared to when taking stimulant medication. There were no significant differences between the narcolepsy and control groups with respect to the other two actigraph variables that measured overall activity level (Activity) and percentage of time during the diurnal period spent moving (Movement). Inspection of the direction of differences across individual case data for Activity and Movement indicated that there was no apparent consistency.

Table 1. Means, Standard Deviations, Univariate and Planned Contrast Results for Unmedicated and Medicated Narcolepsy and Matched Control Subjects.

	Unmed Narcolepsy (n=9)		Control Subjects (n=9)		Med Narcolepsy (n=9)		Univariate Results		Unmed Narcolepsy vs. Med Narcolepsy	Unmed Narcolepsy vs. Control	Med Narcolepsy vs. Control
	Mean	SD	Mean	SD	Mean	SD	<i>F</i>	<i>p</i>	Planned contrast/ t-test (see text) <i>p</i>	Planned contrast <i>p</i>	Planned contrast <i>p</i>
Activity	3.54	(1.77)	4.23	(4.79)	4.49	(2.19)	1.66	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Movement	42.51	(10.33)	37.04	(22.29)	49.44	(13.57)	1.91	<i>ns</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Immobility	1.49	(0.94)	0.29	(0.04)	0.37	(0.072)	15.81	0.0001	.006	0.005	0.03
POMS total	29.55	20.9	-6.66	17.34	21.09	35.93	5.18	0.021	<i>ns</i>	0.001	0.056
Epworth Sleepiness Scale	18.43	(4.36)	5.12	(2.16)	15.12	(5.83)	21.42	0.0001	<i>ns</i>	0.0001	0.005
Number of Naps	3.94	(1.33)	00	(00)	2.43	(1.38)			0.048		
Nap Duration	73.54	(23.37)	0	(00)	34.79	(33.43)			.056		

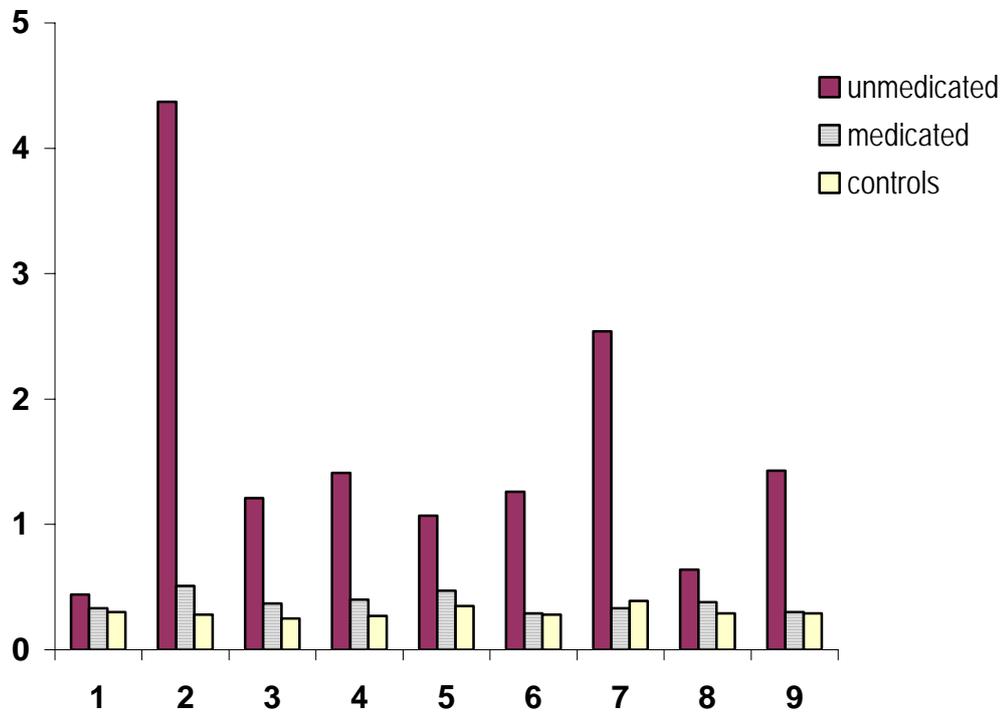


Figure 1. Comparison of Actigraph Immobility Scores of Individual Narcoleptics (when Unmedicated and Medicated) with Matched Control Subjects.

Treatment Effects And Discriminant Analysis

In order to focus specifically on treatment effects, all seven dependent variables were submitted to a step-wise discriminant analysis performed between medicated and unmedicated narcolepsy subjects. The only variable to enter the analysis was the actigraph variable of Immobility and this variable accounted for 42% of the total between treatment variance (Wilks lambda=0.579, $p=0.005$; Eigen value =0.728). The Immobility variable correctly classified 89% of cases into medicated or unmedicated narcolepsy (8/9), with 77.8% of medicated cases and 100% of unmedicated cases correctly classified.

To facilitate comparisons with the above, a second discriminant analysis was performed between medicated and unmedicated narcolepsy using only the four self-report variables (ESS, POMS total, Nap Duration and Nap Number). Nap Duration was the only variable to enter the analysis, accounting for 31% of the total explained between treatment variance (Wilks lambda =0.687, $p=0.02$; Eigen value =0.455) and correctly classified 66.7% of cases (6/9 in both medicated and unmedicated narcolepsy subjects).

Self-Report Variables

Details of mean values and results of analyses for these variables are shown in Table 1. The control group did not report any napping and medicated narcolepsy subjects spent less time napping than unmedicated subjects with narcolepsy. The mean number of reported naps differed significantly between medicated and unmedicated narcolepsy. Seven of the nine narcolepsy subjects had less naps when on medication, one the same number and one more naps when medicated. Dividing mean Nap Duration values by the mean Number of Naps showed that medicated narcolepsy subjects had fewer naps and that, on average, naps were four minutes shorter than naps in the unmedicated condition.

Significant differences were found between the control group and both the medicated and unmedicated narcolepsy treatments for ESS scores. However, there was no difference between ESS scores for medicated and unmedicated treatments.

There was significant difference between the unmedicated narcolepsy and control subjects, and a trend for medicated narcolepsy subjects to differ from control subjects on the POMS Total scores. Given the significant difference between unmedicated narcolepsy subjects and control subjects for POMS Total scores a more detailed exploration was carried out to determine which of the individual POMS factors contributed to this difference. Means, standard deviations and paired samples *t*-Test results for control versus unmedicated narcolepsy subjects for the POMS factors are shown in Table 2. Table 2 shows that unmedicated narcolepsy subjects reported significantly more confusion, fatigue, depression, tension and less vigor than control subjects.

Table 2. Means and Standard Deviations for the POMS Factors for Unmedicated and Medicated Narcolepsy and Matched Control Subject Groups and Paired Sample *t*-Test Comparisons between Unmedicated Narcolepsy and Matched Control Subjects.

POMS Factors	Unmed Narcolepsy s (n=9)		Control Subjects (n=9)		Med Narcolepsy s (n=9)		Unmed Narcolepsy vs. Control Subjects (df=8)	
	Mean	SD	Mean	SD	Mean	SD	<i>t</i>	<i>p</i>
Confusion/ Bewilderment	8.64	4.92	2.42	2.09	7.03	5.36	3.27	0.011
Vigour	8.00	7.09	17.75	8.80	13.12	6.60	2.68	0.028
Fatigue	15.19	8.90	3.41	3.80	9.60	7.84	3.07	0.015
Depression/ Dejection	5.00	4.07	1.19	1.81	6.79	10.79	2.42	0.042
Tension/Anxiety	4.86	2.44	2.47	1.89	5.61	4.47	2.75	0.025
Anger/Hostility	3.86	5.25	1.58	2.42	5.33	6.26	1.15	<i>ns</i>

Correlations For Self-Report and Actigraphy Variables

For the medicated and unmedicated narcolepsy and control subjects correlations between the three actigraph and four self-report variables were calculated (Table 3). It was found that the POMS Total score correlated with Movement for medicated and unmedicated narcolepsy subjects and control subjects with a significance level greater than $p = 0.03$ (Table 3). Significant correlations were also found between POMS Total and Immobility for unmedicated narcolepsy and between POMS Total and Activity for control subjects. Scatterplots confirmed the fundamental linearity of the relationships. Correlations showed that increased Movement/Activity was associated with a more negative mood (higher POMS Total). In order to explore whether there were particular mood factors contributing to these correlations, further correlations were calculated between Movement and the six individual POMS factors for all three groups. For medicated narcolepsy subjects the factors tension, depression, anger and fatigue correlated with Movement in descending order of magnitude (from $r=-0.86, p=0.003$ to $r=-0.69, p=0.038$). For control subjects Movement was correlated with anger, depression and vigour (from $-0.76, p= 0.018$ to $0.669, p=0.049$). There were no significant correlations between Movement and individual POMS factors in the unmedicated condition.

Table 3. Pearson Correlation Coefficients for the POMS Total Scores with the Three Actigraphy Variables Scores for Unmedicated and Medicated Narcolepsy and Matched Control Subjects.

	Unmed N (n=9)		Med N (n=9)		Control (n=9)	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Activity	-0.51	ns	-0.57	ns	-0.69	0.03
Movement	-0.77	0.01	-0.85	0.004	-0.71	0.02
Immobility	0.71	0.03	0.59	ns	0.13	ns

DISCUSSION

The finding of the present study showed that actigraphy is a useful tool for examining diurnal stimulant medication treatment effects in narcolepsy when the dependent variable Immobility is used. Planned contrast tests yielded highly significant differences on the Immobility variable (Table 1) with all nine narcolepsy subjects showing differences in the expected direction (Figure 1). Immobility was the only variable that entered the discriminant analysis and was able to correctly classify 89% of cases as medicated or unmedicated. This compared favourably to the self-report variables, where Nap Duration only classified 66.7% of cases as medicated or unmedicated.

The trend for differences in the Nap Duration between medicated and unmedicated narcolepsy treatments and the significant difference in number of reported naps may be contributing to the difference in Immobility. Webster et al. (1982) believed actigraph Immobility predominantly reflected features of sleep-wake behaviour. Similarly, Middelkoop et al. (1995) attributed higher diurnal Immobility values in narcolepsy to intermittent episodes of sleep during the major wake period. However, it is not clear whether the Immobility differences can be fully accounted for by differences in reported nap behaviour or whether unmedicated narcolepsy subjects may be unaware of having more intermittent short episodes of sleep (Mitler et al., 1982). The fact that the other actigraphy variables, Activity and Movement, did not differ between medicated and unmedicated treatments suggests that the lack of medication does not lead to an overall significant reduction in activity level. Similarly, Middelkoop et al. (1995) found no differences in these two actigraphic variables between unmedicated narcolepsy and control groups during the day. This may arise because people with narcolepsy maintain a higher motor activity level than controls between immobile periods. Perhaps they stay "on the go" more to help maintain arousal.

While medication brought the treated narcolepsy subjects closer to control subjects' values of Immobility, a difference was still apparent. This confirms findings from other studies using different evaluation methods, such as the Maintenance of Wakefulness Test (Mitler et al., 1992) and

home polysomnographic recorders (Rogers et al., 1994), that stimulant medication improves daytime sleepiness in narcolepsy but not to levels that are non-pathological. In the current study, during the medicated phase subjects still slept an average of 34.8 minutes during the day and had 2.43 naps. These findings are comparable with those of Rogers et al. (1994) where 25 medicated narcolepsy patients averaged somewhat more daytime sleep (43 minutes) but did so with less naps (1.6). The differences found between narcolepsy and control subjects were also consistent with the findings of Middelkoop et al. (1995) who found that the measure of actigraphic Immobility was the most sensitive discriminator between unmedicated narcolepsy and control subjects in both diurnal and nocturnal sleep periods.

The control subjects scores on the ESS for sleep propensity showed differences from both medicated and unmedicated treatments. Mean values reported by control subjects and unmedicated narcolepsy subjects were similar to those reported previously (Johns 1991). Comparing medicated and unmedicated narcolepsy ESS scores from the current study to those reported by Parkes (1994), shows that medicated narcolepsy subjects had comparable values, but that unmedicated narcolepsy people had higher ESS values in Parkes study (20.2 versus 18.4 in present study). This finding provides some tentative support for the contention that any rebound sleepiness effect from stimulant medication withdrawal during this study would be minimal. This contention is also supported by the lack of a significant difference in sleepiness in the unmedicated narcolepsy group from the first to the third day of actigraphy recording.

There was no difference found between medicated and unmedicated narcolepsy for POMS Total scores (Table 1). However, the mean values suggested that further exploration with a larger sample may be warranted. With a larger sample it would be interesting to compare scores assessing mood on and off medication over a period of several days with the findings of Zwicker et al. (1995) where acute mood improvement over a 90-minute period was found with stimulant intake in 40 narcolepsy

subjects. With respect to individual mood factors it would be of particular interest to explore changes in depressed mood. As the current study (involving the mean of four daily ratings) suggests highly variable depression ratings when comparing medicated and unmedicated phases (assessed via inspection of individual data and the large standard deviations). While the Zwicker et al. study examined *acute* effects, the current study rating period covered four whole day periods where subjects experienced both the active, acute therapeutic effects of stimulants and the period where the stimulants were wearing off (reported to be associated with negative affect in some patients).

The findings with respect to the individual POMS factors (Table 2) suggest that compared to control subjects, unmedicated people with narcolepsy are more confused, fatigued, tense, depressed and have less vigour. However, some caution needs to be used in interpreting this data. Comparison of the unmedicated narcolepsy subjects' mean POMS scores with norms for college populations and outpatients (with no psychiatric disorder) (POMS Manual) (McNair et al. 1981) shows that all unmedicated narcolepsy scores were within one standard deviation of the normative group means, except for Vigour which was below this range.

While actigraphy measures have been shown not to correlate with subjective Sleep Diary reports in narcolepsy (Middelkoop et al., 1995), the association between actigraph variables and mood in narcolepsy has not previously been explored. Strong negative correlations were found between the POMS Total score and the actigraphy variable of Movement in medicated and unmedicated narcolepsy and control subjects. Narcolepsy and control subjects who reported more negative affect showed a lower percentage of movement epochs across the day. Interestingly, the correlations between the actigraphy variable and mood occurred in the absence of correlation of the actigraphy variable with sleep propensity estimates (ESS), Nap Duration, or Number of Naps. Given the small sample size, over interpretation of the particular POMS factors contributing to the strong association with Movement should be avoided. However, these preliminary data suggest that the

mood factors of tension, depression and anger may be strongly associated with Movement in the clinical and control populations. Low levels of daytime activity, measured with actigraphy, has been related to the severity of depression in psychiatric (Teicher 1995) and non-psychiatric depressed patients (Mendlowicz et al.1999). Consistent with this, treatment effects of antidepressants have been successfully monitored in major depressive disorder using diurnal actigraphy (Volkers et al., 2002). The findings of a negative association between movement and mood in both narcolepsy and control groups suggests that it may be useful to include the POMS questionnaire in studies involving actigraphy in a variety of other clinical and non-clinical populations.

The actigraphic study of nocturnal sleep has seen the development of many different algorithms with various degrees of correlation with polysomnographic measures (Hajek et al., 1989). The study of diurnal functioning using actigraphs has had to adopt different measures. Given the current results, together with those found by Middelkoop et al. (1995), it would be potentially valuable for all daytime actigraphic studies to include an analysis of the mean duration of Immobility as a dependent variable.

Comparison of the current mean scores for Activity and Movement with the values obtained in a study using similar populations but a different brand of actigraph (Middelkoop et al., 1995) shows quite different values. However, the scores for the Immobility variable are comparable across the two studies. Thus, both would appear to have similar movement detection thresholds. Useful comparisons of Immobility scores across studies would be possible if the same threshold for activity movement detection was adopted internationally.

The use of actigraphy in the clinical assessment of both sleep disorders and psychopharmacology is becoming widespread, with a growing literature of review papers, validation studies and practice

parameters (ASDA 1992; Sadeh et al.,1995, Ancoli-Israel et al., 2003, Littner et al., 2003, de Souza et al., 2003, Stanley 2003). The current study suggests that actigraphy may have a useful role in assessing treatment effects in narcolepsy and that further research is required to determine how robust the Immobility measure is in a variety of clinical settings. This could include further short-term and longitudinal study of pharmacological and behavioural treatment efficacy as well as further study of the association between actigraphy and subjective reports of mood.

ACKNOWLEDGEMENTS

This study was funded by an Australian Research Council (ARC) Small Grant (Bruck & Kennedy). The authors wish to thank members of NODSS for their cooperation and assistance with this study; Mark Brookes for developing the NEWVUT activity analysis software and Dr Bernadette Hood for helpful comments on the manuscript.

REFERENCES

- Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollack CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003, 26 (3), 342-359.
- ASDA (American Sleep Disorders Association) Report, The clinical use of the Multiple Sleep Latency Test. *Sleep* 1992, 5(3), 268-76.
- Broughton R, Dunham W, Newman J, Lutley K, Duschesne P, River M. Ambulatory 24 hour sleep-wake monitoring in narcolepsy-cataplexy compared to matched controls. *Electroencephalography and Clinical Neurophysiology* 1988, 70, 473-81.
- Roth T, Roehrs TA, Carskadon MA, Dement WC. Daytime sleepiness and alertness. In *Principles and Practice of Sleep Medicine*. 2nd ed. Kryger MA, Roth T, Dement WC, Eds.; WB Saunders: Philadelphia, 1994; 40-49.
- De Souza L, Benedito-Silva AA, Pires MLN, Poyares D, Tufik S, Calil HM. Further validation of actigraphy for sleep studies. *Sleep* 2003, 26(1), 81-85.

Guilleminault C, Billiard M, Montplaisir J, Dement WC. Altered states of consciousness in disorders of daytime sleepiness. *Journal of Neurological Sciences* 1975, 26, 377-93.

Hajek M, Meier-Ewert K, Wirz-Justice A, Tobler I, Arendt J, Dick H, Fink G. Bright light does not improve narcoleptic symptoms. *European Archives of Psychiatric Neurological Science* 1989, 238, 203-7.

Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep* 1991, 14, 540-45.

Littner M, Kushida MD, Anderson M, Bailey D, Berry RB, Davila DG, Hirshkowitz M, Kapen S, Kramer M, Loubé D, Wise M, Johnson SF. Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. *An American Academy of Sleep Medicine Report, Sleep* 2003, 26(3), 337-341.

McNair DM, Lorr M, Droppleman LF. Profile of mood states manual. San Diego: Educational and Industrial Testing Service, 1981.

Mendlowicz MV, Jean-Lois G, von Gizycki H, Zizi F, Nunes J. Actigraphic predictors of depressed mood in a cohort of non-psychiatric adults. *Australian and New Zealand Journal of Psychiatry* 1999, 33(4), 553-8

Middelkoop HAM, Lammers GJ, Van Hilten BJ, Ruwhof C, Pijl H, Kamphuisen HAC. Circadian distribution of motor activity and immobility in narcolepsy: Assessment with continuous motor activity monitoring. *Psychophysiology* 1995, 32, 286-91.

Mitler MM, Erman M, Hajdukovic R. The treatment of excessive somnolence with stimulant drugs. *Sleep* 1993, 16, 203-6.

Mitler MM, Gujavarty KS, Sampson MG, Brownman CP. Multiple daytime nap approaches to evaluating the sleepy patient. *Sleep* 1982, 5, S119-S127.

Mitler MM, Hajdukovic RM, Erman M, Koziol JA. Narcolepsy. *Journal of Clinical Neurophysiology* 1990, 7, 93-118.

Mitler MM, Hajdukovic RM. Relative efficacy of drugs for the treatment of narcolepsy. *Sleep* 1991, 14, 218-20.

Parkes JD. Introduction to the mechanism of action of different treatments of narcolepsy. *Sleep* 1994, 7, S93-S96.

Parkes JD, Dahlitz M. Amphetamine prescription. *Sleep* 1993, 16(3): 201-203.

Rogers AE, Aldrich MS, Caruso CC. Patterns of sleep and wakefulness in treated narcoleptic subjects. *Sleep* 1994, 17(7), 590-97.

Rosenthal LD, Nykamp K, Day R, Syron ML, Roehrs T, Fortier J, Roth, T. The detection of brief daytime sleep episodes. *Sleep* 1999, 22(2), 211-14.

Sadeh A, Hauri PJ, Kripke DF, Laurie P. The role of actigraphy in the evaluation of sleep disorders. *Sleep* 1995, 18(4), 288-302.

Sangal RB, Mitler MM, Sangal JM. Subjective sleepiness ratings (Epworth sleepiness scale) do not reflect the same parameter of sleepiness as objective sleepiness (maintenance of wakefulness test) in patients with narcolepsy. *Clinical Neurophysiology* 1999, 110(12), 2131-5.

Stanley N. Actigraphy in human psychopharmacology: A review. *Human Psychopharmacology Clin Exp*, 2003, 18: 39-49.

Teicher MH. Actigraphy and motion analysis: new tools for psychiatry. *Harvard Review of Psychiatry*, 1995, 3(1), 18-35.

Volkers AC, Tulen JH, Van den Broek WW, Bruijin JA, Passchier J, Peplinkhuizen L. 24-Hour motor activity after treatment with imipramine or fluvoxamine in major depressive disorder. *European Neuropsychopharmacology* 2002, 12(4), 273-8.

Webster JB, Kripke DF, Messin S, Mullaney DJ, Wyborney, G. An activity-based sleep monitor system for ambulatory use. *Sleep* 1982, 5, 389-99.

Zwicker J, Bruck D, Parkes JD, Broughton RJ. Acute mood improvement after dextroamphetamine and methylphenidate in narcolepsy. *Journal of Sleep Research* 1995, 4, 252-55.