A Comparison of Three Different Sleep Schedules for Reducing Daytime Sleepiness in Narcolepsy

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Study Objective: To determine if the combination of scheduled sleep periods and stimulant medications were more effective than stimulant medications alone in controlling the excessive daytime sleepiness experienced by narcoleptic patients.

Design: Twenty-nine treated narcoleptic subjects were randomly assigned to one of three treatment groups: 1) two 15-minute naps per day; 2) a regular schedule for nocturnal sleep; or 3) a combination of scheduled naps and regular bedtimes. Measures of symptom severity and unscheduled daytime were obtained at baseline and at the end of the two-week treatment period, using the Narcolepsy Symptom Status Questionnaire (NSSQ) and 24-hour ambulatory polysomnographic monitoring. No alterations were made in stimulant medications during the study period.

Setting: N/A

Patients or Participants: N/A

Interventions: N/A

INTRODUCTION

FREQUENT, REGULARLY SCHEDULED NAPS,1-4 AND REGULAR TIMES FOR ARISING AND RETIRING EACH NIGHT,4,5 are widely recommended as an adjuvant therapy for narcolepsy. Patients are advised to take three to six 15-minute naps per day,6 or two longer naps (30—60 minutes each).7 Sleep loss is to be avoided and regular bedtimes are encouraged.4,6 Although these prescriptions require substantial adjustment in patient lifestyle, there has been only a limited evaluation of their efficacy.

With one exception,8 all previous studies testing the efficacy of sleep satiation via ad libitum sleep,9,10 daytime naps,11-14 and pharmacologically mediated consolidation of nocturnal sleep15,16 have involved untreated narcoleptic subjects. Although napping can produce a transient improvement in alertness and performance,12,14,17 it does not reduce the number or duration of unscheduled daytime naps. Nor does reducing or eliminating nocturnal sleep disruptions with benzodiazepines or gamma-hydroxybutyrate9,15,16 have any effect on daytime sleepiness. Extending the nocturnal sleep period to 12 hours, reduced subjective sleepiness and significantly improved mean sleep latencies the following day.10 However, the mean sleep latency increased only 3.6 minutes, resulting in a mean sleep latency of 7.8 minutes on the MSLT (Multiple Sleep Latency Test).

During our pilot study,8 16 narcoleptic subjects, serving as their own controls, took three 15-minute naps per day, but did not alter their (stimulant) medication regime or usual sleeping habits at night. One month later, despite statistically significant increases in mean sleep latencies on the MWT (Maintenance of Wakefulness Test), there was no change in the number of successful trials (20 minutes without sleep). Finally, there was no change in the number of sleep attacks recorded in the subjects’ diaries, and no significant improvements in symptom severity as measured by the Narcolepsy Symptom Status Questionnaire (NSSQ).

It is possible that discrepancy between the objective (MWT) and subjective measures of alertness (sleep diaries and NSSQ scores) was due to differences in the setting for data collection. Objective data about the subjects’ ability to remain alert was recorded in the laboratory, while subjective data reflected the subjects’ experiences outside the laboratory. Since it is probably inappropriate to assume that laboratory measures of alertness will accurately reflect subjects’ ability to remain alert in other circumstances, we next designed a study where both objective and subjective measurements of alertness would reflect the subjects’ experiences while carrying out their usual activities. It was hypothesized that the combination of scheduled sleep periods and stimulant medications would be more effective than stimulant medications alone.
METHODS

In order to determine if the combination of scheduled sleep periods and stimulant medications were more effective than stimulant medications alone, we first obtained baseline information, then randomly assigned narcoleptic subjects to one of three treatment protocols: 1) two regularly scheduled 15-minute naps per day; 2) a regular schedule for arising and retiring each day; and 3) a combination of scheduled naps and regular bedtimes. Subjects who were assigned to take two regularly scheduled 15-minute naps per day (Groups 1 and 3) were encouraged to take the first nap in the morning and the second in the afternoon. We did not attempt to designate specific times for these naps, but encouraged patients to choose times that were compatible with their work and/or school schedules. After they chose their nap times, we programmed an inexpensive wristwatch to indicate when the subject was to start and end their scheduled naps, and instructed the subject to wear that watch during the study period. Subjects assigned to a regular schedule for arising and retiring (Groups 2 and 3) were also allowed to select times for nocturnal sleep that were compatible with their lifestyles. We made no attempt to increase the duration of their nocturnal sleep. Subjects were requested to follow their assigned sleep schedule for two weeks but make no other alterations in their medications or usual daily activities. At the end of the two-week period, a second 24-hour ambulatory polysomnographic recording was obtained.

Subjects

Twenty-nine treated narcoleptic subjects were obtained from three sites; Evanston Hospital (Evanston, IL), Ingham Medical Center (Lansing, MI), and the University of Michigan Medical Center (Ann Arbor, MI). All met the following inclusion criteria: age 18—65; a history of recurrent daytime naps occurring almost daily for at least three months; a mean sleep latency of less than five minutes and two or more sleep onset rapid eye movements periods (SOREMS) on MSLT; an absence of other sleep disorders as determined by a clinical evaluation and nocturnal polysomnography; no other neurological disorder, mental illness, or alcoholism; HLA-DR15 and DQw6 positive; no concurrent use of analeptic medications other than those prescribed for narcolepsy; and major sleep period at night. Written, informed consent was obtained from all subjects, and all subjects were paid for their participation.

Seventeen subjects (58.6%) were female and 12 subjects (41.4%) were male. Ages ranged from 18—64 years, with a mean age of 43.7 years (SD=13.9). All narcoleptic subjects were taking stimulant medications; 21 subjects (72.4%) had prescriptions for methylphenidate, five subjects (17.2%) had prescriptions for dextroamphetamine, and the remaining three subjects (14.3%) had prescriptions for pemoline. Almost half of the subjects (44.8%) were also taking medications to control cataplexy.

Procedure

The severity of five common symptoms of narcolepsy was assessed pre and post treatment using the Narcolepsy Symptom Status Questionnaire (NSSQ). This questionnaire, developed by Mitler and his colleagues, asks subjects to indicate on a seven-point scale the severity of their symptoms (sleepiness, sleep attacks, cataplexy, sleep paralysis, and hypnagogic hallucinations) during 12 typical daily situations and mood states (e.g., working, driving, sitting, watching TV, exercising, anger, sadness, tension, boredom). Although this questionnaire is not often used, it is both reliable and sensitive. In order to test the reliability of this questionnaire, 20 stable treated narcoleptic patients completed the clinical questionnaire once a week for two weeks. Test-retest reliability for the entire questionnaire was quite good. The particular sub-scales of interest for this study, sleepiness, and sleep attacks, and cataplexy were also quite reliable (r = .91, . and r=.83, and r=.68 ). Furthermore, when Mitler and his colleagues, evaluated the effectiveness of low, moderate, and high doses of methylphenidate, pemoline, protriptyline, and viloxazin in controlling sleepiness, performance, and cataplexy, they found that decreases in scores on the clinical status questionnaire (improvement) were highly correlated with improvements in the ability to stay awake during the Maintenance of Wakefulness Test. Drugs that produced no improvements in objective alertness (protriptyline, and viloxazin) as measured by the MWT did not alter the scores on the NSSQ.

Twenty-four-hour ambulatory polysomnographic recordings were made before starting the assigned sleep schedule and at the end of the two-week treatment period using the Oxford Medilog 9000 recorder. On the day of the recording, subjects came to the sleep laboratory at 17:00h to discuss the study, give informed consent, complete two questionnaires and to review the sleep diaries that they would be completing during the study period. Subjects were instructed to push the event marker on the side of the recorder just before lights out at night and again in the morning (lights on). The following montage was used for all 24-hour recordings; electroencephalogram (C4-A1, C3-A2), electrooculogram (ROC/A1, LOC/A2), and submental electromyogram (EMG). All recordings were obtained while subjects were carrying out their usual activities; no recordings were obtained during weekends. Recordings started at 18:00h and ended at 1800h the following day.

The cassette tapes were played back through the Medilog 9000 Reply and the SS90-III Sleep Stager System for automatic epoch-by-epoch scoring. All tapes were then replayed a second time and the scoring of the entire record checked by an experienced polysomnographic technologist. Thirty-second epochs were used and visual scoring was done using standardized criteria for staging sleep.

The 24-hour recordings were separated into nighttime and daytime periods based on the event marker for bedtime and awakening. If the subject failed to push the event marker, information about lights out and lights on was obtained from a sleep diary. The following information was calculated from the nocturnal recordings: total time in bed, time asleep, sleep latency, REM sleep latency, wake past sleep onset (WASO), duration and percentage of each sleep stage, number and duration of awakenings, and sleep efficiency. The following information was obtained from the daytime portion of the recordings: total duration of daytime sleep, number and duration of each nap, type and duration of each sleep stage, and percentage of total sleep in 24 hours that occurred during the waking period. The number and duration of daytime sleep periods was determined using the method described by Broughton and Mamelak. To count as a nap, each daytime sleep period had to be at least three minutes...
long and consist of stages 2, 3/4 or REM sleep and be preceded
and followed by at least 15 minutes of wakefulness or stage 1
sleep.

Analysis

Demographic variables and pre-treatment scores were exam-
ined prior to testing our hypothesis. To determine if the three
treatments were more effective in reducing unscheduled daytime
napping than the use of stimulants alone we compared scores
obtained at baseline to scores obtained after two weeks of treat-
ment using Students t-Tests. Regression models were then devel-
oped to determine which of the three treatment protocols was
most effective for reducing unscheduled daytime napping and
subjective symptom severity. We fit a linear regression model of
the change in unscheduled daytime napping on treatment indica-
 tors and pretreatment daytime napping to determine which of the
three treatments was more effective in reducing unscheduled
daytime napping. This model allowed us to study the treatment
effect on reduction of daytime sleep duration after adjusting for
differences in day sleep duration among the three groups at base-
line. Next, we fit a linear regression model of change of NSSQ
scores before and after treatment on treatment indicators and pre-
treatment NSSQ scores. For each analysis, we also fit a model

Table 1—Comparisons of the three treatment groups at baseline

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=10)</th>
<th>Group 2 (n=10)</th>
<th>Group 3 (n=9)</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (yrs)</td>
<td>39.0 ± 14.7</td>
<td>43.2 ± 12.4</td>
<td>49.6 ± 13.3</td>
<td>0.236</td>
</tr>
<tr>
<td>Gender</td>
<td>7 females</td>
<td>5 females</td>
<td>5 females</td>
<td>0.642</td>
</tr>
<tr>
<td></td>
<td>3 males</td>
<td>5 males</td>
<td>4 males</td>
<td></td>
</tr>
<tr>
<td>Symptom Severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration</td>
<td>39.2±41.9</td>
<td>27.8±31.8</td>
<td>76.4±42.5</td>
<td>0.044*</td>
</tr>
<tr>
<td>Daytime Sleep (mins)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score on NSSQ (pretest)</td>
<td>124.3±22.4</td>
<td>127.3±33.2</td>
<td>121.3±24.4</td>
<td>0.969</td>
</tr>
<tr>
<td>Nocturnal Sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in bed (mins)</td>
<td>454.0±104.9</td>
<td>434.3±103.0</td>
<td>463.2±89.7</td>
<td>0.513</td>
</tr>
<tr>
<td>Sleep Duration (mins)</td>
<td>403.1±114.8</td>
<td>354.2±66.8</td>
<td>349.7±81.9</td>
<td>0.302</td>
</tr>
<tr>
<td>WASO (mins)</td>
<td>39.0±33.2</td>
<td>67.1±42.7</td>
<td>101.0±63.2</td>
<td>0.063</td>
</tr>
<tr>
<td>Sleep Efficiency (percent)</td>
<td>88.2±8.0</td>
<td>81.0±11.4</td>
<td>76.0±11.6</td>
<td>0.071</td>
</tr>
<tr>
<td>Total Sleep during recording period (mins)</td>
<td>442.2±109.1</td>
<td>382.0±92.4</td>
<td>437.9±111.4</td>
<td>0.035*</td>
</tr>
</tbody>
</table>

* p<0.05
** the p-values were calculated using the Kruskal-Wallis test for continuous measures and the chi-square test used for gender

Table 2—Effects of scheduled sleep periods

<table>
<thead>
<tr>
<th></th>
<th>Pretreatment</th>
<th>Post Treatment</th>
<th>Mean difference</th>
<th>T</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration</td>
<td>43.5 ± 41.5</td>
<td>30.4 ± 24.5</td>
<td>-13.100</td>
<td>1.451</td>
<td>0.185</td>
</tr>
<tr>
<td>Sleep Daytime (mins)</td>
<td>124.3±22.4</td>
<td>124.4±21.7</td>
<td>0.1111</td>
<td>0.0113</td>
<td>0.9912</td>
</tr>
<tr>
<td>Total Score on NSSQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2 (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration</td>
<td>31.7 ± 39.1</td>
<td>41.0 ± 25.0</td>
<td>9.300</td>
<td>0.800</td>
<td>0.450</td>
</tr>
<tr>
<td>Sleep Daytime (minutes)</td>
<td>130.7 ± 34.3</td>
<td>108.5±26.0</td>
<td>-22.200</td>
<td>-5.268</td>
<td>0.002**</td>
</tr>
<tr>
<td>Total Score on NSSQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3 (n=9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration</td>
<td>76.4 ± 42.5</td>
<td>29.3 ± 25.3</td>
<td>-54.4</td>
<td>-3.64</td>
<td>0.011**</td>
</tr>
<tr>
<td>Sleep Daytime (minutes)</td>
<td>121.3 ± 24.4</td>
<td>101.8±22.0</td>
<td>19.5625</td>
<td>-3.3196</td>
<td>0.013**</td>
</tr>
</tbody>
</table>

* four influential outliers removed from analysis, and two-sample t-tests were used to calculate the p-value
**p<0.05
with interaction between treatment and baseline data and found that the interaction was not significant. We also fit a model controlling for other baseline sleep-related variables besides length of daytime sleep, the NSSQ score, and demographic variables. None of these variables were significant. Regression diagnostic techniques, such as residual plots and Cook distances, were used to identify outlying observations and influential observations. One highly influential outlier in Group 2 (regular bedtimes group) was found and removed from the analysis of daytime sleep duration. For the NSSQ analysis, one highly influential outlier in each of the three treatment groups was found and removed from the analysis.

RESULTS

Although subjects were randomized to treatment groups, subjects assigned to the combination therapy (Group 3) slept longer during the day at baseline, and subjects assigned to the regular bedtime group (Group 2) slept less during the 24-hour than the other two groups of subjects (See Table 1). Our regression analysis adjusted for the difference of the baseline daytime sleep duration when comparing treatment effects. No other differences were found in demographic characteristics, NSSQ scores, or polysomnographic data.

Stimulants Alone Versus the Combination of Stimulants and Scheduled Sleep Periods

As shown in Table 2, only one treatment, the combination of two 15-minute naps and regular bedtimes, significantly reduced the amount of unscheduled daytime sleep in treated narcoleptic subjects (p=0.011). Subjects assigned to treatment Group 3 (combination therapy) averaged 76.4 minutes of unscheduled daytime sleep when treated with stimulant medications compared to 29.3 minutes of unscheduled daytime sleep when treated with stimulant medications and scheduled sleep periods. The amount of unscheduled daytime sleep was not significantly reduced by the addition of two 15-minute naps per day (p=0.185) or regular times for sleep at night (p=0.450).

Although there was no change in the amount of unscheduled daytime sleep recorded during 24-hour ambulatory polysomnographic recordings, subjects assigned to treatment group two (regular bedtimes) reported less severe symptoms at the end of the two-week treatment period (p=0.002). Subjects assigned to the combination treatment group (Group 3), also reported decreased symptom severity at the end of the two-week treatment period (p=0.013). NSSQ scores remained unchanged for subjects taking two 15-minute naps per day (Group 1).

Regression Models

Unscheduled daytime napping Our linear regression analysis suggested that, after adjusting for the effect of pre-treatment daytime sleep, treatment Groups 1 (scheduled naps) and 2 (regular bedtimes) had almost identical reductions in daytime sleep, and treatment Group 3 (combination therapy) had much more reduction in daytime sleep duration than Groups 1 and 2 (See Table 3). Specifically, the mean reduction in unscheduled daytime sleep for treatment Group 2 (regular bedtimes) decreased 0.06 minutes (SE=9.75 minutes) more than subjects in treatment Group 1, a difference between the two groups that was not significant (p-value=0.99). In contrast, subjects in treatment Group 3 reduced their daytime sleep on average by 16.5 minutes (SE=10.8 minutes) more than subjects in treatment Group 1, but the differences were not statistically significant (p-value=0.14).

We also found that longer pre-treatment daytime sleep durations were strongly associated with greater reductions in unscheduled daytime sleep durations at the end of the two-week treatment protocol. Specifically, for every 10-minute increase in pre-treatment daytime sleep duration, the mean reduction in unscheduled daytime sleep duration after treatment increased by six minutes. This effect occurred in all three treatment groups and represented a significant change (p-value=0.0001, (See Table 3).

Subjective Symptom Severity

Our second linear regression analysis suggests that, after adjusting for the effect of pre-treatment NSSQ scores, treatment groups 2 and 3 (regular bedtimes and combination therapy) had similar improvement in NSSQ scores and both groups had significantly more improvement in their NSSQ scores compared to group 1 (naps) (See Table 4). Specifically, the mean improvement in NSSQ scores for treatment Group 2 was 19.3 points (SE=9.2) more than that of treatment Group 1, and the difference between the two groups was statistically significant (p-value=0.047). The mean improvement in NSSQ scores in treatment group 3 (combination treatment) was 21.0 points (SE=8.8) more than treatment Group 1 (naps) and the difference was statistically significant (p-value = 0.02). There were no differences between Groups 2 and 3 in their improvement in NSSQ scores (p-value =0.87).

Table 3—Regression coefficient estimates for the change of daytime sleep

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>SE</th>
<th>T</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>12.10</td>
<td>7.54</td>
<td>1.60</td>
<td>0.12</td>
</tr>
<tr>
<td>Group2</td>
<td>0.06</td>
<td>9.75</td>
<td>0.01</td>
<td>0.99</td>
</tr>
<tr>
<td>Group3</td>
<td>-16.49</td>
<td>10.80</td>
<td>-1.53</td>
<td>0.14</td>
</tr>
<tr>
<td>Pre Daytime Sleep</td>
<td>-0.59</td>
<td>0.11</td>
<td>-5.27</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

R-square=0.74

Note that Group 2 is the dummy variable for group 2 and Group3 is the dummy variable for Group 3 with Group 1 as the reference group.

Table 4—Regression coefficient estimates for the change of NSSQ scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>SE</th>
<th>T</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>55.75</td>
<td>19.25</td>
<td>2.90</td>
<td>0.01</td>
</tr>
<tr>
<td>Group2</td>
<td>-19.25</td>
<td>9.19</td>
<td>-2.12</td>
<td>0.047</td>
</tr>
<tr>
<td>Group3</td>
<td>-21.00</td>
<td>8.82</td>
<td>-2.28</td>
<td>0.027</td>
</tr>
<tr>
<td>Pre NSSQ</td>
<td>-0.45</td>
<td>0.15</td>
<td>-3.04</td>
<td>0.006</td>
</tr>
</tbody>
</table>

R-square=0.46

Note that Group 2 is the dummy variable for Group 2 and Group3 is the dummy variable for Group 3 with Group 1 as the reference group.
Our linear regression analysis, shown in Table 4, also suggests that higher pre-treatment NSSQ scores were strongly associated with greater improvements on NSSQ after treatment. Subjects with more severe symptoms, as measured by the NSSQ, benefited more from the combination of stimulant medications and scheduled sleep than subjects with less severe symptoms. Specifically, for every 10-point increase in pre-treatment NSSQ score, the improvements in NSSQ score increased by 4.5 points (p-value=0.006). This effect occurred in all three treatment groups (See Table 4).

Additional Findings—Effects of Pretreatment Levels of Daytime Sleepiness

To further examine the relationship between the severity of daytime sleepiness and the efficacy of scheduled sleep periods, we divided the subjects into three groups according to the severity of their daytime sleepiness during the baseline recordings. The first group of subjects, the least sleepy group, included six subjects who were able to remain awake for the entire day and two other subjects who had day sleep durations of less than 10 minutes. Subjects in the moderately sleepy group (n=7) had day sleep durations between 10 minutes and 60 minutes. Subjects in the profoundly sleepy group (n=10), those with day sleep durations of over 60 minutes, averaged 97.7 minutes of unscheduled daytime sleep (See Table 5). Although subjects spent approximately the same time in bed at night, subjects who were the least sleepy during the daytime, had more consolidated sleep at night, as evidenced by a fewer minutes awake after sleep onset (WASO), and a higher sleep efficiency.

The addition of scheduled sleep periods did not benefit treated subjects who were alert or only moderately sleepy during the daytime (See Table 6). Only those subjects who were profoundly sleepy during the baseline recording appeared to benefit from the addition of scheduled sleep periods (Students t-test, p=0.028). Mean amounts of unscheduled daytime sleep dropped from 97.7 minutes to 62.9 minutes.

DISCUSSION

This study demonstrated that the addition of scheduled sleep periods may benefit some treated narcoleptic patients. Subjects assigned to the combination therapy group had less daytime sleep and reported less severe symptoms at the end of the two-week treatment period. Although subjects assigned to sleep regular hours at night reported less severe symptoms at the end of the study, their objective level of daytime sleepiness did not change. The addition of two 15-minute naps per day did not alter either the amount of unscheduled daytime sleep or subjective symptom severity.

Although combination therapy appears more effective than the other two treatment approaches tested, the apparent superiority of combination therapy may be more a reflection of the subjects’ baseline levels of sleepiness than inherent superiority of this approach. Subjects assigned to the combination therapy group were significantly sleepier at baseline than the other two groups of subjects, sleeping on average 76 minutes per day (compared to 28 minutes and 39 minutes). All three sleep schedules produced significant reductions in the amount of unscheduled daytime sleep, if pretreatment levels of daytime sleepiness were high. Subjects with severe daytime sleepiness benefited from the addition of scheduled sleep periods, while those who were only moderately sleepy or able to maintain alertness did not benefit from scheduled sleep periods. Thus, it appears that the efficacy of scheduled sleep periods is highly associated with pre-treatment levels of daytime sleepiness.

Several factors should be considered when recommending scheduled sleep periods as an adjunct to stimulant medications.
First, is the patient likely to benefit from the addition of scheduled sleep periods? Our data suggest that blanket statements regarding the necessity of scheduled sleep periods for all patients with narcolepsy should be reconsidered. Although stimulant medications do not "normalize" patient scores on laboratory tests of daytime sleepiness, 24 roughly 30%—40% of the treated narcoleptic patients we have studied using 24-hour ambulatory polysomnographic recordings are able to remain awake throughout the day when engaged in their usual daily activities. 25 Scheduled sleep periods are not necessary for these patients, and should only be recommended if the patient is sleeping for more than 60 minutes during the daytime. Since narcoleptic patients often underestimate the severity their daytime sleepiness, 22,25,26 a sleep log and/or actigraphy should be used to determine how long a patient is sleeping during the day.

Secondly, if scheduled sleep periods are recommended, is the patient likely to comply with your recommendations? Or are there other approaches that may be equally efficacious and/or more acceptable to the patient? It may be quite difficult for some patients to adhere to a regular sleep schedule and/or take two 15-minute naps a day. 8 Finding the time to nap during the workday may be especially difficult, 27,28 especially if it involves disclosing their illness. Finally, many patients may resist altering their lifestyles to accommodate their sleepiness. 22,25,26 A sleep log and/or actigraphy should be used to determine how long a patient is sleeping during the day.

Compliance is an issue with all patient populations, 30,31 and patients with narcolepsy are no exception. 32 Just a little over one-third of the patients in this study (36%) took all of their prescribed medications. Fifty-seven percent of the least sleepy subjects took all of their prescribed medications, compared to 29% of the moderately sleepy group and 25% of the profoundly sleepy subjects. The least sleepy subjects also took a greater percentage of their prescribed stimulant medications than members of the other two groups, 85% compared to 65% of the dosage taken by members of the moderately sleepy group, and 51% taken by members of the profoundly sleepy group. Profoundly sleepy subjects were also more likely to decrease their dosage by larger amounts than the least sleepy subjects (they reduced their dosages by an average of 41% compared to an average dosage reduction of 15% for the least sleepy subjects). Moderately sleepy subjects reduced their dosages on average by 35%. Two-thirds of the profoundly sleepy subjects in this study failed to take their prescribed dosage of stimulant medications, and half of the moderately sleepy subjects had not taken the full amount of their prescribed stimulants. Perhaps if they these subject had taken their prescribed stimulant medications, they might not have such severe daytime symptoms. Subjects who were compliant with their prescribed stimulant regimen, but remained moderately or profoundly sleepy (25% of the subjects in these two groups), might benefit from increasing the dosage of their current stimulant or changing to a more potent stimulant.

However, if stimulant doses are already high, and the patient is taking their medications as prescribed, scheduled sleep periods should be considered as an adjunct therapy for those patients whose have significant amounts of unplanned daytime sleep. They should also be considered if a patient is reluctant to take higher doses of stimulants, experiences adverse side effects with higher doses, or has another illness that rules out the use of higher doses or the use of certain stimulants.

At present it is difficult to recommend one type of sleep schedule over another. Since all three treatments produced significant reductions in daytime sleep durations, when pretreatment levels of sleepiness were high, patient preferences should be considered. For example, patients who are reluctant to request accommodations from their employer may prefer to avoid scheduled daytime naps. Other patients may prefer scheduled daytime naps, or the combination of scheduled daytime naps and regular hours for nighttime sleep. If scheduled daytime naps are used, patients need to know that a nap will increase their alertness for only a short period of time (usually less than two hours). 33 Additional studies are needed to test the efficacy of the three different sleep schedules in a group of profoundly sleepy subjects.

### Table 6—Effects of scheduled sleep periods by severity of daytime sleepiness

<table>
<thead>
<tr>
<th>Severity of Daytime Sleepiness</th>
<th>Pretreatment</th>
<th>Post Treatment</th>
<th>Mean difference</th>
<th>T</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Least Sleepy</td>
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</tr>
<tr>
<td>Mean Duration Sleep Daytime (mins)</td>
<td>1.6±3.1</td>
<td>10.1±12.3</td>
<td>11.6</td>
<td>2.081</td>
<td>0.076</td>
</tr>
<tr>
<td>Total Score on NSSQ</td>
<td>113.6±18.4</td>
<td>102.9±18.0</td>
<td>-10.7</td>
<td>-1.477</td>
<td>0.190</td>
</tr>
<tr>
<td>Moderately Sleepy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration Sleep Daytime (minutes)</td>
<td>33.7±15.6</td>
<td>28.1±17.0</td>
<td>-5.6</td>
<td>-0.652</td>
<td>0.539</td>
</tr>
<tr>
<td>Total Score on NSSQ</td>
<td>131.1±29.1</td>
<td>109.6±22.4</td>
<td>-21.4</td>
<td>-3.205</td>
<td>0.018*</td>
</tr>
<tr>
<td>Profoundly Sleepy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Duration Sleep Daytime (minutes)</td>
<td>97.7±16.1</td>
<td>62.9±39.0</td>
<td>-34.8</td>
<td>-2.671</td>
<td>0.028*</td>
</tr>
<tr>
<td>Total Score on NSSQ</td>
<td>129.5±29.1</td>
<td>128.5±29.8</td>
<td>-5.6</td>
<td>-0.586</td>
<td>0.574</td>
</tr>
</tbody>
</table>

* p<0.05
ACKNOWLEDGMENTS

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REFERENCES
