Do Sleep Deprivation and Time of Day Interact with Mild Obstructive Sleep Apnea to Worsen Performance and Neurobehavioral Function?

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Study Objectives: Sleep deprivation, time of day (circadian influences), and obstructive sleep apnea (OSA) all reduce performance and neurobehavioral function. We assessed the interactive effect of sleep deprivation and time of day on performance and neurobehavioral function in subjects with and without mild OSA.

Methods: This was a cross-over study in which 13 subjects with mild OSA and 16 subjects without OSA had performance and neurobehavioral testing after a normal night’s sleep and after a night of supervised sleep deprivation. All subjects were studied in the sleep laboratory of a university teaching hospital. Subjects were administered questionnaires to collect demographic, physical, and medical information; completed actigraphy and sleep diaries to estimate prior sleep debt before testing; and were tested on the Neurobehavioral Assessment Battery, a personal computer-based driving simulator (AusEd™), and the Oxford Sleep Resistance Test to assess performance and neurobehavioral function.

Results: Sleep deprivation resulted in poorer driving simulator and neurobehavioral performance for most outcome measures. The worst-time performance was often seen at 3:00 PM. Subjects with mild OSA were less aware of their sleepiness due to sleep deprivation and, in 1 reaction time task, showed greater impairment than did subjects without OSA at certain times of the day after sleep deprivation.

Conclusions: The results suggest that subjects with mild OSA are not primarily different than subjects without OSA in their response to sleep deprivation or time-of-day influences. Consistent with previous literature, there were clear effects of sleep deprivation and time of day in all subjects. The finding that perception of daytime sleepiness after sleep deprivation was blunted in subjects with OSA compared with subjects without OSA, despite similar performance decrements, warrants further study.

Keywords: Sleep deprivation, circadian, obstructive sleep apnea, performance, driving

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In particular, the group of drivers with mild OSA deserves special attention, as this subgroup is the largest and their OSA frequently goes undiagnosed. Information on the interaction of mild OSA and other fatigue-promoting factors may additionally aid in decisions about therapy for this group of drivers, especially in the setting of high-risk occupational groups such as commercial drivers.

The aim of this study was to examine the interactive effect of sleep deprivation, time of day, and mild OSA on performance and neurobehavioral function, especially with respect to performance on the driving simulator.

METHODS

Project Design

Twenty-nine subjects (13 with mild OSA, 16 without OSA) underwent polysomnography and performance testing on 2 occasions: under normal sleeping conditions (non–sleep-deprived testing) and after a night of acute total sleep deprivation. Approximately half of each group (with and without mild OSA) was tested first under non–sleep-deprived conditions, with the remaining subjects tested first under sleep-deprived conditions. Generally, both sleep studies were conducted within 2 to 4 weeks of each other. Subjects were instructed to obtain at least 8 hours of sleep per night for the 4 nights preceding each occasion of testing to minimize any preexisting sleep debt at the start of a test. Sleep hours for these 4 nights were also measured subjectively using sleep diaries and objectively with actigraphy.

The protocol was approved by the Central Sydney Area Health Service Ethics Committee (RPA zone) and the University of Sydney Ethics Committee, and informed consent was obtained from each patient.

SUBJECTS

Study Population

Subjects with and without mild OSA were recruited for this study. Men were studied exclusively for several reasons: mild OSA is much more common in men; there is less evidence for increased driving accident risk in women with mild OSA; and finally, to avoid known sex differences in some aspects of performance.22

Eligibility

Subjects were eligible if they were 18 to 60 years old, held a current New South Wales driver’s license, and drove regularly. Subjects were free of significant cardiorespiratory or psychiatric disease or other medical conditions that might affect their ability to adequately and safely perform the experimental protocol (e.g., narcolepsy, epilepsy). Subjects were ineligible if they were taking any medications that might affect daytime alertness, such as antidepressants or benzodiazepines, or if they were currently being treated or had had previous treatment for OSA. Subjects were excluded if they were taking any illicit substances, such as amphetamines, or were heavy drinkers (regular alcohol consumption greater than 40 g per day). Medication and drug use was initially assessed by history and then confirmed by urine drug screen after enrollment into the study.

Recruitment

Patients with mild OSA were identified in hospital-based sleep clinics and then invited to participate, or, alternatively, they were identified through an audit of recent sleep study results from Royal Prince Alfred Hospital Sleep Investigation Unit. Subjects without OSA were recruited from these same sources and also from advertising among university students.

Classification of subjects as having OSA or no OSA was made on the basis of their sleep study results on the weekend without sleep deprivation. Subjects were regarded as having OSA if their total RDI was 5 or greater. Subjects without OSA had a total RDI less than 5 per hour.

Protocol

All testing was performed on weekends (Friday evening to Sunday), when the sleep laboratory was for the most part free, to create a stable testing environment and to minimize any distractions during the testing procedures. Wherever possible, subjects were tested in pairs to increase motivation and to reduce sleepiness and boredom, especially for the period between testing batteries after the night of sleep deprivation. This was achieved for 75% of the subjects.

Subjects were permitted to smoke and to continue their usual caffeine intake on the days prior to attending the sleep laboratory. However, after arrival in the sleep laboratory, subjects were not allowed to consume caffeinated products and or smoke cigarettes for the duration of the weekend testing.

At 7:00 PM on the day of admission to the sleep laboratory, subjects commenced their first performance-testing battery. This consisted of the Neurobehavioral Assessment Battery (NAB) (version 17-063, University of PA), a personal computer-based driving simulator (AusEd™)(Sydney, Australia; Edinburgh, Scotland), and the Oxford Sleep Resistance Test (OSLER) (Osler Chest Unit, Oxford, UK), in that order of testing. This testing battery took 1 hour 45 minutes to complete.

After concluding the 7:00 PM testing battery, the subjects who were undergoing their weekend of testing without sleep deprivation were then set up for overnight polysomnography. Lights out was at 10:15 PM, and the subjects slept, while being monitored, until 6:00 AM. Subjects then showered, had breakfast (no caffeine), and commenced their next testing battery at 7:00 AM. The testing battery was again repeated at 11:00 AM, 3:00 PM, and finally at 7:00 PM. A urine sample was also obtained from the subjects on Saturday for laboratory analysis. The testing weekend without sleep deprivation concluded after the completion of the 7:00 PM testing battery, at 9:00 PM.

Subjects who were being sleep deprived were not set up for polysomnography on the Friday night but, instead, stayed awake overnight. The testing battery was repeated the next day at 3:00 AM, 7:00 AM, 11:00 AM, 3:00 PM, and 7:00 PM. These subjects were supervised by sleep laboratory staff at all times to ensure they did not sleep, either overnight or between the daytime testing bouts. A urine drug screen was also collected. On Saturday evening, these subjects were set up for polysomnography, and a sleep study was performed. After awakening on Sunday morning, subjects went home.

A television, computer, videocassette player, digital video disc player, and videogame play station were available for the subjects’ entertainment for both testing weekends. Subjects were
also free to bring in any other reasonable form of activity, such as reading material or academic work. They were not, however, permitted to exercise or drink alcohol. At all times, subjects were under the close supervision of research staff to ensure that they complied with the protocol conditions.

**Data-Collection Instruments**

The following questionnaires and tests were used to collect the data for this study.

**Participant Questionnaires**

Questionnaires collected basic physical and demographic information, together with information regarding caffeine intake (usual intake and the amount on the day of admission), driving, lifestyle, and medical history. The Epworth Sleepiness Scale was administered on the first testing weekend. All questionnaires were completed during the evening on the day of admission to the sleep laboratory.

**Neurobehavioral Assessment Battery**

The 30-minute computerized NAB was used to measure emotional, performance, and memory variables. This testing battery has been shown to be sensitive to mood and performance changes in studies of total and partial sleep deprivation. It contains subjective questionnaires, including the Stanford Sleepiness Scale (SSS) and the Profile of Mood States; performance measures, including the Psychomotor Vigilance Task (PVT) and the Digit Symbol Substitution Task; and a test of short-term memory (Probed Memory Recall Test). PVT transformed lapses was selected as a primary outcome variable for this group of tests, as it has been shown to be very sensitive to the effects of sleep deprivation.

For technical reasons, the NAB is best administered in a fixed fashion from start to finish. The NAB was administered in its entirety in this way for each testing session. However, analysis of NAB outcomes was limited to the PVT, Digit Symbol Substitution Test, Probed Memory Recall Test, SSS, and Profile of Mood States tests. This was done in order to focus on the NAB outcomes that were most relevant to the aims of this study and, hence, to reduce the risk of type 1 error in the data analysis.

**AusEd Driving Simulator**

A standardized 30-minute run on the AusEd Driving Simulator was performed subsequent to the NAB. Early work suggests that this test is sensitive to driving impairment due to sleep deprivation and alcohol use.

The simulator was installed on a Windows NT workstation in a sound-insulated room, with a 21-inch computer screen, a Thrustmaster T2 steering wheel and pedals (Hillsboro, OR) and dual stereo computer speakers. The AusEd driving simulator is designed to simulate a monotonous night-time drive on a rural road.

A full-screen projection of the view from the driver’s seat of a car is provided, along with a small speedometer in the upper left-hand corner of the screen. The simulator is controlled using an accelerator and brake pedals and the steering wheel. The drive takes place on a dual carriageway at night, with forward vision limited to “low-beam” lights. All room lighting is turned off during testing. On the road during the 30-minute drive, 10 slowly moving trucks appear, driving in the same direction as the subject and disappearing when the subject uses the brake. Otherwise, there are no other cars on the road. There are no traffic signs or markers apart from regularly placed reflective markers on both edges and in the middle of the road, similar to rural roads in Australia.

A continuous, low-frequency (approximately 60 dB) simulated engine noise is played through the computer speakers for the length of the drive. For the purpose of this experiment, 5/7 of the road was straight, while 2/7 of the road consisted of chicanes. The layout of the road and time of presentation of trucks was identical for each drive.

The simulator assesses driving ability through several measures. First, subjects are instructed to keep their speed between 60 and 80 kilometers per hour, using the speedometer as a guide, and velocity deviation from this zone of speed is measured. Because the speedometer lies outside the line of sight for the road, monitoring and maintaining speed represents a divided-attention task also. Second, subjects are instructed to stay as close as possible to the middle of the left-hand lane for the duration of the drive, and steering deviation from this position is measured. Third, crashes are registered under 3 conditions: (1) driving off the shoulder of the road, (2) hitting the back of a truck, or (3) remaining stationary for more than 10 seconds. Finally, the times taken for the subject to brake when the trucks appear in the line of sight are recorded. The AusEd mean reaction time (in milliseconds)—a mean value of the 10 braking episodes—was the primary outcome variable for this test. The standard deviation of the AusEd mean reaction time (in milliseconds) was also measured to reflect performance variability as the result of sleepiness.

**Oxford Sleep Resistance Test**

This test was used to provide an objective measure of daytime sleepiness. It was commenced immediately following the completion of the driving simulator testing. The OSLER test has been shown to discriminate normal subjects from patients with OSA and to be sensitive to the effects of sleep deprivation. A single value, the OSLER sleep latency, is determined at the end of the test (primary outcome variable).

**Urine Drug Screen**

A urine drug screen was performed on both testing weekends to determine whether subjects had taken any substances that might influence their performance tests.

**Other Tests**

Nocturnal polysomnography and estimating prior sleep hours (using a sleep diary and actigraphy) were performed as previously described.

**Statistical Analysis**

Determinants of daytime driving simulator performance and neurobehavioral function were evaluated using analysis of variance with 2 within-subject variables—sleep condition (with and without sleep deprivation) and time of day (7:00 AM, 7:00 PM, 11:00 AM, 3:00 PM, 7:00 PM)—and 1 between-subject variable—the presence or absence of mild OSA. A general linear model was fitted using the method of least squares. Least-squares differences were estimated with 95% confidence intervals. During the sleep-
deprivation condition, an additional night time (3:00 AM) time point was analyzed. Hence, a separate 2-way analysis of variance (OSA status and time of day) was conducted to fully evaluate the effect of diurnal variation on driving simulator performance and neurobehavioral function in the sleep-deprived state. The effect of order of testing, that is, sleep-deprivation condition first or second, was also tested and found not to be a significant predictor of the primary outcomes. Hence, it was not included in the final analyses.

Because of missing data in 5 subjects for the final testing batteries on the weekend without sleep deprivation (7:00 AM), analyses were performed with and without data included from this final time point. When the final time point was included, the analysis of daytime outcomes was limited to 24 subjects with complete data sets (primary analysis). When the final time point was excluded, 28 subjects had complete daytime data sets and could be analyzed (alternative analysis). One subject failed to complete the final 2 testing batteries (3:00 PM, 7:00 PM) on the weekend without sleep deprivation, and, hence, his data were not included in either the primary or alternative analyses for the daytime outcomes.

For the driving simulator and neurobehavioral outcomes, the following potential confounding factors were tested as covariates and retained when they were significant predictors of the outcome variable: age, sleep hours in preceding 4 nights, average caffeine intake, and caffeine intake on the day of admission. Of these, only age and average alcohol intake were significant predictors (p < .05) in any of the analyses.

All interactions were tested, and, when these were significant (p < .05), separate models were constructed for each level of the interaction. Pairwise comparisons between levels of each main independent variable (sleep-deprivation status, time of day, and OSA status) were assessed when the variable was found to be significantly associated with the outcome in the analysis-of-variance model. The magnitude of the effect of each main independent variable was estimated, as differences between levels of the variable, with 95% confidence intervals. P values < .05 were considered statistically significant.

Differences in preceding sleep hours and questionnaire data were assessed with t tests, and results are expressed as mean differences with 95% confidence intervals.

Posthoc power calculations were performed for the 3 principal outcome measures using the observed variance-covariance matrix and observed means. The power to detect a Greenhouse-Geisser F test as significant (p < .05) was estimated for the main effects of sleep-deprivation status and time of day; the interaction between sleep-deprivation status and time of day; and the 3-way interaction between OSA status, sleep-deprivation status, and time of day. Power calculations were performed for actual sample size. A second analysis was undertaken to estimate the sample size that would have been required to achieve 80% for the sleep-deprivation status by time-of-day interaction term. The data analysis described above was undertaken using the SPSS statistical package 10.0.05 (SPSS, Inc., Chicago, IL). The power analysis was undertaken using PASS software (NCSS, Kaysville, UT).

RESULTS

Patient Characteristics

Table 1 presents the general characteristics of the 2 study groups. Subjects with OSA were more overweight, as indicated by an increased body mass index and neck circumference. The mean Epworth Sleepiness Score for both groups was less than 10. Both groups slept less than 8 hours on average for the 4 nights preceding the testing weekends, despite our instructions.

Self-reported motor vehicle accident rates were similar for both groups (mean 0.6 ± 1.3 [SD] in 3 years for subjects without OSA and 0.3 ± 0.5 for subjects with OSA). Both groups reported similar average caffeine intake on the days of admission (1.5 ± 1.6 drinks; 1.9 ± 1.4), similar average usual caffeine intake (2.9 ± 2.4 drinks; 4.3 ± 3.3), and similar average alcohol consumption on work days (0.3 ± 0.7 drinks per day; 1.0 ± 1.7) and on days off (1.1 ± 1.3 drinks per day; 2.8 ± 2.8).

Polysomnography Results During Non–Sleep-Deprived Condition

Table 2 shows the polysomnography results during the non–sleep-deprived condition for the 2 groups. Both groups slept well under the testing conditions, demonstrating good sleep architecture and efficiency (these data have been published previously).55 Subjects with OSA had a mean total RDI of 12, compared with a mean total RDI of 2 in the group without OSA. Similarly, subjects with OSA had a greater RDI during rapid eye movement (REM) sleep, RDI during non-REM (NREM) sleep, and total arousal index compared with subjects without OSA. The effect of sleep deprivation on polysomnographic outcomes in these subjects has been reported previously.55

Daytime Driving Simulator and Neurobehavioral Outcomes

The effects of mild OSA, sleep deprivation, and time of day on daytime driving simulator and neurobehavioral outcomes were assessed by analysis of variance. No subjects had any crashes in...

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Table 1—General Characteristics of the Study Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Without (n = 16)</th>
<th>With (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>38 (± 14.7)</td>
<td>45 (± 14.8)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25.5 (± 5.1)</td>
<td>30.3 (± 4.2)</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>38.9 (± 2.5)</td>
<td>41.4 (± 2.6)</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale score</td>
<td>7 (± 4.2)</td>
<td>9 (± 6.0)</td>
</tr>
<tr>
<td>Recorded sleep preceding 4 nights (average sleep, h/night)</td>
<td>7.1 (± 0.5)</td>
<td>6.6 (± 0.5)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

Table 2—Polysomnography for Subjects With and Without OSA During the Non-Sleep-Deprived Condition

<table>
<thead>
<tr>
<th>Variable</th>
<th>Without (n = 16)</th>
<th>With (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDI, no./h</td>
<td>2 ± 5.1</td>
<td>12 ± 1.4</td>
</tr>
<tr>
<td>REM</td>
<td>8 ± 12.7</td>
<td>20 ± 12.7</td>
</tr>
<tr>
<td>NREM</td>
<td>1 ± 6.1</td>
<td>10 ± 6.1</td>
</tr>
<tr>
<td>Total Arousal Index, no./h</td>
<td>9 ± 6.0</td>
<td>17 ± 6.0</td>
</tr>
<tr>
<td>Subcriterion respiratory events, no./h</td>
<td>1 ± 1.4</td>
<td>2 ± 1.4</td>
</tr>
<tr>
<td>Longest apnea, sec</td>
<td>17 ± 16.6</td>
<td>29 ± 18.3</td>
</tr>
<tr>
<td>Minimum O₂ saturation, %</td>
<td>92 ± 2.4</td>
<td>89 ± 2.6</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD unless otherwise indicated. RDI refers to respiratory disturbance index; REM, rapid eye movement sleep; NREM, non-rapid eye movement sleep.
There was an effect of sleep deprivation and diurnal variation, (i.e., significant diurnal variation in the effect of sleep deprivation on the outcome); where there is no significant diurnal variation, the overall result is shown.

Results include data for 28 subjects and 3 time points; all other results include data for 24 subjects and 4 time points.

CI refers to confidence interval; OSLER, Oxford Sleep Resistance Test; PVT, Psychomotor Vigilance Test.

any of the driving simulator testing sessions, so this AusEd™ outcome could not be analyzed.

### Effect of Sleep Deprivation and Time of Day

There was an effect of sleep deprivation and diurnal variation, or an interaction between these, for many of the daytime driving simulator and neurobehavioral outcomes. Sleep deprivation consistently resulted in poorer driving simulator and neurobehavioral performance for many of the outcome measures. Time of day influenced performance, and the worst daytime performance was often seen at 3:00 PM. These data are presented in tables 3 and 4. Data from subjects with mild OSA and subjects without OSA have been grouped together in these tables because the effect of sleep deprivation, time of day, and the interaction between them did not differ between patients with OSA or subjects without OSA for any of these outcomes. However, this was not the case for the

### Table 3—Effect of Sleep Deprivation on the Primary Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Magnitude of the Effect at (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7:00 AM</td>
</tr>
<tr>
<td>OSLER sleep latency, sec*</td>
<td>-851</td>
</tr>
<tr>
<td>PVT transformed lapses*</td>
<td></td>
</tr>
<tr>
<td>AusEd™</td>
<td>127</td>
</tr>
<tr>
<td>Standard deviation, mean reaction time, ms*</td>
<td></td>
</tr>
<tr>
<td>Mean steering deviation from median position, cm</td>
<td></td>
</tr>
<tr>
<td>Mean reaction time, ms*†</td>
<td></td>
</tr>
<tr>
<td>Mean speed deviation, km/h*†</td>
<td></td>
</tr>
<tr>
<td>Profile of Mood States subscore*</td>
<td></td>
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<tr>
<td>Fatigue</td>
<td></td>
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<tr>
<td>Vigor</td>
<td></td>
</tr>
<tr>
<td>Probed Memory Recall Test, no. correct</td>
<td></td>
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<tr>
<td>Digit Symbol Substitution Test</td>
<td></td>
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<tr>
<td>Number correct, %</td>
<td></td>
</tr>
<tr>
<td>Mean reaction time†</td>
<td></td>
</tr>
</tbody>
</table>

*Differences are relative to preintervention time point, ie, first 7:00 PM testing session prior to either a normal night’s sleep or sleep deprivation.

†Significant interaction between time of day and sleep deprivation (Intervention); where there is no significant interaction, the combined result is shown.

‡Results include data for 28 subjects and 3 time points; all other results include data for 24 subjects and 4 time points.

§Age is a significant covariate.

CI refers to confidence interval; OSLER, Oxford Sleep Resistance Test; PVT, Psychomotor Vigilance Test.

### Table 4—Effect of Time of Day on Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not sleep deprived</th>
<th>Sleep deprived</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSLER sleep latency, sec†</td>
<td>7:00 AM: 117 (-85 to 320)</td>
<td>7:00 AM: -934 (-534 to -1335)</td>
<td>3:00 PM: 106 (42 to 169)</td>
</tr>
<tr>
<td>PVT transformed lapses†</td>
<td>7:00 AM: 0.5 (-0.3 to 1.3)</td>
<td>3:00 PM: 2.1 (1.5 to 3.9)</td>
<td>7:00 AM: 21 (-0.7 to 42.3)</td>
</tr>
<tr>
<td>AusEd™</td>
<td>3:00 PM: 90 (36 to 143)</td>
<td>3:00 PM: 218 (115 to 321)</td>
<td>3:00 PM: 24 (0.1 to 4.8)</td>
</tr>
<tr>
<td>Standard deviation, mean reaction time, ms*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean steering deviation from median position, cm</td>
<td></td>
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<tr>
<td>Mean reaction time, ms*†</td>
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</tr>
<tr>
<td>Profile of Mood States subscore*</td>
<td></td>
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</tr>
<tr>
<td>Fatigue</td>
<td>7:00 AM: 1.2 (-1.5 to 3.9)</td>
<td>11:00 AM: 8.7 (6.0 to 11.4)</td>
<td>7:00 AM: -8.9 (-6.2 to -11.5)</td>
</tr>
<tr>
<td>Vigor</td>
<td>7:00 PM: 2.5 (-0.2 to 5.1)</td>
<td>7:00 AM: 0.5 (-0.2 to 1.1)</td>
<td>7:00 AM: 0.6 (-0.3 to 1.5)</td>
</tr>
<tr>
<td>Probed Memory Recall Test, no. correct</td>
<td></td>
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<tr>
<td>Digit Symbol Substitution Test</td>
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<tr>
<td>Number correct, %</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean reaction time†</td>
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</tbody>
</table>

The effect of sleep deprivation on most of the daytime driving simulator and neurobehavioral outcomes differed according to the time of day at which the test was performed. Table 3 shows that impairments due to sleep deprivation were seen for the 3 primary outcome measures (OSLER sleep latency, AusEd™ mean reaction time, PVT transformed lapses). Other tests of driving ability (AusEd™ standard deviation of reaction time, average speed deviation) were also impaired by sleep deprivation (magnitude of effect, 95% confidence interval; 97 milliseconds, 36-157 milliseconds, for all time points; 1.7 km per hour, 0.1-3.3 km per hour at 7:00 AM and 2.3 km per hour, 0.2-4.4 km per hour at 3:00 PM, respectively). Similarly, mood (Profile of Mood States fatigue and vigor subscores) was adversely affected by sleep deprivation (data not shown). There was no effect of sleep deprivation on the Digit Symbol Substitution Test, a test of attention, or the Probed Memory Recall Test, a test of memory.

### Effect of Time of Day

Table 4 shows that the daytime diurnal effect on most of the driving simulator and neurobehavioral outcomes differed according to whether or not the subject was sleep deprived (Intervention). When daytime driving simulator and neurobehavioral performance was compared with the preintervention time point, i.e., the first 7:00 PM evening testing session prior to either a normal night’s sleep or sleep deprivation, the worst performance was often seen at 3:00 PM, a diurnal time of increased sleepiness. This diurnal effect was seen for 2 of the 3 primary outcome measures (AusEd™ mean reaction time, p < .001; and PVT transformed lapses, p < .001 [both sleep-deprived condition only]) as well as for AusEd™ standard deviation of reaction time (p < .001) and AusEd™ average speed deviation (p = .04, sleep-deprived condi-
Night Time Driving Simulator and Neurobehavioral Outcomes

For the analyses that included the night period after sleep deprivation, a similar time of day effect was again evident. Maximal performance impairment was not seen at 3:00 AM for any of the statistically significant outcomes (data not shown). There was no difference in the effect of diurnal variation between subjects with mild OSA and subjects without OSA.

Power Analysis

The study had a greater than 80% power to detect the observed effects of time of day and of sleep deprivation on all 3 main study outcomes and the observed effects of the interaction between time of day and sleep-deprivation status on 2 of the 3 outcomes (OSLER sleep-latency time and PVT transformed lapses) as significant at the 5% level. However, the power to detect the observed effect of the interaction between time of day and sleep-deprivation status on AusEd™ mean reaction time was only 49%. There was a significant risk of type 2 error in estimating the effect of the 3-way interaction between OSA status, time of day, and sleep-deprivation status.

DISCUSSION

This study examined the added effect of other sleepiness- or fatigue-promoting factors (sleep deprivation and time of day) on driving simulator performance and neurobehavioral function in patients with mild OSA. The results for the most part suggest that this group of patients with mild OSA are not different than the group without OSA in their response to sleep deprivation or time-of-day influences. Consistent with previous literature, there were clear effects of sleep deprivation and time of day in all subjects. However, the subjects with mild OSA were less aware of their impairment due to sleep deprivation, and, in 1 reaction time task, showed greater impairment than did the subjects without OSA at certain times of the day after sleep deprivation.

This study found that sleep deprivation resulted in poorer driving simulator and neurobehavioral performance for most of the outcome measures. There was some variation in the effects of sleep deprivation according to the time of day. Impairments due to sleep deprivation were seen for tests of driving ability, vigilance, sleepiness, and mood. Similar findings have been reported previously.6,36-38

This study found that time of day influenced performance. For some outcomes, this diurnal effect differed according to whether or not the subject was sleep deprived. However, for other outcomes, it was evident with or without sleep deprivation. The worst daytime performance was often seen at 3:00 PM, a diurnal time of increased sleepiness. However, there was no maximal time-of-day effect at 3:00 AM for any of the variables in this study, perhaps due to the fact that subjects had been less sleep deprived at this time point compared with later time points.

This study found that OSA status influenced the effect of sleep deprivation on 2 outcomes, the SSS score and the PVT reaction time, mean fastest 10%. For the SSS score, a measure of subjective sleepiness, the extent of increased subjective sleepiness due to sleep deprivation was less in those subjects with OSA than in those without OSA. Given the consistent effect of sleep deprivation on most of the objective outcome measures, in which there

Effect of OSA Status

Consistent with the effect of sleep deprivation on objective sleepiness (OSLER sleep latency) shown in Table 3, sleep deprivation was also associated with increased subjective sleepiness (SSS score), compared with the non–sleep-deprived state, in subjects with mild OSA (difference 1.3, 0.8-1.7, p < .01) and subjects without OSA (difference 1.9, 1.5-2.3, p < .01). However, the extent of increased subjective sleepiness due to sleep deprivation was less in those subjects with OSA than in those without OSA (p = .03). This difference was not due to differences in initial sleepiness between the groups with and without OSA (comparison of initial difference for SSS and Epworth Sleepiness Scale scores p = .77 and p = .30, respectively). The effect of sleep deprivation on all other daytime outcomes, except the outcome described below, did not differ between subjects with OSA and those without OSA. Similarly, there was no difference in the effect of daytime diurnal variation between subjects with mild OSA and subjects without OSA. Further, subjects with mild OSA did not show different driving simulator performance and neurobehavioral function compared with subjects without OSA.

Impact of Sleep Deprivation on Diurnal Variation Differed with OSA Status

For 1 outcome measure, PVT reaction time, mean fastest 10%, there was a significant 3-way interaction. In other words, the effect of sleep deprivation on diurnal variation in reaction time differed between subjects with and without OSA (p = .02). Separate analyses for both subject groups (subjects with mild OSA and those without OSA) showed that, after sleep deprivation, subjects with mild OSA had significantly poorer performance throughout the day and were worst at the end of the day (mean difference in reaction time from preintervention 7:00 PM time point, 95% confidence interval; at 7:00 PM: 34 milliseconds, 21 to 47 milliseconds), whereas subjects without OSA showed worst performance at 7:00 AM (30 milliseconds, 19 to 41 milliseconds) with a transient relative improvement midmorning (11:00 AM). See Figure 1.

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was no difference between the 2 groups, this apparently paradoxical result may be important. It could suggest that the subjects with OSA were less aware of their impairment due to sleep deprivation. This is important if individuals are relying on their perception of daytime sleepiness to decide when to stop driving if they are fatigued. However, because the difference in SSS scores was small in this study, more work is required in this area to confirm these results.

For the outcome measure PVT reaction time, mean fastest 10%, there was a significant 3-way interaction. In other words, the effect of sleep deprivation on diurnal variation in reaction time differed between subjects with and without OSA. Further analyses showed that subjects with mild OSA had poorer performance throughout the day, whereas subjects without OSA showed a transient relative improvement midmorning. This suggests that subjects with OSA are sleep deprived, they may be less affected by diurnal improvements in performance for some tasks, compared with subjects without OSA.

Although this study did not show any other differences or interactions for daytime or night time performance outcomes between the subjects in the groups with and without OSA, the effect of OSA status on the above 2 outcomes within the study limitations that are discussed below, suggests that more work is needed in this area before definite conclusions can be made. Such work should study a greater number of subjects and also focus on the additive or interactive effects of chronic partial sleep deprivation on performance in subjects with OSA, as the effect of chronic sleep deprivation may differ from that of acute sleep deprivation. It is possible that our test battery was not sufficiently sensitive in the population with mild OSA and, other neurobehavioral measures should also be tested.

Our study subjects, in general, did not report excessive daytime sleepiness, as measured by the group’s mean Epworth Sleepiness Scale score (9 ± 6.0). Hence, our study subjects with OSA are more representative of those patients with OSA alone (snoring, nocturnal apneas, obstructive respiratory events on polysomnography), rather than those with “sleep apnea syndrome” (clinical combination of OSA and excessive daytime sleepiness).

It is possible that these 2 different groups of patients with OSA differ in other respects, e.g., in their interactive response to sleep deprivation or time-of-day effects. Unfortunately, this study was not adequately powered to examine separately the patients with mild OSA and higher Epworth Sleepiness Scale scores and those patients with mild OSA and normal Epworth Sleepiness Scale scores. Importantly, the results of this study cannot also be extrapolated to patients with moderate or severe OSA, as these patients may behave differently than patients with mild OSA, with respect to the study outcomes.

An attempt was made to reduce clinic selection biases in the group without OSA by recruiting university students via an advertisement. However, part of the group without OSA was still recruited from patients seen at hospital sleep clinics, which may have biased the study against finding a difference between the 2 study groups.

Sleep measurement by actigraphy and sleep diary showed that our subjects were mildly sleep deprived preceding the test nights (6.7–6.9 hours sleep per night on average). This may have limited the ability to detect an interactive effect of acute sleep deprivation and OSA. However, this level of chronic partial sleep deprivation is very frequent in society. A major strength of this study is that we requested that subjects avoid sleep deprivation, measured prior sleep hours by 2 different methods, and found this not to differ significantly between groups or testing conditions.

The effects of sleep deprivation on performance and neurobehavioral function that have been observed in this study are not explained by extraneous factors. Sleep debt prior to testing, caffeine intake on the day of laboratory admission, average caffeine intake, average alcohol intake, and age were assessed and tested as potential confounders in the multivariate analysis. The risk of type 1 error arising from the multiple endpoints that have been tested has been limited by defining 3 primary outcome variables that are most relevant to the study objectives. We have shown that the study was adequately powered to detect the effect of diurnal variation and of sleep deprivation on the main study outcomes.

For 2 of the 3 primary outcomes, the study was also adequately powered to detect true differences in diurnal variation between the sleep-deprived and the non–sleep-deprived status. However, true differences in the effect of OSA on this interaction may have been missed.

This study has examined the interaction between mild OSA, the most common form of OSA, and other driver-fatigue risk factors (sleep deprivation and time of day). The results of this study, for the most part, suggest that individuals with mild OSA are not different from individuals without OSA in their response to sleep deprivation or time-of-day influences. However, the subjects with mild OSA did show differences, as compared with the group without OSA, in 2 outcome measures, suggesting that the additive effects of OSA and other risk factors for fatigue need to be further investigated with more research. This would be particularly important for commercial drivers, who are often exposed to many fatigue-promoting factors, apart from OSA.

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