The Effects of REM Sleep Deprivation on the Level of Sleepiness/Alertness

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Study Objectives: The purpose of this study was to evaluate the effects of acute REM deprivation on daytime sleepiness/alertness, as measured by the MSLT.

Participants: Twenty-six healthy, normal volunteers (14 males and 12 females) participated in this study. Participating subjects were in good physical and psychological health and were asymptomatic as to sleep/wake complaints.

Interventions: Subjects spent 5 nights and 5 days in the laboratory. The first night and day were utilized for screening purposes. The remaining stay in the laboratory consisted of a baseline night and day, 2 deprivation nights and days, and a recovery night and day. Each night, a nocturnal polysomnogram was employed to monitor subjects’ sleep. Each day, subjects underwent an MSLT to evaluate their sleepiness/alertness. Subjects were randomized into REM-deprivation (RD) and yoked-control (YC) groups. On deprivation nights, RD subjects were awakened each time they entered stage REM sleep, and the YC subjects were awakened concomitantly with the RD subjects, assuming they were not in stage REM sleep.

Results: The REM-deprived subjects did not demonstrate any changes in MSLT scores across experimental days. In contrast, the YC subjects documented significantly lower MSLT scores on deprivation days due to decreased total sleep time.

Conclusion: The REM-deprivation procedure antagonized the effects of sleep loss on daytime sleepiness, resulting in increased alertness for RD subjects compared to YC subjects. The mechanism by which REM deprivation exerts its alerting effects is unknown and will require future research.

Key words: REM sleep; REM deprivation; sleepiness; alertness; CNS excitability

WITH THE ADVENT of the multiple sleep latency test (MSLT),1 researchers have objectively characterized the effects of total sleep loss,2 sleep restriction,3 and sleep disruption4 on daytime sleepiness. These studies have confirmed earlier subjective reports that sleep loss and sleep disruption increase daytime sleepiness. Indeed, acute sleep-deprivation studies have documented a linear relationship between nocturnal sleep and daytime sleepiness.5,6

In addition to daytime sleepiness, acute sleep deprivation has been documented as having profound effects on the length of recovery sleep. Using an enforced 24-hour recovery period, a 72% recovery of lost sleep has been demonstrated.7 Changes in the composition of the sleep architecture have also been demonstrated following sleep-deprivation protocols. Dement et al demonstrated that a reduction in total sleep time over several nights resulted in an increased percentage of slow-wave sleep (SWS) during recovery sleep.8 Borbély et al demonstrated a significant increase in SWS intensity on 2 contiguous recovery nights following 40 hours of total sleep deprivation.9 Furthermore, extended sleep in the morning,10 and late-afternoon naps,11,12 have been shown to significantly
decrease the amount of SWS during nocturnal sleep when compared to baseline levels. Daytime naps have also been shown to facilitate the reversal of daytime sleepiness following acute sleep deprivation. Lumley et al positively correlated the length of daytime naps and the amount of SWS present during the naps with mean MSLT scores after sleep loss.13

In contrast to SWS sleep, REM sleep appears to be primarily determined by circadian variations rather than putative homeostatic responses to acute total sleep loss.14-21 During 24-hour nap studies, the presence of REM sleep was more dependent on the time of day, whereas SWS was more dependent on the degree of sleep restriction and the length of prior wakefulness.16,17 Indeed, acute total sleep deprivation only minimally disrupts the 90-minute cycle of REM sleep.3,9,20 However, Bennington and Heller suggested that REM sleep propensity accumulates during NREM sleep, and should only occur following NREM sleep.22 They described a linear function directly relating the amount of NREM sleep to the amount of REM sleep. Alas, in normal, healthy subjects, REM sleep has been demonstrated to occur every 90 minutes throughout nocturnal sleep only after sufficient NREM sleep.23,24 In addition, the amount of REM sleep also appears to be a function of previous REM deprivation. Selective REM-sleep-deprivation studies, while minimizing the loss of NREM sleep, have demonstrated a substantial increased propensity for REM sleep, as manifested by a significant rebound in REM sleep on recovery nights.8 In rats, REM deprivation results in most of the same “sleep deprivation effects” as total sleep deprivation and NREM sleep deprivation, including increased energy expenditure and immunosuppression. Both human and animal REM-deprivation studies indicate that REM sleep is a vital homeostatic process. REM deprivation has also been shown to result in a general enhancement of activity, increased sexual activity, and decreased electroconvulsive-seizure threshold in healthy subjects.26-28

The available data point to REM sleep as a necessary component of sleep/wake homeostasis. The animal literature has described the vital role of REM and NREM sleep in the survival of the organism. The human literature has demonstrated the importance of total sleep time and the consequences of sleep restriction on the level of daytime sleepiness. Studies have also suggested the particularly important role of SWS in the alleviation of sleepiness. In contrast, the role of REM sleep during acute sleep-deprivation studies remains unclear. In fact, no study has systematically evaluated the effect of REM sleep manipulations on the level of daytime sleepiness/alertness. The present study was designed to evaluate the effects of acute REM-sleep deprivation on the level of daytime sleepiness/alertness, as measured by the MSLT.

<table>
<thead>
<tr>
<th>Table 1. The screening sleep characteristics of the REM-deprived and yoked control groups</th>
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<td>Sleep efficiency (%)</td>
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<td>Stage 1 (%)</td>
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<td>Stage 2 (%)</td>
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<td>Stage 3/4 (%)</td>
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<td>Stage REM (%)</td>
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± standard deviation

METHODS

Subjects

Twenty-six healthy, normal volunteers (14 males and 12 females) participated in the study. Subjects responded to advertisements presented in local newspapers, and were screened over the telephone in order to establish that they had regular sleep/wake schedules (ie, an average of 6.5-8.5 hours of sleep time per night without habitual napping), no recent drug use, and no medical or psychiatric conditions. In addition, subjects were required to pass a physical examination, a psychological evaluation, and a urine toxicology analysis prior to entry into the study. Participants in the study signed a written consent form explaining the requirements of participation and the monetary compensation they would be receiving for their participation.

Procedures

Participating subjects were in good health as determined by a screening physical examination, and were asymptomatic as to sleep/wake complaints. An 8-hour nocturnal polysomnogram (PSG) was employed for the purposes of screening subjects for sleep disturbances. A four-nap MSLT was administered the following day to assess subjects’ sleepiness/alertness. Subjects had no evidence of a sleep disorder on screening PSG and had a mean MSLT score ≥8 minutes (mean = 13.0±3 minutes). Subjects with REM onset on the MSLT were excluded from the study. Subjects spent the next 4 nights and days in the laboratory. They were randomized to the REM-sleep-deprivation group (RD; n=13) or to the yoked-control group (YC; n=13). If possible, participation in the study was coincident for each pair of experimental and yoked subjects.
Subjects were required to refrain from consuming alcohol and caffeine for 5 hours prior to arrival on the screening night and throughout the study. On the screening night and each of the 4 experimental nights, electrodes were placed on subjects for unipolar monitoring of the central and occipital electroencephalograms (EEG), electrooculograms (EOG), submental electromyogram (EMG), and an electrocardiogram (EKG). Tibialis anterior EMG to monitor periodic leg movements, and a thermistor placed at the nose and mouth to monitor respiration, were used to screen for sleep apnea. On each of the study days, an MSLT was administered to determine subjects’ level of sleepiness/alertness. The standard MSLT protocol was utilized for each MSLT. On the screening day, subjects were asked at 10:00, 12:00, 14:00, and 16:00 hours, to lie down, close their eyes, and attempt to fall asleep. On experimental days (1–4), five naps were administered (10:00, 12:00, 14:00, 16:00, and 18:00 hours). Naps were terminated following 20 minutes of wakefulness or 15 minutes after the first epoch of sleep. Between naps, subjects were monitored to ensure that they remained awake.

Time in bed (TIB) on nights 1 and 4 (baseline and recovery) was 8 hours (23:30 to 07:30 hours), and all subjects were allowed to sleep undisturbed. On nights 2 and 3 (deprivation nights), subjects in the RD group were experimentally awakened following one epoch of unequivocal stage-REM sleep. They were kept awake for 15 minutes before being allowed to return to sleep. Each time RD subjects were awakened, the YC subjects were also awakened if they were not in stage REM. If the YC subjects were in REM sleep, the awakening was delayed until they entered NREM sleep. TIB on nights 2 and 3 was extended to 9 hours and 15 minutes (22:15 to 07:30 hours) as compensation for the loss in total sleep time due to the experimental awakenings. Nocturnal PSG recordings were scored in 30-second epochs according to the rules of Rechtschaffen and Kales with an interrater reliability ≥ 90 percent. Subjects were asked to complete the Positive Affect/Negative Affect Scale (PANAS) and the Profile of Mood States (POMS) three times each day (10:30, 14:30, and 16:30) throughout the study. PSG variables, MSLT scores, and mood variables were analyzed using the Multivariate General Linear Hypothesis testing utilities of Systat, version 5.2 for Macintosh (Evanston, Ill: Systat, Inc., 1992). The between-group variable was group (RD or YC), and the repeated measure was the 4 consecutive experimental nights/days. Probabilities reported were corrected for multiple comparisons using the Greenhouse-Geiser method. Tukey’s post hoc comparisons were performed when appropriate.

### RESULTS

Both of the groups were comparable, with seven males and six females each, and had comparable ages of 21±3 years. There were no group differences in sleep characteristics on screening night (see Table 1).

#### Sleep Characteristics on the Experimental Nights

The sleep characteristics were submitted to a two-factor ANOVA, with one between-group factor (RD and YC) and one repeated-measures factor (experimental nights). RD subjects were awakened 9±2 times during the first deprivation night, which was comparable to the number of experimental awakenings for YC subjects (8±2). The number of awakenings during the second deprivation night was significantly higher (p<.01) for both RD (11±3) and YC (10±3) subjects. Experimental awakenings were comparable between RD and YC subjects on the second deprivation night.

Total sleep time (TST) did not reveal a significant main effect of group or group-by-night interaction (see Table 2). However, the experimental awakenings during the depriva-
tion nights resulted in a significant decrease in TST ($F[3,72]=121.5, p<.01$). On recovery night, TST was comparable to baseline. The latency to stage 1-NREM sleep (minutes) did not reveal a significant main effect of group, but did reveal a significant main effect of night ($F[3,72]=6.41, p<.01$). Post hoc comparisons revealed the latency to stage 1-NREM on baseline and recovery nights to be comparable but significantly shorter ($p<.05$) than those on experimental nights. The 2 experimental nights were comparable. A group-by-night interaction was not documented for latency to stage 1-NREM.

Percent stage 1 NREM was significantly higher ($F[3,72]=21.12, p<.01$) on the 2 deprivation nights than either baseline or recovery. Deprivation night 1 was higher than deprivation night 2 ($p<.05$). There was no effect of group or group-by-night interaction. Stage 2 results show a significant night effect ($F[3,72]=4.33, p<.01$). Percent stage 2 was higher on baseline than any other night. This difference was significant ($p<.05$) in comparison to deprivation night 1 and recovery, but not deprivation night 2. There was again no effect of group or group-by-night interaction. SWS revealed a significant main effect of night ($F[3,72]=6.20, p<.01$), but no group effect or interaction. Post hoc comparison revealed that SWS percent was lower on baseline than any other experimental night.

Importantly, a significant main effect of group ($F[1,24]=21.78, p<.01$), a significant main effect of night ($F[3,72]=37.66, p<.01$), and a significant group-by-night interaction ($F[3,72]=19.00, p<.01$) was documented for REM percent. The percentage of REM sleep for RD subjects was significantly reduced ($p<.01$) from baseline levels on both deprivation nights (see Table 2). Recovery REM sleep was significantly higher than on both deprivation nights, but only slightly higher ($p<.08$) than baseline. The 2 deprivation nights showed comparable REM sleep. In contrast to the RD subjects, the percentage of REM sleep for YC subjects was similar on all experimental nights. Tukey’s post hoc revealed significant ($p<.01$) group differences in the percentage of REM sleep on nights 2 and 3 (see Table 2). Latency to REM was also affected by the REM-deprivation procedure. A significant main effect of group ($F[1,24]=4.23, p<.05$) was documented for latency to REM. The RD group exhibited shorter latencies to REM sleep when compared to YC subjects. The RD group had an overall REM latency of 56.8±11.4 minutes, while the YC group’s REM latency was 89.6±53.8 minutes. There was not a significant main effect of night or a significant group-by-night interaction for REM latency.

**Daytime Assessment**

MSLT scores did not reveal a main effect of group, but did demonstrate a main effect of night ($F[3,72]=15.91, p<.01$). A significant ($p<.05$) decrease in mean MSLT scores on deprivation days 2 (11.6±4 minutes) and 3 (11.0±4 minutes) when compared to baseline (13.7±3 minutes) and recovery (15.0±4 minutes) days was documented. Critically, a significant group-by-night interaction was documented ($F=6.29, p<.01$) for MSLT scores. RD subjects demonstrated comparable MSLT scores across days (baseline=12.9±3 minutes; deprivation day 1=13.3±3 minutes; deprivation day 2=12.2±3 minutes; recovery=14.9±2.7 minutes). However, YC subjects documented lower MSLT scores on deprivation days 1 (9.8±4 minutes) and 2 (9.8±4 minutes) when compared to baseline (14.5±3 minutes) and recovery (15.1±2.4 minutes) days. Furthermore, when compared to RD subjects, YC subjects had significantly lower ($p<.05$) MSLT scores on deprivation days 1 and 2 (see Fig. 1).

A nap-by-nap analysis was performed for the daytime MSLTs. There were no group differences in sleep latency patterns across the days. However, a significant main effect of nap ($F[4,96]=27.7, p<.01$) was documented. The latency to sleep for the nap at 10:00 hours (7.9±3.5 minutes) was significantly shorter ($p<.05$) than the latency to sleep on naps at 12:00 hours (12.0±4.2 minutes) and 14:00 hours (12.5±3.7 minutes). The nap at 16:00 hours (14.6±4.1 minutes) documented a significantly longer ($p<.05$) latency to sleep than the naps at 12:00 and 14:00 hours. Finally, the nap at 18:00 hours (17.1±2.4 minutes) documented a significantly longer ($p<.05$) latency to sleep than the nap at 16:00 hours. A group-by-nap interaction was not documented.

An analysis of the number of sleep-onset REM periods (SOREMPs) present during MSLTs was carried out, and there were not any significant effects of group or night, or group-by-night interaction (see Table 3).
Previous studies have suggested that selective REM deprivation results in enhanced CNS excitability. Cohen and Dement first described the effects of REM deprivation as being “a generalized increase in neural excitability.” 78 They demonstrated that after rats were deprived of REM sleep, their threshold to electroconvulsive shock significantly decreased. In a subsequent paper, the same group described increases in sexual activity as a result of REM deprivation. 31 Furthermore, this general increase in CNS drive following REM deprivation has also been manifested by increased motivational behaviors, 27 increased aggression, 32 and increased preference for novel stimuli. 33 In contrast to these studies, subjects restricted in total sleep time and/or deprived of NREM sleep demonstrated decreased motivation and performance retardation. 34–36

More importantly, sleep restriction and sleep fragmentation have resulted in increased daytime sleepiness, as manifested by the MSLT. 3 – 5 In spite of comparable numbers of awakenings and sleep loss on experimental nights, the REM-deprived group in the present study maintained its level of sleepiness/alertness, while the yoked control group experienced increased daytime sleepiness.

Bennington and Heller (1994) theorized that the primary function of REM sleep is to antagonize the restorative effects of NREM sleep. Moreover, NREM sleep is characterized by synchronized EEG waves and an inert CNS, whereas REM sleep is characterized by desynchronized EEG waves and a highly reactive CNS. 37 Thus, if the functions of REM sleep and NREM sleep appear to be antagonistic, and the physiology of REM sleep and NREM sleep are paradoxic, it is plausible to hypothesize that the effects of REM deprivation should be antipodal to the effects of NREM deprivation. In fact, the results of the present study largely confirm this hypothesis.

A previous study by Glovinsky et al documented a shortening of MSLT latencies for subjects awakened during stage 2 sleep and for subjects awakened during REM sleep. 38 The authors concluded that a “reduced sleep time instead of altered sleep composition was responsible for the observed daytime decrements.” In the Glovinsky et al study, subjects were only required to remain awake for 3 minutes following REM awakenings, resulting in 12 and 18 experimental awakenings on deprivation nights 1 and 2 respectively. As a consequence of these awakenings, TST was reduced to 331 minutes, but REM sleep was only reduced to 9% of TST. In contrast, subjects in the present study were required to remain awake for 15 minutes following REM awakenings, resulting in 9 and 11 awakenings on deprivation nights 1 and 2 respectively. Interestingly, this resulted in a mean TST of 295 minutes and a significant reduction in REM sleep to 4.5 percent of TST. It is conceivable that the effect of sleep fragmentation and sleep loss in the study by Glovinsky et al inundated the

### Table 3.—The number of subjects with multiple sleep-onset REM periods during their MSLT

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Deprivation day 1</th>
<th>Deprivation day 2</th>
<th>Recovery</th>
</tr>
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<tbody>
<tr>
<td>RD group</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>YC group</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
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</table>

### DISCUSSION

The present study evaluated daytime sleepiness/alertness in subjects selectively deprived of REM sleep. Subjects with awakenings yoked to the REM-deprivation subjects were also evaluated for daytime sleepiness/alertness in order to control for the effects of the nocturnal awakenings. The yoked control group experienced increased sleepiness due to the increased number of awakenings and overall sleep loss on deprivation nights. The REM-deprived group did not exhibit any changes in MSLT scores throughout the study. It should be noted that both the REM-deprived and the yoked control groups documented an increase in nocturnal latency to stage 1 NREM sleep on both deprivation nights. This is not, however, a function of the experimental awakenings, but rather an artifact of the earlier bedtimes for subjects on deprivation nights to account for reduced total sleep time.
alerting effect of the REM deprivation, whereas in the present study, the CNS excitability caused by significant REM deprivation compensated for the loss of sleep which resulted in no changes in sleepiness/alertness from baseline levels.

In summary, the results of this study emphasize the delicate balance between NREM and REM sleep homeostasis. While an increase in CNS excitability is suggested as explanatory for the compensation of alertness seen in the RD group, the mechanism by which REM deprivation exerts its effects on CNS excitability has not been extensively explored. An elucidation of these mechanisms may pave the way for a greater understanding of the function of REM sleep.

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