Sleep latency measures of caffeine effects during sleep deprivation

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Abstract

Studies of stimulants during sleep deprivation have used performance assessment batteries (PABs) and occasionally the multiple sleep latency test (MSLT) as measures. Another type of sleep latency test, the maintenance of wakefulness test (MWT), assesses ability to remain awake without assistance, rather than ability to go to sleep. The MWT previously has not been used in studies of stimulants during sleep deprivation. This study of caffeine during 64 h without sleep included a PAB, the MSLT, and a single MWT trial per day. The PAB and the MSLT were sensitive to caffeine effects during the first 24 h without sleep. The MWT demonstrated that caffeine improved ability to remain awake even after 2 nights of sleep deprivation. Ability to go to sleep and ability to stay awake during sleep deprivation appear to be affected differently by caffeine. PAB testing may fail to detect this stimulant effect because technicians prevent subjects from nodding off during PAB testing, an external support not available to subjects during the MWT and also not available in many real-world work environments. The MWT was more sensitive to stimulant amelioration of sleep-deprivation effects. The findings need to be validated with MWTs at other times of day and with other stimulants. © 1997 Elsevier Science Ireland Ltd.

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1. Introduction

The multiple sleep latency test (MSLT) was developed as a measure of excessive daytime sleepiness (Richardson et al., 1978; Mitler et al., 1979). In the MSLT, subjects are placed in a bed in a darkened room at intervals during the day and given 20 min to try to go to sleep. It generally is considered the 'gold standard' measure of sleepiness, and in addition to clinical studies, it has been used to evaluate sleepiness in studies of sleep deprivation and stimulants (Rosenthal et al., 1991).

The maintenance of wakefulness test (MWT) is an alternative form of sleep latency testing (Mitler et al., 1982a; Mitler et al., 1982b). It was developed as a practical measure for evaluation of patients with sleep disorders. While ability to fall asleep if you try is a good gauge of physiological sleepiness, in the conduct of daily life the ability to remain awake is what is important. Lower sleep latency on MSLT does predict occurrence of unintentional sleep episodes. However, sleep latency on MWT may provide a more accurate prediction. Additionally, the 'floor effect' under conditions when the MSLT sleep latency approaches zero, may limit the sensitivity of the MSLT (Sugerman and Walsh, 1989). In the MWT, the subject sits in a semidarkened room at intervals during the day and is told to try to stay awake. Durations ranging from 20 to 40 min have been used for this test. Studies have shown that the MWT and the MSLT correlate well in some individuals and under some conditions, but they can be widely disparate in others (Sangal et al., 1992b).

In most situations where stimulants are administered, the practical concern is with people's ability to remain awake and perform, rather than their ability to go to sleep if they try. However, we are not aware of previous studies of stimulant administration during sleep deprivation that included the MWT.
Caffeine probably has been studied more than any other stimulant. Certainly, it is the most widely used stimulant. Caffeine has been reported to benefit many measures of cognitive performance and mood (Weiss and Laties, 1962; Baker and Theologus, 1972; Clubley et al., 1977; Childs, 1978; Lieberman et al., 1987; Penetar et al., 1993). However, research findings on caffeine’s cognitive effects have been somewhat inconsistent (James, 1991). Most caffeine studies have involved daytime administration of caffeine to subjects who have not been sleep deprived. Since stimulants in general show maximum benefit when performance is most deteriorated, leaving more room for improvement (Weiss and Laties, 1962), larger caffeine effects would be expected with administration during sleep deprivation. Studies of caffeine administration at night (Schweitzer et al., 1992; Bonnet and Arand, 1994) and during sleep deprivation beyond a single night (LeBlanc et al., 1989; Penetar et al., 1993; Bonnet et al., 1995) have provided evidence of caffeine benefitting performance under those conditions. However, one recent study comparing the effects of caffeine on MSLT and auditory vigilance after normal and restricted sleep failed to show the expected increased caffeine effect with restricted sleep (Rosenthal et al., 1991).

A previous report has documented the effects of repeated caffeine administration on performance and the MSLT during a 2-night sleep-deprivation protocol (Bonnet et al., 1995). It was found that caffeine improved performance in a dose-response fashion during the first 24 h of sleep deprivation, but did little to maintain performance thereafter. Subjects treated with caffeine showed evidence of improved alertness as measured by the MSLT after a single night of sleep deprivation, but not after 2 nights of sleep deprivation. A subset of subjects in that protocol underwent a single MWT-type session each day. This report will compare the findings of the different sleep latency tests for subjects treated with 300 mg of caffeine every 6 h during sleep deprivation.

2. Methods and materials

This was a double-blind, parallel-group study. Subjects were nonsmoking males who used low to moderate amounts of caffeine (averaged no more than 250 mg/day, based on a questionnaire). A detailed description of the protocol has been published previously (Bonnet et al., 1995). A night of accommodation sleep was followed by a day of training on study procedures, a night of recorded sleep, a 64-h period without sleep with repeated testing, a night of recorded recovery sleep, and follow-up testing the next day. MSLT sessions occurred every 3 h, and a single MWT session occurred at 1330 each day, about 30 min before one of the MSLT sessions. MWT scores and scores for the MSLT trials that occurred 30 min after the MWT testing each day will be discussed in this paper.

Standard procedures were used for the MSLTs and MWTs (Mitler et al., 1982a,b; Carskadon, 1986). For the MSLT the room was dark and subjects lay flat in bed. For the MWT the head of the bed was elevated to 45° and the room was dimly lit. Sessions ended after the first epoch of Stage 2 or REM sleep (Rechtschaffen and Kales, 1968) or after 20 min if no sleep occurred. Technicians walked the subjects around between the MWT session and the following MSLT session to prevent any residual effects from carrying over.

Starting at 23:20 h on the first night without sleep, each subject took a capsule at about 6-h intervals (7 doses total; 23:20, 04:50, 11:20, 17:20, 23:20, 04:50, 17:20). Two groups of subjects will be discussed here. One group (n = 14, age = 21.0 ± 4.1 years) received a placebo each time. One group (n = 11, age = 19.5 ± 1.8 years) received 300 mg of caffeine each time. Caffeine levels were monitored using a salivary assay (McGeoy et al., 1992).

Each individual’s sleep latency prior to sleep deprivation was subtracted from his latencies during sleep deprivation to adjust for any baseline differences among subjects. Twenty minutes was used as the sleep latency for trials where the subject did not go to sleep. Two-way analysis of variance (ANOVA) (Group × Day) (BMDP Statistical Software, Los Angeles, CA) was applied to the difference-score data for the 2 sleep-deprivation days, followed post hoc Tukey’s HSD t-tests when indicated. A separate t-test was performed on the data collected after the recovery sleep.

3. Results

The raw sleep-latency data from the MWT-type trial at 1330 each day and the MSLT-type trial at 1400 each day are plotted in Figs. 1 and 2, respectively. The ANOVA on the MWT difference scores showed a Group effect (F(1,22) = 10.15, P < 0.005) and a Day × Group interaction (F(1,22) = 5.73, P < 0.03). There was no significant Day effect. The post-hoc t-tests on the data after one and 2 nights of sleep deprivation showed that the caffeine group’s sleep latency changed less from baseline than the placebo group after one night of sleep deprivation (P < 0.05), with a much larger difference after 2 nights of sleep deprivation (P < 0.01). The t-test on the MWT difference-score data from after the recovery sleep did not show a significant group difference.

The ANOVA of the MSLT difference scores during sleep deprivation showed a Day effect (F(1,23) = 18.66, P < 0.001). There was no Group effect and no Group ×
Day interaction, and post-hoc testing of the individual-day data showed no evidence of a group difference on either day. The MSLT difference scores for the session after the recovery sleep were similar between groups.

4. Discussion

The data from this study suggest that sleep deprivation in normal subjects has similar effects on sleep latency when subjects are trying to stay awake and when they are trying to go to sleep. The placebo group showed similar patterns of change in the 2 tests (compare Fig. 1 and Fig. 2), with progressive shortening of sleep latency during sleep deprivation. In contrast, during sleep deprivation, caffeine affects the ability to fall asleep and the ability to stay awake quite differently, having a larger and more persistent effect on the ability to stay awake. On the MWT, the caffeine group maintained sleep latency near baseline levels throughout the sleep deprivation (Fig. 1). The superiority of the caffeine group was not seen in the MSLT sessions 30 min later (Fig. 2). On the MSLT, the caffeine group showed a fairly similar pattern to the placebo group. These findings suggest that the MWT may be a better test than the MSLT for detecting stimulant effects during sleep deprivation. Clearly, a single sleep latency session per day is a less reliable test of sleepiness than the usual full MSLT. However, this should be equally true for the isolated wakefulness test, and even the full MSLT was unable to detect caffeine effects after 2 nights of sleep deprivation (Bonnet et al., 1995). The data suggest that after prolonged sleep deprivation, caffeine will assist subjects in remaining awake if they try, but still will allow them to sleep should the opportunity arise, a desirable pattern of effects for situations such as military sustained operations. However, these data do not tell us what the quality of sleep would be. Even though caffeine does not interfere with ability to fall asleep under these conditions, it may still decrease the quality of sleep, as it does individuals who are not sleep deprived.

The finding that a wakefulness test is a more sensitive measure of stimulant effects under these conditions than a sleepiness test is consistent with previous reports of studies of patients with narcolepsy. The MWT has repeatedly been shown to be sensitive to stimulant effects in narcoleptic patients (Mitler et al., 1982a; Mitler et al., 1982b; Mitler and Hajdukovic, 1991; Mitler et al., 1990). Sangal et al. (1992a) administered MSLTs and MWTs to 47 patients with sleep disorders before and after 6 months of stimulant treatment. The MSLT revealed no evidence of stimulant effects. However, a marked improvement was evident in the ability to stay awake as measured by the MWT.

Previously published results indicated that it was not possible to maintain cognitive performance or alertness throughout such a prolonged period of sleep deprivation with the doses of caffeine administered (Bonnet et al., 1995). Cognitive performance and the MSLT showed evidence of caffeine benefits during the first 24 h of sleep deprivation, but little beyond that.

It seems likely that methods required in laboratory studies of sleep deprivation may mask stimulant effects on performance that would be apparent under real-world conditions. During this study, technicians aroused subjects who nodded off or failed to respond during the performance testing. This is standard in studies of sleep deprivation. Allowing subjects to sleep would decrease their sleep deprivation as compared to other subjects and could invalidate the results. However, if subjects treated with caffeine were able to keep themselves awake to perform the tasks without assistance, but subjects treated with placebo were not, then arousing subjects would mask the caffeine benefits. In real-world work, there often will be nobody available to keep others awake. The superiority of the caffeine group on this test of ability to keep oneself awake might indicate that high doses of caf-
feine during sleep deprivation would benefit performance in situations where personnel alertness could not be closely supervised by non-sleep-deprived individuals.

The data from this study indicate that administration of caffeine during sleep deprivation has a greater and more persistent effect on ability to keep oneself awake than on the ability to go to sleep. The MWT may be a better measure of the effects of caffeine, and perhaps other stimulants, during sleep deprivation. Further studies including MWTs at other times of day and with other stimulants are needed to confirm these findings.

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