Laboratory and Field Studies of Naps and Caffeine as Practical Countermeasures For Sleep-Wake Problems Associated With Night Work

Paula K. Schweitzer, PhD[1]; Angela C. Randazzo, PhD[1]; Kara Stone, MA[1]; Milton Erman, MD[2]; James K. Walsh, PhD[1,3]

[1]Sleep Medicine and Research Center, affiliated with St. John's Mercy Medical Center and St. Luke's Hospital, St. Louis, MO; [2]Pacific Sleep Medicine, La Jolla, CA; [3]Department of Psychology, St. Louis University, St. Louis, MO

Study Objectives: To evaluate the effects of napping, caffeine, and napping plus caffeine on performance and alertness in both laboratory and field settings.

Design: (1) Laboratory Study: parallel-groups design with random assignment to 1 of 4 experimental conditions. (2) Field Study: crossover design.

Setting: Sleep laboratory and field settings.

Participants: (1) Laboratory Study: 68 healthy individuals; (2) Field Study: 53 shiftworkers who worked nights or rotating shifts.

Interventions: (1) Laboratory Study: an evening nap opportunity before the first 2 of 4 consecutive simulated night shifts plus placebo taken all 4 nights, caffeine taken nightly, the combination of the nap and caffeine conditions, or placebo. (2) Field Study: an evening nap on the first 2 of 4 consecutive night shifts plus caffeine taken nightly versus placebo taken nightly without naps.

Measurements and Results: (1) Laboratory Study: Napping, caffeine, and their combination all improved alertness and performance as measured by Maintenance of Wakefulness Test and Psychomotor Vigilance Task, but the combination of napping and caffeine was best in improving alertness. (2) Field Study: Napping plus caffeine improved performance as measured by Psychomotor Vigilance Test and decreased subjective sleepiness in individuals working the night shift.

Conclusions: Napping plus caffeine helps improve performance and alertness of night-shift workers.

Keywords: Naps, caffeine, shift work, sleepiness, performance

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INTRODUCTION

THE ALERTNESS AND PERFORMANCE CAPABILITIES OF NIGHT WORKERS ARE OFTEN IMPAIRED ON THE JOB. FOR EXAMPLE, SHIFT WORKERS WITH NIGHT WORK have a 1.6 relative risk of experiencing unintentional sleep at work, even when controlling for reports of disturbed sleep.[1] The results of a study that included ambulatory electroencephalogram recordings indicated that 20% of shift workers fell asleep during a single night shift, whereas none slept during the afternoon or evening shift.[2] Similarly, ambulatory recordings of train drivers have revealed that electroencephalogram indicators of sleepiness increase markedly during a 4.5-hour night trip but not during a day trip of equivalent duration.[3]

Human performance also declines to its lowest in the early morning hours for most skills, including vigilance, reaction time, logical reasoning, serial addition/subtraction, spatial orientation, and flight-simulator operation.[4-6] The magnitude of reduction in night versus daytime levels of performance in the laboratory ranges from approximately 10% to 35% of the 24-hour mean level of performance.[5,7] Field studies of actual shift-worker performance are rare because of methodologic difficulties. Classic studies have found that switchboard operators respond to calls 112% more slowly from 3:00 AM to 4:00 AM than their mean speed between 8:00 AM and 10:00 PM,[8] and the rate of data-recording and calculating errors by gasworks personnel is 98% higher at 3:00 AM than during day and evening hours.[9] Vidacek and colleagues estimate that industrial productivity declines about 5% at night, as compared with day work.[10] In addition to a decline in productivity, accidents and injuries are 1.3 times more likely to occur on the night shift than on the day shift.[11]

The 2 main sources of reduced alertness and performance during night work hours are the circadian rhythm of sleepiness and alertness and increasing homeostatic sleep pressure related to the duration of wakefulness preceding work time.[12] Night work disturbs the critical temporal relationship of the circadian and homeostatic factors that regulate sleep and alertness (i.e., the 2-process model)[13] and that maintain reasonable levels of alertness throughout the waking day in individuals sleeping at night. That is, the temporal relationship of the 2 processes in the night-work situation does not allow the circadian alerting process to counteract increasing homeostatic drive for sleep during work hours, and, additionally, the circadian process interferes with sleep attempted during the daytime.

Only partial, and often minimal, adaptation of circadian rhythms to night work occurs over time. Laboratory and field

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Address correspondence to: Paula K. Schweitzer, PhD, Sleep Medicine and Research, 232 S. Woods Mill Road, Chesterfield, MO 63017; Tel: (314) 205-6325; Fax: (314) 205-6025; E-mail: schwpk@stlo.mercy.net

studies demonstrate that endocrine, sleep, body temperature, adrenaline, alertness, and other physiologic rhythms do not fully adjust after 2 or 3 weeks of a schedule of daytime sleep and nighttime wakefulness.[14-16] Adjustment of circadian rhythms to even permanent night work is opposed by night workers' exposure to the natural light-dark cycle, family and social contacts during the day, and reversion to a pattern of wakefulness during the daytime and sleep at night on nonwork days.[17]

The majority of persons who work at night report that their sleep during the day is disrupted and nonrefreshing[18] and that those sleep difficulties become more common and more severe with increasing age.[19,20] Objective sleep recordings have confirmed that total sleep time is significantly reduced to approximately 5 to 6 hours per day in both permanent night workers and in workers rotating on and off the night shift.[2,21,22] Because the effects of sleep restriction are cumulative (i.e., sleepiness and performance impairment increase over successive days of reduced sleep time[23-26]) any intervention that significantly reduces the sleep loss associated with night work may improve alertness and performance on the night shift.

Napping as a Countermeasure

Multiple laboratory studies have demonstrated improved alertness, performance, or both alertness and performance following naps in sleep-deprivation studies, including during nighttime hours,[27-30] as well as in real or simulated night-work situations.[27,31] Dinges et al found that the circadian placement of a nap was not important in terms of beneficial effects on reaction-time performance and suggest that placement of the nap just prior to a night of sleep loss will maximally aid performance that night.[32] Although the benefits of napping before a single night shift are fairly clear, the benefit of napping on 2 or more successive nights has rarely been studied. Uncontrolled studies of shift workers suggest that naps are associated with reduced sleep quality during daytime sleep periods[29,33]; however, the direction of the causal effect, if any, cannot be determined from these studies. There is also evidence in laboratory studies that minor reductions in total nocturnal sleep time and slow-wave sleep may occur following daytime naps.[28,34] For example, Werth and colleagues have demonstrated reduced slow-wave activity during nighttime sleep following an evening nap, which they interpret as a reduction in homeostatic pressure as a result of the nap.[35] Thus, it is also important to measure the effect of naps taken before the night shift on main sleep episodes the following day.

Workers nap most frequently prior to night-shift work and average between 1.5 and 2.5 hours per nap.[31,33,36] Nap onset is most commonly between 7:00 PM and 8:00 PM,[31] most likely reflecting family and social obligations earlier in the day. Two experimental studies[29,37] that allowed either a 3- or 4-hour period in which to nap before a simulated night shift showed remarkably similar mean total sleep times during the nap opportunity: 143.0 minutes and 139.9 minutes.

Caffeine as a Countermeasure

The enhancing effects of caffeine ingested around 10:30 PM to 1:30 AM upon alertness and performance in the laboratory during typical night work hours are well established.[29,37-44] One study[34] found that 300 mg of caffeine taken at 11:00 PM improved performance until 8:00 AM in 4 experienced shift workers. Another study showed that a 400-mg dose ingested at 1:20 AM significantly improved alertness and performance at 5:30 AM.[38] In that same study, a lesser degree of improvement was seen with 150-mg or 300-mg doses. A dose of caffeine equivalent to 4 mg/kg of body weight, given at approximately 10:30 PM, has been shown to decrease sleepiness from 11:00 PM to 5:00 AM on a single night for both mild and moderate caffeine users.[43] In a similar study, 4 mg/kg improved performance on a single night of simulated assembly line work from 11:00 PM to 6:30 AM.[29] A novel caffeine-administration schedule, which involved a low dose given hourly in a forced desynchrony paradigm, largely eliminated the wake-dependent deterioration seen with placebo for more than 20 hours.[40] These findings and others are consistent with the hypothesis that adenosine mediates the wake-dependent increase in sleep drive, as caffeine is a specific adenosine antagonist.

In humans, tolerance to some physiologic actions of caffeine has been demonstrated, but there is limited evidence of tolerance to the alerting effects of caffeine.[43,46] This may be related to the fact that no tolerance is detectable with regard to caffeine's effect on cerebral metabolism, especially in neural systems involved in sleep regulation.[47] The results of 2 studies[48,49] suggest the possibility of tolerance when caffeine is given in more than 1 daily dose. A slight, but statistically significant, reduction in sleep latency during the day across 4 administrations of caffeine (two 250-mg doses per day on 2 consecutive days) was interpreted as a demonstration of tolerance, although individuals taking caffeine remained more alert than those on placebo.[48] A study of 400 mg of caffeine, given 3 times per day for 7 days as an experimental model of insomnia, indicated that, by day 7, sleep was disrupted less than on day 1.[49] However, even on day 7, sleep was significantly disturbed, as compared with baseline. Moreover, the reduced sleep disruption on night 7 may reflect increased sleep drive associated with several nights of disrupted sleep. Therefore, data supporting the concept of tolerance to the alerting effects of caffeine in humans are limited and restricted to multiple administrations and moderate to large daily dosages (500-1200 mg). The hourly dosing study of Wyatt et al,[40] however, provided no suggestion of tolerance despite frequent dosing.

In a single study involving caffeine administration during the first 3 of 5 consecutive simulated night shifts, alertness was significantly improved on all 3 nights, and performance was improved on the first night.[41] Importantly, there was no significant effect of abruptly discontinuing caffeine. That is, performance and alertness on night shifts 4 and 5 were no different between caffeine and placebo groups. Further, daytime sleep in this study was minimally affected by nocturnal caffeine administration.

Caffeine Combined with Napping

Only 1 study[50] has combined napping and caffeine interventions; however, only a single night was evaluated. A 2.5-hour evening nap plus 200 mg of caffeine administered at 1:30 AM improved alertness and performance between 4:00 AM and 7:00 AM significantly more than napping alone. Bright light and caffeine together have also been shown to be more effective than either countermeasure alone in enhancing alertness and performance at night.[44] Thus, combining night-shift interventions appears to be a promising means to counter sleep-related problems associated with shift work.

This paper describes 2 studies: (1) a laboratory study evaluat-

ing the effects of 3 interventions (napping, caffeine, and napping plus caffeine) versus placebo on performance and alertness during a simulated 4-night work paradigm and (2) a field study evaluating the effects of the combination of napping and caffeine on performance during night-shift work.

METHODS

Laboratory Study

Subject Recruitment, Selection and Training

Participants were recruited primarily through the media. Interested individuals were initially screened via structured telephone interview to exclude those with significant medical conditions, psychiatric disorders, irregular sleep schedules, those habitually consuming excessive alcohol (> 10 drinks/week) or caffeine (> 400 mg/day), or those routinely taking central nervous system active medications. Potential participants then received a detailed explanation of the research and provided written informed consent during a visit to the laboratory. Those individuals signing a consent form completed a medical history; had a physical examination, urine drug screen and pregnancy test performed; and completed a psychological assessment, including the Zung Anxiety and Depression scales (excluded if either score > 50). Participants passing this screening procedure were scheduled for a polysomnogram to adapt them to laboratory procedures and to exclude those with sleep apnea (respiratory disturbance index > 10 or SaO_2 < 85%) or periodic limb movement disorder (10 or more limb movements with arousal per hour). A Multiple Sleep Latency Test[51] was conducted the following day to exclude individuals displaying a pathologic level of sleepiness (mean latency < 5 minutes). Individuals with excessive sleepiness during the daytime were excluded to minimize the contribution of sleep debt to nighttime performance and alertness.

Training for all performance tests and subjective questionnaires was accomplished on the day of the medical evaluation and the day of the Multiple Sleep Latency Test. Participants were instructed to maintain a regular sleep-wake schedule and limit caffeine and alcohol consumption each to 1 drink per day or less for a minimum of 1 week prior to randomization.

Experimental Design, Methods and Measures

Participants were randomly assigned to 1 of 4 experimental conditions: (1) a 2.5-hour nap opportunity (from 7:30 PM to 10:00 PM) before the first 2 of 4 consecutive simulated night shifts (NAP) plus placebo taken 30 minutes prior to all 4 night shifts; (2) 4 mg/kg of caffeine taken 30 minutes prior to all 4 night shifts (CAF); (3) the combination of the NAP and CAF conditions (NAP+CAF); (4) placebo before all 4 simulated night shifts (PBO) with no naps on any evening. The 4mg/kg dose was used because it was found in our prior simulated shiftwork studies to improve alertness and performance for about 6 to 7 hours without interfering with subsequent daytime sleep.[29,41-43] Random assignment and running 2 individuals simultaneously provided reasonable control for season of the year and associated change in day length.

Figure 1 shows a schematic of the study schedule. If a nap opportunity was scheduled, participants reported to the laboratory at 6:30 PM. Naps were terminated (1) after 2.5 hours, (2) upon request if a subject did not fall asleep within 60 minutes, or (3) upon request if the patient slept but then was awake for 30 minutes or more. If no nap was scheduled, participants reported to the laboratory at 9:30 PM. Sleep at any time other than that scheduled during laboratory sessions was prohibited; participants wore actigraphs to help enforce and monitor compliance with the protocol.

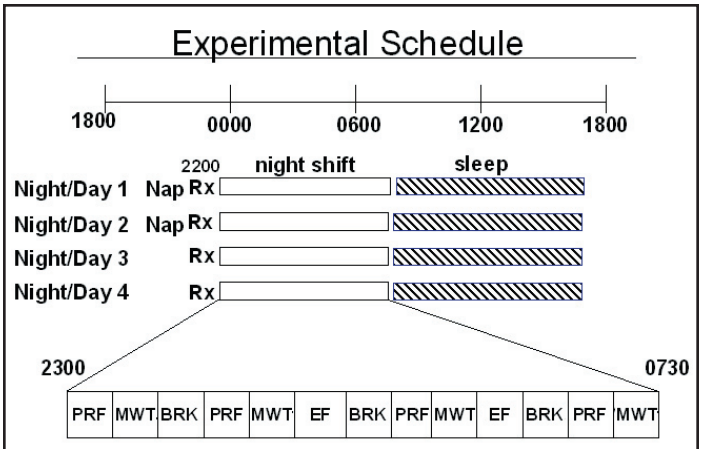

Figure 1—Schematic of schedule for laboratory study. PRF refers to performance battery, MWT, Maintenance of Wakefulness Test; BRK, break; EF, executive function tests.

From 11:00 PM until approximately 7:30 AM, participants performed a variety of tasks, including the Maintenance of Wakefulness Test (MWT),[52] the Psychomotor Vigilance Task (PVT),[53] the Digit Symbol Substitution Test,[54] and subjective measures including the Stanford Sleepiness Scale,[55] and the Karolinska Sleepiness Scale (KSS)[56] Each task was administered 4 times nightly at approximately 2-hour intervals. In addition, tests of executive function (which varied nightly) were conducted at 2:15 AM and either 4:15 AM or 5:00 AM (counterbalanced between conditions). The dependent measures are described later in this section.

Following the end of testing at approximately 7:30 AM, a 30-minute period of sunlight exposure ensued (near a large window) to partially simulate the light exposure during a morning commute. Actual intensity of light exposure was not controlled or measured on each morning, but illumination measures in the location the participants occupied, taken on multiple days, showed a range of approximately 500 to 1500 lux. Sleep was monitored polysomnographically each day, beginning between 8:15 AM and 8:30 AM. Participants slept in noise-attenuated, darkened, single rooms; they slept ad lib with the restriction that time in bed was a minimum of 6 hours and maximum of 8 hours. The minimum time in bed guarded against participants prematurely terminating the study for personal reasons and imposing significant sleep restriction upon themselves. Since night-shift workers rarely sleep more than 8 hours during the day, the maximum time in bed was set at 8 hours. Standard polysomnographic methods were used to record[57] and score[58] sleep.

Following each polysomnogram, participants were free to leave the laboratory to carry out their usual activities, typically between 3:00 PM and 9:30 PM, depending on the night and whether an evening nap was scheduled. They were instructed to avoid naps, not to use medications unless approved by the investigator, and to limit caffeine consumption to 1 cup per day. Compliance was monitored via actigraphy and daily diary. Food consumption, light exposure, and exercise were not controlled during the time away from the laboratory.

Dependent Measures

Maintenance of Wakefulness Test

The MWT was performed according to consensus procedures,[59] with the exception of the recommended 20-minute subtest duration. As has been discussed,[59] when testing individuals with a low level of sleepiness, or assessing treatment response, minimizing the potential for a "ceiling" effect by using a longer duration is preferable. Since we expected low sleepiness levels early in the night shift, a 30-minute test duration was employed.

To promote a constant level of subject motivation over repeated nights of MWT testing, the criterion for termination (but not scoring) of each subtest was modified. Each 30-minute subtest of the MWT was conducted using standard procedures until the sleep-latency criterion was met. Terminating the test at that time (in accord with standard research MWT guidelines) could serve as a "reward" because it would end the aversive experience of fighting sleep during a time of intense sleep pressure. Instead, the test was extended (beyond the point that the sleep-latency criterion was met) by instructing participants to "keep your eyes open" 2 to 5 times (variably) at the appearance of drowsiness or sleep. This procedure continued to minimize the amount of sleep obtained during each subtest and avoided providing participants with a cue that the test would be terminated if they fell asleep. Mean latency to the first epoch of any sleep stage was the dependent measure. A latency of 30 minutes was recorded if a subject remained awake during the entire 30-minute subtest. A minimum of 15 minutes elapsed from the termination of the MWT until the onset of the next procedure in order to minimize the effect of sleep on the MWT (although only a few minutes of sleep was allowed) upon performance

Psychomotor Vigilance Task

The PVT is a computer-based reaction-time test designed to evaluate the ability to sustain attention and respond in a timely manner to salient signals. PVT performance has been demonstrated to be highly sensitive to alertness fluctuations in a variety of situations and conditions.[60-67] A computerized version of the PVT with task duration of 15 minutes was employed for each PVT session. PVT performance is sensitive to the duration of the task, with more lapses and longer reaction times as time on task increases.[68] The primary variables are (1) frequency of lapses, which refers to the number of times the subject fails to respond to the signal within 500 milliseconds (i.e., the number of reaction times > 500 milliseconds), and (2) the mean of the slowest 10% reaction times, a metric that reflects vigilance response slowing.[61]

Digit Symbol Substitution Task

The Digit Symbol Substitution Test[54] assesses cognitive throughput (speed and accuracy) and has been shown to be sensitive to sedation and sleepiness in psychopharmacologic and sleep-deprivation research. Participants match digit-symbol pairs as rapidly and as accurately as possible for 90 seconds. The variable analyzed was number of correct responses.

Actigraphy

Continuous actigraphic recordings allowed assessment of each subject's compliance to the napping intervention instructions. A wristwatch-size activity recorder (Actiwatch, Mini-Mitter Co., Inc., Bend, OR.) was attached to the subject's nondominant wrist on the day before the first of a series of consecutive night shifts and was worn 24 hours a day (except for bathing).

Tests of Executive Function

One of 4 versions of the Optimal Telegram,[69] a test of verbal reasoning, was administered each night at 2:15 AM. The versions were not counterbalanced, since equivalence of the 4 versions is not established. During a second test period each night, which was either from 4:15 to 4:45 AM or 5:00 to 5:30 AM (time varied for logistical reasons), the following tests were given: on night 1, the Torrance Test of Creative Thinking-Verbal (TTCT-V),[70] which measures verbal fluency, originality, and flexibility (all expressed as standard scores); on night 2, the Wisconsin Card Sorting Test,[71] which evaluates concept formation and abstraction ability, Thurstone's Word Fluency Test (WFT),[72] which evaluates verbal fluency, and the Anagram Task[73]; on night 3, the Torrance Test of Creative Thinking-Figural (TTCT-F),[70] which assesses communication of unusual and unique ideas through drawing; on night 4, the Category Test,[74] which measures ability to identify connecting ideas or principles, Letter-Number Sequencing,[75] a test of working memory, and the Sentence Completion Test,[76] which evaluates ability to resist closure and avoid perseveration.

Baseline data were obtained for the TTCT-V and TTCT-F on the day of the screening Multiple Sleep Latency Test, typically between the third and fourth Multiple Sleep Latency Test subtest, approximately 6.5 to 7.5 hours after awakening (about 1:30 PM to 3:30 PM).

Subjective Measures

These measures included the KSS,[56] the Profile of Mood States,[77] the Stanford Sleepiness Scale,[55] and several visual-analog scales.

Statistical Analysis

All data were scored without knowledge of treatment condition. Data analyses consisted of mixed-model analyses of variance (ANOVAs) (4 groups by 4 nights by 4 time points) for MWT, PVT, and most subjective measures. The Huynh-Feldt adjustment was used to control for sphericity for within-subject factors. Follow-up analyses varied depending on the question of interest, the model, and the results of the omnibus analysis of variance (ANOVA) but typically involved examination of group differences on a nightly basis. Prior to undergoing ANOVA procedures, PVT lapses underwent square root transformation to normalize distributions, compress large counts, and prevent scores of 0. PVT slowest 10% reaction times underwent reciprocal transformation to compress the range of scores. ANOVAs were conducted for executive function tests, with difference scores (change from baseline) used for TTCT variables, followed by paired comparisons as appropriate.

RESULTS

Laboratory Study

Sixty-eight individuals met entrance criteria and were randomized into the study. Four individuals did not complete the study

Table 1—Demographic Data in the Laboratory Study

Group	No.	Age, y (range)	Men/women, no.
NAP+CAF	17	27.5 (19-46)	7/10
CAF	17	30.1 (19-62)	11/6
NAP	17	34.3 (18-65)	7/10
PBO	16	33.2 (20-52)	6/10

NAP+CAF refers to nap prior to first 2 night shifts plus caffeine prior to all night shifts; CAF, caffeine prior to all night shifts; NAP, nap prior to first 2 night shifts; PBO, placebo prior to all night shifts.

(all withdrew for personal reasons) and were excluded from data analyses. Three participants from the placebo arm of a separate study[78] with identical procedures were also included. These individuals were selected according to age and sex to balance the groups to the degree possible and without knowledge of their experimental data. Thus the final sample consisted of 67 individuals. Mean age and sex distribution (see Table 1) did not differ significantly among groups

Table 2 shows mean minutes of sleep during evening naps and during daytime sleep periods for each group. Nap duration did not differ between groups ($F_{1,32} = 0.9$, $P > .35$) or between nights ($F_{1,32} = 2.5$, $P > .12$), nor was there an interaction. Although mean nap duration for the 2 groups ranged from 73 to 99 minutes, there were 3 individuals in each nap group who did not sleep during evening nap 2. Daytime total sleep time did not differ among groups ($F_{3,62} = 0.7$, $P > .55$), but there was a trend for a group-by-day interaction ($F_{9,186} = 1.7$, $P = .10$). Posthoc analyses (using Sidak or Tukey contrasts for multiple comparisons) showed that the PBO group slept less on day 4 compared to both day 1 ($P = .012$) and day 2 ($P = .005$) and that there was a trend for PBO to sleep less than CAF on day 4 ($P = .077$). Although total sleep time was numerically increased in both nap groups on day 3 (the first sleep period without a prior nap), these changes were not significant. There was a main effect for day ($F_{3,186} = 5.7$, $P = .001$), with decreased sleep duration on day 4 (mean of all groups = 334.8) compared with day 3 (mean of all groups = 374.8 minutes), probably attributable to anticipation of completion of study participation on day 4. Indeed, total recording time was slightly (but significantly) less on day 4 (mean of all groups = 409.1 minutes) compared with day 3 (mean of all groups = 433.3, $P = .001$).

MWT data are presented in Figure 2. ANOVA indicated a night by group interaction ($F_{9,189} = 2.581$, $P = .008$), a night by time-of-night interaction ($F_{9,567} = 4.32$, $P < .001$), and main effects for group ($F_{3,63} = 3.55$, $P = .019$), night ($i_{3,189} = 3.44$, $P = .018$), and time-of-night ($F_{3,189} = 92.1$, $P < .001$). The time-of-night main effect refers to the within-night pattern of latencies becoming much shorter as the night shift progressed. The night main effect is described by a cubic polynomial ($F_{1,66} = 13.2$; $P = .001$), with mean latencies on night 2 greater than those on night 1 ($P = .035$) and night 3 ($P = .002$), while night 4 latency was greater than night 3 latency ($P = .045$). Comparisons among groups showed that, on night 1, NAP, NAP+CAF, and CAF all had longer latencies compared with PBO ($P < .001$ to .033). In addition, NAP+CAF was more alert than both NAP ($P = .007$) and CAF ($P = .033$). On night 2, only NAP+CAF was more alert than PBO ($P = .019$), and there was a trend for NAP+CAF to be more alert than NAP ($P = .077$). On night 3, there was a trend for NAP+CAF to be more alert than PBO ($P = .052$), while NAP+CAF was more alert than NAP ($P = .008$). MWT latencies did not differ among groups on night 4, although there was a trend for NAP+CAF to be more alert than PBO ($P = .09$).

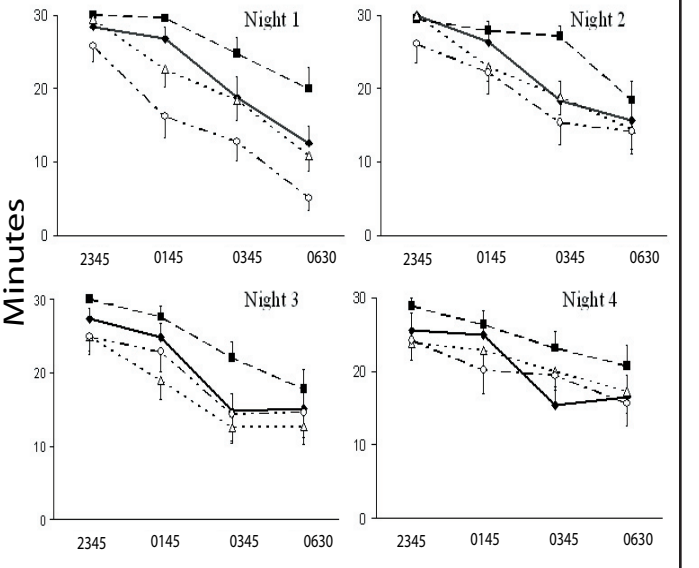

Figure 2—Maintenance of Wakefulness Test. Mean latency to sleep onset in minutes with standard errors from the laboratory study. Closed squares with dashed line = nap (NAP)+caffeine (CAF) group; closed diamonds with straight line = CAF group; open triangles with dotted line = NAP group; open circles with dashed/dotted line = placebo (PBO) group.

PVT lapse data (square root transformed) are presented in Figure 3. Analysis of PVT transformed lapses showed a significant group by time-of-night interaction ($F_{9,189} = 4.2$, $P = .002$) and main effects for group ($F_{3,63} = 2.97$, $P = .038$), night ($F_{3,189} = 20.8$, $P < .001$), and time of night ($F_{3,189} = 231.4$, $P < .001$). Lapse frequency increased as the night shift progressed and worsened slightly across the 4 nights. The group by time-of-night interaction indicated fewer lapses in the early morning hours (3:00 AM to 5:45 AM) for NAP, NAP+CAF, and CAF compared with PBO ($P = .002$ to .046). In addition, at 1:00 AM, NAP and NAP+CAF

Table 2—Total Sleep Time in Minutes for Evening Naps and Daytime Sleep Periods in the Laboratory Study

Group	Nap 1	Nap 2	Day 1	Day 2	Day 3	Day 4
NAP+CAF	99.4 (40.2)	99.4 (47.8)	338.9 (87.5)	353.4 (52.3)	388.5 (65.0)	334.1 (74.2)
CAF	NA	NA	369.8 (74.4)	360.4 (77.2)	379.5 (69.1)	370.9 (62.1)
NAP	99.1 (33.2)	73.0 (49.3)	346.2 (75.7)	332.3 (81.6)	389.3 (80.6)	325.0 (89.7)
PBO	NA	NA	365.0 (86.7)	361.1 (76.7)	346.0 (67.3)	306.9 (71.8)

Data are presented as mean ± SD.
NAP+CAF refers to nap prior to first 2 night shifts plus caffeine prior to all night shifts; CAF, caffeine prior to all night shifts; NAP, nap prior to first 2 night shifts; PBO, placebo prior to all night shifts.

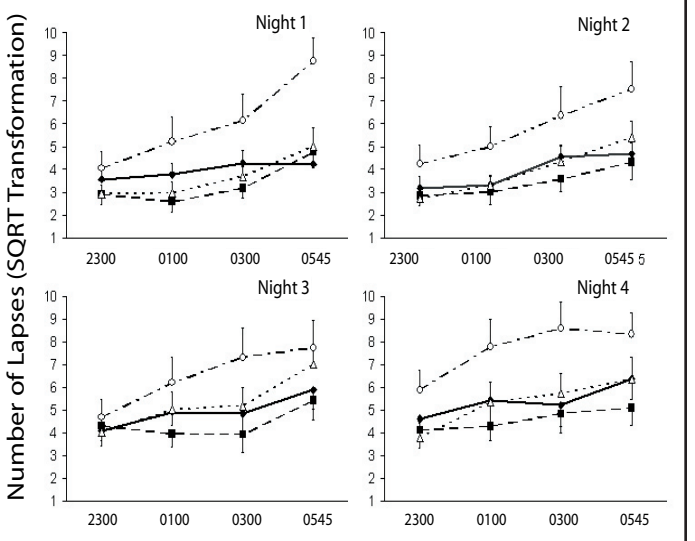

Figure 3—Psychomotor Vigilance Task. Mean number of lapses (square-root transformed [SQRT]) with standard errors from the laboratory study. Closed squares with dashed line = nap (NAP)+caffeine (CAF) group; closed diamonds with straight line = CAF group; open triangles with dotted line = NAP group; open circles with dashed/dotted line = placebo (PBO) group.

had fewer lapses compared with PBO (P = .005 and .008, respectively), while there was a trend for CAF to be improved relative to PBO at this time point (P = .08). There were no group differences at the first measure of the night (11:00 PM). NAP, NAP+CAF, and CAF did not differ from each other at any time point.

PVT data were similar for the mean of the slowest 10% of reaction times (RT10; reciprocal transformation), with significant group by time-of-night ($F_{9,189}$=2.1, P = .03) and night by time-of-night ($F_{9,567}$=2.2, P = .03) interactions and main effects for group ($F_{3,63}$=2.8, P = .046), night ($F_{3,189}$=29.3, P < .001), and time of night ($F_{3,189}$ = 58.8, P < .001). As with PVT lapses, groups did not differ at 11:00 PM. RT10 were shorter for CAF and NAP+CAF than PBO at 1:00 AM, 3:00 AM, and 5:45 AM (P = .003 to .038) and for NAP compared with PBO at 3:00 AM (P =.049)

Digit Symbol Substitution Test (number correct) analysis showed main effects for night ($F_{3,177}$=21.7, P < .001) and time of night ($F_{3,177}$=298.6, P < .001) but no group effects or interactions. The number correct declined as the night progressed (means = 56.2, 55.6, 55.0, and 53.8 for the 4 time points) and improved slightly across nights (means = 52.7, 54.8, 55.7, and 57.4 for the 4 nights.) The percentage of correct responses on the Digit Symbol Substitution Test was high throughout (generally > 97.5%) and showed only a time of night effect ($F_{3,177}$=4.95, P = .024).

The KSS showed a night by group interaction ($F_{9,180}$=10.3, P = .014), a night by time-of-night interaction ($F_{9,540}$ =6.1, P < .001), and main effects for night ($F_{3,180}$=23.3, P = .001) and time of night ($F_{3,180}$=561.3, P < .001). KSS scores, which vary from 1 (very alert) to 9 (very sleepy), indicated that subjective sleepiness increased as the night progressed (mean KSS = 3.6 [SD 1.4] at the start of the night and 7.1 [SD 1.7] at the end of the night) and decreased slightly across nights (mean KSS on night 1 = 5.6 [SD 1.8], night 4 = 5.3 [SD 1.8]). Group differences were present on night 1 only, with CAF (mean KSS = 5.4 [SD 1.9]) and NAP+CAF (mean KSS = 4.8 [SD 1.7]) reporting less sleepiness than PBO (mean KSS = 6.8 [SD 1.6]); P = .029 and P = .001, respectively) with a trend

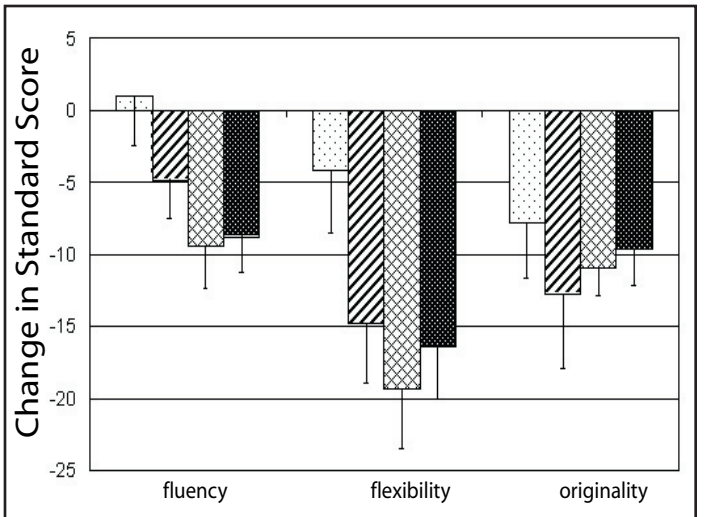

Figure 4—Torrance Tests of Creative Thinking – Verbal. Mean change from baseline standard scores with standard errors for fluency, flexibility, and originality from the laboratory study. Bars (left to right): dotted white = nap (NAP)+caffeine (CAF) group; striped = CAF group; crosshatched = NAP group; black = placebo (PBO) group.

for NAP (mean KSS = 5.7 [SD 1.8]) to be less sleepy than PBO (P = .07). Data were similar for the Stanford Sleepiness Scale, the Profile of Mood States fatigue scale, and the visual-analog scales of sleepiness.

TTCT-V standard scores are presented in Figure 4 as change from baseline. Baseline values, which showed no group differences, were measured during the daytime. TTCT-V scores were typically worse during the night shift. Verbal fluency showed a main group effect ($F_{3,63}$=2.76, P = .05), and verbal flexibility showed a trend for a main group effect ($F_{3,63}$=2.64, P = .057). Verbal originality showed no group differences. For both fluency and flexibility, scores during the night shift were reduced less for NAP+CAF compared with both PBO (P = .021 and .04, respectively) and NAP (P = .013 and .01, respectively). CAF scores were midway between those for NAP+CAF and those for both PBO and NAP and not significantly different from any other group. There were no significant group differences for the TTCT-F variables.

Optimal Telegram data (time to completion and score, a rating of test quality) were analyzed separately for each night and also averaged across the 4 nights. The only significant difference noted was time to completion of the telegram on night 3 ($F_{3,63}$=4.7, P = .005), which is likely a chance finding.

Analysis of data from the Wisconsin Card Sorting Test showed no significant effects, although there was a trend toward a main effect for group ($F_{3,62}$=2.3, P = .08) in overall errors, with NAP+CAF (standard score = 101.4) and CAF (standard score =102.3) making fewer errors than PBO (standard score = 90.9), P = .035 and .021, respectively). The remainder of the executive-function tests showed no group differences.

METHODS

Field Study

The objective of the field study was to determine if 300 mg of caffeine given nightly for 4 nights plus an evening nap taken prior to the night shift on the first 2 nights would produce greater performance and alertness during night shift work.

Subject Recruitment, Selection and Training

Individuals 18 to 65 years of age were recruited, primarily with media advertisements, for participation in St. Louis and in San Diego. A screening office visit occurred 2 to 14 days prior to randomization. Screening procedures and entry criteria were identical to those used in the laboratory study, except that each participant's work schedule had to include at least 5 night shifts per month with at least 3 of the nights consecutive, with shift length being 7 to 10 hours, including at least 5 hours between the hours of 10:00 PM and 8:00 AM. Additionally, exclusion criteria were less restrictive for average caffeine and alcohol consumption (> 600 mg caffeine per day; > 15 alcoholic drinks per week). Finally, travel across 2 or more time zones during the week before participation was prohibited. All participants provided written informed consent. They were paid for participation in the study.

Experimental Design, Methods and Measures

A crossover design was used to compare 2 conditions, (1) caffeine (all nights) plus an evening nap on the first 2 nights (NAP+CAF) and (2) placebo (all nights) with no nap (PBO). Each condition consisted of 4 consecutive night shifts. Individuals were randomly assigned to condition order in a counterbalanced manner. Conditions were separated by 3 to 24 days. Caffeine, 300 mg or placebo, was taken at the start of each night shift. On napping nights, participants were scheduled to take a 2-hour nap at home in the evening prior to the night shift. Nap start time was approximately 3 to 4 hours before shift start time and was specified for each subject on an individual basis. Participants were instructed to stay in bed for a minimum of 1 hour and a maximum of 2 hours, setting an alarm to mark the 2-hour time point, and to avoid napping at any other time.

Three times during each study night, participants completed a 20-minute test battery including a 15-minute PVT (hand-held units, Ambulatory Monitoring, Inc.), the Profile of Mood States, and the KSS. Times for this test battery were determined individually for each subject, depending on his or her work schedule, but adhered roughly to the following schedule: (1) shortly before the start of the night shift, approximately 10:00 PM to midnight; (2) midway through the night shift, approximately 2:00 AM to 4:00 am; and (3) at the conclusion of the night shift, approximately 6:00 AM to 8:00 AM.

Following each night shift, participants slept at home during their usual night-shift sleep hours. Participants were instructed to go to bed between 7:00 AM and 11:00 AM (specific time was determined individually for each subject), not to vary bedtime by more than 30 minutes each day of the study, and to remain in bed for a minimum of 5 hours and a maximum of 8 hours. Participants continuously wore actigraphs (Mini-Mitter, Inc.) on the nondominant wrist (except for bathing) throughout the study period to monitor activity and estimate sleep time during naps and main sleep periods. Actigraphs were set to store data in 1-minute epochs. Subjects were instructed to press the event marker on the actigraph when they began to attempt sleep for all naps and main sleep periods and when they ended each of those attempts to sleep. In addition, participants kept a diary to indicate time in bed, sleep, work periods, and medication use.

At the end of each study week, each subject reported to the study center. The study drug container was checked, and all study data were downloaded and inspected for compliance. Inquiries were made to detect adverse events. Urine was collected for a drug screen (performed at the discretion of the investigator). Study drug was provided for the subsequent study week, and all instructions were reviewed.

Statistical Analysis

ANOVAs with repeated measures for condition, night, and time of night were initially used for analysis of PVT and KSS. However, complete PVT and KSS data were available for only 32 individuals (of 39 whose data were included in analysis). Therefore, except for assessment of effects across nights, data were also evaluated for each individual night. The Huynh-Feldt adjustment was used to control for sphericity for within-subject factors. For PVT data, reciprocal transformation was used for RT10, and square root transformation was applied to lapses. Although participants were instructed to complete the PVT and other measures shortly before starting their work shift, midway through the work shift, and at the end of the work shift, in practice, the completion times for these measures varied considerably within and across individuals. After examining the distribution of the completion times, 2 time intervals were chosen for data analysis; time interval 1 included all trials completed between 8:00 PM and 2:00 AM, and time interval 2 included all trials completed from 2:00 AM to 10:00 AM. If an individual completed more than 1 trial during a time interval, the data were averaged to provide 1 value for the interval. Trials completed outside these intervals were not included.

Raw actigraph data were visually inspected by a trained observer (PKS) to identify rest-activity periods. Individuals whose actigraph and diary data were significantly discrepant (e.g., visual inspection of actigraph data indicated extended period of quiescence when the subject's diary indicated a night shift, along with continuous activity during the daytime when the diary indicated a sleep period) or who were noncompliant with the study protocol (e.g., napping during the nonnap week) were excluded from all analyses prior to breaking the blind. Sleep duration was estimated using the manufacturer's algorithm (Actiware-Sleep v 3.4), which has been validated in populations with sleep disorders.[79] Actigraph recordings were scored in 1-minute epochs with the analysis program set to "medium" sensitivity for detecting movement. This setting was chosen based on our prior experience with this equipment in comparing actigraph-determined total sleep time with simultaneous polysomnography recordings (unpublished observation). Start and stop times of analysis periods of evening naps and daytime sleep periods were determined by event markings in the data files. If markers were not present in the data, self-reported bedtimes and wake times were used. Actigraphy and diary data for evening naps and daytime sleep were analyzed with condition by day repeated measures ANOVAs, also using the Huynh-Feldt adjustment for the within-subjects factor. Daytime sleep data were evaluated only for the days following the first 3 night shifts, since many individuals truncated sleep on the fourth day as they were shifting to a day-work/night-sleep schedule.

RESULTS

Field Study

Fifty-three individuals met all entry criteria and were random-

Table 3—Actigraphic and Subjective Sleep Duration in Minutes for Evening Naps and Daytime Sleep Periods in the Field Study

Data Source	Condition	Nap 1	Nap 2	Day 1	Day 2	Day 3
ACTIGRAPH	NAP+CAF	72.2 (39.6)	57.7 (41.2)	262.5 (97.0)	300.8 (99.4)	299.8 (93.1)
(N=33)	PBO	NA	NA	303.2 (100.1)	342.2 (100.8)	320.8 (89.3)
DIARY	NAP+CAF	83.2 (38.6)	75.0 (47.0)	322.6 (72.3)	340.6 (67.7)	361.4 (79.3)
(N=39)	PBO	NA	NA	355.0 (75.1)	401.6 (80.1)	397.5 (70.6)

Data are presented as mean ± SD.
NAP+CAF refers to nap prior to first 2 night shifts plus caffeine prior to all night shifts; CAF, caffeine prior to all night shifts; PBO, placebo prior to all night shifts.

ized. Six persons did not complete the study (3 because of changes in work schedule or job, 3 because of noncompliance with the protocol). Data from 8 persons were excluded (prior to breaking the blind for condition order) because of technical problems (1 person) or protocol violations (6 persons: napping during the non-nap week (n=2), not attempting to nap during the nap week (n=1), actigraphic evidence of non–night-shift work (n=3), and nonconsecutive night work (n=1)). Thirty-nine subjects complied with the protocol and completed both study arms (28 men, 11 women; mean age 33.5 years, range 20-55 years).

Table 3 contains actigraphic and sleep-diary estimates of sleep duration for naps and for main sleep periods for each day and condition. Complete actigraphy data for both conditions were available for only 33 individuals because of technical problems. Mean actigraph-estimated and diary-estimated sleep duration during the 2 evening naps for NAP+CAF did not differ between nights ($t = 1.5$, $P = .15$ for actigraphy; $t = 1.2$, $P = .26$ for diary). Actigraph-estimated sleep durations during days 1 to 3 did not differ between conditions ($F_{1,27}=2.4$, $P = .13$). In contrast, daytime sleep durations from diary reports were shorter following NAP+CAF compared with PBO ($F_{1,37}=23.6$, $P < .001$).

PVT mean RT10 (reciprocal transformation) data are presented in Figure 5. Reciprocal RT10 decreased across nights 1 to 4 ($F_{3,93} = 16.9$, $P < .001$), meaning that mean RT10 increased. There was a condition by time-of-night interaction ($F_{1,31} = 7.8$, $P = .009$). For PBO only, reciprocal RT10 decreased from time interval 1 to time interval 2 ($P < .001$). In addition, during time interval 2, reciprocal RT10 was less during PBO than during NAP+CAF ($P = .05$).

Analysis of PVT transformed lapse data produced similar results. There was a trend for a condition by time-of-night interaction ($F_{1,32}=3.6$, $P = .066$) and main effects for night ($F_{3,96} = 14.2$, $P < .001$) and time of night ($F_{1,32} = 6.5$, $P = .016$). Lapse frequency increased across nights 1 through 4 with significant linear ($P < .001$) and quadratic components ($P = .028$). Mean raw lapses collapsed across conditions were 2.15 on night 1, 3.11 on night 2, 4.53 on night 3, and 4.22 on night 4. Performance worsened from shift start (NAP + CAF = 3.61, PBO = 3.5) to shift end (NAP + CAF = 3.5, PBO = 4.5) only for PBO ($P = .002$). Individual night analyses showed condition by time-of-night interactions for night 1 ($F_{1,37}=7.7$, $P = .009$), night 2 ($F_{1,37}=9.1$, $P = .005$), and night 3 ($F_{1,34}=4.4$, $P = .042$). Lapse frequency increased from shift start to shift end for PBO on night 1 ($P < .001$) and night 3 ($P = .014$), with a trend on night 4 ($P = .11$), while there was no change for NAP+CAF during the night. There was a trend for PBO to be worse than NAP+CAF at the end of the night shift on night 1 ($P = .09$) and night 3 ($P = .11$).

Subjective sleepiness as assessed by the KSS showed a condition by time-of-night interaction ($F_{1,31}= 9.1$, $P = .005$) and a main effect for time-of night ($F_{1,31}=45.6$, $P < .001$). Although subjective sleepiness increased at shift end compared with shift start for both conditions ($P < .001$ for both), subjective sleepiness was greater at shift end for PBO (grand mean KSS = 6.29) compared with NAP+CAF (grand mean KSS = 5.66; $P = .011$).

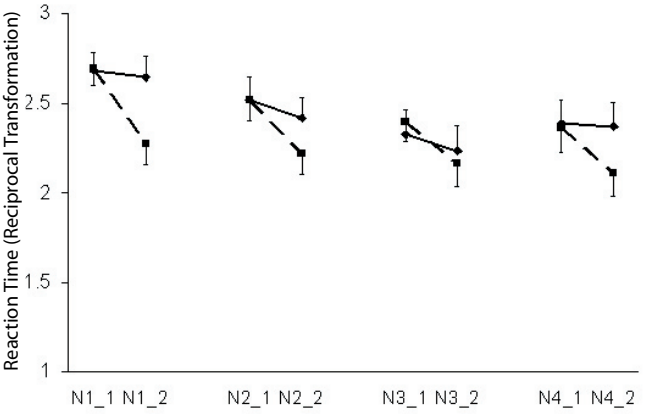

Figure 5—Psychomotor Vigilance Test (PVT): Mean (and standard error) of slowest 10% of reaction times (reciprocally transformed) from the field study for time intervals 1and 2 during nights 1 to 4. Reciprocal transformation results in smaller numbers representing slower reaction times and larger numbers representing faster reaction times. Diamond with straight line = nap (NAP)+caffeine (CAF) condition; square with dashed line = placebo (PBO) condition.

DISCUSSION

Caffeine, napping, and a combination of caffeine and napping improved both alertness and performance during 4 simulated night shifts in our laboratory investigation. Improvements in alertness on the MWT (see Figure 2) relative to PBO occurred with all treatments on the first night shift, with NAP+CAF being the most alerting countermeasure. The significant alerting effect of NAP+CAF persisted into the second night of MWT measurement, and there was a strong trend in the same direction on nights 3 and 4. After night 1, the NAP and the CAF groups did not differ from PBO on the MWT. The lack of effect appears to be the result of increased latencies in the PBO group, rather than a decreasing effect of the experimental manipulations. The change in the PBO group from nights 1 to 4 is not surprising, since, by the end of night 1, no sleep had been obtained for approximately 24 hours; whereas on nights 2 to 4 the period of sustained wakefulness at the end of the shift was only about 14 to 15 hours.

Effect sizes for the MWT nightly means were highest in the NAP+CAF group and high on all 4 nights (Cohen's $d^{80} = 1.8$, 0.8, 0.7, and 0.6 for the 4 nights, respectively). For the CAF and NAP groups, effect sizes were high on night 1 (1.0 and 0.8 for CAF and NAP, respectively), moderate on night 2 (.4 and .3), and low on

nights 3 and 4 (0.1 to 0.2)

The increase in alertness on the MWT on the 4 nights of our laboratory study, when comparing NAP+CAF with PBO (increase of 11.1, 6.3, 5.2, and 4.9 minutes on the 4 nights, respectively) was roughly equivalent to the difference between 200 mg of modafinil and placebo in a similar study performed in our laboratory over 4 nights (increase of 8.8, 2.5, 4.9, and 5.2 minutes, respectively).[78] Nonetheless, for all countermeasures, ability to maintain wakefulness decreased significantly during the night.

In contrast with the MWT, PVT data showed that all 3 countermeasures differed from PBO on all nights, and there were no differences among the active treatment groups (see Figure 3). PVT improvements with all 3 countermeasures were maximal on the first night shift and persisted across subsequent shifts. For PVT transformed lapses, effect sizes were highest for NAP+CAF (0.7 to 0.9) and were generally moderate to high for NAP (0.5 to 0.7) and CAF (0.3 to 0.8) on all nights. These effect sizes and the magnitude of change in PVT performance were also similar to those seen with modafinil in a prior study.[78] By the end of the night, however, performance for all 3 countermeasures was below levels typically seen in alert individuals during the daytime following 8 hours in bed the previous night[82] but were still markedly better than those of the PBO group, whose performance by the end of the night was worse than daytime levels in individuals with no sleep the night before.[81] Combined with the MWT results, these findings may mean that reducing the performance deficits associated with night work may require only a modestly heightened level of alertness.

The combination of napping plus caffeine resulted in better TTCT verbal fluency and flexibility compared with PBO or napping alone (see Figure 4) and fewer Wisconsin Card Sorting Test errors compared with PBO, results similar to those found with modafinil in another simulated-shiftwork study.[78] The TTCT and Wisconsin Card Sorting Test assess higher-level cognitive capability. It is important for workers, employers, and clinicians to realize that the behavioral impact of sleepiness on the night shift (or associated with other conditions) is not limited to lower-level neurobehavioral performance but also includes degradation of executive functions, such as problem solving and creative thinking. Countermeasures such as those tested here effectively reduce executive-function degradation. Similarly, physical performance at the end of an overnight period of duty, which has been shown to be poorer than daytime baseline levels, is enhanced beyond baseline levels by the use of caffeine.[82] Thus, wakefulness at night is characterized by widespread behavioral and cognitive deficits, consistent with the 2-process model, and most of the deficits are attenuated with selected countermeasures.

Because of the wide age range of the participants, we considered the possibility that a small number of outliers may have influenced the reported statistical findings. Inspection of raw data gave no indication that outliers were differentially present among groups on key dependent measures. Moreover, statistical analyses for MWT and PVT transformed lapses were repeated after excluding all participants over 49 years of age. The results of the analyses were identical to the results reported above.

The numerical (but nonsignificant) differences in total sleep time between the 2 napping groups and the nonnapping groups on days 1 and 2 and the numerical increase in total sleep time from days 1 and 2 to day 3 in the 2 napping groups suggest that daytime sleep may be shortened on days following an evening nap. This is consistent with a predicted reduction of process S as a result of a shortened period of wakefulness prior to daytime sleep. Moreover, when both daytime sleep and a nap occur before a night shift, total sleep time in the past 16 hours is increased by about 1 hour (relative to the no-nap condition), and the duration of wakefulness from last sleep to the start of the night shift is reduced by about 6 to 7 hours. Both of these factors would reduce Process S during the subsequent night shift.

The field study examined the effectiveness of caffeine and napping in actual night-shift workers and documented that the combined intervention had positive effects on performance (see Figure 5) and subjective sleepiness in the early morning hours. To our knowledge, this is the first demonstration of objectively measured benefit of a countermeasure for night work-related performance impairment in actual shift workers in the work place. Garbarino et al[83] reported a reduced risk of motor vehicle accidents in shift workers who nap prior to the night shift, but their study used a model-based method to evaluate observational data. Our field study also showed clear decline in performance and alertness late in the night shift, as would be predicted from circadian influences. Effect sizes for PVT reciprocal RT10 in the early morning hours were 0.5, 0.3, 0.1, and 0.3 on nights 1 to 4, respectively. For KSS in the morning hours, effect sizes were 0.5, 0.5, 0.2, and 0.3 for nights 1 to 4. The generally lower effects sizes in the field study are predictable given the loss of experimental control inherent in field research, as compared with laboratory investigations.

Because of the nature of the crossover design and the fact that subjects were not blind to the occurrence of napping, sleepiness ratings or motivation on the PVT task may have been influenced by study condition. Expectancy was not assessed, and this is a limitation of our field study. However, if KSS ratings and PVT performance were influenced by expectancy, we would predict that KSS ratings and PVT performance at the beginning of the shift (as well as at the end of the shift) would be better in the NAP+CAF condition. This was not the case, and we conclude that knowledge of the study conditions did not have a major effect on our findings.

Actigraph-determined sleep durations were consistently shorter than subjective reports. This discrepancy may have been the result of the actigraph scoring algorithm, which has not been validated in normal subjects or in shift-work populations, or unreliable diary reporting. Demand characteristics of the study (instructions to spend a minimum of 5 hours in bed during the main daytime sleep period) may have caused subjects to overestimate sleep duration. Nonetheless, daytime sleep durations, whether estimated from actigraphy or subjective report, were consistent with prior laboratory and field studies[18,20,21,22] and frequently less than 6 hours. An evening nap added approximately 1 hour of additional sleep time to the daytime sleep duration. Total sleep time in the past 24 hours, however, is not the only factor when judging the benefit of naps. Proximity to the night shift (and thus reduction of time since last slept) also needs to be considered. As demonstrated by Jewett et al,[81] performance and alertness improve in a saturating exponential fashion as a function of duration of prior sleep. That is, proportionally more improvement occurs following 2 hours of sleep relative to longer periods of sleep. It is possible that the recuperative value for night workers of 6 hours of sleep, split into a main sleep episode of 4 hours and a 2-hour nap prior to work, may have more value than a main sleep bout of 6 hours duration taken in the morning. This is clearly an area for empirical study.

We did not select workers with symptoms diagnostic of shift work sleep disorder,[84] which may represent a more severely affected subgroup.[85] It seems likely that the benefit of napping and caffeine may be enhanced in those with more severe sleepiness at night, as would be expected in those with shift work sleep disorder. As would be predicted from shift-work simulation studies, Czeisler et al[86] have reported that the use of modafinil increases alertness and improves performance of workers with shift work sleep disorder tested in a laboratory environment during usual night-shift hours.

Generalizing our findings and methods to successful implementation in the real world involves significant behavior change on the part of workers. Utilization of caffeine as a drug, as was done in our studies, may require abstinence from (or at least minimal use of) routine social consumption of caffeine. Novel caffeine-administration schedules, such as the schedule demonstrated to be highly effective in an experimental situation by Wyatt and colleagues,[40] should be tested in applied settings. It seems likely that alertness and performance will be improved if workers comply with a repeated, low-dose, caffeine regimen administered during night work. However, the effect on daytime sleep may be negative, as in the Wyatt study, the maximal disruptive effect on sleep came when sleep was attempted near the peak circadian alerting phase. Night-shift workers have truncated sleep, at least in part, because the last few hours of their sleep period occur as circadian alerting strengthens (circa 2:00 PM-5:00 PM). If low-dose caffeine enhances this disturbance, sleep complaints may increase, and the net benefit of caffeine consumption on night-shift performance and alertness may be somewhat lower.

Systematically incorporating naps into the lives of shift workers may be even more challenging than designing optimal pharmacologic therapies. Significant personal and family schedule changes are likely to be needed to routinely include a 1- to 2-hour evening nap. Monk[87] and others have emphasized that family-social components of shift work (e.g., child care, conflicting work schedule of spouse) must be considered in addition to circadian and sleep factors when designing interventions for the sleep-wake disturbances associated with shift work.

In conclusion, these data from both a highly controlled efficacy study and a field-effectiveness investigation provide rather convincing evidence that alertness and performance of night workers will degrade significantly less with the use of napping and caffeine, as applied in our research. Presumably, the risk of errors and accidents will decrease in association with these improvements but will not likely return to daytime levels. Clinicians, such as those involved in occupational medicine, should consider active and preventative implementation of these strategies as they care for night-shift workers, particularly those involved in high-risk occupations.

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