Archives Italiennes de Biologie, 139: 253-267, 2001.

SUSTAINED ATTENTION PERFORMANCE DURING SLEEP DEPRIVATION: EVIDENCE OF STATE INSTABILITY

S.M. DORAN, H.P.A. VAN DONGEN, AND D.F. DINGES

Division of Sleep and Chronobiology, Department of Psychiatry, and Center for Sleep and Respiratory Neurobiology, University of Pennsylvania School of Medicine, 1013 Blockley Hall, 423 Guardian Drive, Philadelphia, Pennsylvania, 19104 USA

INTRODUCTION

For more than a century, the primary focus of experiments on the effects of sleep deprivation on humans has been to identify the nature of neurobehavioral incapacitation during sustained wakefulness. Early investigators assumed that because remaining awake for 3 or 4 days was so difficult, the ability to perform neurobehavioral tasks (ranging from finger tapping to IQ tests) should be lost when healthy, motivated persons were deprived of sleep. Although the seminal experiment by Patrick and Gilbert (25) reported that 90 hours of continuous wakefulness caused both motor and cognitive deficits in three adults, these findings were not replicated in early 20th century experiments (27, 28, 30). Between 1923 and 1934, Nathaniel Kleitman published a series of reports on sleep deprivation ("experimental insomnia") that were intended to clarify the literature. Kleitman, and a few associates, remained awake between 60 hours and 114 hours but were unable to provide conclusive evidence that sleep loss eliminated the ability to perform specific motor or cognitive functions, because subjects could often transiently perform at baseline levels even after days without sleep (16, 20). However, Lee and Kleitman (20) did report that when a color-naming task was extended from 1 to 12 minutes, significant slowing of response time and increases in errors could be seen. They suggested that during sleep deprivation most abilities could be maximally utilized by a "new effort" but that "the effect of increased effort disappeared when the test became one of endurance" (p. 150).

The failure to find that sleep deprivation eliminated the ability of subjects to carry out specific neurobehavioral tasks directed the experimental focus toward evaluation of other aspects of performance change (see 5 for a review). One of the first insights into the possibility that sleep deprivation affected neurobehavioral functions by initially destabilizing performance, rather than by eliminating the capacity to perform, came from Warren and Clark (34). They reported that while modal performance on three neurobehavioral tasks remained relatively stable during 65 hours of sleep deprivation, the frequency of slow response times increased markedly. Williams, Lubin and Goodnow (36) later adopted this approach and reported that 78 hours of sleep deprivation caused an 18-fold increase in the number of performance 'lapses' (i.e., reaction times greater than twice the subject's baseline mean), even though subjects were occasionally able to respond fast and accurately throughout the 78 hours of waking. Consistent with the findings of

Bjerner (2), Williams and colleagues (36) found that lapses were most likely to occur when the electroencephalographic waveforms of a subject attempting to perform showed evidence of transition to sleep onset (1, 22). This observation led to the "lapse hypothesis", which posited that performance during sleep deprivation was punctuated by brief moments of low arousal during which subjects appeared to be unable to respond to the task at hand. The lapse hypothesis provided an important heuristic for investigating performance during sleep loss because it drew attention to increased performance variability, rather than to the search for functional lesions of specific neurobehavioral capabilities. Performance must be sampled frequently to detect increased variability during sleep deprivation; perhaps for this reason most studies of sleep deprivation during the 40 years since the articulation of the lapse hypothesis have ignored response variability in favor of global measures of performance.

We hypothesize that the effects of sleep deprivation on performance variability, as evidenced by intermittent lapsing, involve escalating wake "state instability" brought about by an elevating homeostatic drive for sleep, resulting in rapid and uncontrolled sleep initiation (3, 23), which subjects seek to resist using increasingly greater compensatory effort to perform (4). When the homeostatic drive for sleep prevails, response slowing and lapses will occur until prolonged lapses progress into uncontrolled sleep attacks that eliminate wakefulness itself (17, 32). When compensatory effort prevails, performance will appear to be relatively normal, at least for a short period of time (36). This "state instability" hypothesis (13, 14) posits that sleep deprivation particularly affects performance that relies on fundamental neurobehavioral processes sensitive to state instability. It is well established that lapses are more likely to occur in tasks that required sustained attention (4, 6, 12, 15, 18, 21, 35), and that lapse frequency increases with time on task (18, 21, 35). Consequently, components of attention, and in particular the ability to sustain *attention over time*, which is a requirement of many performance tasks beyond those referred to as vigilance tasks (24, 26), are prime candidates for the fundamental neurobehavioral processes that may be particularly vulnerable to instability when the homeostatic drive for sleep is elevated (4).

We conducted an experimental test of the "state instability" hypothesis by systematically evaluating performance on a high-signal-load, short-duration, sustained-attention task across 88 hours of acute total sleep deprivation compared to a control condition of 88 hours of partial sleep restriction. The experiment sought to determine if there is evidence that, as sleep loss progresses, variability in performance increases in a manner that reflects the interaction of the homeostatic drive for sleep and the endogenous circadian promotion of wakefulness. This experiment also sought to determine if increased performance variability is present in all subjects, regardless of their vulnerability to sleep loss (i.e., irrespective of the wide range of individual differences commonly observed in response to sleep deprivation). This study was also able to help determine if escalating response variability occurs in the presence of increasing compensatory effort to respond as sleep loss progresses. Finally, we sought evidence that response slowing and lapsing increase more rapidly as a function of time on task as sleep deprivation progresses.

METHODS

Subjects.

The data presented here comprise the placebo conditions for two experimental arms of a study of caffeine effects during sleep deprivation. A total of n = 28 healthy male subjects were randomized to two experimental conditions; n = 13 underwent 88 hours of total sleep deprivation (TSD group: mean age 27.3 y, range 22-37 y) and n = 15 were given a 2-hour (time in bed) nap opportunity once every 12 hours throughout the 88-hour period (NAP group: mean age 28.0 y, range 21-47 y). (A separate n = 30 subjects were randomized to low-dose caffeine conditions, the results of which are not reported here.) The NAP group served as a control for the TSD group by providing a condition that did not elevate the homeostatic drive for sleep as high as in the TSD condition, while allowing for neurobehavioral measurements every 2 hours across the entire 88 hours of the protocol. Subjects were screened extensively to assure they were physically and psychologically healthy; free of sleep disorders; non-smokers; free of alcohol and drugs of abuse; maintaining normal diurnal patterns of waking activity and normal nocturnal sleep durations; and capable of performing all neurobehavioral tests required by the protocol. All subjects gave informed consent and were paid minimum wage for their participation. The University of Pennsylvania's Institutional Review Board for ethics in human research approved the experimental protocol.

Protocol.

During the week prior to the experiment, daily sleep duration was fixed to 8 hours per night (21:30-07:30) as verified with sleep diaries, actigraphy, and calls to a time-stamped voice recorder. Upon entering the General Clinical Research Center's isolated laboratory for the 10-day protocol, subjects underwent a single adaptation night with sleep recordings, followed by two additional baseline days and nights with bedtimes from 23:30 until 07:30. At 17:00 on the final baseline day, subjects were fitted with an in-dwelling intravenous catheter for blood sampling for hormones. The catheter remained in throughout the 88-hour experimental deprivation period and throughout the first day of recovery (i.e., for a total of 6 days). The 88-hour sleep restriction period began immediately after the third baseline night. The NAP (control) group had seven scheduled 2-hour nap periods (i.e., 2-hour time in bed), occurring once every 12 hours at 14:45 (until 16:45) and 02:45 (until 04:45), beginning with the afternoon of the first day of the 88-hour period (i.e., after 7 hours awake), and ending with the afternoon the last day of the 88-hour period. Sleep was polysomnographically recorded, but will not be reported here. Subjects in the NAP conditions averaged a cumulative total between 11.5 and 13.5 hours of sleep across the 88-hour experimental period, with the five naps taken after the first 24 hours each involving nearly 2 full hours of physiological sleep.

Twenty-two hours into the 88-hour experimental period (i.e., at 05:30 on day 2) all subjects in the TSD and NAP conditions began receiving a placebo pill every hour (except for the hour in the middle of the scheduled 2-hour naps for the NAP condition), which continued for the remaining 66 hours (of the 88-hour period). As part of the randomized, double-blind, controlled trial, subjects were not aware they were receiving placebo for every pill administration, but instead were told that any given pill could be either placebo or low-dose caffeine (0.3 mg/kg). Results reported here were available only after data acquisition in the trial was complete and the blind was broken.

Throughout the 10-day protocol, subjects remained in the laboratory, under constant behavioral observation. They were isolated from time cues, and from contact with the outside world (other than experiment staff), and kept in ambient light less than 50 lux. Mild behavioral/social stimulation was used to keep them awake. Throughout the 10 days in the laboratory, including the 88-hour experimental period, subjects were maintained on isocaloric diets, adjusted for body mass. They received 3 nights of recovery sleep in the laboratory following the 88-hour experimental period.

Neurobehavioral testing.

Every 2 hours during wakefulness, subjects underwent computerized neurobehavioral testing while in a sitting position. They were closely monitored during these test bouts and repeatedly admonished to perform to the best of their ability. Between test bouts all subjects remained in bed and were allowed to eat, watch videotapes, read, or converse—but not to sleep unless it was specifically scheduled (i.e., NAP condition). The neurobehavioral test bout consisted of a 35-minute computerized questionnaire and performance battery. About 6 minutes into the test bout, subjects began a 10-minute psychomotor vigilance task (PVT; ref. 7), which has been extensively documented to be sensitive to increased homeostatic drive for sleep and circadian rhythmicity (7, 8, 19, 29, 38).

The PVT is a relatively high-signal load, sustained attention (vigilance) performance task requiring a button press response to the onset of a visual millisecond counter (red digits on a black background) presented in the center of a 14-inch computer monitor at a distance of about 20 inches, such that the counter subtended a visual angle of about 1 degree. The PVT has virtually no learning curve and all subjects achieved asymptotic responding capability within one test bout. Stimuli were presented with a random inter-stimulus interval of 2 to 10 seconds duration programmed to begin anew 2 seconds after each completed response. The digital counter showing reaction time to the light stimulus remained visible and stopped counting immediately at the subject's response. All responses were displayed digitally in milliseconds (ms), with incorrect responses (i.e., false start, incorrect key press, or keeping the button pressed) coded into the recording as errors. Stimuli not responded to after 30 seconds (i.e., non-responses) evoked an auditory warning tone, were logged as 30-second response durations, and the next trial began immediately.

Since the computerized test battery was administered every 2 hours, data were available for a total of 44 PVT test bouts (10 minutes each) completed by all subjects throughout the 88-hour experimental period. Subjects produced between 60 and 100 responses during each 10-minute PVT test bout (depending on their average speed of responding), for a total of approximately 2,640 to 4,400 reaction times (RTs) per subject, per 88-hour period (a grand total of 101,516 PVT responses were gathered across the 88-hour experimental period for the $n = 28$ subjects). Only the second RT through the seventy-first RT in each 10-minute trial were used in the analyses in order to eliminate effects of orienting to the task and to allow all subjects to contribute a similar number of trials to all analyses. False start trials (i.e., pressing the response button when no stimulus was present) were combined with RTs less than 100 ms to evaluate PVT response errors denoting anticipatory responses. Repeated-measures ANOVAs (with Huynh-Feldt adjustment for sphericity) were used to evaluate the effects of condition (i.e., TSD, NAP) and time across the 88-hour experiment (i.e., 44 test bouts across 88 hours), time on task (minutes 1 through 10) mean reaction times, standard deviations of reaction times, and number of errors. For evaluation of time-on-task effects, reaction time data was reciprocally transformed in order to normalize the data.

RESULTS

Reaction times and response errors.

The PVT performance difference between the TSD and NAP groups, which differed by the degree of homeostatic drive for sleep present across the 88-hour experimental phase, was evaluated by comparing their mean reaction times and error rates (Figure 1). As expected, both groups maintained relatively fast and error-free responding across the first 16 hours of wakefulness. Beginning 18 hours into the experimental period, TSD subjects showed a progressive deterioration in performance, while NAP subjects were able to maintain near baseline performance throughout the experimental period. The deterioration in performance was evidenced

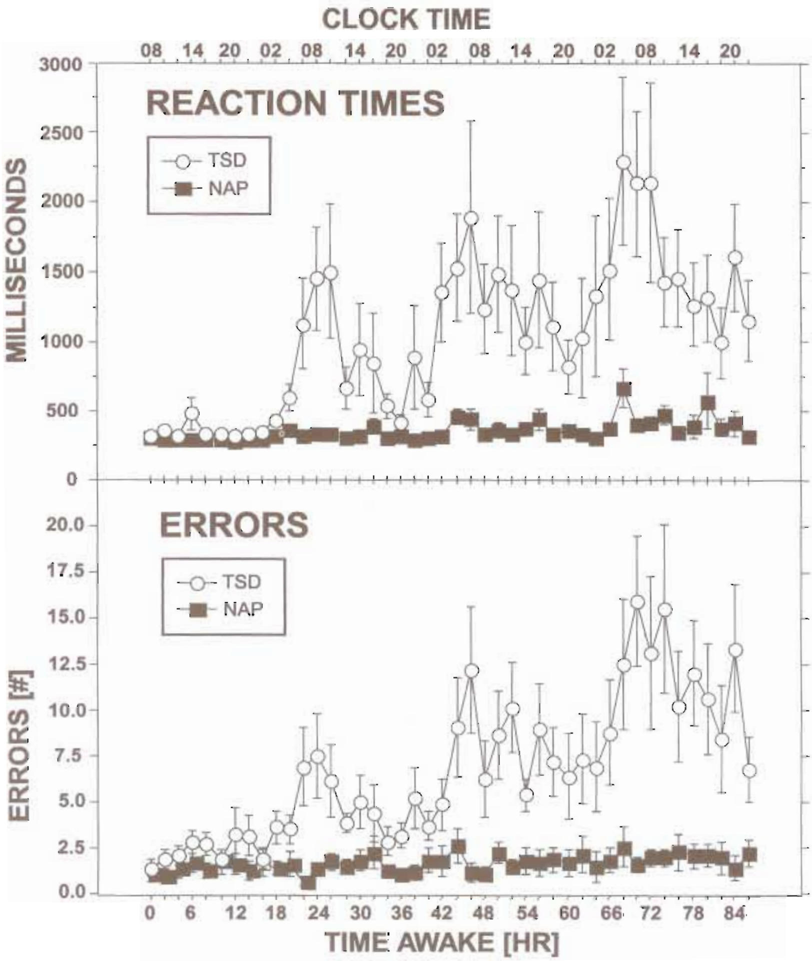

Fig. 1. - *Psychomotor vigilance task (PVT) performance mean reaction times (top panel: in ms ± 1 SE) and PVT mean number of errors (bottom panel: ± 1 SE) for each test bout during 88 hours of continuous wakefulness for the TSD group (open circles) and the NAP group (filled squares).*

The NAP group was given a 2-hour (time in bed) nap opportunity once every 12 hours (02:45-04:45 and 14:45-16:45) throughout the 88-hour period (nap times are not shown in the figure).

by increases in both PVT reaction times (Figure 1, top panel) and PVT response errors (Figure 1, bottom panel) for the TSD group relative to the NAP group. These effects were evident in the results of the repeated-measures ANOVA, which yielded significant main effects of condition (TSD vs. NAP) for PVT reaction time ($F_{1,26} = 12.8$, $p = 0.0014$) and for the number of PVT response errors ($F_{1,26} = 13.7$, $p = 0.0010$); as well as main effects of time in the 88-hour period for both reaction time ($F_{43,1118} = 5.3$, $p < 0.0001$) and errors ($F_{43,1118} = 3.3$, $p = 0.0009$). In confirmation of the data shown in Figure 1, there was a different influence of time in the 88-hour period between the two conditions (TSD vs. NAP), reflecting the differential rates of increase in the homeostatic drive for sleep; significant interactions between group and time in the 88-hour period were obtained for both PVT reaction time ($F_{43,1118} = 3.6$, $p = 0.0030$) and PVT response errors ($F_{43,1118} = 2.5$, $p = 0.0096$).

The mean reaction time and response error graphs for the TSD condition showed the well-established interaction of the homeostatic drive for sleep and the endogenous circadian pacemaker (14). Importantly, the profiles of mean reaction time and of response errors within each condition (TSD, NAP) were remarkably similar. There was a significant correlation between the TSD mean reaction times graph (top panel) and the TSD mean number of response errors (bottom panel) shown in Figure 1 (Pearson's $r = 0.85$, $p = 0.0001$).

Response variability with increasing homeostatic drive for sleep.

Visual examination of the TSD condition data presented in Figure 1 reveals that as sleep deprivation increased, between-subject variance (shown as standard error of the mean) increased in both mean RT and total errors. This suggests that in addition to increases across deprivation in mean PVT reaction time, inter-subject variability was also increasing in the TSD group across time in the 88-hour period. To quantify this apparent effect, average standard deviations for PVT reaction time were calculated for each time point for each condition. These results are displayed in Figure 2. Significant main effects were found for condition ($F_{1,26} = 17.0$, $p = 0.0003$), and for time in the 88-hour period ($F_{43,1118} = 6.7$, $p < 0.0001$), as well as for the interaction of condition and time ($F_{43,1118} = 4.5$, $p < 0.0001$).

The standard deviations of PVT response times across the 88-hour experimental period (Figure 2) showed a profile that is remarkably similar to mean PVT response times (Figure 1, top panel). In order to evaluate this apparent relationship more closely, standard deviations were plotted as a function of the mean for all test bouts for each subject in both conditions. The graphical results are displayed in Figure 3. When a least-squares linear trend was fit to these data points within each condition (TSD and NAP), a significantly good fit was found for each condition (NAP $r^2 = 0.83$, $p < 0.0001$; TSD $r^2 = 0.90$, $p < 0.0001$). The regression slopes were very similar (NAP slope = 1.65; TSD slope = 1.45; $t = 0.88$; $p = 0.77$). Although, as can be seen in Figure 3, the NAP group expressed this linear relationship between mean and standard deviation over a smaller range of values, both groups demonstrated the same basic linear relationship between response variability and mean response time. The proportionality shown in Figure 3 is indicative of increasing inter-individual differences, and the primary contributor to this variability was escalating sleep deprivation (continuous time awake in the TSD condition; and cumulative partial sleep loss in the NAP condition).

Increasing between-subject variability across sleep deprivation (Figures 2 and 3) may reflect that some subjects are more vulnerable to neurobehavioral impairment than others, but it reveals nothing about within-subject variability as a function of escalating homeostatic drive for sleep. The question of whether each individual subject also showed proportionality between mean and standard deviation of PVT reaction times across the 88-hour period was evaluated for subjects in the TSD condition (there was little within-subject variability in the NAP control condition).

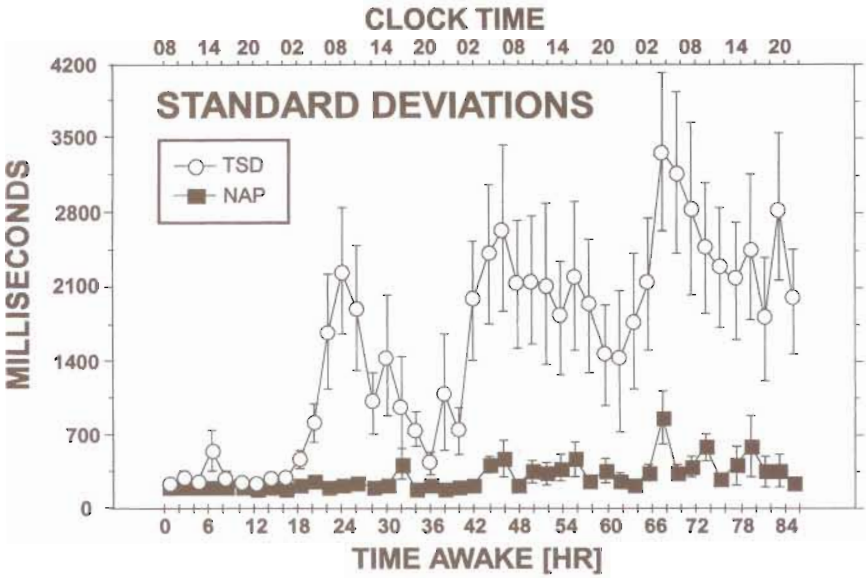

Fig. 2. - *TSD group (open circles) and NAP group (filled squares) average standard deviations (in ms ± 1 SE) for PVT performance at each test bout across the 88-hour experimental period.*

The NAP group was given a 2-hour (time in bed) nap opportunity once every 12 hours (02:45-04:45 and 14:45-16:45) throughout the 88-hour period (nap times are not shown in the figure).

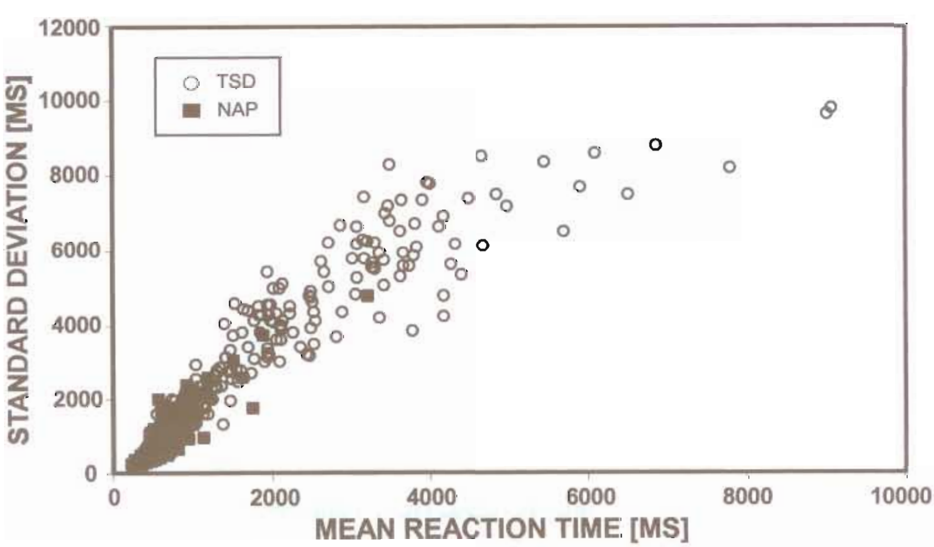

Fig. 3. - *Psychomotor vigilance task (PVT) reaction time standard deviations (in ms) plotted as a function of PVT mean reaction times (in ms) from all PVT test bouts for all subjects.*

Filled squares represent NAP group data and open circles represent TSD group data.

Linear trend fits were computed for each individual subject and plotted in Figure 4. Goodness-of-fit was high in all subjects with r^2 ranging from 0.85 to 0.98 (all p's < 0.0001) and the regression slopes ranged from 1.20 to 2.51. This positive correlation between each subject's PVT means and standard deviations indicates that all subjects experienced both response slowing and an increase in response variability during the 88-hour experimental period. Furthermore, examination of the 13 linear fit lines in Figure 4 reveals that while all subjects demonstrated response instability during the 88 hours of sleep deprivation, the magnitude of impairment differed among subjects. This is visible as differences in the length of the linear fit lines, and appears to be the primary source of inter-individual differences in response to TSD.

Response variability within PVT trials: Time on task.

The final analyses concerned the issue of how reaction times changed within each 10-minute PVT trial for each subject, as sleep loss increased. This was accomplished by focusing on response-to-response changes as a function of time on task (what Kleitman referred to as "endurance"). Sustained attention task performance normally degrades as a function of time on task, a phenomenon known as vigilance decrement. These time-on-task decrement slopes can vary as a function of sleep loss (e.g., 18). An ANOVA on reciprocal reaction times for minute-by-minute time on task in the TSD condition focused on the test bouts that occurred at 20:00 on each of the 4 sleep deprivation days. Significant main effects were found for day of deprivation ($F_{3,48} = 7.5$, $p = 0.0030$); time on task ($F_{9,432} =$

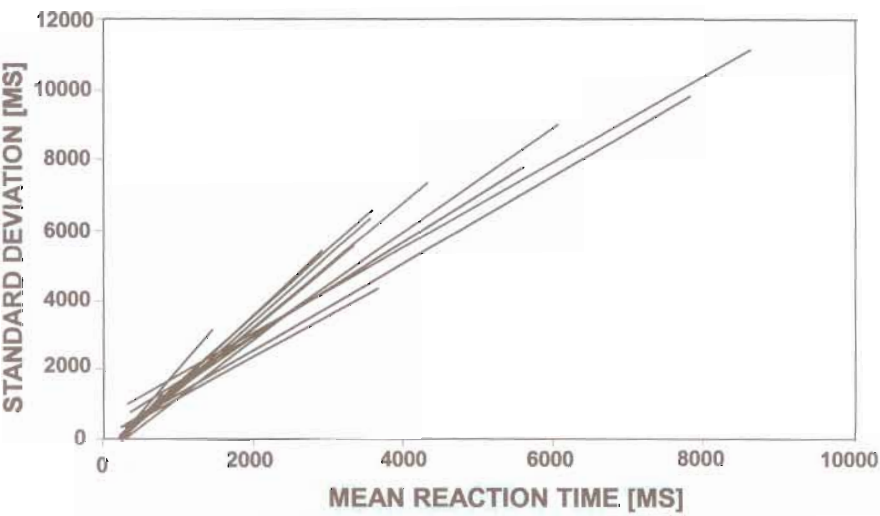

Fig. 4. - *Least-squares regression lines fit for the linear relationship between mean and standard deviation of psychomotor vigilance task (PVT) reaction times (in ms) for each of the 13 subjects in the TSD condition.*

Regression lines for 2 of the 13 subjects are obscured by other lines.

6.8, $p = 0.0001$); and their interaction ($F_{27, 432} = 2.4$, $p = 0.0003$). When standard deviations of reaction times were analyzed, significant effects were again observed for day of deprivation ($F_{3,43} = 7.1$, $p = 0.0005$); time on task ($F_{9,387} = 3.9$, $p = 0.0019$); and the interaction ($F_{27, 387} = 2.0$, $p = 0.0169$). (Note that degrees of freedom in this analysis vary slightly as not all subjects produced enough response trials in all 60-second periods to calculate a standard deviation).

To illustrate this effect, Figure 5 shows all the sequential PVT reaction times for a single subject in the TSD condition for each of his 20:00 test bouts across the 88 hours of continuous wakefulness. Fast, stable responding was possible throughout the 20:00 hour trial of the first day (i.e., at 10 hours awake) and for the first 10 RTs (i.e., approximately the first minute of responding) of all other test bouts, regardless of the severity of sleep deprivation. However, after one night without sleep (i.e., ≥ 34 hours awake) reaction time fluctuated wildly from response to response as time on task proceeded from minutes 2 to 10. Latency to the loss of stable performance decreased with increasing sleep deprivation. The duration of longer reaction times (i.e., lapses) also increased. In addition, the presence of false starts (i.e., pressing the response key when no stimulus was present) can be seen in Figure 5 (as blank columns) together with frequent long-duration lapses on days 3 and 4 (i.e., at 60 and 84 hours without sleep). However, even in the last half of the 20:00 test bouts on these days, the subject was able to produce a few normal, fast responses.

DISCUSSION

This experiment tested the hypothesis that the effects of sleep deprivation on neurobehavioral performance involve an escalating "state instability" that is particularly evident in performance requiring sustained attention. The state instability hypothesis considers lapses in performance to be a product of the fundamental increase in moment-to-moment variability of attention brought about by the interaction of the homeostatic drive for sleep, the endogenous circadian promotion of wakefulness, and the compensatory effort exerted by subjects to perform (4, 5). Variability is the critical feature of performance in this conceptualization. The state instability hypothesis does not assume that sleep loss completely eliminates (i.e., makes impossible) any specific neurobehavioral function.

Results from the experiment of psychomotor vigilance performance across 88 hours of sleep deprivation supported the hypothesis that state instability was developing. PVT performance variability increased within each individual subject as a function of exposure to sleep deprivation (e.g., Figure 4). As expected, relative to subjects in the NAP control condition (i.e., partial sleep permitted), subjects in the TSD experimental condition had much greater variability in performance as sleep loss continued (e.g., Figure 2), indicating that the increasing PVT variability was due to cumulative time awake (i.e., increasing homeostatic drive for sleep). Nevertheless, even among subjects in the NAP condition, there was a tendency for variability of performance to increase in a linear relationship to mean performance,

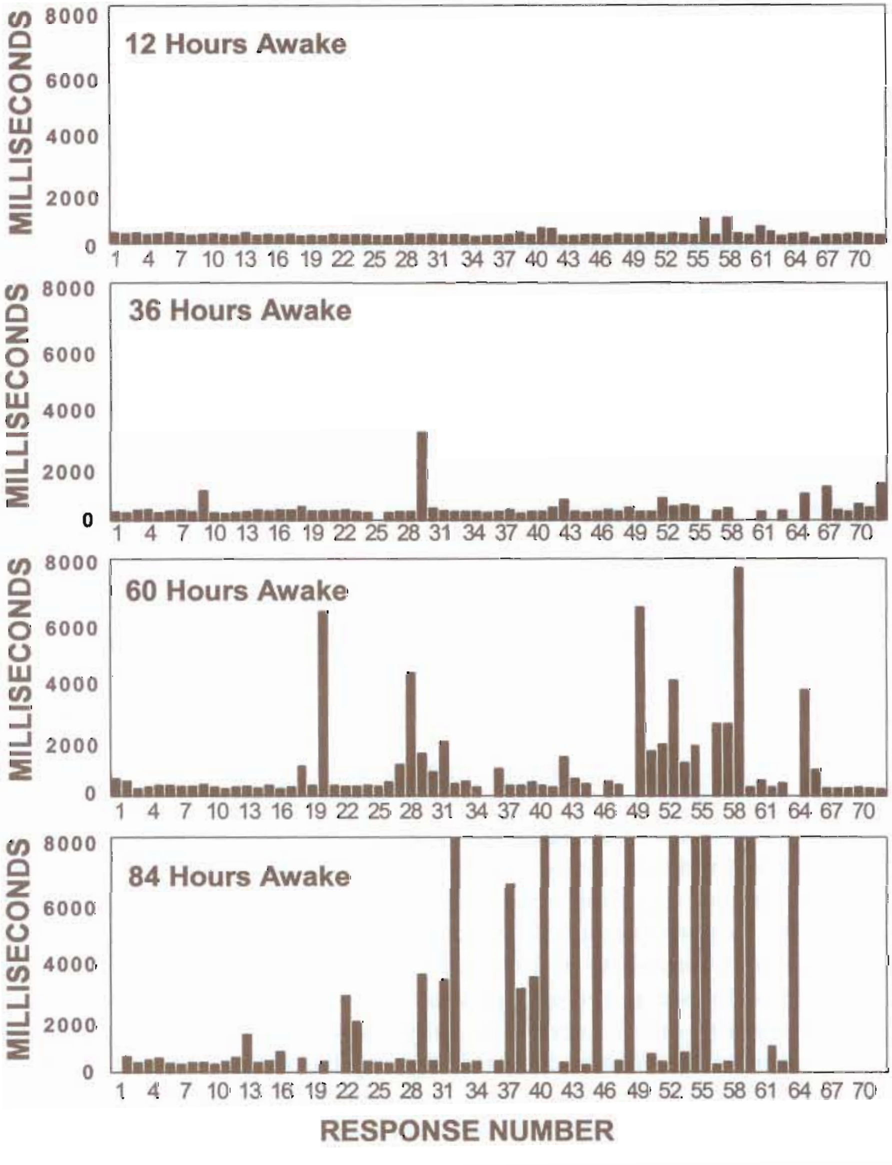

Fig. 5. - *Individual PVT reaction times (ms) for a representative single TSD subject in each of the 20:00 hour test bouts for the four consecutive days without sleep.*

On the first day of testing (i.e., 12 hours awake), modest-duration response lapses (i.e., slightly slowed responses represented by taller black columns) are evident at response numbers 56 and 58, and there are no response errors (i.e., false starts represented by blanks). On the second day of testing (i.e., 36 hours awake), response lapses were more evident (response numbers 9, 29, 65, 67, 73) and response errors (i.e., false starts) became apparent near the end of the task (response numbers 56, 59, 62, 64, 66). By the third day (i.e., 60 hours awake), lapses were frequent following the first few minutes of performance (response numbers 18, 20, 27-31, 37, 43, 49-58, 65-66). On the fourth day of testing (i.e., 84 hours awake) this subject showed many long-duration lapses (> 8000 ms), as well as more response errors (note that the 10-minute test bout ended at response number 64.

as sleep debt accumulated across the four days. Consequently, regardless of the severity of PVT performance impairment that each subject ultimately experienced, mounting performance variability became evident as the drive for sleep increased.

It is noteworthy that PVT performance variability during sleep deprivation reflected a combination of three outcomes: (1) lapses (i.e., not responding in a normal timely manner); (2) response errors (i.e., responding when no stimulus was present); and (3) normal timely responses. This pattern was especially pronounced as time on task progressed during the 10-minute PVT task. It appeared after 1 night without sleep, and after 2 nights of sleep loss it was evident typically within 1-2 minutes of PVT performance initiation (e.g., Figure 5). These data confirm the original observation of Lee and Kleitman (20) that the effects of sleep deprivation—even on neurobehavioral processes that appear to be particularly sensitive to sleep loss—do not involve elimination of the ability to perform. Rather, the effects are much more evident in the ability to maintain basal performance as a function of time on task—Kleitman considered this vigilance decrement a deficit of endurance induced by sleep loss (15).

It has been well established that response slowing and lapses contribute to greater vigilance decrements as sleepy subjects continue performing (4, 6, 10, 12, 15, 18, 21, 35). However, this experiment presents the first systematic evidence that such vigilance decrements reflect escalating variability in moment-to-moment performance responses when sleep drive is elevated. The fact that this outcome has not been described in other studies of vigilance performance during sleep deprivation is likely due to the widespread use of long-duration, low-signal-load vigilance tasks (e.g., 35) that involved only infrequent samples of performance during time on task.

Horne (11, 12) has attributed the effects of sleep deprivation on long-duration, low-signal-load, vigilance or signal detection tasks (35), as well as on simple sustained-attention, high-signal-load tasks such as the PVT (8), to monotony and boredom that lead to a reduced motivation to perform. This argument was predicated on experimental observations that incentives (e.g., monetary rewards; end of deprivation) improved vigilance performance to near-baseline levels even after 70 hours of sleep deprivation (13). In contrast to this view, Kleitman (6) and other investigators (13, 14) have argued that heightened motivation (rather than reduced motivation) during sleep deprivation masks the more serious effects of deprivation through increased compensatory effort. A number of aspects of our results provide support for Kleitman's perspective. In our experiment subjects were pushed to perform to the best of their ability at each PVT test bout. There was no indication in their behaviors at the test console or from their comments after test bouts and post-experimentally that they failed to do so. More importantly, PVT performance after as little as 18 hours awake was characterized by normal short reaction times intermixed with both long-duration lapses (i.e., errors of omission) and responses when no stimulus was present (i.e., errors of commission). Errors of commission and errors of omission closely covaried across total sleep deprivation ($r = 0.85$ [$p = 0.0001$] between TSD graphs in the top and bottom panels of Figure 1). This is evidence that subjects were attempting to compensate (errors of commission) for having missed signals (errors of omission)—examples of this can be seen in Figure 5 for responses 58-67 after 36 hours awake; for responses 34-64 after 60 hours awake; and for responses 16-64 after 84 hours awake. The fact that normal RT responses also occur during these periods, and at the beginning of PVT test bouts even after severe sleep loss, further supports the conclusion that loss of motivation was not the basis for the effects of sleep deprivation on PVT performance. The state instability hypothesis would predict that even though normal responses emerge after substantial sleep loss, they can be rekindled briefly, but they cannot be sustained over time, even in the face of continuing rewards and compensatory effort, due to the chronic intrusion of sleep initiation processes into wakefulness.

The state instability hypothesis is similar to the lapse hypothesis (36) in that both view sustained attention tasks as the most sensitive markers of sleep deprivation, and both emphasize performance variability. The lapse hypothesis posits that performance during sleep deprivation is normal until it is punctuated by brief moments of low arousal during which a lapse occurs (36). However, there is evidence that the lapse hypothesis cannot account for all of the performance deficits seen even on simple sustained-attention tasks such as the PVT (for a review see 13, 14). The state instability hypothesis posits that performance during sleep deprivation is increasingly variable due to the influence of sleep initiating mechanisms on the endogenous capacity to maintain alertness. For example, our results revealed that as sleep loss progressed, variability in performance increased in a manner that reflected the interaction of the homeostatic drive for sleep and the endogenous circadian drive for wakefulness (Figures 1-2). That is, variability in PVT performance followed the well-established temporal output of the two basic neurobiological processes regulating alertness (33). Other investigators have also reported both circadian and homeostatic regulation of PVT performance (38). Thus, the state instability hypothesis posits that sleep-initiating mechanisms begin to occur in the presence of waking neurobiology, making sustained performance labile and increasingly dependent on compensatory mechanisms (13). Therefore, compensatory effort and compensatory stimulation (e.g., motor activity, social contact, emotional excitement, cognitive and environmental stimulation) take on a greater role in maintaining wakefulness and performance as sleep drive increases. Withdrawal of these factors and exposure of the underlying endogenous capacity to remain alert, by requiring subjects to sustain attention and respond in a timely manner (e.g., PVT performance demands), reveals a fundamentally unstable state that cannot be characterized as either fully awake or asleep; that fluctuates within seconds; and that can rapidly progress to physiological sleep if not resisted (and at some point even when resisted, such as occurs in drowsy-driving crashes).

Finally, we note that neurobehavioral performance tasks requiring attention seem especially prone to state instability when sleep drive is elevated. Attention is a requirement of many goal-directed activities (24, 26). Neuroimaging studies suggest that neural structures subserving selective and sustained visual attention (i.e., thalamus, basal ganglia, cingulate gyrus, prefrontal cortex) are among the most likely areas of the brain to show reduced metabolic rates during sleep deprivation (5, 9, 31, 37). Much more work is needed on the basic neurobiological mechanisms that contribute to the state instability evident in sustained attention during sleep deprivation.

SUMMARY

Nathaniel Kleitman was the first to observe that sleep deprivation in humans did not eliminate the ability to perform neurobehavioral functions, but it did make it difficult to maintain stable performance for more than a few minutes. To investigate variability in performance as a function of sleep deprivation, n = 13 subjects were tested every 2 hours on a 10-minute, sustained-attention, psychomotor vigilance task (PVT) throughout 88 hours of total sleep deprivation (TSD condition), and compared to a control group of n = 15 subjects who were permitted a 2-hour nap every 12 hours (NAP condition) throughout the 88-hour period. PVT reaction time means and standard deviations increased markedly among subjects and within each individual subject in the TSD condition relative to the NAP condition. TSD subjects also had increasingly greater performance variability as a function of time on task after 18 hours of wakefulness. During sleep deprivation, variability in PVT performance reflected a combination of normal timely responses, errors of omission (i.e., lapses), and errors of commission (i.e., responding when no stimulus was present). Errors of omission and errors of commission were highly intercorrelated across deprivation in the TSD condition ($r = 0.85$, $p = 0.0001$), suggesting that performance instability is more likely to include compensatory effort than a lack of motivation. The marked increases in PVT performance variability as sleep loss continued supports the "state instability" hypothesis, which posits that performance during sleep deprivation is increasingly variable due to the influence of sleep initiating mechanisms on the endogenous capacity to maintain attention and alertness, thereby creating an unstable state that fluctuates within seconds and that cannot be characterized as either fully awake or asleep.

Acknowledgments. - This investigation was supported by AFOSR F49620-95-1-0388 and NIH M01-RR00040, and in part by NIH NR04281, NASA NCC 9-58 with the National Space Biomedical Research Institute, and ARO DAAD 19-99-1-0120. We thank John W. Powell, Michele M. Carlin, Matthew Martino, Michal Atzram, Kim McConnell, and Nicholas Price for help in data acquisition and analyses.

REFERENCES

1. Armington, J.C. and Mitnick, L.L. Electroencephalogram and sleep deprivation. *J. Appl. Physiol.*, **14**: 247-250, 1959.
2. Bjerner, B. Alpha depression and lowered pulse rate during delayed actions in a serial reaction task: A study of sleep deprivation. *Acta Physiol. Scand.*, **19** (Suppl. 65): 1-93, 1949.

3. Carskadon, M.A. and Dement, W.C. Nocturnal determinants of daytime sleepiness. *Sleep*, **5** (Suppl. 2): 73-81, 1982.
4. Dinges, D.F. The nature of sleepiness: Causes, contexts, and consequences. Pp. 147-179. In: Stunkard, A.J. and Baum, A. (Eds.), *Eating, Sleeping, and Sex*. Hillsdale, NJ, Lawrence Erlbaum Ass. Inc., 1989.
5. Dinges, D.F. and Chugh, D.K. Physiologic correlates of sleep deprivation. Pp. 1-27. In: Kinney, J.M. and Tucker, H.N. (Eds.), *Physiology, Stress, and Malnutrition: Functional Correlates, Nutritional Intervention*. New York, NY, Lippincott-Raven Publ., 1997.
6. Dinges, D.F. and Kribbs, N.B. Performing while sleepy: Effects of experimentally-induced sleepiness. Pp. 97-128. In: Monk, T.H. (Ed.), *Sleep, Sleepiness and Performance*. New York, NY, John Wiley and Sons, 1991.
7. Dinges, D.F., Pack, F., Williams, K., Gillen, K.A., Powell, J.W., Ott, G.E., Aptowicz, C., et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep*, **20**: 267-277, 1997.
8. Dinges, D.F. and Powell, J.W. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behav. Res. Meth. Instr. Comp.*, **17**: 652-655, 1985.
9. Drummond, S.P.A., Brown, G.A., Gillin, J.C., Stricker, J.L., Wong, E.C. and Buxton, R.B. Altered brain response to verbal learning following sleep deprivation. *Nature*, **403**: 655-657, 2000.
10. Findley, L.J., Suratt, P.M. and Dinges, D.F. Time-on-task decrements in "steer clear" performance of patients with sleep apnea and narcolepsy. *Sleep*, **22**: 804-809, 1999.
11. Horne, J.A. Dimensions to sleepiness. Pp. 169-196. In: Monk, T.H. (Ed.), *Sleep, Sleepiness and Performance*. New York, NY, John Wiley and Sons, 1991.
12. Horne, J.A., Anderson, N.R., and Wilkinson, R.T. Effects of sleep deprivation on signal detection measures of vigilance: Implications for sleep function. *Sleep*, **6**: 347-358, 1983.
13. Horne, J.A. and Pettitt, A.N. High incentive effects on vigilance performance during 72 hours of total sleep deprivation. *Acta Psychol.*, **58**: 123-139, 1985.
14. Johnson, M.P., Duffy, J.F., Dijk, D.K., Ronda, J.M., Dyal, C.M. and Czeisler, C.A. Shortterm memory, alertness and performance: a reappraisal of their relationship to body temperature. *J. Sleep Res.*, **1**: 24-29, 1992.
15. Kjellberg, A. Sleep deprivation and some aspects of performance: II. Lapses and other attentional effects. *Waking and Sleeping*, **1**: 145-148, 1977.
16. Kleitman, N. The effects of prolonged sleeplessness on man. *Am. J. Physiol.*, **66**: 67-92, 1923.
17. Konowal, N.M., Van Dongen, H.P.A., Powell, J.W., Mallis, M.M. and Dinges, D.F. Determinants of microsleeps during experimental sleep deprivation. *Sleep*, **22** (Supp. 1): S328-S329, 1999.
18. Kribbs, N.B. and Dinges, D.F. Vigilance decrement and sleepiness. Pp. 113-125. In: Ogilvie, R.D. and Harsh, J.R. (Eds.), *Sleep Onset. Normal and Abnormal Processes*. Washington, D.C., American Psychological Association, 1994.
19. Kribbs, N.B., Pack, A.I., Kline, L.R., Getsy, J.E., Schuett, J.S., Henry, J.N., Maislin, G., et al. Effects of one night without nasal CPAP treatment on sleep and sleepiness in patients with obstructive sleep apnea. *Am. Rev. Resp. Disease*, **147**: 1162-1168, 1993.
20. Lee, M.A.M. and Kleitman, N. Studies on the physiology of sleep: II Attempts to demonstrate functional changes in the nervous system during experimental insomnia. *Am. J. Physiol.*, **67**: 141-152, 1923.

21. Lisper, H. and Kjellberg, A. Effects of 24-hour sleep deprivation on rate of decrement in a 10-minute auditory reaction time task. *J. Exp. Psychol.*, **96**: 287-290, 1972.
22. Mirsky, A.F. and Cardon, P.V. A comparison of the behavioral and physiological changes accompanying sleep deprivation and Chlorpromazine administration in man. *Electroencephalogr. Clin. Neurophysiol.*, **14**: 1-10, 1962.
23. Mitler, M.M., Gujavarty, K.S. and Browman, C.P. Maintenance of Wakefulness Test: A polysomnographic technique for evaluating treatment efficacy in patients with excessive somnolence. *Electroencephalogr. Clin. Neurophysiol.*, **53**: 658-661, 1982.
24. Parasuraman, R. *The Attentive Brain*. Cambridge, MA, MIT Press, 1998.
25. Patrick, G.T.W. and Gilbert, J.A. Studies from the psychological laboratory of the University of Iowa: On the effects of loss of sleep. *Psychol. Rev.*, **3**: 469-483, 1896.
26. Posner, M.I. Attention in cognitive neuroscience: An overview. Pp. 615-624. In: Gazzaniga, M.S. (Ed.), *The Cognitive Neurosciences*. Cambridge, MA, MIT Press, 1995.
27. Robinson, E.S. and Herrmann, S.O. Effects of loss of sleep. 1. *J. Exp. Psychol.*, **5**: 19-32, 1922.
28. Robinson, E.S. and Richardson-Robinson, F. Effects of loss of sleep. 2. *J. Exp. Psychol.*, **5**: 93-100, 1922.
29. Rosekind, M.R., Gander, P.H., Miller, D.L., Gregory, K.B., et al. Fatigue in operational settings: Examples from the aviation environment. *Human Factors*, **36**: 327-338, 1994.
30. Smith, M. A contribution to the study of fatigue. *Brit. J. Psychol.*, **8**: 327-350, 1916.
31. Thomas, M.L., Sing, H.C. & Belenky, G. Cerebral glucose utilization during task performance and prolonged sleep loss. *J. Cerebr. Blood Flow and Metab.*, **13**: 5531, 1993.
32. Torsvall, L. and Åkerstedt, T. Sleepiness on the job: Continuously measured EEG changes in train drivers. *Electroencephalogr. Clin. Neurophysiol.*, **66**: 502-511, 1987.
33. Van Dongen, H.P.A. and Dinges, D.F. Circadian rhythms in fatigue, alertness and performance. Pp. 391-399. In: Kryger, M.H., Roth, R. and Dement, W.C. (Eds.), *Principles and Practices of Sleep Medicine*. 3rd Ed. Philadephia, PA, W.B. Saunders, 2000.
34. Warren, N. and Clark, B. Blocking in mental and motor tasks during a 65-hour vigil. *J. Exp. Psychol.*, **21**: 97-105, 1937.
35. Wilkinson, R.T. Sleep deprivation: Performance tests for partial and selective sleep deprivation. Pp. 28-43. In: Abt, L.E. and Riess, B.F. (Eds.), *Progress in Clinical Psychology: Dreams and Dreaming*. New York, NY, Grune and Stratton, 1968.
36. Williams, H.L., Lubin, A. and Goodnow, J.J. Impaired performance with acute sleep loss. *Psychological Monographs: General and Applied*, **73**: 1-26, 1959.
37. Wu, J.C., Gillin, J., Buchsbaum, M.S. and Hershey, T. The effect of sleep deprivation on cerebral glucose metabolic rate in normal humans assessed with positron emission tomography. *Sleep*, **14**: 155-162, 1991.
38. Wyatt, J.K., Dijk, D.-J., Ronda, J.M., Jewett, M.E., Powell, J.W., Dinges, D.F. and Czeisler, C.A. Interaction of circadian- and sleep/wake homeostatic-processes modulate psychomotor vigilance test (PVT) performance. *Sleep Res.*, **26**: 759, 1997.