EFFECTS OF HYPNOTIC DRUGS ON PERFORMANCE BEFORE AND AFTER SLEEP

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This report is a summary of the research conducted in the Sleep Research and Treatment Center supported in part by NASA Grant NGR-009-204. This research was carried out between 1 June 1971 and 28 February 1975. The general goals of this grant were three-fold: (1) A continuing evaluation was made of the effects of various hypnotics on various sleep stage parameters and on the parameters of effectiveness. (2) A continuing evaluation was also made of the effects of several commonly used yet distinctly different hypnotics on performance. (3) At the request of NASA, the effects on performance of two non-hypnotics commonly used in the space program were also evaluated.

Until the last decade there has been little exacting and objective research into the fundamental biological process of sleep even though approximately one-third of our lives are spent in this state. Our sleep laboratory along with others have now begun to make inroads into this complex subject. Recent research has already provided significant contributions to the diagnosis and treatment of sleep disorders and mental disorders and to a better understanding of the aging process as well as to the effects of drug action on the central nervous system. Sleep laboratory studies have also evaluated the relationship between a night's sleep and daytime performance, e.g., the effects of varying amounts of sleep loss. An area that has not been thoroughly studied is the effects on daytime performance of commonly used hypnotics taken the previous night.

I. EFFECTS OF HYPNOTICS ON SLEEP STAGE AND EFFECTIVENESS PARAMETERS

Past Studies

Effects of Short-Term Hypnotic Use on Sleep Stages

In our past studies, we have utilized a standard eight-night protocol to determine if hypnotic drugs altered sleep patterns. The first placebo night allows for adaptation to the laboratory, while the second and third placebo nights are used for baseline measurements. On the next three nights, the active drug is administered at "lights out" and the initial and short-term cumulative effects of the drug on sleep patterns can be measured. On the last two nights, placebo is again administered and withdrawal effects, if any, are observed.

A number of our short-term studies based on this eight-night protocol have shown that many drugs produce significant alterations in REM sleep. The following drugs, in the doses listed, produce a decrease in REM sleep and were followed by a rebound of REM sleep (increase above baseline levels) on withdrawal: glutethimide (Doriden) 500 mg; secobarbital sodium (Seconal) 100 mg; pentobarbital sodium (Nembutal) 100 mg; methyprylon (Noludar) 300 mg, methaqualone (Quaalude) 300 mg; and diphenhydramine (Benadryl) 500 mg. On the other hand, the following drugs produced either no decrease or minimal changes in REM sleep in the doses given, nor were they (with one exception) followed by REM rebound on withdrawal: chloral hydrate 500 mg and 1000 mg; chlordiazepoxide (Librium) 50 mg; diazepam (Valium) 10 mg; and promethazine (Phenergan) 25 mg. However, following withdrawal of promethazine there was a marked increase in REM sleep on withdrawal.

Further, we have evaluated several benzodiazepine drugs, e.g., flurazepam (Dalmane) 30 mg; triazolam (U33030) 5 mg and flunitrazepam (RO54200) 1 and 2 mg each of which produced decreases in REM sleep during initial administration. Upon withdrawal REM sleep returned to normal values without a rebound of REM sleep. Finally, there are a few drugs which produce an immediate increase in REM sleep during administration. These include thioridazine (Mellaril) 50, 75 and 100 mg and ORF 8063 (20 mg), an investigational benzodiazepine drug.

Because we scored all stages of sleep (often not previously done), our studies also demonstrated that in addition to producing changes in REM sleep, a number of drugs produce decreases in stage 4 sleep. These included three hypnotics: flurazepam 30 mg; glutethimide 50 mg and diazepam 10 mg. The most marked decreases in stage 4 sleep occurred following the administration of the benzodiazepine drugs, flurazepam and diazepam. The decrease in stage 4 sleep occurred on the first night of pentobarbital administration, while the decrease in stage 4 sleep with the other four drugs did not occur until the second or third consecutive drug nights.

Evaluation of Hypnotic Drug Effectiveness

A particular focus of hypnotic evaluation has been the degree and length of the effectiveness of these drugs in inducing and maintaining sleep in insomniac patients. The experimental protocol for these studies is described as follows: The first placebo night allows for adaptation to the laboratory environment and then on nights

2-4 baseline measurements are obtained. On nights 5-7, initial and short-term effectiveness in inducing and maintaining sleep is measured. Nights 17-18 mark the end of the two-week period of drug administration and these laboratory nights allow for determining if the drug is still effective or if tolerance has developed.

We have evaluated individually the following drugs and dosages with this 22 night protocol: chloral hydrate 1000 mg; ethclorvynol (Placidyl) 500 mg; glutethimide 500 mg; methaqualone (Sopor) 150 and 300 mg; methaqualone HCL (Parest) 400 mg; secobarbital 100 mg; flurazepam 30 mg and triazolam 0.5 mg.

We found that all of the drugs were intially moderately to markedly effective in inducing or maintaining sleep, or both However, we found that at the end of the two-week period of drug administration, a loss of effectiveness had developed for either sleep induction or maintenance or both, with all of these drugs except flurazepam 30 mg.

Effectiveness of Hypnotic Drugs Used Chronically

The most striking finding in a study previously described of chronic hypnotic drug users was the poor sleep experienced by these insomniac patients in spite of their continued hypnotic use. The results showed that all of these patients had as great or greater difficulty, either in falling asleep, staying asleep or both, when compared to age-matched insomniac control subjects who were not taking drugs. Seven of the ten patients taking medication had values for total wake time which were either similar to or greater

than the insomniac controls. At least one of the three key parameters for measuring hypnotic drug effectiveness - sleep latency, wake time after sleep onset, or total wake time - was evaluated in every patient over the insomniac controls.

We consider the continued effectiveness and safety of a hypnotic drug to be the primary factor in recommending its use. However, there have been very few studies in which the effectiveness of a hypnotic drug has been evaluated beyond several consecutive nights to one week of drug administration let alone for periods of months. The major implication of our sleep laboratory studies evaluating hypnotic drug effectiveness relates to the need for clearly establishing the effectiveness of a hypnotic drug with continued use.

Drug Withdrawal Insomnia

We have described a condition which we refer to as Drug Withdrawal Insomnia, which results from both psychological factors and physiological changes involved in drug withdrawal. When a patient abruptly withdraws from the regular and prolonged use of multiple doses of a hypnotic, he frequently first experiences marked insomnia, i.e., difficulty in falling asleep. This insomnia is due to psychological apprehension over his ability to get along without the drug and also an abstinence syndrome which includes jitteriness and nervousness. In addition, once the patient falls asleep, his sleep is frequently fragmented and disrupted.

If the hypnotic which is abruptly withdrawn is a REM suppressant and there is a marked increase or rebound in REM sleep there may also be associated an increased intensity and frequency of dreaming. At times even nightmares may occur. It should be emphasized that altered sleep patterns and Drug Withdrawal Insomnia can occur not only when a drug is intentionally withdrawn but also on an actual drug night when the patient slept past the duration of pharmacologic action of the drug.

Current Studies

Effects of Long-Term Hypnotic Use

Within this current grant period, we have evaluated flurazepam 30 mg and pentobarbital 100 mg when administered for a one month period. The protocol was as follows: 1-4 placebo-laboratory; 5-7 drug-laboratory; 8-15 drug-home; 16-18 drug-laboratory; 19-29 drug-home; 30-32 drug-laboratory; 33-36 placebo-laboratory; 37-44 placebo-home and 45-47 placebo-laboratory. The results of this study are briefly summarized in Table 1A and 1B. Within the table are the mean values for 4 effectiveness parameters (sleep latency, wake time after sleep onset, total wake time and number of wakes). These are followed by two sleep stage parameters, % slow wave sleep (stage 3 and 4 sleep) and % REM sleep. The P values represent the probability levels obtained when contrasting a specified condition mean with the baseline via a Dunnett multiple comparison test.

The results seen with pentobarbital administration are similar to what have been seen previously. This drug is initially effective,

i.e. total wake time is significantly decreased from 62.2 min. on baseline to 41.5 min. on short-term drug. This effectiveness is not, however, maintained. By the end of two weeks the total wake time has returned to baseline levels and remains there.

Flurazepam administration, showed similar initial effectiveness. The total wake time decreased from 67.1 on baseline to 34.5 on short-term drug ($P < .01$). At the end of two weeks and three weeks administration, the total wake time of this drug was still significantly ($P < .01$) decreased (29.4 & 38.5 min. respectively).

The two drugs showed a different picture in terms of sleep stages also. They both produced a decrease in % REM sleep. Pentobarbital decreased the % REM from 22.5 to 21.7, 20.8, & 21.5 during short, intermediate, and long-term drug administration. There was a suggestion of a rebound following initial withdrawal (24.4). With flurazepam administration a similar but significant decrease in % REM was seen (26.2 vs. 22.9, 19.4, & 22.2). Upon withdrawal there was no evidence of rebound (26.2 vs. 25.5, & 25.2).

With slow wave sleep, pentobarbital initially produced a decrease from 7.9 to 5.0. The % slow wave returned to baseline by the end of two weeks of drug administration. By the end of four weeks, the % slow wave had exceeded baseline values (7.9 vs. 9.5) and continued to rise upon initial drug withdrawal (10.2). Flurazepam administration decreased slow wave sleep significantly ($P < .01$) across all conditions (16.4 vs. 9.2, 7.2, & 5.6). These sleep stages partially returned with initial withdrawal (6.0%) and were similar to baseline after two weeks

of withdrawal (13.0%).

This study supported what we had previously reported both in terms of sleep stages and in terms of effectiveness. Both drugs were initially effective. At the end of two weeks administration, only flurazepam was still effective and its effectiveness was mantained throughout the one month of drug administration. Both drugs decreased REM and slow wave sleep. Flurazepam did this significantly across all conditions. With pentobarbital there was a nonsignificant increase in REM sleep on withdrawal which was not seen with flurazepam.

II. PERFORMANCE FOLLOWING ADMINISTRATION OF HYPNOTICS

The second area of investigation in this grant concerns the effects of administrating various commonly prescribed hypnotics upon subsequent daytime performance. Most performance studies have been criticized (e.g. Chiles) as being extremely difficult to relate to the "real world." He suggests that this is due to the fact that few experimental tasks exist which can approximate the complexity of the real world. One reason for this is due to the desire of most researchers to simplify the tasks so that they can be measured and quantified easily. Alternatively, most experimental tasks are prevented from their goal of being realistically complex because not enough time is available or allowed due to pressures at the moment. Further, the facilities necessary to conduct this type of research are rarely available, due to prohibitive costs. Thus, part of what we are reporting here is the evolvement of our Performance Evaluation Laboratory towards the more complex types of tasks alluded to by Chiles above. Specifically, our measurements evolved over a period of time from very simple observational techniques to the more objective paper and pencil evaluation of mood and performance. As we progressed to more active non paper and pencil evaluations, we more rigidly controlled our measurement task by isolating our subjects to eliminate the interaction among our subjects and other external contaminants. Then we began the inclusion of more complex tasks which ultimately included the subject's time-sharing of multiple tasks. This step has brought us closer to the real world in terms of the realistic complexities within our tasks, while at the same time

keeping our measurements and analysis task at least managable.

Past Work

In order to place what we have done during this contract in a better perspective, we will first b iefly summarize our previous work that was supported in part by prior NASA grants and contracts.

1. In one study, 4 subjects were involved in an evaluation oi chlordiazepoxide 50 mg, chloral hydrate 1000 mg and secobarbital 100 mg counter-balanced with placebo. The tasks employed were Wilkinson's Addition, Digit Symbol Substitution Test, Pursuit Rotor and Flow Maze. The subjects were evaluated over a four hour period following four hours of sleep.
2. A nine night protocol (PPPPDDPPP) was employed to evaluate 3 different drugs (secobarbital 100 mg, glutethimide 500 mg and flurazepam 30 mg). Three subjects were tested in three separate 9 night protocols (counter-balanced for drug condition) with the Wilkinsor Addition, Digit Symbol Substitution Test, Moscowitz Vigilance and Divided Attention and the Pursuit Rotor.
3. The same subjects were again evaluated using the same drugs in a three night protocol (P D P). This time they were evaluated 90 minutes following administration.
4. Two insomniac subjects were studied over a 22-night protocol in which there were 4 placebo baseline nights, 14 drug nights (secobarbital 100 mg) and 4 placebo withdrawal nights. The

task used was a card sorting one described by Crossman which was done immediately upon arising in the A.M.

The data that was compiled in these studies was summarized by looking at the time course of the various drugs in terms of how much intervening sleep was allowed. These conclusions though speculative were helpful in designing further research. Glutethimide was eliminated from this summary as the effects of this drug were not sufficiently consistent.

Performance 90 Minutes After Drug Administration Without Intervening Sleep

All of the tests which resulted in consistent trends suggested that at the approximate peak action of flurazepam and secobarbital there was a decrement when compared to placebo. This decrement was somewhat greater on secobarbital. These tests included cognitive-association type (Wilkinson Continuous Addition Task and Digit Symbol Substitution Test) and motor coordination (Pursuit Rotor).

Performance Four Hours After Drug Administration With Intervening Sleep

The drugs studied were secobarbital, chloral hydrate and chlordiazepoxide. In this instance the cognitive-association type tests (Wilkinson Continuous Addition Task and Digit Symbol Substitution Test) showed a decrement, again somewhat greater with secobarbital. On the other hand, the motor coordination tasks (Pursuit Rotor and Flow Maze) showed an enchancement over placebo on all drug conditions. (These results may be partially confounded with sleep deprivation and with previous drug administration).

Performance 8 Hours After Drug Administration With Intervening Sleep

In the cognitive-association type tasks, there appeared to be a general decrement with both flurazepam and secobarbital. With secobarbital the decrement was significant. In the motor-type tasks there was a significant decrement with secobarbital. The card sorting task (decision process) suggested that a decrement occurred with both secobarbital and flurazepam, and this decrement was greater with secobarbital. With long-term administration of secobarbital, both the effectiveness of the drug and the decrement in performance decreased considerably.

Current Work

Study One

Two major studies were carried out in this section. In the first study, eight male and eight female subjects were used. These 16 subjects were studied across a 4-week period. They slept in the laboratory the same 2 consecutive nights each week in four groups of four subjects each. The first night in the laboratory was considered an adaptation night and the subjects all received placebo. The second night in the laboratory the subjects received one of the 4 drug conditions specified. These were flurazepam 30 mg, secobarbital 100 mg, phenobarbital 100 mg and placebo. The subjects were assigned to one of these four groups in terms of their daily schedule. Within the groups the assignment to the specific protocol was according to a randomized Latin square. This counter-balancing was done in such a way that each drug was present in each group for every testing session.

Two complete practice sessions were made at the subjects' convenience prior to testing sessions. During the testing sessions, the

subjects were tested twice each week. The first time was in the evening prior to the administration of the drug. Thus, this session was also considered practice. The second testing session was the following morning. This testing session was preceded by drug administration and 8 hours of sleep.

The testing session itself involved all four subjects simultaneously. They each were seated around a 3' X 8' table which was partitioned into 4 equal 1.5' X 4' areas. The partition was 2' tall and was built of accoustical material such that communication among the 4 subjects was maintained at a minimum.

The testing schedule every morning was as follows:

0700 Awaken and dress

0720 Juice and roll and fill post sleep questionnaire

0730 Begin test session

0845 End test session

The test schedule for the evening was similar except that no juice or roll was supplied and no questionnaire was filled out.

The performance tasks that were used in this study are as follows:

1. Simple Reaction Time - This task employed the traditional pradigm in that a warning tone preceded the visual stimulus which was a single flash of a photostimulator by approximately 5 seconds. 50 stimuli were presented to obtain a valid representative of the response speed. A single variable was obtained from this task (mean response latency).
2. Critical Flicker Frequency - This task along with the next one were included as they have been shown to detect drug differences

and are reportedly measuring arousal or cortical excitability. The stimulus was prsesented via a Grass Photostimulater (PS-2). Three consecutive fusions for all subjects were used as the criteria to finish a trial. Four trials for each session were collected using the traditional method of constant stimuli. The mean frequency of fusion was the only variable obtained.

3. Auditory Flutter Frequency - This task has been reported by previous authors to be more sensitive to drug effects than the critical flicker frequency. The method of collection was the paired comparison technique. This method forced a decision between a 100 cycle flutter and a variable frequency flutter between 10 and 100 cycles in steps of 10. The variable derived from this task was the mean fusion frequency.
4. Wilkinson Vigilance Task with Reactive Time - This task consists of a tone which occurs once every 2 seconds for a 1 hour period. Periodically one of these tones is slightly shorter than the rest. The shorter tones are the stimulus and the subject is requested to identify them by pushing on a hand held push button. The tones are masked in white noise such that a well trained observer will perceive about 80% of the stimuli. Test and training tapes were obtained from RT Wilkinson of Cambridge, England. Several variables were obtained from this task including the number of correct responses, the number of incorrect responses, the number of attempted responses, the mean latency between stimulus onset and response onset, d' (this is a detection therapy estimate of discriminability between signal and noise) and an estimate of habituation. This

latter estimate was derived from the number correct within the first fifteen minutes minus the number correct within the last fifteen minutes.

5. Paced Math - This task consisted of a prerecorded verbal presentation of two numbers followed by a pause. During the pause the subject's task was to add the two digits and record the answer. Preliminary work showed that the pace employed in most sleep loss studies (1.5-2 sec) was inadequate for our subjects. We chose a pace of 0.25 sec per stimulus presentation, i.e., the first stimulus was followed by the second in 0.25 sec which was followed by a 0.25 sec pause before the next two stimulus were presented. Possibly, the major difference between our subjects and previously published results is that our subjects were of high or above average intelligence, i.e., medical students, graduate students and their wives. Three variables were derived from this task. The number of correct additions, the number of additions attempted and a measure of efficiency derived from the percent correct.
6. Pursuit Rotor - This task consisted of a turntable with a ½" diameter spot near the outer edge. The turntable was rotating at a speed of 60 RPM. The subject held a stylus in his preferred hand and attempted to keep this stylus in contact with the rotating spot. The variable derived from this task was the mean time on target derived from three 30 second trials.

The post sleep questionnaire was included as a non-performance measure to yield a subjective estimate of the previous nights sleep. The specific questions that were asked were:

1. How long do you think it took you to fall asleep last night?

   _____hours_____min.

2. How much sleep do you think you got last night?

   _____hours_____min.

3. Did you wake up during the night? If yes, how many times_____?

The statistical analysis of these data were carried out at two levels. First, a three way analysis of variance within each variable was made (sex, subject and condition with the sex and condition parameters fixed). This analysis tested specifically whether there were any systematic differences between the male and female samples that could be detected. Whenever a significant ($P < .05$) interaction between sex and condition was detected any further analysis was made with the male and female sample rather than the total sample.

The analysis of the total sample that was used to detect differences due to drug conditions employed the Dunnett comparison test. The error term for this analysis was the subject by condition interaction term derived from the analysis of variances described above. If, on the other hand, a significant sex difference was detected in the three way analysis of variance then the subject by condition error term for the Dunnett was derived from the male and female samples separately. The results of the performance tasks of this first study are described in Table 2. Within this table, the mean response of each of the various tasks is given for the males, females and for the total sample. In general, there was demonstrated a difference due to sex across all variables. These differences were significant within the simple reaction time, vigilance d', and vigilance correct, positive slope

variables. Thus, the analysis within these three var'ables was carried out within the male and female samples rather than the total samples. Table 2 also describes the conditions that were significantly different from placebo in terms of probability. Whenever possible the total sample was employed.

The simple reaction time task was not analyzed for the total sample since a sex difference was detected. In other words, the male sample was significantly faster than the female sample (246.5 msec vs. 304.9 msec). Within the male sample all three drug conditions (253.0, 252.0 & 251.2 msec) showed a significant decrement when contrasted with placebo (229.9 msec). This drug effect was not seen within the female sample (309.6, 249.9 & 300.0 msec vs. 311.5 msec).

There were slight decrements suggested when contrasting flurazepam administration with placebo in the critical flicker frequency task (48.6 FPS vs. 49.6 FPS). With phenobarbital administration, there was a decrement suggested with the critical flicker frequency (48.4 FPS vs. 49.6 FPS). The auditory flutter frequency task suggested a slight increase due to both secobarbital (72.9 FPS) administration and phenobarbital (71.0) administration when contrasted to placebo (70.6).

There were several variables derived from the vigilance task. In general, these results were rather complimentary with themselves and with the other tasks. First, the number of correct positives was slightly decreased with flurazepam administration (18.3), significantly decreased with phenobarbital (17.2) and slightly increased with secobarbital (20.8) when contrasted with placebo (19.3). There was no

change detected in the number of false positives during flurazepam administration (4.0), and an increase related to both of the barbiturate administrations (5.6 & 4.6) when contrasted with placebo (4.0). The number attempted showed a decrease from 23.2 on placebo to 22.3 on flurazepam and 21.8 on phenobarbital. During secobarbital administration, a significant trend in terms of an increase in the number attempted was detected (23.2 vs. 26.3). There was also a tendency to take longer to react within the vigilance task across all conditions (728.4 msec vs. 739.0, 740.2 & 765.2 msec). The estimate of d' from the vigilance data was analyzed separately for the two sexes. In general, for both sexes there was a tendency to increase d' on flurazepam and to decrease d' on the barbiturates except for phenobarbital with the male sample. Finally, the slope of the correct positives detected a significant difference within the male sample for both of the barbiturates (-0.8, 0.4 vs. 2.5) and no change with flurazepam administration (2.5 vs. 2.5).

The paced math task was evaluated in terms of three variables. There was a tendency for fewer correct responses to be made across the three drug conditions (48.4, 47.8, 46.6 vs. 50.4). There was also a tendency for fewer responses to be attempted across all conditions (54.5, 56.4, 53.4 vs. 57.5). Finally within the paced math task, there was a significant decrement in terms of efficiency (percent correct) with secobarbital administration (83.5% vs. 86.9%).

The final performance task to be evaluated within this study was the pursuit rotor in terms of time on target. There was a tendency for both flurazepam and phenobarbital administration to enhance this

task while secobarbital administration suggested a slight decrement. We were able with these subjects to get a subjective estimate of each subjects sleep during the 8-hour sleep period the night previous to the performance testing. Table 3 summarizes the subjective estimate of sleep latency, total sleep time, and the number of wakes for each condition. Within each condition a mean is given for the male and female sample and for the total sample. These data were analyzed in a manner identical to the performance data. In other words, these data were first evaluated for differences due to sex. There were no differences obtained, th s, ..e remaining analyses were all done on the total sample. Table 3 also summarizes these results in terms of probability that the mean drug condition is different from the placebo baseline.

All three drug conditions demonstrated a decrease in sleep latency (24.4 min. vs. 18.8, 15.0 & 21.5 min.) for placebo vs. flurazepam, secobarbital and phenobarbital. All three drugs also produced anincrease in total sleep time (7.0 hours vs. 7.5, 7.3, and 7.2 hours). Flurazepam showed a significant increase ($P < .05$). All three drugs also produced a decrease in the number of awakenings reported (2,9 vs. 2.7, 2.7, 2.8). None, however, were significantly different.

The pattern of changes detected within this study strongly suggest that there are drug effects on daytime performance following a single administration of a commonly used hypnotic. It is also apparent that each of these drugs produce a different pattern of effects on the performance tasks employed here.

The simple reaction time task measures the general responsiveness of an individual in terms of speed. An increase in reaction time may not necessarily be related only to a decrease in arousal but as we will discuss later may be related to an increase in arousal. Within this study, the male sample was significantly faster than the female regardless of the condition. This finding is in agreement with previous reports. There was also a difference between the male and female sample of how they reacted to the effects of the different drug administrations. Within the male sample but not the female sample, all three drug conditions caused a significant decrement in reaction time.

The critical flicker frequency and auditory flutter frequency have been used to measure cortical excitability or general arousal level. An increase in the fusion frequency indicates an increase in the general arousal. Previous studies evaluating the acute effects of hypnotic drugs demonstrated that detectable changes can be found with auditory flutter frequency for up to 10 hours following hypnotic drug administration. The critical flicker frequency, on the other hand, has shown changes with these same hypnotics for up to 8 hours following administration. It is important to establish the effects that a drug may be having on general arousal, as this will affect performance in a differential manner. It has been documented that a possible waning effect of the barbiturates is a phase of excitment.[7] Further it has been demonstrated that as the arousal of a subject increases or decreases beyond an optimal point, performance will begin to deteriorate. These two tasks suggest that there may be an increased arousal present with secobarbital and perhaps a decreased arousal with flurazepam.

Within the vigilance task following flurazepam administration, there was a tendency to respond less with a resulting decrease in the number of correct responses. On the other hand, d' was increased. What this suggests is that the signal was easier to detect from noise but the subject was just responding less. Secobarbital administration, in contrast, produced a tendency to respond more, make more false responses along with correct responses and have a decreased d'. In other words, the subjects were responding more and finding it more difficult to detect a signal. Further, contrary to all previous literature there was little or no habituation or fatigue detected within the one hour task following barbiturate administration. These data strongly suggest the hypotheses that there is a decrease in arousal following flurazepam administration which is affecting performance. With secobarbital and less so phenobarbital we note an increase in arousal which also results in performance decrements.

Finally, in the one task that required sustained concentration (paced math) the secobarbital administration produced the only significant decrement. Again, this supports the hypothesis that by increasing the arousal past the optimal point, the performance efficiency will deteriorate.

In making a decision between the three drugs evaluated in this study, one needs only to look at the number of significant changes that were detected. The analysis summary in terms of number of significant changes supports the further hypothesis that the two barbiturates are more severe in there detectable performance decrements.

This hypothesis carries more impact when one considers that the subjects estimated that flurazepam was more effective in enhancing total sleep time.

Study Two

In this second study, the effects of two commonly used hypnotics on performance was evaluated by employing tasks which have a high face validity and an increased complexity. The hypnotics evaluated were flurazepam, 30 mg and secobarbital, 100 mg. Nine male subjects aged 21-31 years of age with a mean of 24.5 years were tested individually on the same day each week. Each subject was assigned randomly to one of 3 different counter-balanced orders. The subjects were above average in intelligence as all were either medical or graduate students. All of the subjects abstained from the use of any drugs including marijuana and alcohol for the duration of the study.

All performance evaluation was carried out within an accoustically, light and temperature controlled chamber (Industrial Accoustics Co. #402). The subjects were seated in a comfortable reclining chair which was facing a screen on which the various stimuli were projected tachistoscopically from a two-channel projecting tachistiscope (Ralph Gerbrands #G1170). Auditory stimuli and instructions were transmitted between the experimenter and the subject through headsets. This allowed the subjects to be completely isolated from all external or uncontrolled stimuli. All tasks were presented in a completely automated manner via magnetic tape so that each subject was presented exactly the same material in the same order.

Prior to the actual testing period, each subject was thoroughly trained. In each of three complete practice sessions, subjects were allowed to take as much time and to ask as many questions as were necessary to understand the task involved. This training method enabled subjects to become skilled enough in these tasks so that the effects due to learning could be minimized.

Each subject arrived at the sleep laboratory at 10:15 P.M. At 11:00 P.M. the subject was in bed and administered either drug or matching placebo. Lights out was immediately following drug administration. The next morning at 7:00 A.M. the subject was aroused and allowed to dress and fill out the post sleep questionnaire. Breakfast followed which consisted of hospital cafeteria food without any stimulants. Session I began at 8:00 A.M. and finished by 10:00. From 10:00 to 10:15 A.M., a rest period was scheduled. At 10:45, Session II began and ended at 12:15 P.M. Following the end of Session II, a one hour break for lunch (all stimulants excluded) was taken within the hospital cafeteria. Session III and Session IV were repeated in a similar manner with a fifteen minute rest period between the two sessions. Thus, Session III began at 1:15 and Session IV was completed at 5:30 P.M..

Each testing day consisted of four 2 hour sessions with every subject following the same routine within a session. The wobble board task began each session. The subject then entered the chamber and was presented the remaining tasks. Following the completion of these tasks the subject was again tested on the wobble board.

The tasks employed in this study were as follows:

1. Wobble board - This test estimates gross stability or cerebellar coordination similar to the Romberg test. Each subject stood on a slightly raised platform. This platform was capable of torsionally tilting approximately 2 degrees in any direction. Any movement of this platform was detected and in this way, the number of postural changes were tabulated. The subject's task was to stand in a relaxed manner with his eyes open for 30 seconds, visually fixating on a spot on the wall directly in front of him. The subject was then instructed to close his eyes and again remain motionless for 30 seconds. This whole procedure was then repeated for a total of six 30 second samples alternating between the conditions of eyes open and eyes closed. This task resulted in 4 variables which were the number of counts for each of the four conditions.
2. Wilkinson Vigilance - This task and variables were described within the previous study.
3. Shooting Gallery - This test evaluates performance ability where target identification and accuracy are required. The task was patterned after a "penny arcade shooting gallery." In the first phase the subject, following a brief warning tone, responded to a 100 msec flash of light on the screen directly in front of him by aiming and firing a hand held light-gun as quickly and accurately as possible at a small target.

The target was a cadmium sulphide photo cell, one inch in diameter. In this frist phase of this task, fifty stimuli were presented approximately ten seconds apart. The length of time in milliseconds between the onset of the stimulus and the firing of the gun was recorded along with the number of times the target was hit.

In the second phase of this task, the subject responded to a set of visual stimuli presented in the same manner as in the first phase. The visual stimuli were chosen from all possible combinations of four colors (red, green, yellow and blue) and four shapes (triangle, circle, square, and diamond). Four of these color-shape combinations were identified during the training sessions as being correct and requiring a response. All possible combinations were presented in each session. Each of the correct responses (red circle, yellow square, green triangle, and blue diamond) were presented twelve times for a total of forty eight. The remaining twelve possible combinations were presented once each for a total of twelve presentations. Thus, the "no response" rate for any given session was 20%. The response, in this second phase, was again to aim and fire at the target as quickly and accurately as possible. However, this time a decision had to be made whether to shoot or not and if the shot was made, which target of four possible targets was the correct one. The targets were the same as in th first phase except that they were located in the four corners of the screen. In this phase, the latency to shooting response was again

recorded. The number of correct responses (shoot vs. no shoot) was tabulated along with the number of correct hits. In both phases, a hit was counted if at least a corner of the photo cell target was hit by the light spot projected from the gun. This task resulted in eight variables, the reaction time, number attempted and number hits for the simple and choice phase. The choice phase had further the number of correct and false positives.

4. Baddely Reasoning Test - This task samples "higher mental" functioning and has previously been shown to be sensitive to certain drug effects. This test also employed visual stimuli projected onto the screen following a brief warning tone. A series of statements followed by a pair of letters were projected onto the screen, one at a time. Examples of these stimuli are: "A follows B - AB", "B is not followed by A - BA." The subjects task was to push the response key if the statement was correct in relation to the pair of letters that followed. Thus, this task resulted in two variables, the number of correct and false positives.
5. Auditory Flutter Fusion - This task was described within the previous study.
6. Digit Symbol Substitution Test - This test measures short-term memory and consisted of a series of digits that were arbitrarily assigned to a series of symbols. The subject was allowed 30 seconds to study the digit-symbol relationships. His task was to substitute the appropriate symbol for each number represented during the next three minutes. The digit-

symbol relationships were changed with each subsequent presentation of the test. This task had two variables, the number attempted and the number correct.

7. Post Sleep Questionnaire - This questionnaire was described within the previous study.

The analysis of these data was based upon a single score for each day for each subject. These daily subject scores were then analyzed with the Dunnett multiple comparison t-test contrasting the two hypnotic conditions with placebo. The results of this study are described within Table 4. This table presents the mean of each of the three conditions within each of the task variables. Within this same table are the results of the Dunnet analysis in terms of probability values for the contrasts made between each drug condition and placebo.

It can be seen from close inspection of this table that the data analyzed in terms of an overall daily mean do not show any consistent changes in relation to the control on placebo condition. There is only one significant trend. The number correct in the digit-symbol sunstitution test is decreased ($P<.1$) during flurazepam administration (135.6 vs. 123.1). This is supported by a slight suppression of the auditory flutter frequency (56.4 vs. 52.8), d' of the vigilance task (2.1627 vs.2.0207) and the reaction scores seen within the shooting gallery (simple - 510.6 vs. 571.1 ms & choice - 1552.5 vs. 1607.4 ms). None of these values were statistically significant. They are however consistent with the first study.

The analysis of the subjective estimate of each nights sleep derived from the post sleep questionnaire is described in Table 5.

Both flurazepam and secobarbital produced a decrease in the estimate of sleep latency over placebo (58.9 min. vs. 37.7 & 30.5 min. respectively). Both drugs also increased the total sleep time 16. ours vs. 7.1 & 7.0 hours) and decreased the number of wakes (2.4 vs. 0.6 & 1.0). The number of wakes was significantly decreased with both drugs while a significant trend was seen with flurazepam in terms of total sleep time and with secobarbital in sleep latency.

It would appear that the changes seen within the performance tasks in the first study were no trong enough to effect an overall day long score. There was, however, a trend suggesting an overall decrement with flurazepam. If these data were reanalyzed to include the 2 hour sessions as a parameter it may be possible to ascertain whether some of the hypothesized effects seen within the first study were seen within this study. For example, it is possible that changes of an oscillating nature following barbiturate administration are present. While we noted an aroused or excited state after awakening in the morning, we did not note any differences in the average daily response. Thus, it is possible that the original excited state led to one type of error and a subsequent hypoaroused st te to an opposite error, the two cancelling out each other. At this point we can not rule out the possibility that something such as this is going on.

It is also possible that the effects seen in the first study may have been washed out by the increased time between arousal and testing and/or the inclusion of a meal wtihin this second study. In previously reported studies, for example, some of the reported effects which were due to hypnotic drug administration could be changed or eliminated with the simple administration of a stimulant such as coffee. Obviously,

if this is the degree of the decrement, then probably under most conditions there is little to be concerned about. On the other hand, when one considers a manned space flight where split second decisions are extremely important and lives and countless of millions of dollars are at stake, then the effects of hypnotic drugs on performance are critical.

In conclusion, we have noted changes in performance that are due to the administration of a single dose of a hypnotic. These changes appear to be strongest, upon awakening in the morning. In addition, these decremental effects appear to be stronger, at least in the morning, with the barbiturates than with flurazepam. These effects also appear to be detectable on occasion throughout the entire day following drug administration. The question remains regarding how strong these effects really are, e.g., can they be effectively eliminated with a single cup of coffee? In other words, there still remains the question of whether we are at times failing to detect changes in performance because there are no changes there or because our measuring devices are relatively insensitive to real world complexities.

III. Non-Hypnotic Performance Evaluation

Study One

At the request of NASA we evaluated two different kinds of non-hypnotic compounds. The first was to evaluate the amount of barbiturate potentiation that might be expected from the administration of Lomotil. This drug is used routinely on NASA manned space flights to slow down the formation of feces during space flight.

We employed the critical flicker frequency to evaluate this drug in combination with secobarbital. We used four male subjects aged 22-27 who slept in our laboratory for four consecutive nights fc 8 hours each night. The first night was for adaptation purposes so no evaluation was done. The first two nights, the subjects received matching placebo at h.s. The third and fourth nights the subjects received the active drug which was secobarbital 100 mg plus Lomotil 2.5 mg at h.s. The morning following nights 2,3 and 4, each subjects' critical flicker frequency was established approximately one half hour after arousal.

There was a decrease in fusion frequency from 56.1 on baseline to 55.0 and 54.1 during drug administration, days 1 and 2 respectively. The difference between the fusion frequency obtained on the second day of drug administration and baseline was significant ($P < .05$).

The morning evaluation of arousal was further supported by the subjects' reports of side effects of drowsiness throughout the day. These subjective symptoms of drowsiness did not decrease on the second day of administration, rather they increased.

These data suggest that the use of Lomotil in conjunction with secobarbital can be decremental to performance. As we would have expected, rather strong changes in several performance measures occurred in conjunction with the decreased arousal. This hypothesis is clear even though we did not include a control group. Our data reported in Study One with secobarbital alone, suggested an increase in arousal with subjects tested at approximately the same time following arousal from sleep. Further, in two previously published studies where secobarbital was administered for several consecutive days, the effects detected by a card sorting task and the Wilkinson. Vigilance task decreased across the several days of administration. Thus, the results of this study support the hypothesis that a barbiturate related decrement can be potentiated with the simultaneous administration of Lomotil. This could be a potentially dangerous combination in someone performing an extremely critical job.

Study Two

At a further request of NASA we set up to evaluate the effects of two motion sickness compounds upon performance that are commonly used by NASA astronauts. These were a combination of a) scopalamine (.35 mg) and dexedrine (5 mg) and b) promethazine (25 mg) and ephedrine (50 mg). We were able to monitor only three subjects in a pilot study in preliminary work with the latter combination. However, the clinical investigation committee of our institution was unable to allow further work on either of these compounds because they were not FDA approved nor was there an IND number available.

This study represents the furthest evolvement of the Performance Evaluation Laboratory. Within this study, we completely redesigned the tasks such that the tasks employed were more complex and were beginning to yield some measures of face validity. The major difference between this study and the previous evaluations was that a single complex task battery was used rather than a set of separate tasks. The multiple-complex battery was developed within our laboratory along the lines of that described by Alluisi.[1] The task itself requires a greater level of skill than any we had employed previously, primarily because it required time sharing of multiple simultaneous tasks. This variable of time sharing is considered to be one of the most important variables required to make a task relatable to the complexity of the "real world" (Chiles).

The subjects were seated within the previously described accoustically controlled chamber in a reclining chair. A response panel was constructed which rested on the arms of their chair and housed the response keys. A movable stimuluus panel was positioned above the response panel and housed the meters and warning lights. Above the stimulus panel and on the wall was located a screen on which were projected stimuli via a projecting tachistoscope.

The response panel consisted of 6 (series 2N) lighted "microswitches". These panel switches have an exposed surface area of 1" x 3/4". They were oriented in an 8" arc 2 1/4 " apart. The set of switches to be used and the conditional set of stimuli to be monitored were identified by whether or not a switch was lit and by its color. The stimulus panel consisted of a panel 12" x 18". On this panel were located a pair of warning lights which shifted from yellow to red and a pair of meters (3" x 1 1/2") which were continually oscillating.

The multiple-complex battery was developed from a set of tasks which were as follows:

(1) The Wilkinson Vigilance - this task has been previously described.

(2) Probability Monitoring - The two meters on the response panel were driven such that they were continually oscillating with a mean of zero. Periodically, this mean would shift slightly. The subjects' task was to respond to this mean shift as quickly as possible by pressing the appropriate response key. If the subject responded within 10 seconds, a response latency in milliseconds was recorded. If the subject responded within 3 minutes, a correct response was recorded and if the subject did not respond within 3 minutes an error was recorded. When the subject responded or the 3 minute interval was surpassed, the meter reset itself again to a mean of zero. The two meters were activated independently and in a quasi-random manner.

(3) Simple Reaction Time - This task has been previously described.

(4) Target Identification - The stimuli presented in the shooting gallery task (previously described) were projected on the screen with a projecting tachistoscope. The subjects' task was to respond as quickly as possible to the correct key. There were 4 possible responses and one inhibited response - each of which were equally likely. The number correct and incorrect were recorded along with the reaction time in terms of milliseconds.

(5) Warning Lights Monitoring - This task consisted of two pairs of lights which periodically shifted from yellow to red. The subjects' task was to respond as quickly as possible by pressing the appropriate key on the response panel. As with the probability monitoring task the time to respond was recorded in milliseconds if the subject responded in less than 10 seconds. If he responded in less than 3 minutes a positive response was recorded. A negative or missed response was recorded if the subject did not respond within 3 minutes. If the subject responded or the 3 minute interval was up without a response, the light was reset to its original setting. The two warning lights functioned independent of each other and of the probability monitoring task.

(6) Wobble Board - This task has been previously described.

The three subjects were all male between the ages of 22 and 25. They were trained with three complete training sessions as had been previously employed. The subjects remained in the hospital or laboratory for the duration of the 5 day study. A drug or matching placebo was administered each day at 8 A.M. and 8 P.M. On days 1 and 2, the subjects received placebo and on days 3 through 5 the subjects were administered the promethiazine and ephedrine compound. Three 2-hour testing sessions were employed each day at 8:30, 1:30 and 5:30. Each subject was assigned to one of these sessions. Thus, we confounded subjects with testing sessions.

The subject began the multiple complex battery when the fourth response key from the left turned red. This signaled to the subject

that the auditory vigilance task was to be monitored by itself. At the end of the first half hour, the switch light in this task along with the two keys to the right of it were lit green. This change signaled the subject that the auditory task was to be monitored along with the probability and warning light monitoring. At the end of the second half hour, the auditory task ceased and the subject had to monitor only the probability and warning light tasks. At the end of the third half hour, tne fourth key from the left was again lit (red) by itself. This was followed by a warning tone and a series of 50 simple reaction times to a 10 msec flash. The first 4 switches from the left then came on (yellow) and following the next warning tone, the choice stimuli were presented on the screen and the subject completed 64 choice stimuli responding with the appropriate key. This completed the multiple complex battery task. The subject was removed from the chamber and a wobble board assessment was obtained. The results of this study are described in Table 6. This table has a mean value for the baseline and for each of the 3 days of drug administration. It also has the probability level that a specific drug condition was different from the baseline based upon the Dunnett multiple comparison test.

The strongest effects were obtained within the vigilance task. In this task a decrease was detected in the number of correct positives across the three days of drug administration (9.3, 8.9 and 10.3) which contrasted with baseline (11.7). The number of false positives was significantly decreased (7.7, 5.6, 2.3 vs. 16.0). The d' level increased slightly on day 1 and 2 (1.8875 and 1.8977 vs. 1.7197) and

significantly ($P < 0.1$) on day 3 (2.3745). The number attempted on this task was likewise significantly decreased across the 3 days (17.0, 14.7 and 12.7 vs. 27.7 at a probability of .1, .05 and .05). The reaction time decreased initially on day 1 (858.9 vs. 809.5) and then increased on day 2 (883.7) and day 3 (962.1).

Within the probability monitoring task there was a non significant increase in the percentage detected in the > 10 sec < 3 min category across all 3 days (15.3 vs. 26.9, 23.6 and 27.2). The warning light monitoring task demonstrated a similar increase (9.4 vs. 23.3). The target identification phase also showed this same initial decrement. In other words, day 1 reaction time was 714.1 vs. 648.3 for baseline and the number correct for day 1 was 43.3 as compared to 47.3.

Within the total multiple complex task, there was a decrement detected within the three subjects following administration of the motion sickness compound. The results are consistent with the expected generalized effects. In other words, the reported complaint of the astronauts and the expected side effects of these drugs would have predicted a carry over in terms of drowsiness during the day. That this decrement appears to increase with continued drug administration clearly in the case of the vigilance task and perhaps also with the monitoring type tasks, should be taken with great alarm. The fact remains that in order to show statistical significance with only 3 subjects, the effect must be large and consistent. Thus, a great deal more work needs to be done to evaluate the safety of this and the other motion sickness preparation. Finally, this study clearly

demonstrates that our Performance Evaluation laboratory has attained the sensitivity and utility to answer certain practical questions.

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Table 1A

Long Term Hypnotic Administration
Pentobarbital 100 mg

Source	BSLN	STD	ITD	LTD	W_1	W_2
Sleep Latency	29.4	22.3	29.9	27.7	28.6	31.0
WTASO	32.8	19.2 †	31.3	27.9	32.1	32.3
Total Wake Time	62.2	41.5 †	61.2	55.6	60.7	63.3
Number Wakes	24.2	17.4 o	18.2 o	17.5 o	22.2	25.8
% REM	22.5	21.7	20.8	21.5	24.4	22.7
% Slow Wave	7.9	5.0	7.5	9.5	10.2	9.8

Table 1B

Flurazepam 30 mg

Source	BSLN	STD	ITD	LTD	W_1	W_2
Sleep Latency	38.8	23.6	16.8	24.7	34.9	39.5
WTASO	28.3	10.9 o	12.5 *	13.8 *	24.9	13.0
Total Wake Time	67.1	34.5 †	29.4 †	38.5 †	60.0	52.5
Number Wakes	14.8	8.8 o	10.3	12.2	16.7	15.7
% REM	26.2	22.9 o	19.4 †	22.2 c	25.5	25.2
% Slow Wave	16.4	9.2 †	7.2 †	5.6 †	6.0 †	13.0

P< .10 = *
P< .05 = o
P< .01 = †

Table 2

Mean Performance Measures for Sex and Total Samples

SOURCE	PLACEBO			FLURAZEPAM 30 mg			SECOBARBITAL 100 mg			PHENOBARRITAL 100 mg		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Simple Reaction Time	229.9	311.5	270.7	253.0 °	309.6	281.3	252.0 °	294.9	273.4	251.2 °	300.1	275.7
Critical Flicker Frequency	4` 4	50.8	49.6	46.4	50.8	48.6	48.3	50.6	49.5	47.5	49.4	48.4
Auditory Fusion Frequency	71.2	70.0	70.6	71.2	66.7	69.0	75.0	70.8	72.9	71.7	70.4	71.0
Vigilance Correct Positive	22.8	15.9	19.3	22.1	14.5	18.3	23.5	18.1	20.8	21.4	13.0	17.2
Vigilance False Positive	3.8	4.2	4.0	2.5	5.5	4.0	4.8	6.4	5.6	4.0	5.1	4.6
Vigilance Number Attempted	26.5	20.1	23.3	24.6	20.0	22.3	28.1	24.5	26.3*	25.4	18.1	21.8
Vigilance d'	2.3146	2.1640	2.2393	2.5526	2.2136	2.3831	2.2278	2.0662	2.1470	2.5346	1.8941	2.214
Vigilance Correct Positive Slope	2.5	1.0	1.8	2.5	0.2	1.4	-0.8 +	0.8	0.0	0.4°	0.8	0.6
Vigilance Reaction Time	673.1	783.8	728.4	730.9	747.1	739.0	663.4	817.1	740.2	716.6	813.9	765.2
Paced Math Number Correct	54.0	46.9	50.4	50.4	46.5	48.4	51.4	44.1	47.8	46.5	46.8	46.6
Paced Math Number Attempted	59.6	55.4	57.5	53.8	55.2	54.5	57.9	55.0	56.4	54.6	52.2	53.4
Paced Math Percent Correct	91.2	82.5	86.9	92.8	79.5	86.1	88.6	78.4	83.5 °	86.1	86.4	86.2
Pursuit Rotor	859.4	568.9	714.1	850.5	600.7	725.4	886.0	499.0	692.5	882.5	635.4	759.1

P<.10 = *
P< .05 = o
P< .01 = +

Table 3

Subjective Sleep Estimate

	PLACEBO			FLURAZEPAM			SECOBARBITAL			PHENOBARBITAL		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Sleep Latency	20.6	28.1	24.4	15.0	22.5	18.8	11.2	20.6	15.9	16.9	26.2	21.5
Total Sleep Time	7.2	6.9	7.0	7.7	7.3	7.5 °	7.4	7.2	7.3	7.3	7.2	7.2
Number Wakes	2.8	3.0	2.9	3.0	2.4	2.7	3.0	2.4	2.7	3.3	2.4	2.8

P< .10 = *
P< .05 = o
P< .01 = †

Table 4

Hypnotic Drug Mean Performance Measures and Probability Values

SOURCE	PLACEBO	FLURAZEPAM	SECOBARBITAL
Wilkinson Vigilance			
d'	2.1627	2.0207	2.1218
Number Attempted	24.0	21.7	24.6
Reaction Time	750.3	737.2	693.7
Shooting Gallery			
Simple Reaction Time	510.6	571.1	523.2
Number Attempted	49.8	50.0	49.2
Number Hits	30.4	25.5	27.2
Choice Reaction Time	1552.5	1607.4	1589.7
Number Attempted	47.7	48.0	48.0
Number Hits	20.6	19.4	17.9
Number Correct Positives	47.6	47.6	47.4
Number False Positives	0.1	0.3	0.3
Baddeley			
Number Correct Positives	29.7	29.8	29.5
Number False Positives	1.4	1.4	1.4
Auditory Flutter Frequency	56.4	52.8	54.8
Digit Symbol Substitution Test			
Number Attempted	135.9	123.5	133.1
Number Correct	135.6	123.1 *	132.3
Wobble Board			
Pre-Eyes Opened	57.0	56.6	59.7
Pre-Eyes Closed	101.2	103.1	100.7
Post-Eyes Open	67.9	65.0	60.0
Post-Eyes Closed	110.1	105.9	96.6

P< .10 = *
P< .05 = o
P< .01 = †

Table 5

Subjective Sleep Estimates

	PLACEBO	FLURAZEPAM	SECOBARBITAL
Sleep Latency	58.9	37.7	30.5 *
Total Sleep Time	6.5	7.2 *	7.0
Number Wakes	2.4	0.6 †	1.0 o

P< .10 = *
P< .05 = o
P< .01 = †

Table 6

Mean Performance Measures for Motion Sickness Preparation

SOURCE	BSLN	DRUG		
		Day 1	Day 2	Day 3
Vigilance				
Number Correct Positive	11.7	9.3	8.9	10.3
Number False Positive	16.0	7.7 °	5.6 †	2.3 †
d'	1.7197	1.8875	1.8977	2.3745
Number Attempted	27.7	17.0 *	14.7 °	12.7 °
Reaction Time	858.9	809.5	883.7	962.1
Probability Monotoring				
Reaction Time	3017.5	3806.9	3008.6	3309.4
% > 10 sec < 3 min	15.3	26.9	23.6	27.2
Warning Light Monitoring				
Reaction Time	1015.0	1710.8	1437.8	1843.0 *
% > 10 sec < 3 min	9.4	23.3	9.2	19.3
Simple Reaction Time	288.7	323.2	288.6	260.8
Target Identification				
Reaction Time	648.3	714.1	644.8	648.2
Number Correct	47.3	43.3	44.7	45.3
Wobble Board				
Eyes Open	26.8	28.7	19.0	20.11
Eyes Closed	108.4	90.0	59.9	62.7

P< .10 = *
P< .05 = o
P< .01 = †