

- (1) **Title of grant:** Individual Differences in Response to Sleep Deprivation: Assessment of Fatigue Following Sleep Loss
- (2) **Type of Report:** Summary of Research
- (3) **Name of Principal Investigator:** Mary A. Carskadon, Ph.D.
- (4) **Period covered by the grant:** 11/15/1994 to 11/15/1997
- (5) **Name and address of the recipient's institution:** E.P. Bradley Hospital
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Introduction

Previous work has indicated that a small but significant number of participants in sleep deprivation studies or in simulated shift work experiments manifests an exaggerated performance decrement when they reach a critical point in the experiment, usually near the trough of the circadian cycle or the middle of the night. Those who show this exaggerated response do not appear to differ from other normal volunteers in any substantial way according to usual screening criteria or baseline values. The present study aims to examine factors that may provide the basis for this extreme response.

We propose that a preexisting sleep deficit—as manifested by low values on the Multiple Sleep Latency Test (MSLT)—may account for extreme responders. Roth and colleagues (1993) have shown that among normal volunteers screened for a variety of studies, approximately 20 to 25 percent show low (≤ 6 minutes) MSLT scores on a consistent basis, whereas a like proportion shows consistently high MSLT scores (≥ 13 minutes). Additionally, studies by this group have indicated that subjects with low MSLT scores may suffer from chronic insufficient sleep (Roth et al., 1993), as further substantiated by the finding that they have consistently higher nocturnal sleep efficiency and that their MSLT scores rise to normal values when sleep is extended (Roehrs et al., 1996). We hypothesize that the short MSLT subjects have a significant long-term sleep deficit that leads to a marked intolerance for sleep deprivation or shift work.

We further suggest that this sleep debt may signify an increased sleep need in these individuals that is not met either due to personal preference or to societal pressures (or both). If this speculation is accurate, then we predict that the tolerance for sleep deprivation in such individuals can be increased by "pretreatment" with sleep extension. Thus, the present study is designed to test the following two hypotheses:

- subjects with nominal sleep patterns who have low MSLT scores (e.g., Sleepy subjects) will show an exaggerated response (performance decrement) to sleep loss compared to subjects who have high MSLT scores (Alert subjects) on a nominal sleep schedule.
- when permitted to extend sleep—thus discharging their sleep debt—the Sleepy subjects will show a sleep-loss response resembling that of the Alert subjects.

Participants

Participants were recruited by advertising in local newspapers for normal healthy individuals ages 18 to 35 interested in taking part in a sleep study. Initial screening consisted of a telephone interview in which prospective participants were asked about recent medical history, habitual sleep schedule, recent substance use, and current and recent work schedules. Further participation was excluded for those who were outside the age range, reported habitual nocturnal sleep less than 7.5 hr or greater than 8.5 hr, inconsistent sleep schedule, history of sleep disorders (including family history of narcolepsy or sleep apnea syndrome), current medical illness, history of psychiatric illness, excessive (>10 per week) alcohol use, recreational drug use in the past month, habitual cigarette smoking (more than 5 cigarettes per day), current use of medications that might affect sleep or wakefulness (such as sedatives, anti-convulsants, antihistamines, antidepressants), or history of shift work within the last 3 months. Participants who passed the initial telephone screening completed a second phase of screening.

Screening Phase 2 included two nights wearing a wrist activity monitor at home, followed by a one-day in-lab session for the Multiple Sleep Latency Test (MSLT). Home actigraphic monitoring was used to confirm that the participant's normal sleep was within the cutoff range of 7.5 to 8.5 hours. MSLT was used to determine the participant's group designation. The MSLT is a measure of sleep tendency in which an individual is requested to attempt to fall asleep at 2-hr intervals in standard conditions of minimal environmental stimulation (Carskadon and

Dement, 1977; Carskadon et al., 1986). The variable of interest is the interval between the start of the test and the first 30-sec epoch scored as sleep. Five tests were administered at 2-hr intervals across the screening day. Cutoffs for inclusion were average sleep latency for the 5 naps of ≤ 6 min (Sleepy group) or average of ≥ 12 min (Alert group). Participants who were not compliant with the screening protocol or whose MSLT scores fell in a range between these averages were excluded from further participation.

Twenty-eight volunteers fulfilled the screening requirements. Of this group, five declined to participate in the full study, two completed the first sleep loss study but were unable to return for the second, and three were asked to leave before the study ended due to noncompliance or illness. Thus, 18 volunteers completed all aspects of the study. These participants included 9 in the Sleepy group (5 male, 4 female; mean screening MSLT = 4.6 ± 1.5 min) and 9 in the Alert group (4 male, 5 female; mean screening MSLT = 15.8 ± 2.4 min). The average age of participants in the Sleepy group was $22.8 (\pm 4.3)$ years; mean age of Alert participants was $24.2 (\pm 3.6)$ years.

Methods

Participants took part in the study for three weeks, during which they underwent a 40-hr sleep loss during week 1 and week 3. Week 2 included actigraphically monitored sleep at home to provide adequate time to recover from the in-lab sleep loss experience. Participants were assigned at random to a counterbalanced order of conditions stratified within group. Every participant experienced both "pretreatment" sleep schedules. The schedules during the Baseline phases of the protocol included either 8 (midnight to 0800) or 10 (2200 to 0800) hours in bed attempting to sleep for the five consecutive nights before the sleep loss procedure. The first two of these five nights occurred at home. Participants wore the wrist actigraph, kept a sleep-wake diary, and telephoned the laboratory at bedtime and rise time. On the third and fourth nights, participants reported to the laboratory before bedtime and slept in the lab. Sleep on these nights was monitored only by wrist actigraphy. The in-lab portion of each trial began on the fifth night before sleep loss, with polysomnographically monitored sleep. A 40-hr sleep-loss vigil was followed by a recovery sleep episode of 20 hours (midnight to 2000).

From the start of each in-lab session through the end of recovery (approximately 70 hr), participants wore electrodes to measure electroencephalogram (EEG) from central (C3 and C4) and occipital (Oz) placements, electrooculogram (EOG) from right and left outer canthi, and chin electromyogram (EMG). Continuous recordings of EEG and EOG were made using portable 8-channel Medilog recorders. For all sleep episodes (baseline and recovery nights and all MSLTs), simultaneous chart recording of EEG, EOG, and EMG was performed using Grass Model 7 polygraphs. These records were scored in 30-sec epochs according to standard criteria (Rechtschaffen and Kales, 1968).

During the sleep-loss sessions, sleepiness and performance were assessed with the following measures. Introspective measures of sleepiness/alertness included the Stanford Sleepiness Scale (SSS, Hoddes et al., 1973), a visual analog (VAS) sleepiness scale, the fatigue scale of the Profile of Mood States (POMS, McNair et al., 1971), and the deactivation-sleepiness scale of the Activation-Deactivation Adjective Checklist (ADACL, Thayer, 1978). The SSS and VAS were administered half-hourly, the ADACL every 2 hours, and the POMS every 4 hours. Performance was assessed with the Psychomotor Vigilance Task (PVT, Dinges et al., 1994) of simple visual reaction time, a Divided Attention Task (DAT, Roehrs et al., 1989), and a 4-word-pair probed memory recall task. These tests were given as a battery every 2 hours following the MSLTs.

The variables were analyzed using repeated measures MANOVA, with Time (into the sleep loss protocol) as the repeated measure to assess the effects of Group (Sleepy vs. Alert) and Condition (8 or 10 hours of presleep).

Results

Every variable showed a significant ($p < .001$) effect of Time. This effects is illustrated in the first series of illustrations in the appendix (Figures 1-3), showing a decline in scores across trials, particularly those trials occurring during the usual sleeping hours. As illustrated, participants reported feeling sleepier on the VAS (Figure 1), the deactivation-sleepiness scale of the ADACL (Figure 2), and the POMS fatigue scale (Figure 3). Not illustrated, but also statistically significant, participants were sleepier on the objective (MSLT) sleepiness measures, and performance also declined significantly on all performance tests. These are all expected effects of sleep deprivation.

Our first main hypothesis anticipated a significant Group effect, with the Sleepy participants faring worse than the Alert group during sleep deprivation. Three of 14 measures analyzed demonstrated a significant Group effect supporting this hypothesis. The MSLT (Figure 4), mean central reaction time on the DAT, and mean peripheral reaction time on the DAT showed the anticipated Group effect. The Sleepy group was sleepier on the MSLT and slower on the DAT reaction times throughout the majority of the 40-hour protocols. When we examined significant Group-by-Time interactions, several additional variables showed a significant effect demonstrating that the Sleepy group was more greatly impaired than the Alert group at times during the sleep deprivation procedure. These findings are illustrated in the Figures 5-9 in the appendix. As shown in Figure 5, Sleepy and Alert groups were distinguished on the POMS fatigue scale until approximately 8 am, after sleep loss.

Two other introspective measures—the VAS (Figure 6) and the deactivation-sleepiness scale of the ADA CL (Figure 7) showed a similar pattern. Figures 8 and 9 illustrate that the grand median reaction time on the PVT and the slowest 10% of trials on the PVT were generally worse (slower) for the Sleepy group, with occasional spikes of profoundly worse performance in the Sleepy participants. [Please note: in Figure 9, the slowest 10% reaction time scores have been subject to a mathematical transformation in which the poorer scores are represented by a downwards deflection.] Thus, eight of the variables demonstrated some significant decrement in Sleepy versus Alert subjects during the study.

Our second major hypothesis predicted that the performance of the Sleepy group would be preferentially enhanced by extending the predeprivation sleep quotient. Three variables demonstrated a significant Group-by-Condition interaction, two of which support the hypothesis. Two of the DAT variables—mean central (Figure 10) and mean peripheral (Figure 11) reaction time—showed significantly better performance with 10 versus 8 hours of presleep (significant condition effects were found): performance enhancement with 10 hours of sleep in the Sleepy group was greater for both measures than that of the Alert group. The other Group-by-Condition interaction was seen for the total number of errors on the PVT (Figure 12), in which the Alert group performed better on 10 hours of sleep than 8 hours of sleep, while the sleepy performed worse with 10 hours of sleep than with 8 hours of sleep.

Discussion

These data indicate that preexisting sleepiness indeed has a significant impact on subjective sleepiness and certain aspects of performance during sleep deprivation. In general, sleepier individuals feel worse and perform worse than those who are alert. The improvement of performance with extended sleep also indicates that sleep extension may be a useful countermeasure, with its benefits most beneficial for individuals who are sleepy when obtaining a nominal amount of sleep (8 hours). One problematic issue in the interpretation of this study arises when considering the impact of repeated assessments of sleep deprivation. Although not detailed in this report, a number of measures demonstrated a significant effect of or interaction with order of condition presentation, in which performance and other measures were worsened during the second session regardless of the sleep condition. Thus, motivation or other effects complicate the interpretation of the findings.

In summary, human error underlies more than two-thirds of air carrier accidents (Nagel, 1988). Human factors accidents can result from diverse causes, but some types of errors, such as inattention or failure to monitor, detect, and respond to critical information are more common and often more costly. It has long been recognized that fatigue is a major source of accidents of inattention (Dinges & Graeber, 1989; Dinges et al., 1989; Rosekind et al., 1993). The Fatigue Countermeasures Program in the Flight Human Factors Branch at NASA-Ames has as one of its primary objectives the development of techniques that can reliably detect fatigue states (e.g., sleepiness, reduced vigilance) in operational environments for the purpose of preventing performance impairment (Rosekind et al., 1993). Although human error is an unequivocal factor in aviation accidents, and although fatigue is often cited as a source of such errors, clearly not every fatigue-inducing event or person in whom fatigue might be considered to be problematic results in an incident or accident. Studies such as the one performed here provide important information regarding potential factors that may help explain individual differences in susceptibility to fatigue-related adverse events.

Negative Inventions Statement: No inventions came out of this research.

Inventory Report of Federally Owned Property: No federally owned property is at the principal investigator's location. One computer (Macintosh G3) was purchased with the grant; four PVTs are on permanent loan from David F. Dinges, Ph.D., but are not federally owned.

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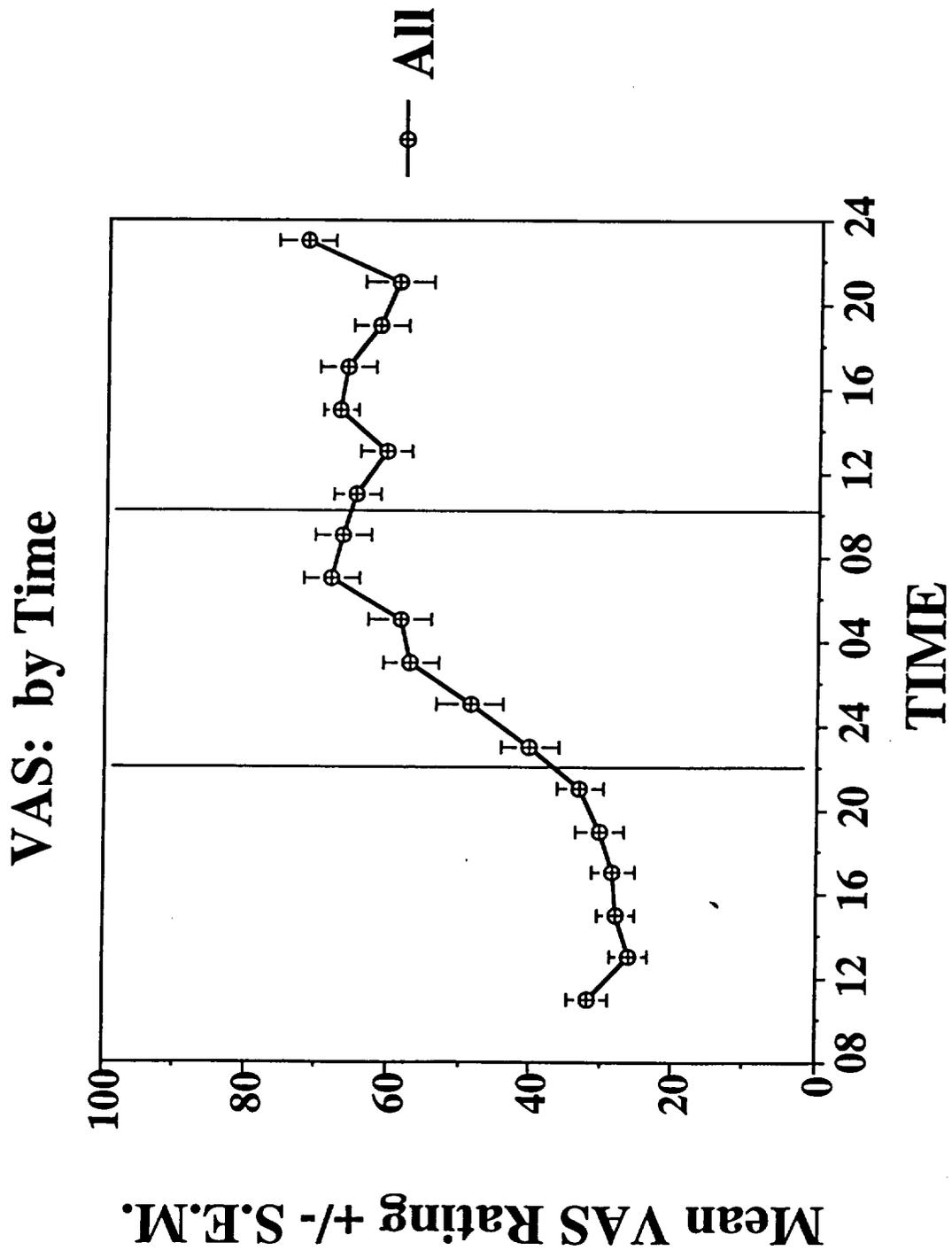


Figure 1

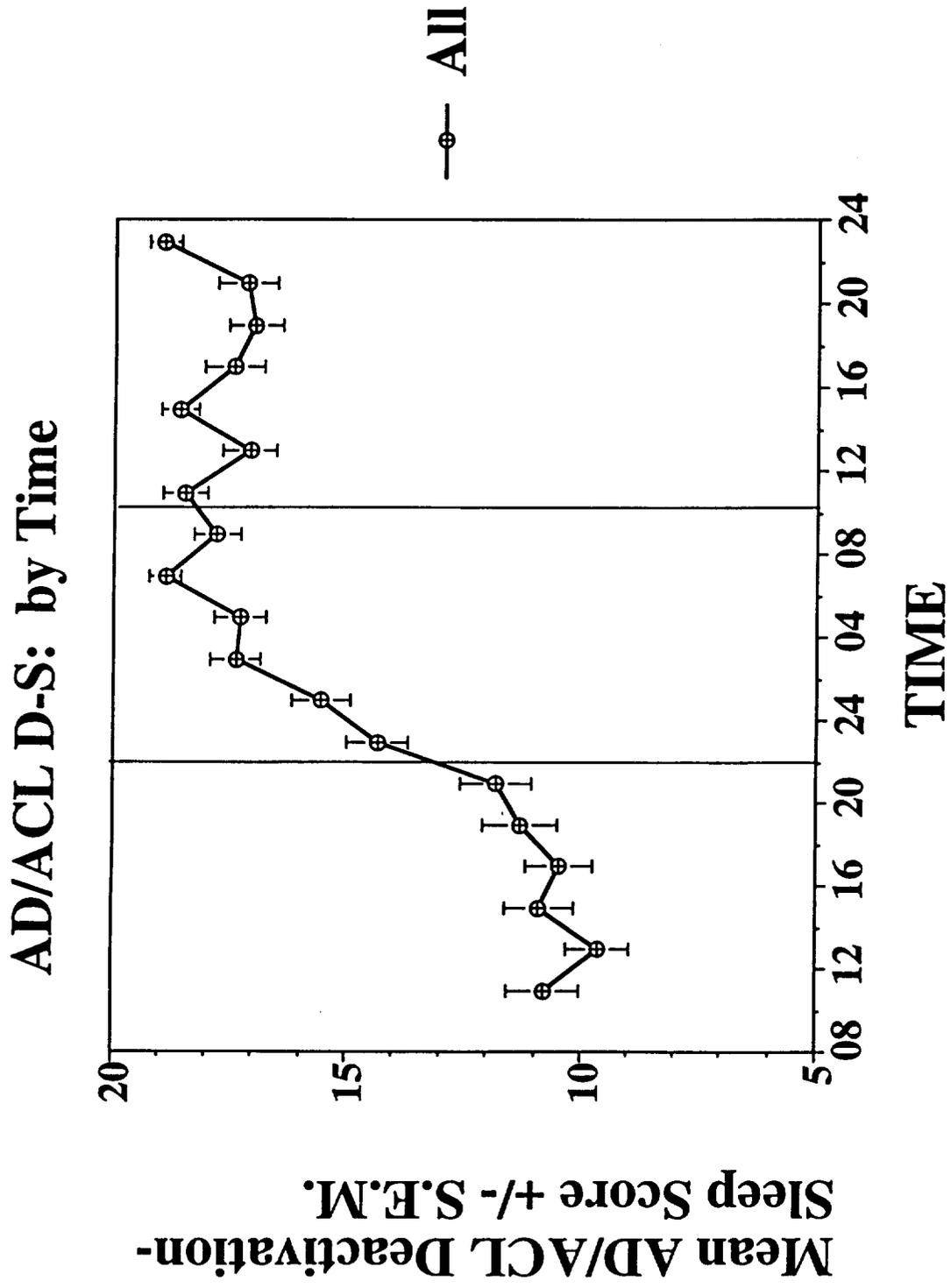


Figure 2

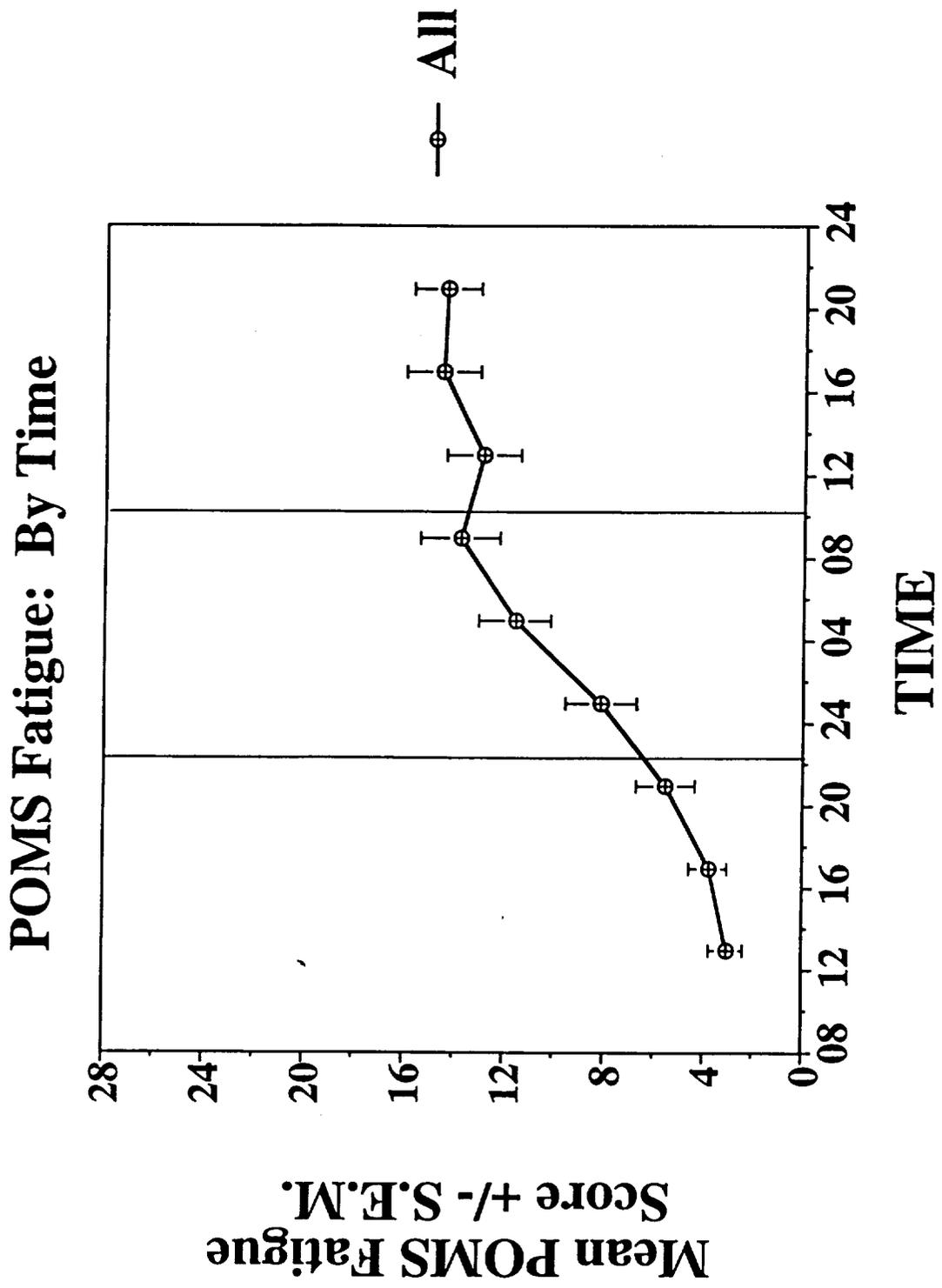


Figure 3

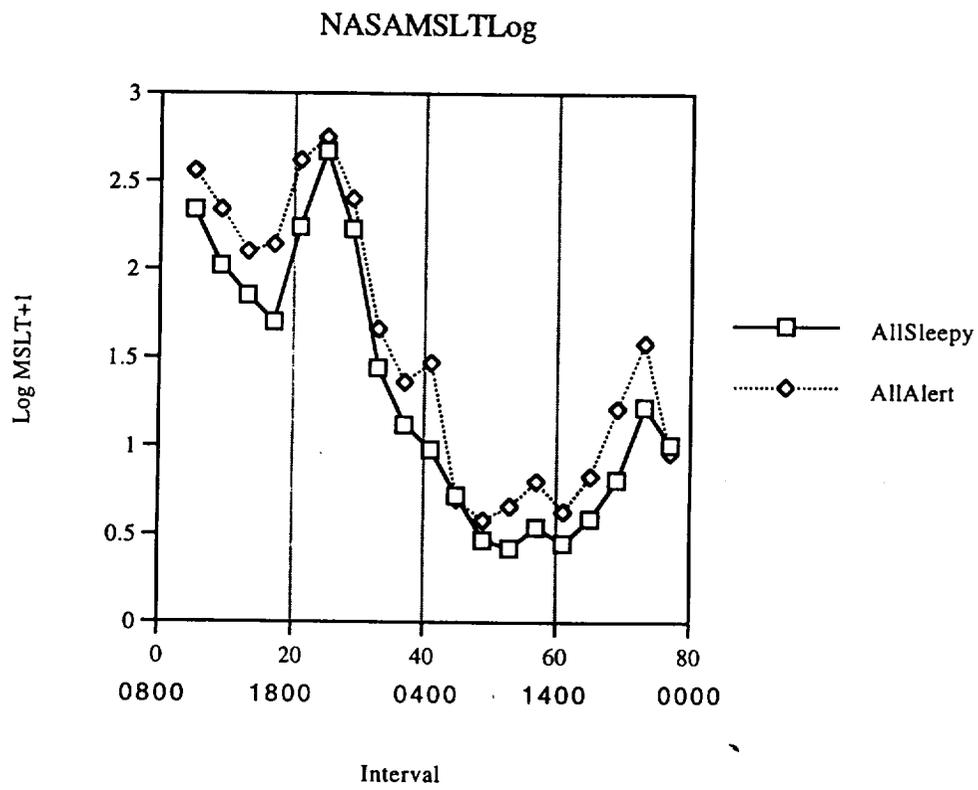


Figure 4

POMS Fatigue: Group by Time

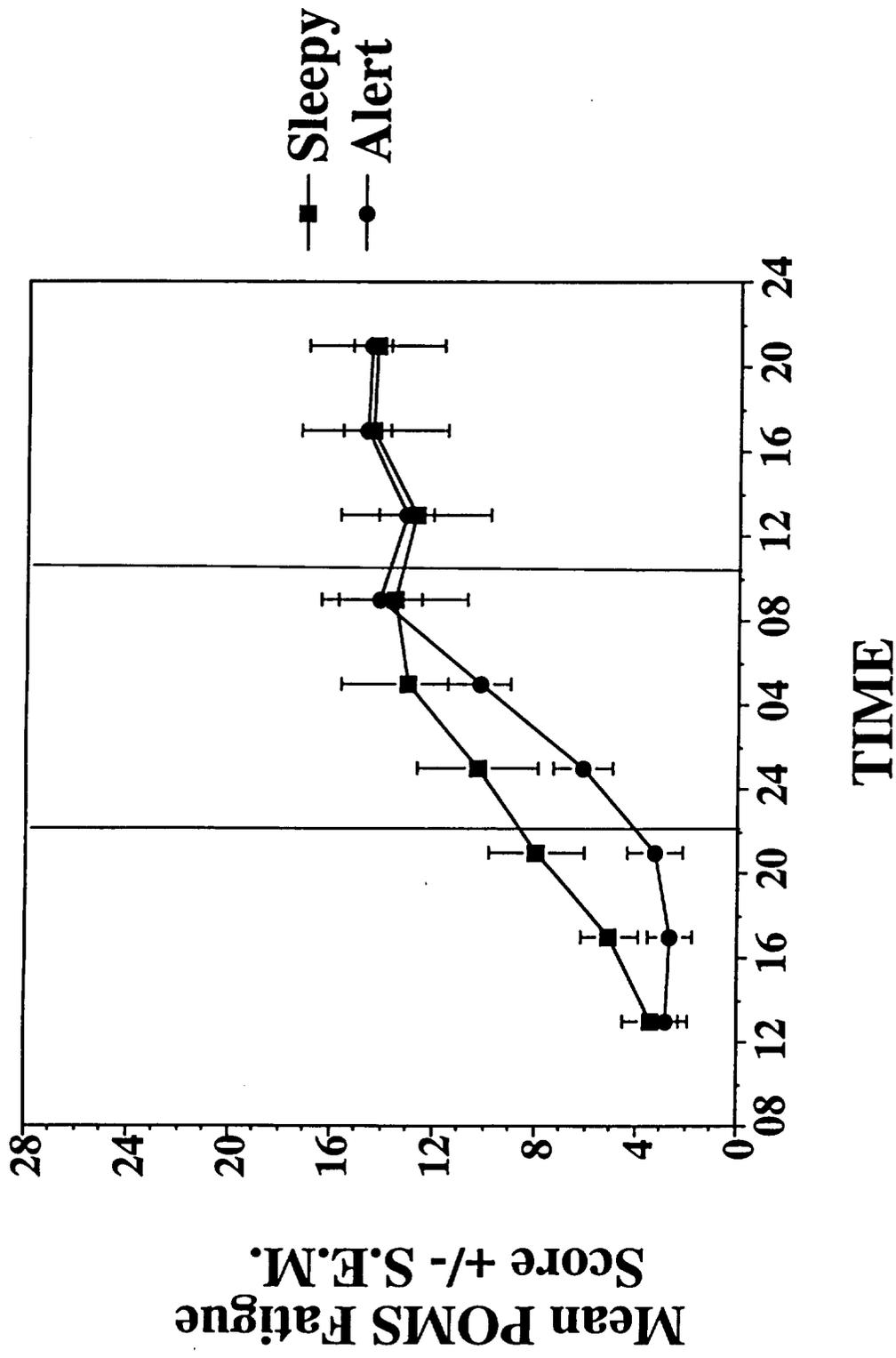


Figure 5

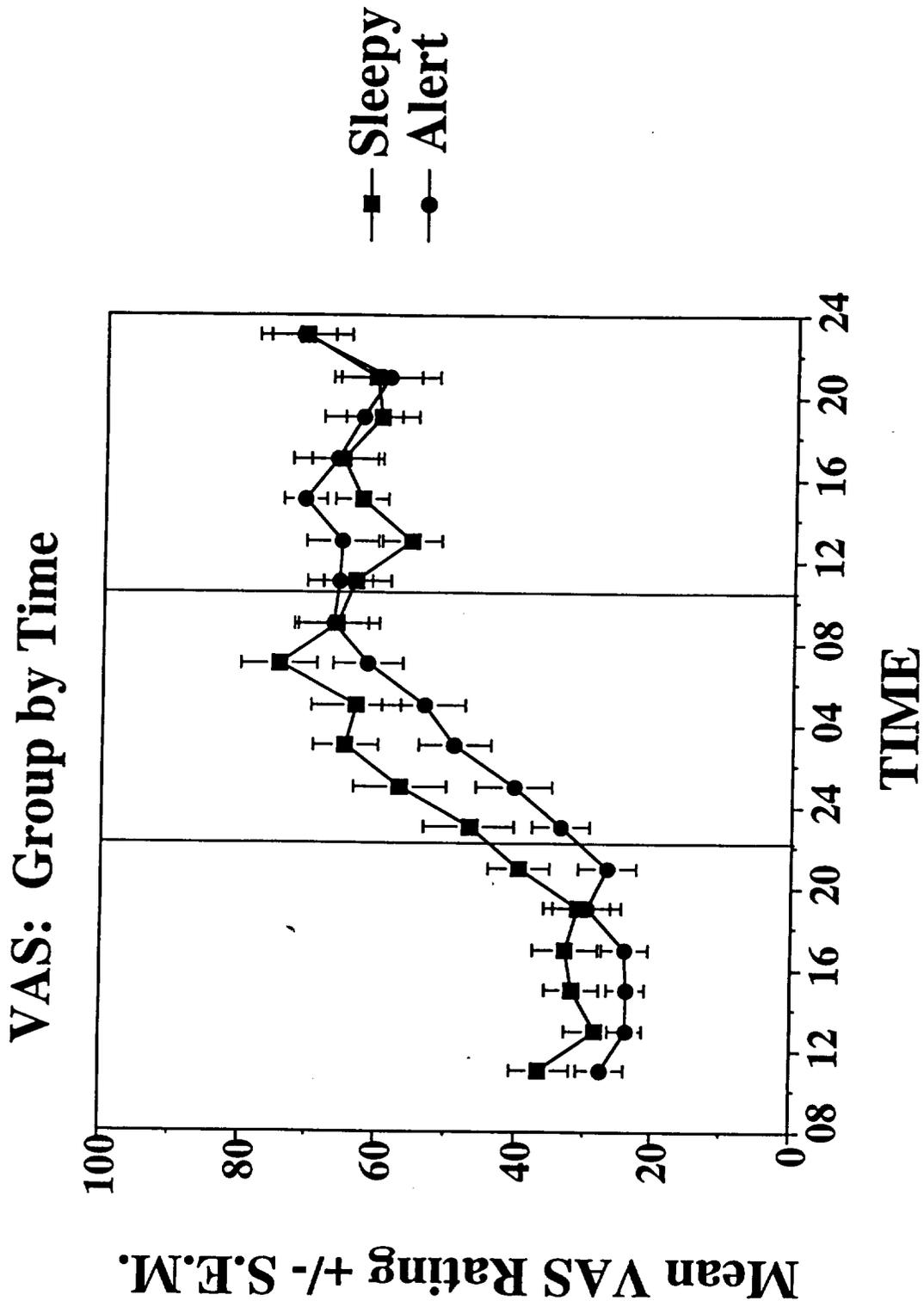


Figure 6

AD/ACL D-S: Group by Time

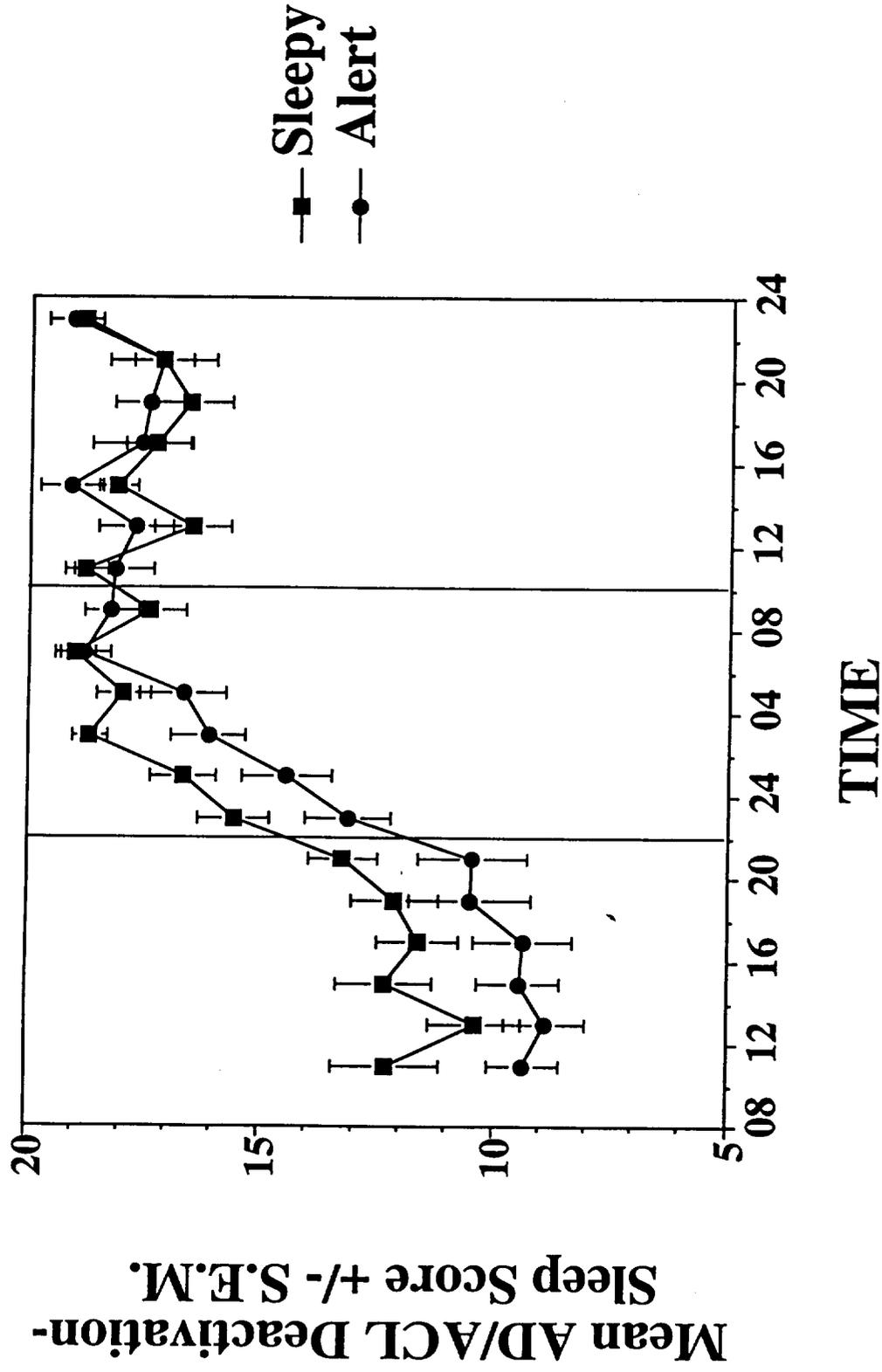


Figure 7

PVT: Grand median response time: by group

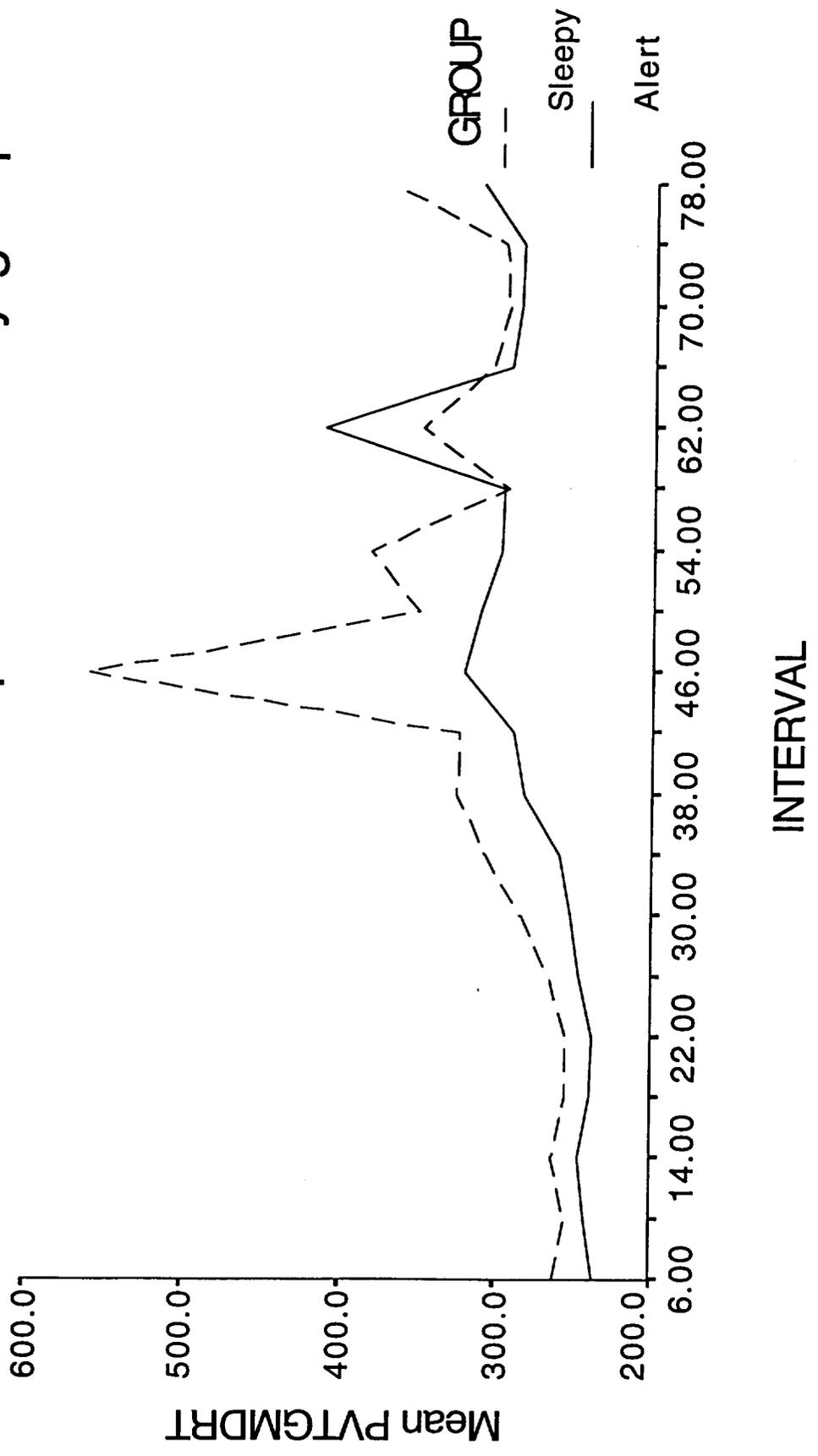


Figure 8

PVT: Slowest 10% of responses: by group

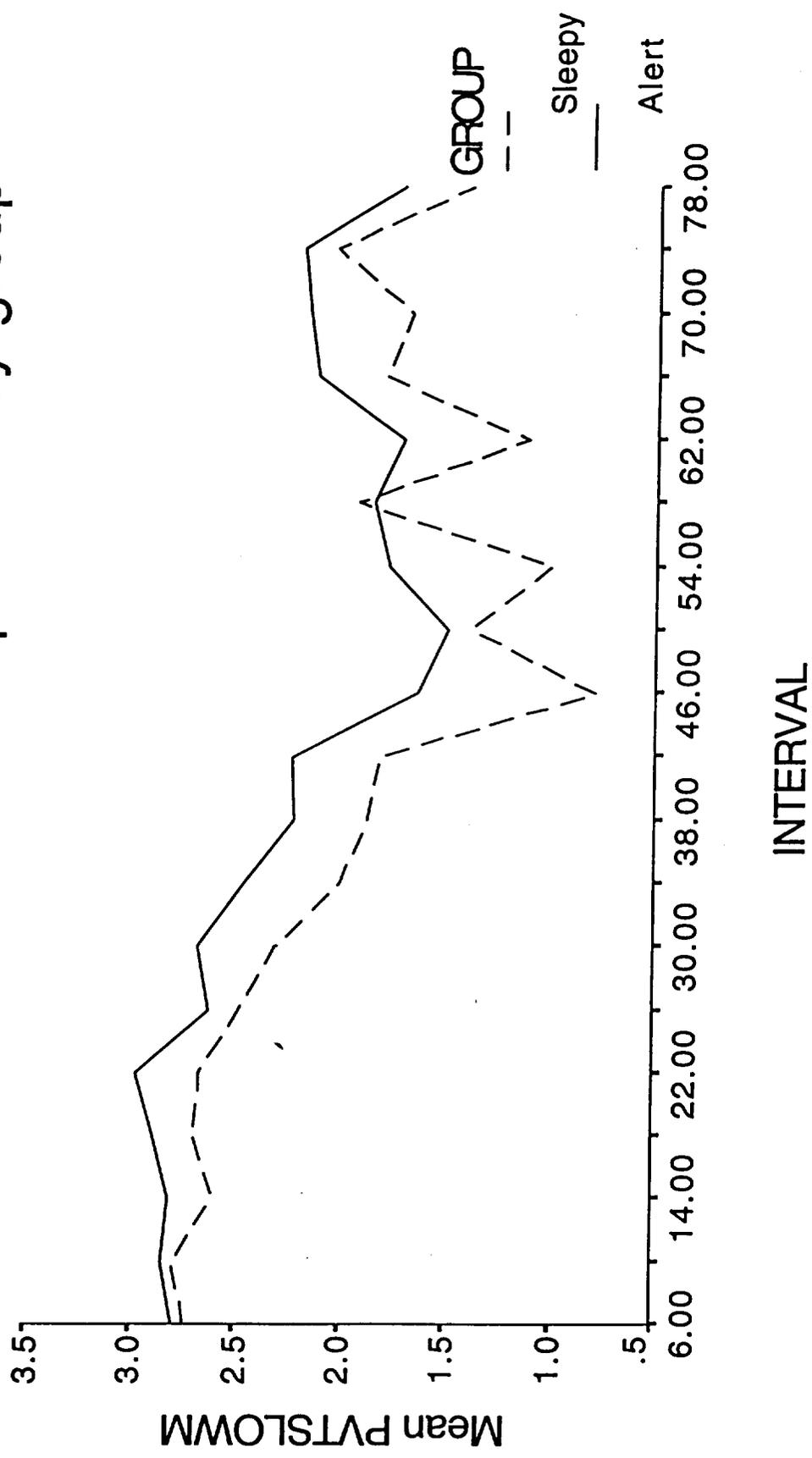


Figure 9

DAT: Central response time: group by condition

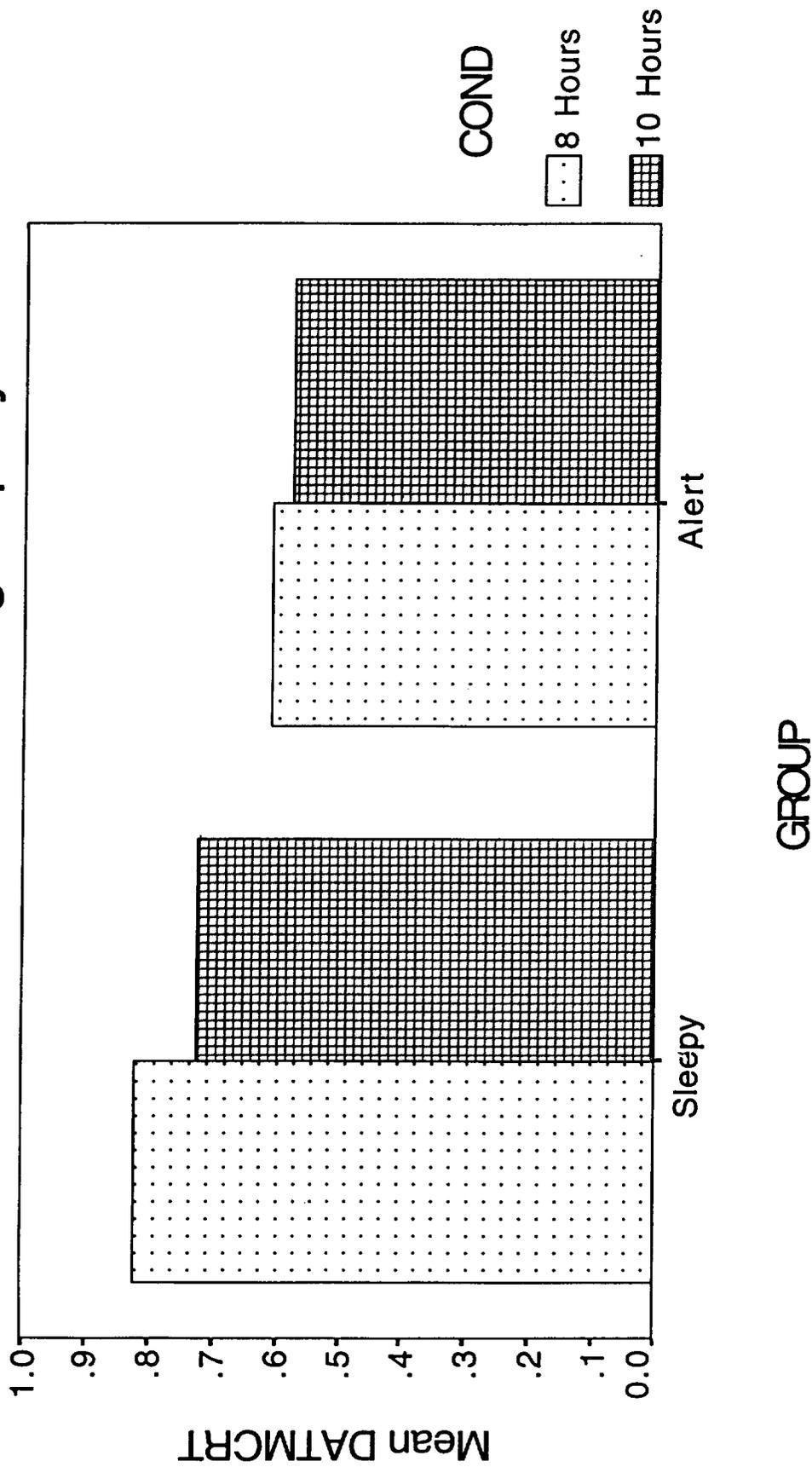


Figure 10

DAT: Peripheral response time: group by condition

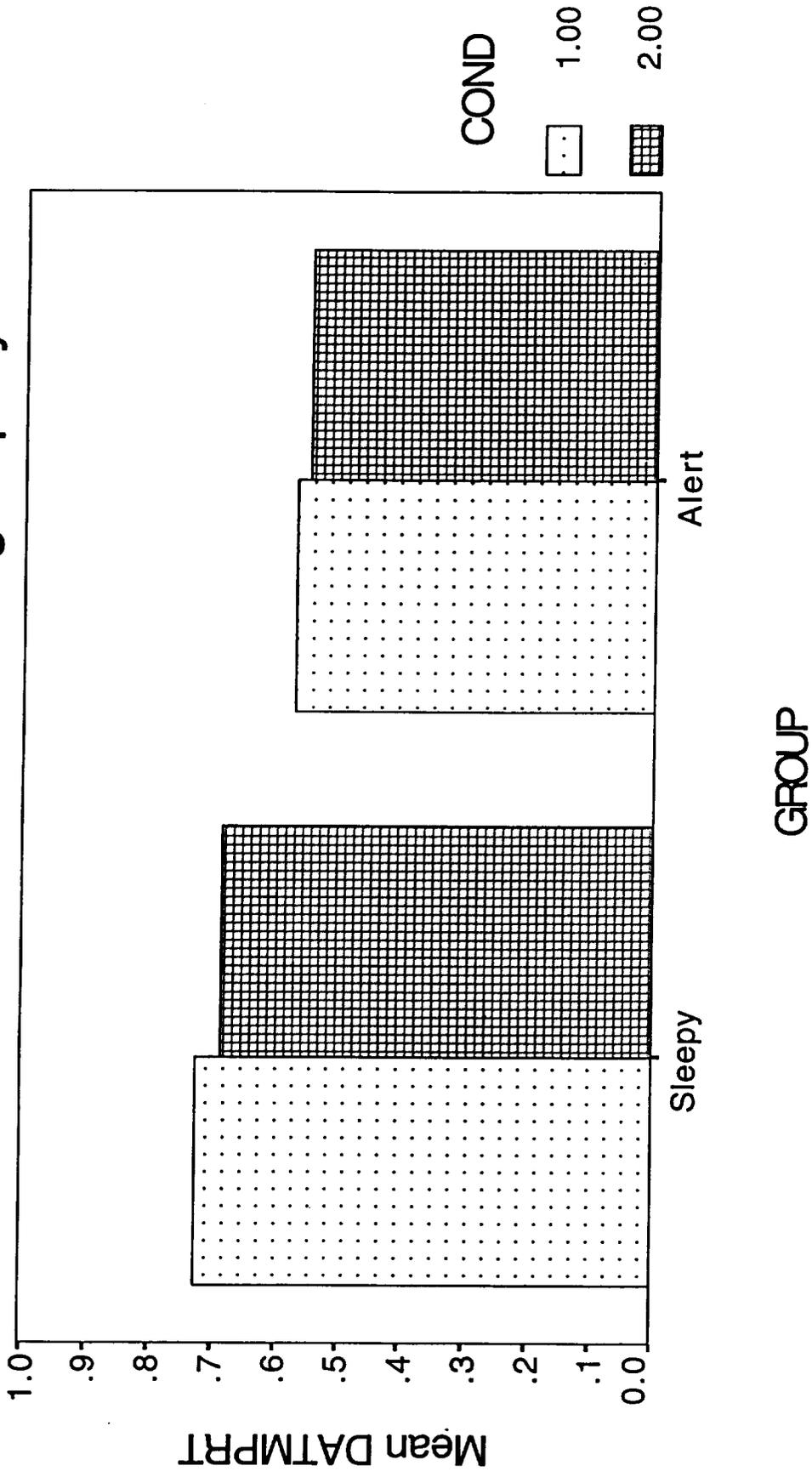


Figure 11

PVT: Total response errors: group by condition

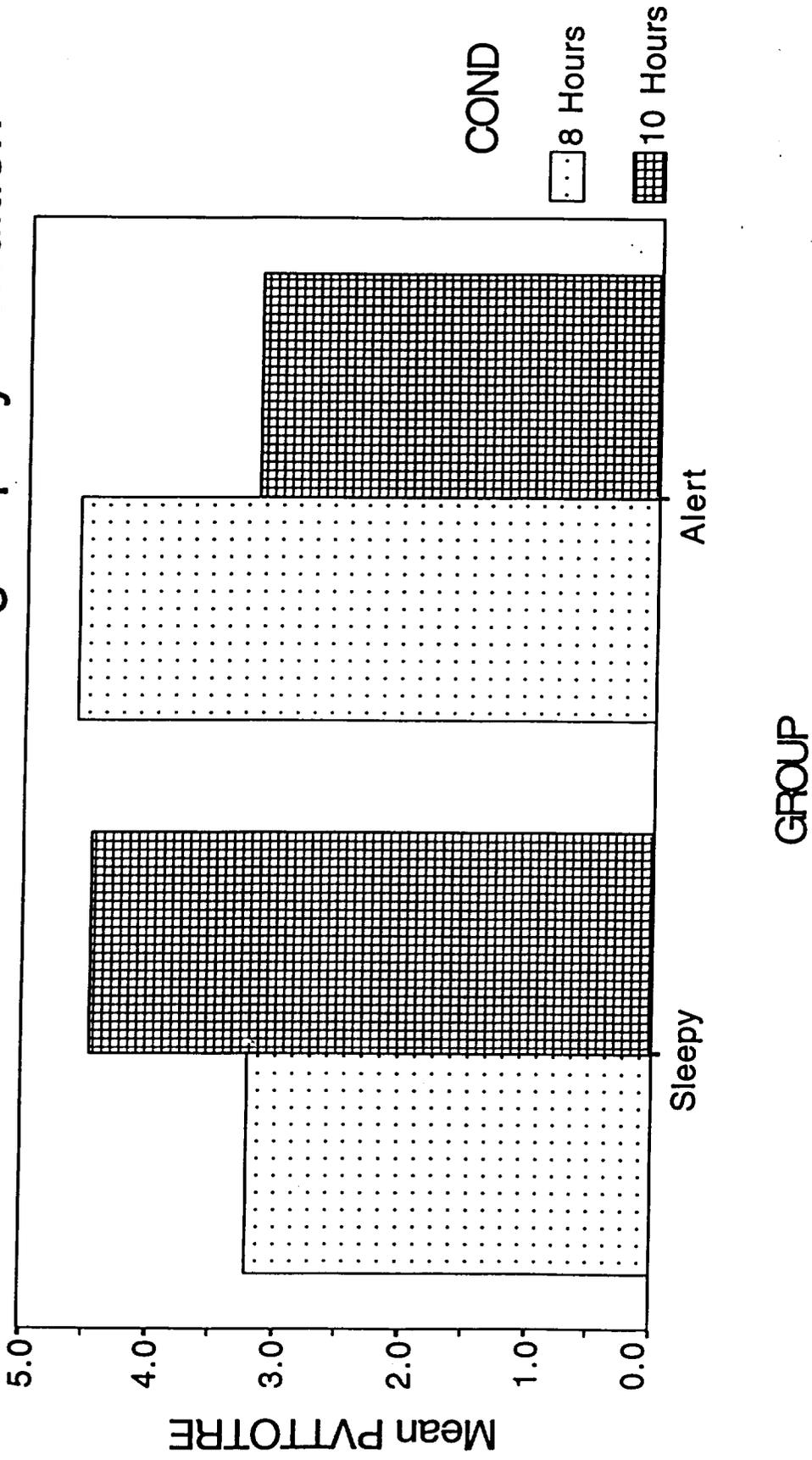


Figure 12