Final Technical Report

Effectiveness of Circadian Countermeasures
in Simulated Transmeridian Flight Schedules

NASA Cooperative Agreement No. NCC 2-253

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1. Aim of the Study

The symptoms of jet-lag commonly afflict travelers who cross time zones. Insomnia during the new "night", daytime fatigue, malaise, sleepiness, and gastrointestinal disturbances can occur for as long as 3 weeks after jet travel across even a few time zones. These symptoms are largely due to the slow rate of adjustment of the internal circadian timing system to the new time zone. Since business (or pleasure) can be seriously interrupted by such symptoms, it is important to determine ways to speed up the adjustment process to ameliorate the symptoms.

Airline pilots have reported that they frequently nap to counter their symptoms of jet lag, and that they view this as a useful technique. Napping as a countermeasure would be attractive since it is practical and would take advantage of a naturally occurring phase of sleepiness after lunch. Napping also makes sense since insomnia is a common jet lag symptom. Thus, a laboratory simulation of jet lag was designed to test the ability of napping to increase the rate of adjustment following a time zone shift in a population of middle-aged men.

2. Experimental Design

These studies were conducted in a time isolation facility at the Institute of Chronobiology, Westchester Division, New York Hospital-Cornell Medical Center. Each time isolation apartment excludes all external time information from sources such as windows, televisions, radios and clocks. Time zone shifts can be simulated easily in such a facility by manipulating the schedules of subjects.

Twelve middle-aged male subjects were recruited for the study. Each was physically and emotionally healthy as determined by a thorough screening procedure that included physical and psychological examinations and tests. A subject agreed to participate in two 15 day studies. Informed written consent was obtained.

Six of the subjects participated in the "eastbound" direction, and 6 in the "westbound" direction. One of the 15 day sessions served as a control (no countermeasure used). During the other session, the nap countermeasure was applied. Each day of the study was structured, with meals, sleep periods and exercise scheduled. For the first 5 days of the study, the subjects went to sleep and were awakened according to their usual schedules at home, as determined by a log maintained for 2 weeks prior to the study. Jet lag then was induced by changing the schedules of the subjects by 6 hours once, either by waking the eastbound subjects early or by delaying the sleep of the westbound subjects. This technique was used to simulate the sleep deprivation which often accompanies transmeridianal travel. After the shift, the same intervals between scheduled events were maintained on a 6 hour advanced (east) or delayed (west) schedule. Subjects in the nap countermeasure were allowed to nap for up to 2 hours beginning one hour after lunch on each on the two days following the shift. Subjects were not allowed to nap on other days during the nap countermeasure or at all during the control session.

Throughout the study, data were collected on the following variables: (1) core temperature; (2) sleep parameters; (3) mood; (4) performance; (5) alertness; (6) activities.

3. Results

3.1. Core Temperature

Methods. Core temperature was measured rectally using a thermister system. Samples were taken every minute and recorded both on computer tapes and on paper. Data from the tapes were transferred to the mainframe computer for analysis. Phase of the temperature rhythm was determined by a cosine based technique. The acrophase (time of peak temperature) and the amplitude of the rhythm (degrees F from the center of the curve to the top) were determined.

Eastbound Shifts. The temperature rhythm adjusted to the shift according to a linear recovery function. By the end of the 9 post-shift days, the temperature rhythms had not yet fully resynchronized to the 6 hour advance shift. The amplitude of the temperature rhythm decreased after the shift when compared to control values, and like the phase adjustment, also showed a linear increase over time. This linear adjustment pattern will be in contrast to the sleep and performance adjustment data as will be described below.

Westbound Shifts. The temperature rhythm adjusted to the phase delay linearly, as can be seen in Figures T-1 and T-2. However, the rate of adjustment was faster in the westbound than in the eastbound direction. By the end of the study, the control group had nearly completely shifted by the 6 hours. The amplitude of the temperature rhythms was more variable after the phase delay than during the baseline days. Napping did not increase the rate of adjustment of the temperature parameters.

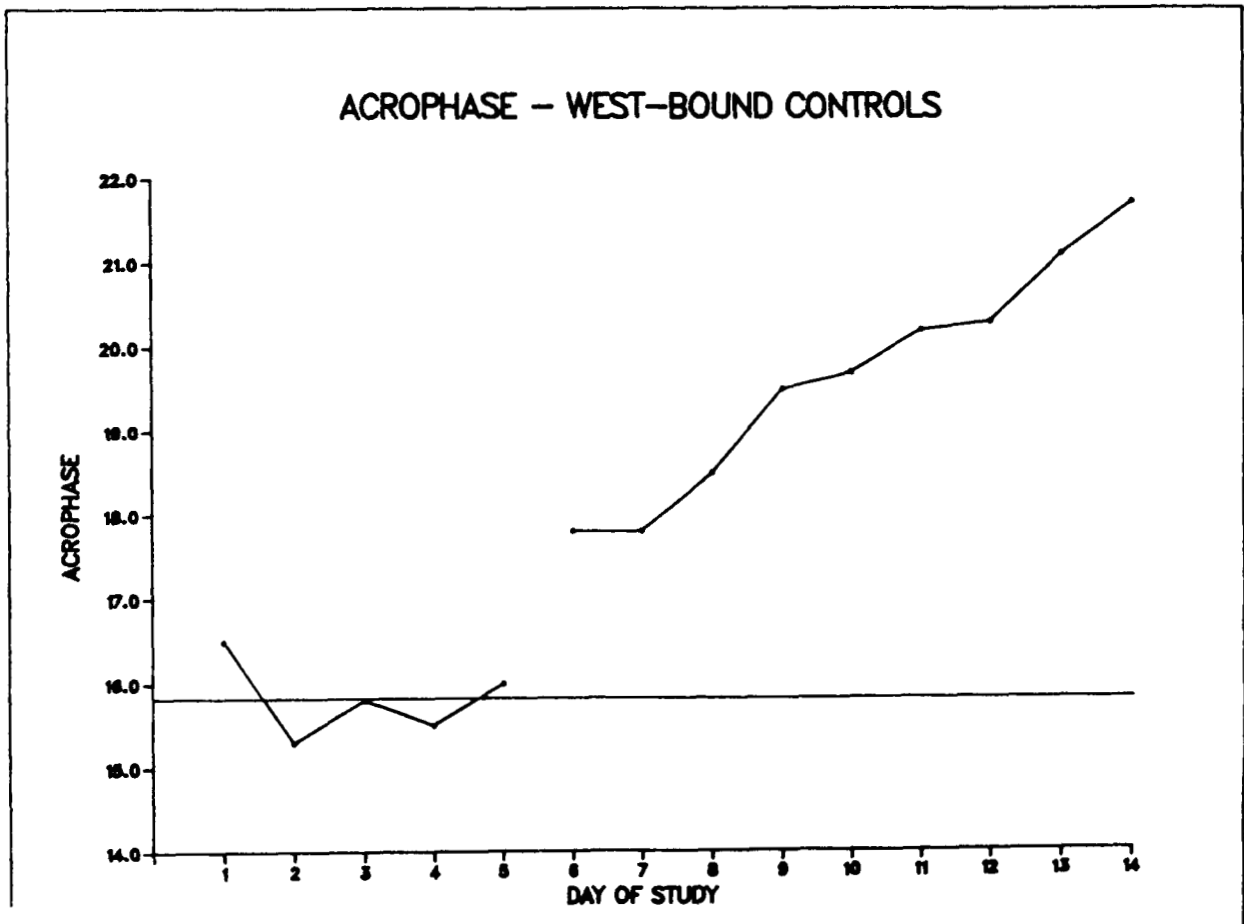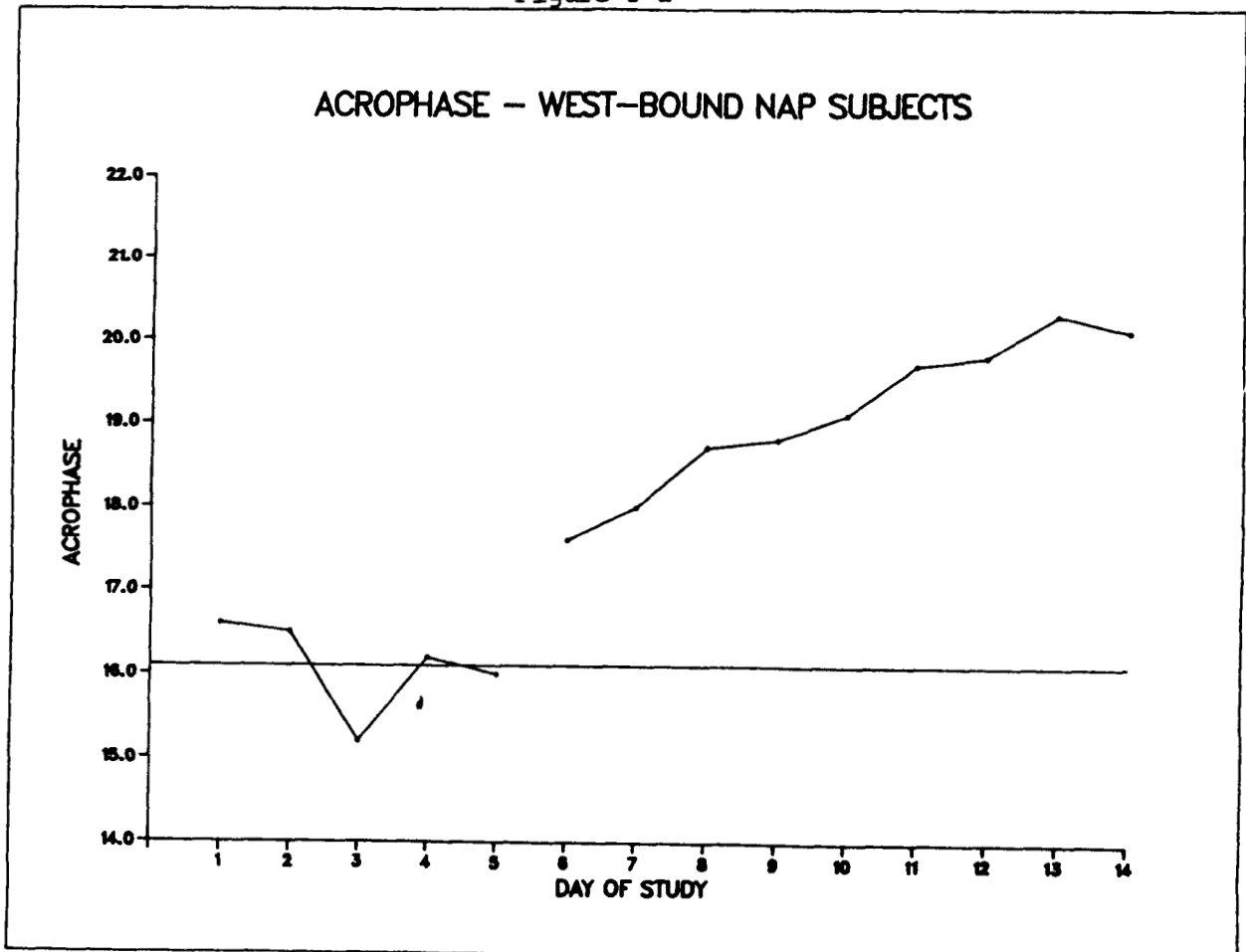## ACROPHASE – WEST–BOUND CONTROLS

ACROPHASE – WEST–BOUND NAP SUBJECTS

3.2. Sleep Parameters

Methods. Each sleep or nap was recorded polygraphically and scored according to standard techniques. Comparisons were made between the nap and no nap conditions in each shift direction and between napping in the two directions.

Results from Eastbound (Advanced) "Travel"

Total Sleep Time. Total sleep time refers to the duration of time spent actually sleeping when a subject is in bed with the lights off. Sleep efficiency is the percentage of time spent sleeping.

In the subjects who were phase advanced ("eastbound travel"), mean total sleep time in minutes was decreased in the nap group (heavy line) on the first night following the shift when compared to the control group (light line; Figure S-1). Total sleep time in both groups did not return to pre-shift values by the end of the study. Please note that the sixth night is the abbreviated sleep episode (120 min of sleep or less).

Sleep efficiency of the night sleep episodes showed a alternating pattern, especially in the control group (Figure S-2). This is presumably due to the competition between the need for sleep and the inability of a person to sleep at a phase of the day that is too advanced compared to normal.

The decrease in sleep efficiency could be due either to an increase in the time needed to fall asleep (sleep latency), more time spent awake during the sleep period, or early awakening. The data indicate that sleep latency was not affected by the shift on average in the control and nap groups. Subjects in both groups tended to wake earlier than usual. Thus, the decrease in
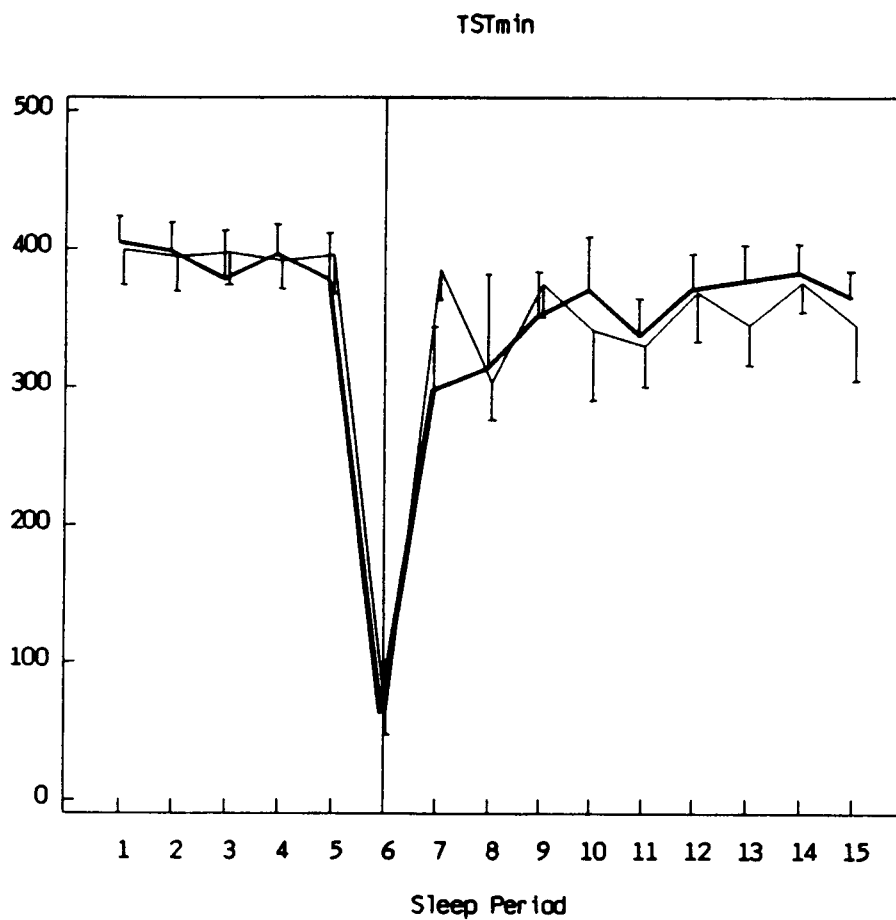
TSTmin

Sleep Period

Figure S-1
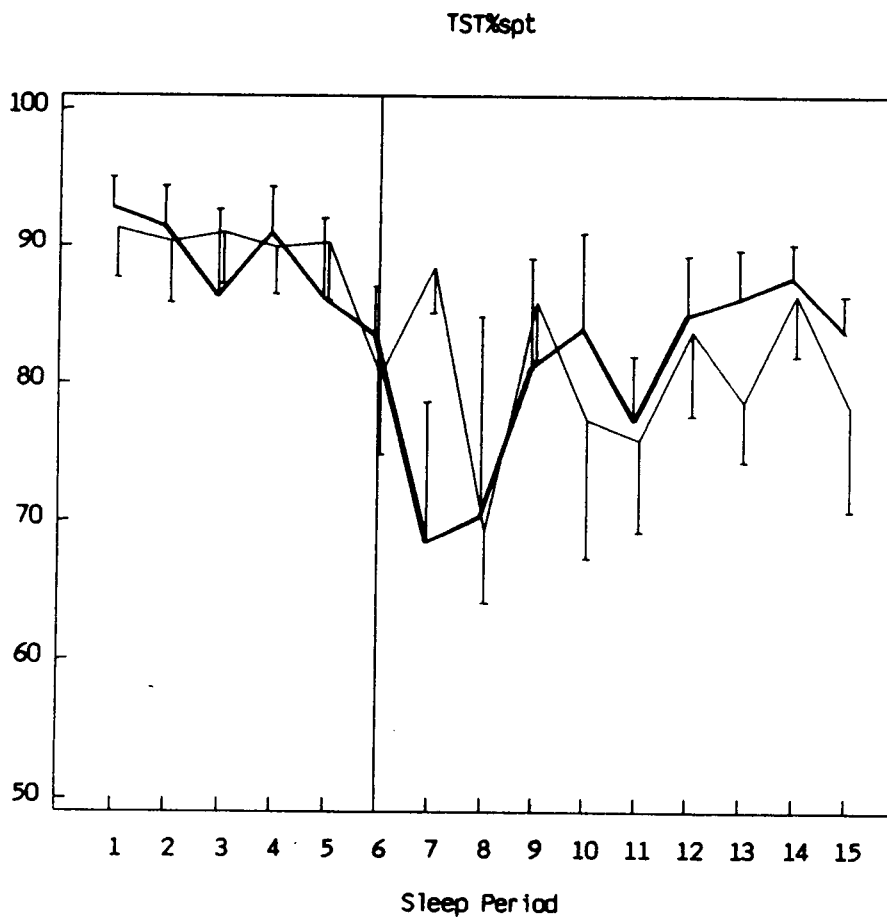Total Sleep Time
Eastbound

TST%spt

Sleep Period

Figure S-2
Sleep Efficiency
Eastbound

total sleep time and sleep efficiency was due more to problems maintaining sleep and to early morning awakening.

When naps are taken into consideration, the total sleep time is somewhat different (Table S-1).

Total Sleep Time (min)

Day After Shift	Night Sleep Without Nap	Night Sleep After Nap	Nap Added In	Difference
1	386	297	408	+22
2	303	280	292	+89

Thus, napping during the afternoon of the new time zone decreased the subsequent night sleep. However, when the total minutes of sleep were compared, the napping group did have more sleep.

Slow Wave (Deep) Sleep. Slow wave sleep (SWS) increased transiently in the control group following the phase advance (Figure S-3). The duration of SWS in the night sleep in the nap group, however, was much less following the two afternoon naps. When the minutes of SWS from the naps were added to the night sleep SWS, the difference between groups narrowed. On average, the control group had 78 minutes of SWS during the first night sleep after the shift, while the nap group had 38 minutes at night and 23 minutes during the nap (78 vs. 61 minutes). On the second day after the shift, the control group averaged 48 minutes, and the nap group 45 minutes (nap + night sleep).

Rapid Eye Movement (REM) Sleep. REM sleep decreased following the shift in both groups, and returned gradually to the preshift baseline (Figure S-4). REM latency shortened slightly in both groups following the shift (Figure S-5).
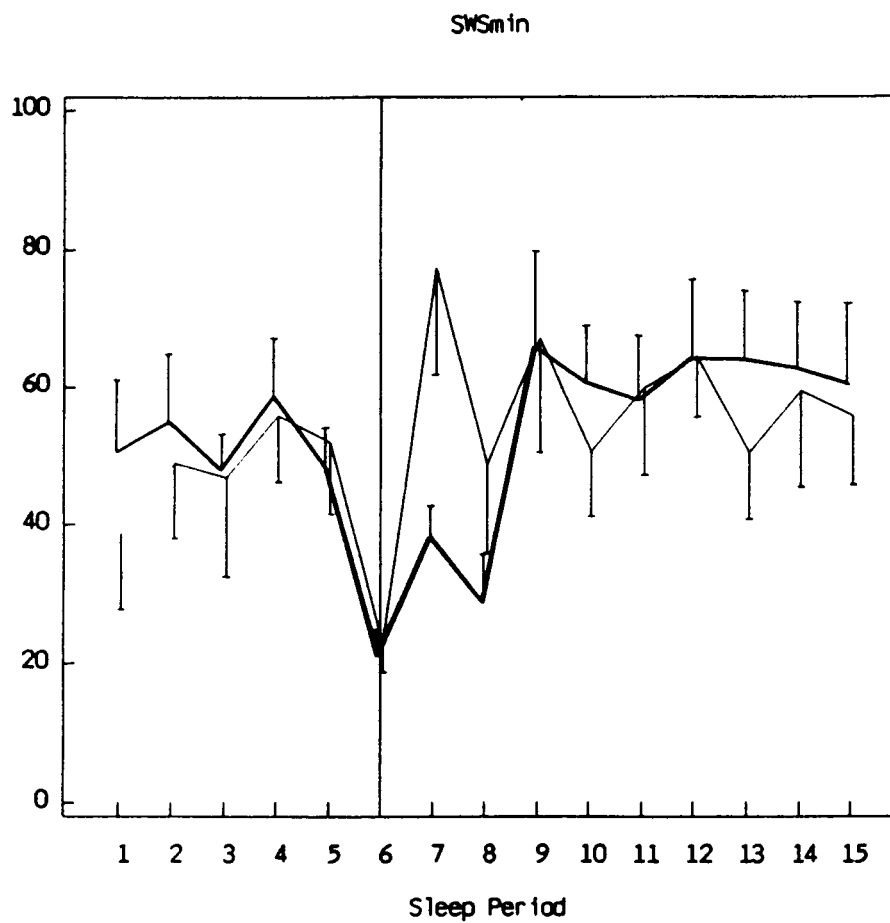
SWSmin

Sleep Period

Figure S-3
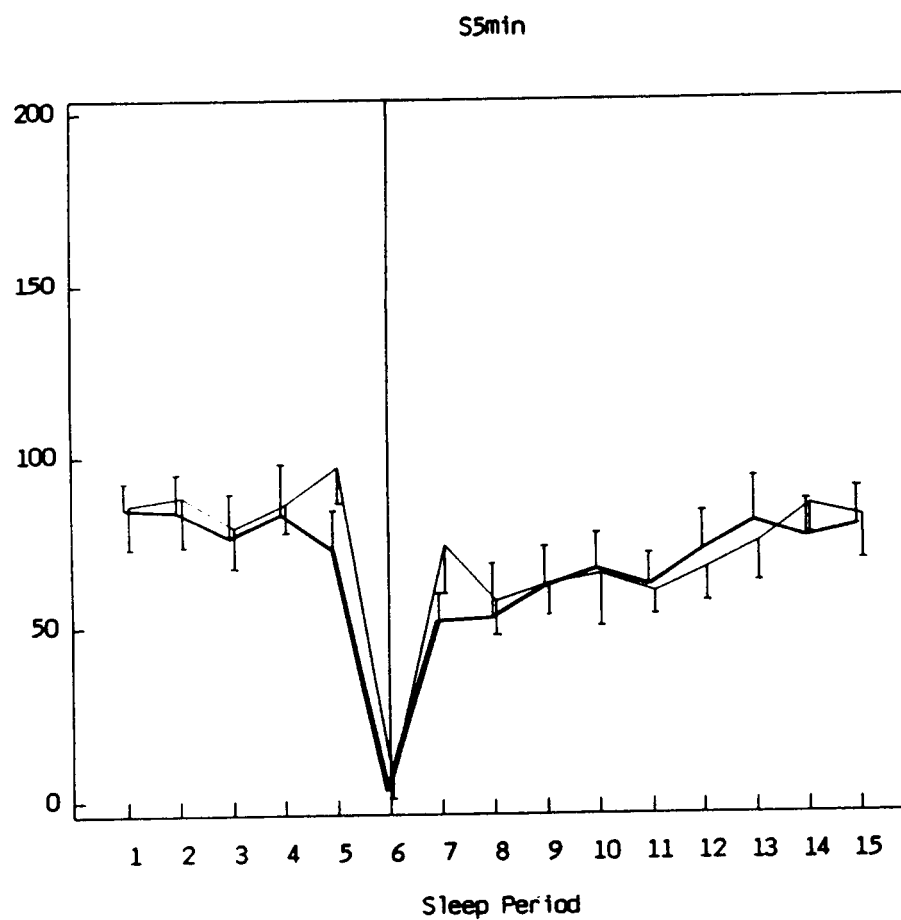Slow Wave Sleep
Eastbound

S5min

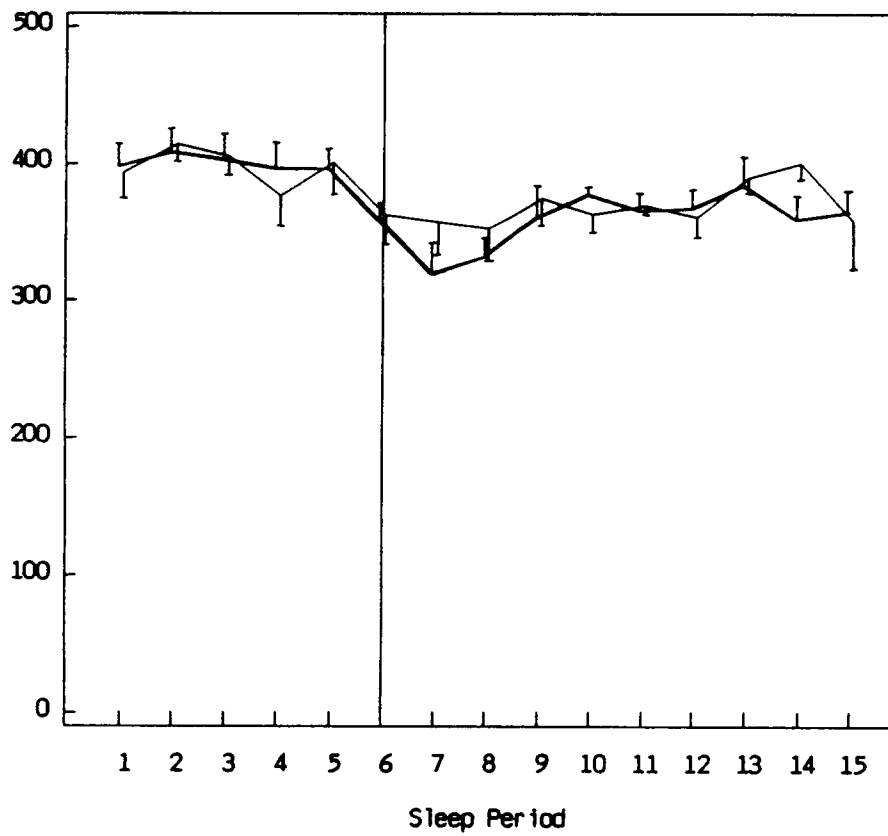Sleep Period

Figure S-4
REM Sleep
EAstbound

REMLat

Sleep Period

TSTmin

Sleep Period

Results from Westbound (Delayed) "Travel"

Total Sleep Time. Total sleep time decreased following the phase delay in both groups (Figure S-6). Sleep efficiency decreased as well (Figure S-7), more so in the nap group during the first two night sleeps after the delay. Mean sleep efficiency remained below the pre-shift mean for the remaining nights of the study.

When napping is taken into consideration, a similar result was obtained:

		Total Sleep Time (min)		
Day After Shift	Night Sleep Without Nap	Night Sleep After Nap	Nap Added In	Difference
1	357	319	394	+37
2	353	331	396	+43

Thus, westbound napping subjects had more total sleep when the naps were included, but less sleep on those nights following the naps.

Much of the decrease in sleep efficiency can be accounted for by an increase in terminal wake latency, which is the duration of time that a person is awake at the end of the sleep period. In other words, subjects who awakened early had a long terminal wake latency. This effect can be observed in Figure S-8. No differences in sleep latency were observed in either the control or the nap group.

Slow Wave Sleep. SWS decreased transiently only in the napping group (Figure S-9). The difference between control and nap group was removed when the minutes of SWS from the naps were added into the total: 53 vs 57 minutes (control vs nap groups) on the first day after the shift; and 57 vs 56 minutes on the second day.
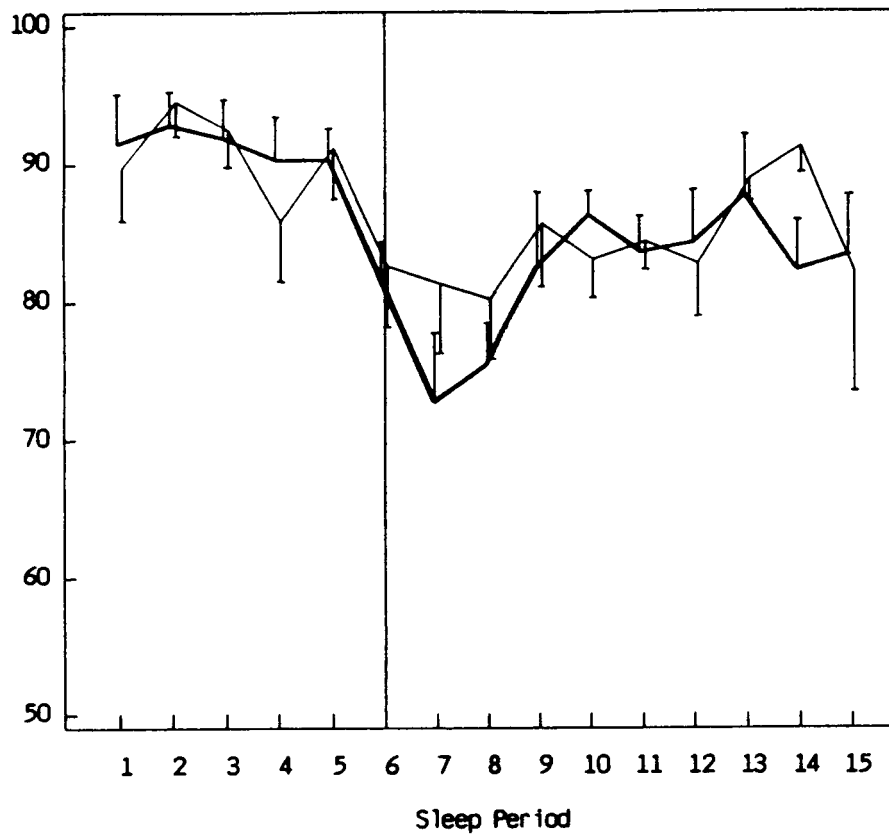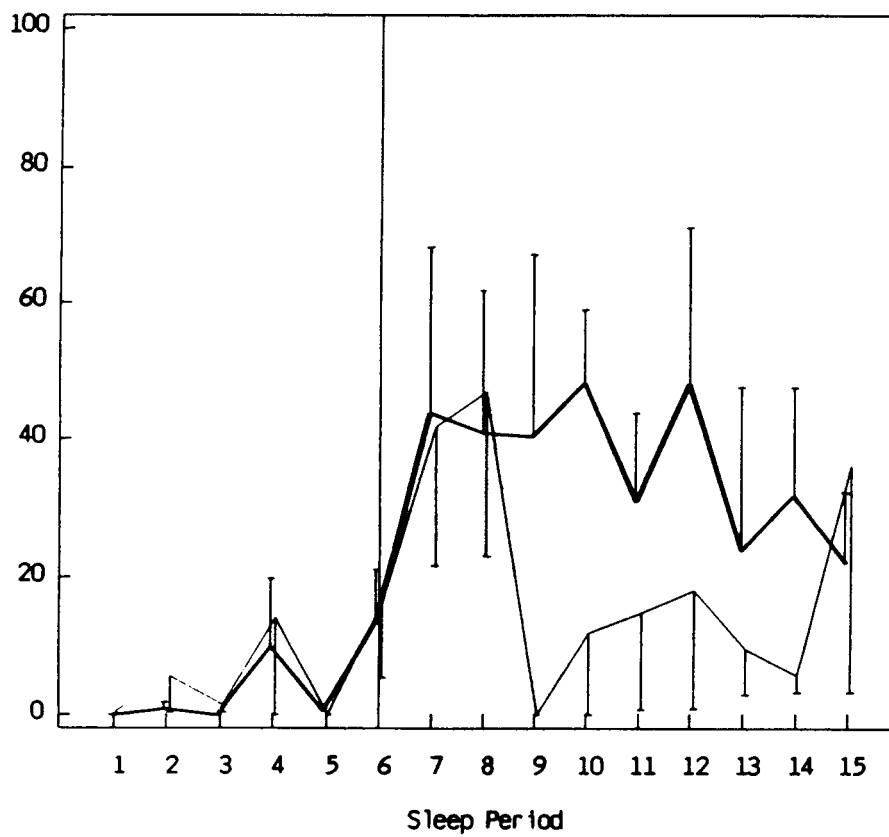
TST%spt

Figure S-7
Sleep Efficiency
Westbound

Sleep Period

TWL

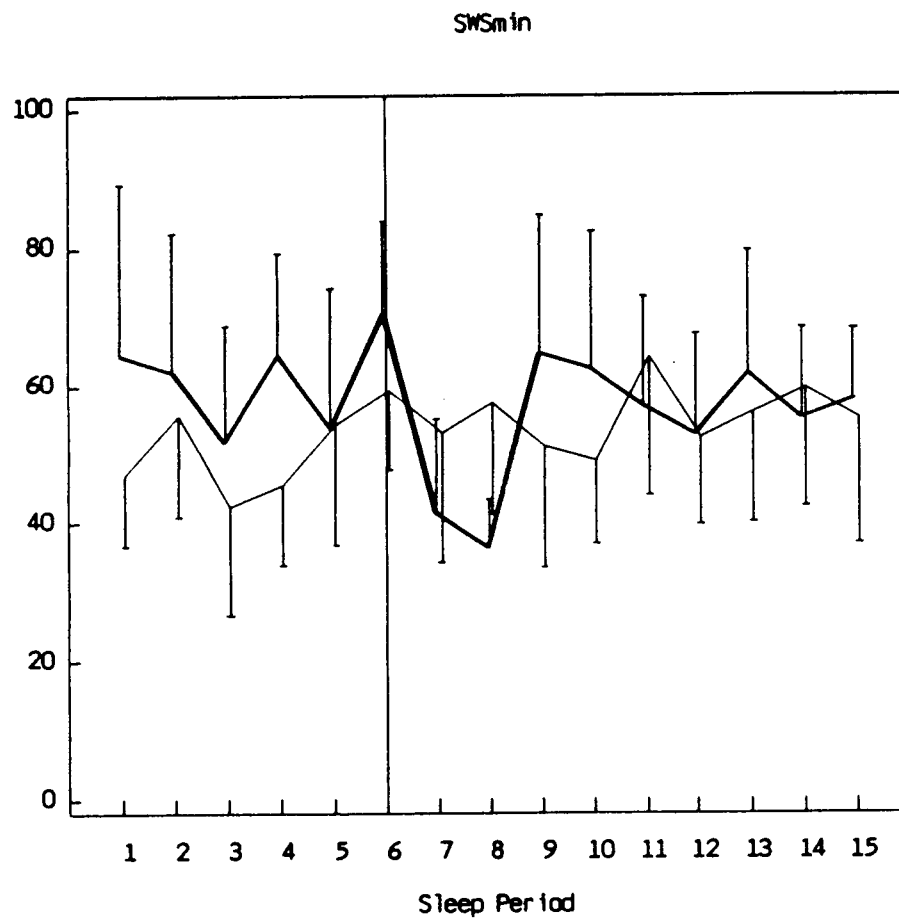Figure S-8
Terminal Wake Latency
Westbound

Sleep Period

SWSmin

Figure S-9
Slow Wave Sleep
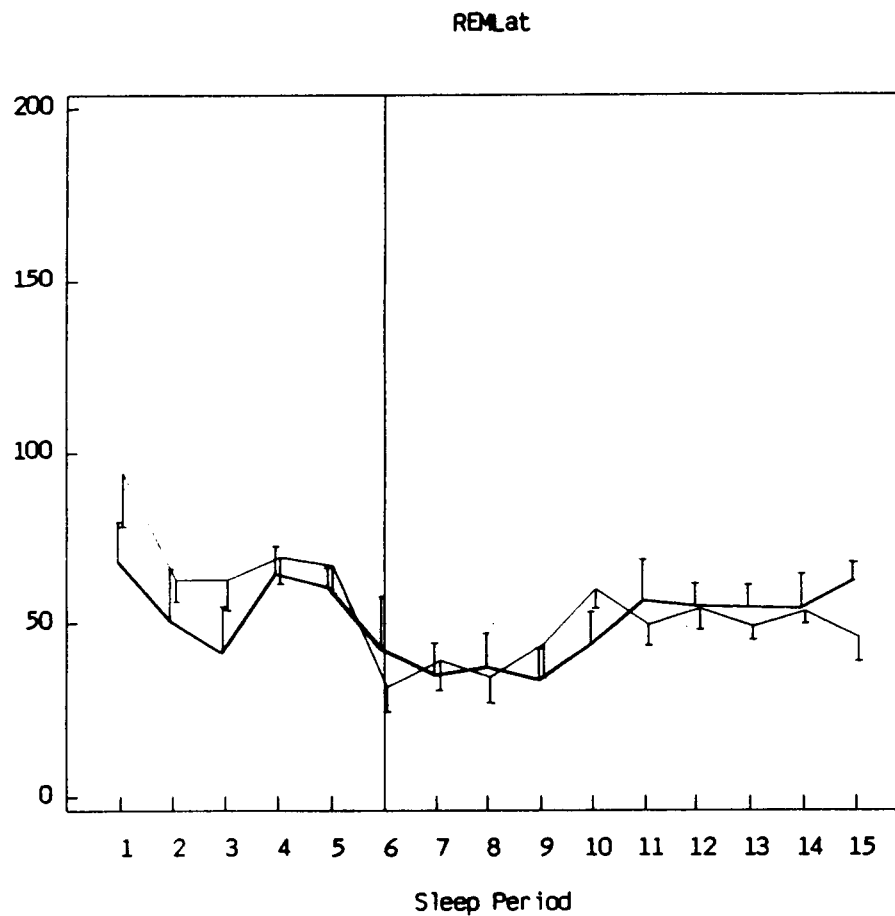Westbound

Sleep Period

REMLat

Figure S-10
REM Latency
Westbound

Sleep Period

REM Sleep. REM latency decreased after the shift in both groups (Figure S-10), which was an expected finding. The percentage and minutes of REM sleep did not differ between the control and nap conditions.

Eastbound vs Westbound Naps

Eastbound naps were longer, with a mean duration of 112 minutes out of a possible 120, with a sleep efficiency of 93%. In contrast, westbound naps averaged 70 minutes out of 120, with a sleep efficiency of 58%.

More SWS was obtained in the eastbound naps; 2 of the westbound subjects had no SWS in their naps at all. All of the eastbound nappers had some REM sleep in the naps, while about half of the westbound nappers did.

These differences can be explained in terms of the phase of the day at which they were scheduled. After the eastbound shift, the nap was scheduled at what was near the end of the sleep episode before the shift. That is a time that corresponds to high REM probability. Conversely, the nap in the westbound direction was scheduled during what had been the early evening, a time during which it is usually difficult to initiate sleep. Thus, it is not altogether surprising that the subjects who were advanced had longer naps, with more REM than their phase delayed counterparts.

3.3. Mood, Alertness and Performance Measures

Methods. Mood and performance were assessed approximately six times per day (not at "night") using a computer-based technique. Nine visual analog scales were given, and the results combined (Monk, 1989) to give one global measure of vigor or activation (alertness, sleepiness, weariness, motivation loss; GV) and one of affect (happiness, sadness, calmness, tension; GA) with

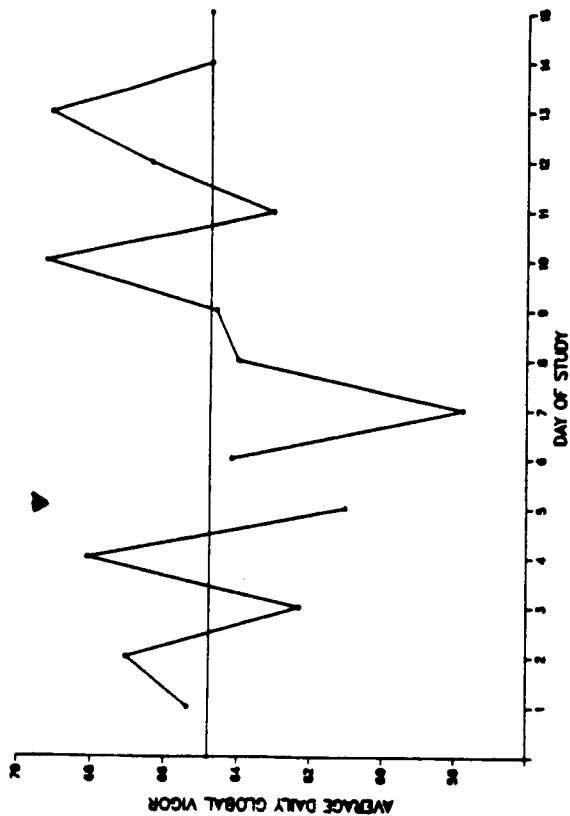each measure ranging from 0 to 100. Mean daily values are reported.

Three performance tests were given, and speed (time taken) was analyzed. The tests were (1) searching through 32 lines, each of 30 random letters, to detect the presence or absence of the letter E; (2) a version of the Baddeley reasoning test in which the subject decides whether a sentence accurately describes a letter pair; and (3) 25 holes of the simple Purdue Pegboard manual dexterity test (once with the dominant hand, and a second time with the non-dominant hand). The tests given on a particular day were averaged to yield a daily measure of performance level.

Eastbound and westbound control conditions. Figure P-1 shows the results for eastbound (phase advance) and westbound (phase delay) conditions in measures of vigor and affect. Readers should note that the scale is expanded in the westbound condition.

In measures of vigor, there was a disruption due to the phase shift (denoted v) in both conditions, although it was more marked and longer lasting in the eastbound condition. In each case, the recovery function tended to be alternating, rather than monotonic, a result discussed in detail in Monk, Moline and Graeber (1988). This appeared to indicate effects stemming both from the misaligned circadian system and from fatigue built up from disrupted and shortened "nights" of sleep, as was also observed in the sleep data.

Measures of affect were interesting in that disruptions were observed in both eastbound and westbound conditions. This clearly bears upon the relation between circadian dysfunction and depression currently under considerable debate (see, for example, Wehr and Goodwin, 1983; Kupfer, Monk and Barchas, 1988). However, the presence of disruptions in affect under both conditions
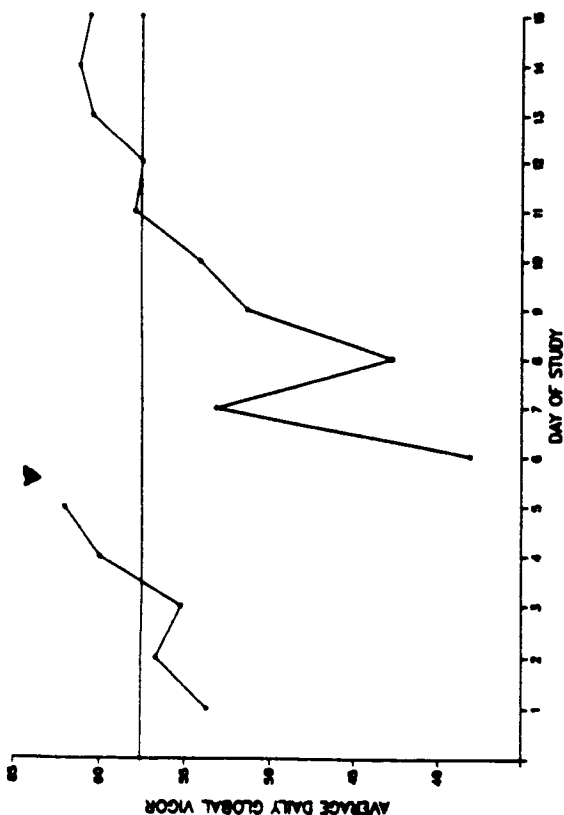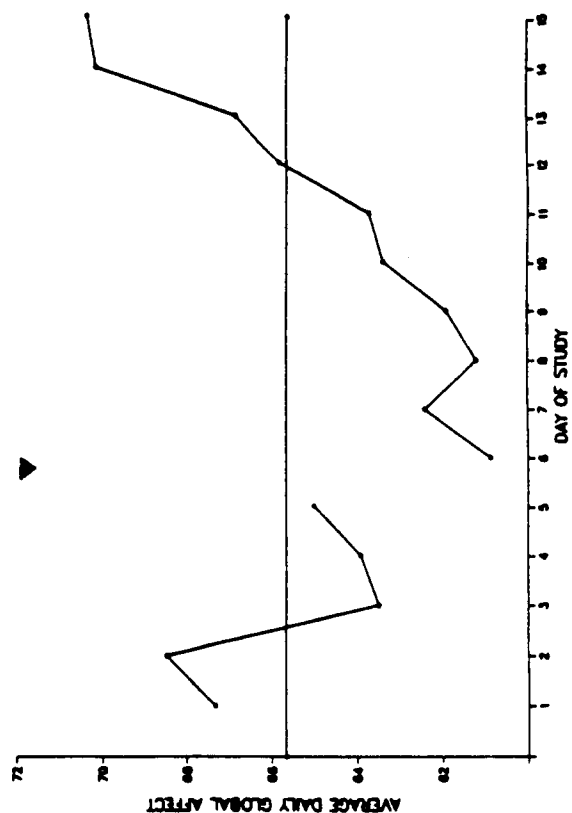
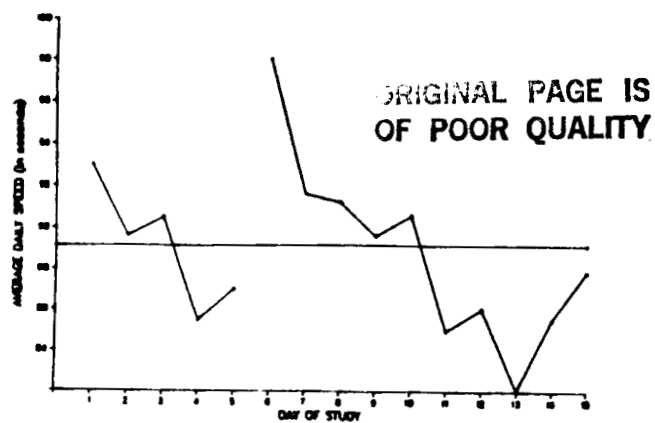GLOBAL VIGOR – WEST-BOUND SUBJECTS

GLOBAL VIGOR – EAST-BOUND SUBJECTS
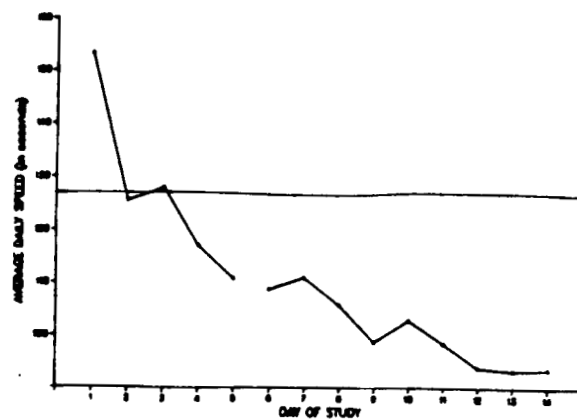
GLOBAL AFFECT – WEST-BOUND SUBJECTS

GLOBAL AFFECT – EAST-BOUND SUBJECTS

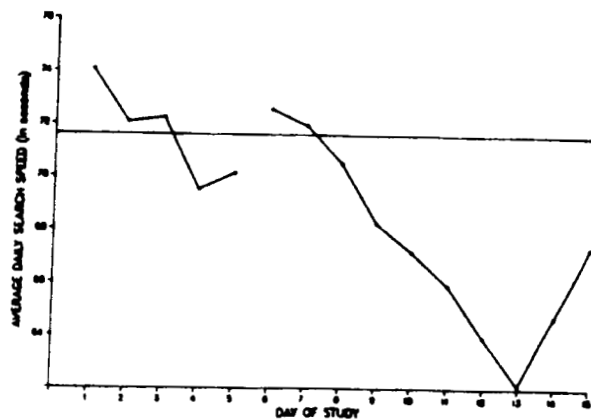MC TASK – EAST-BOUND SUBJECTS

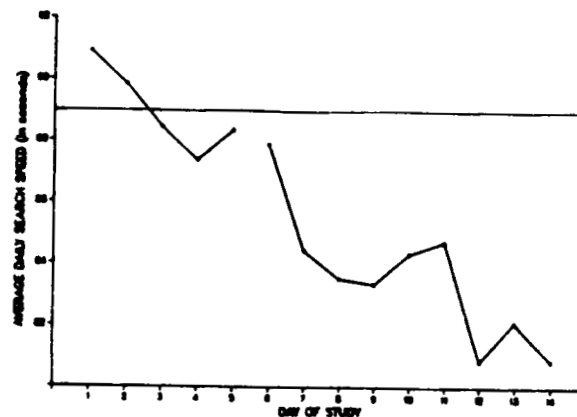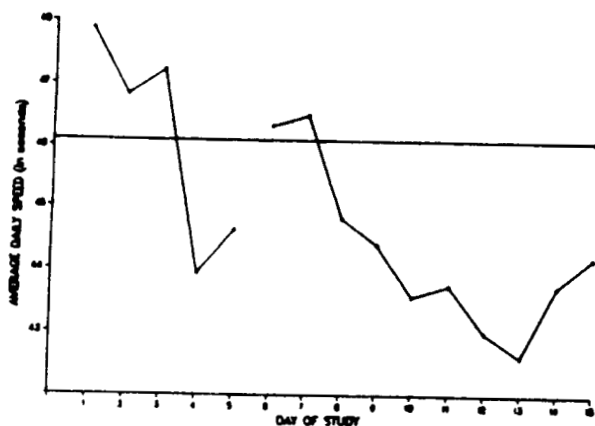

MC TASK – WEST-BOUND SUBJECTS
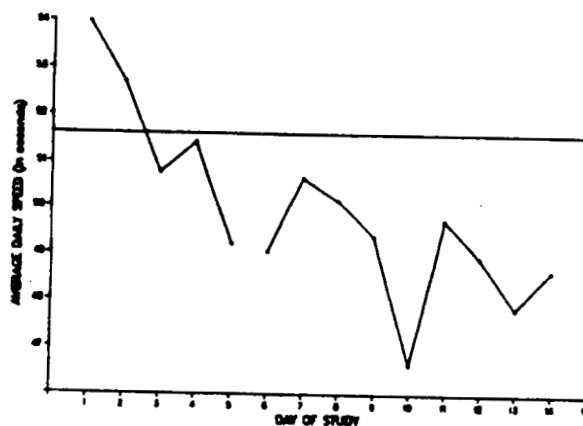

VISUAL SEARCH TASK – EAST-BOUND SUBJECTS
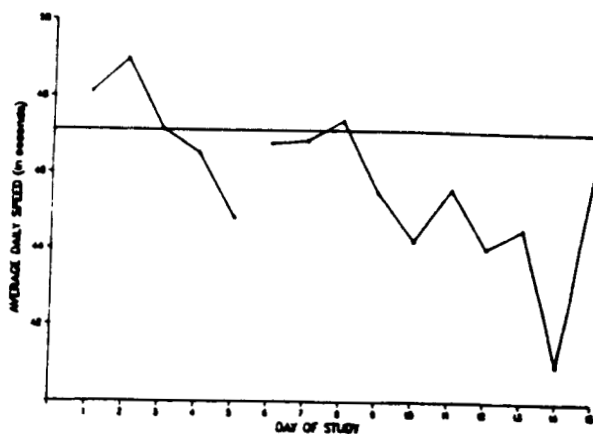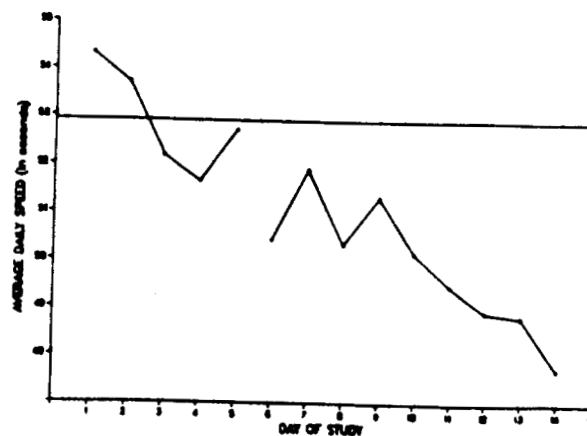

VISUAL SEARCH TASK – WEST-BOUND SUBJECTS

MANUAL DEXTERITY TASK (DOMINANT HAND) – EAST-BOUND SUBJECTS

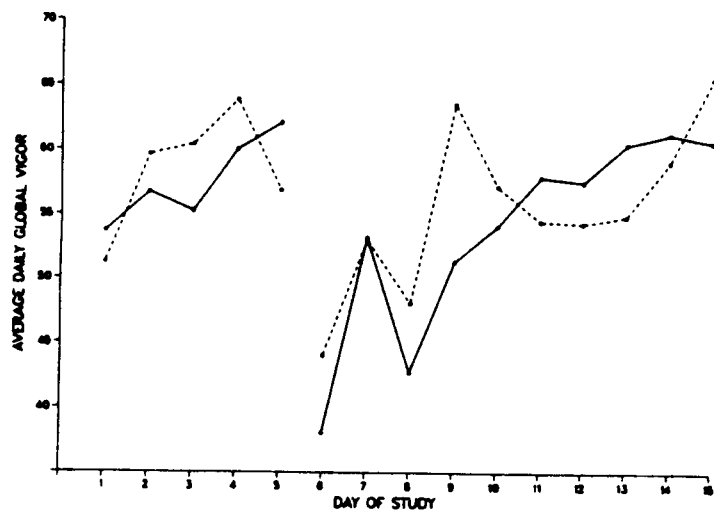MANUAL DEXTERITY TASK (DOMINANT HAND) – WEST-BOUND SUBJECTS

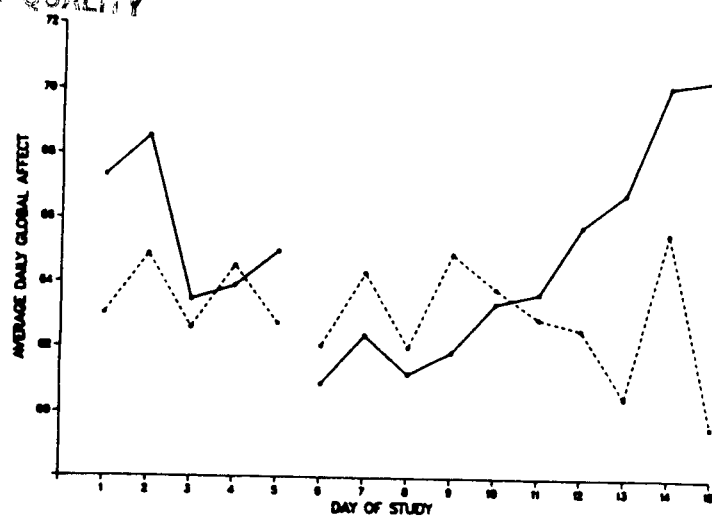MANUAL DEXTERITY TASK (NON-DOMINANT HAND) – EAST-BOUND SUBJECTS

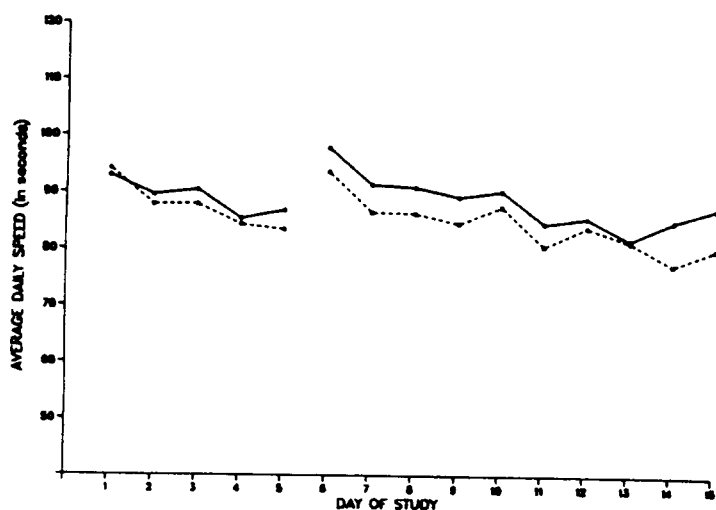MANUAL DEXTERITY TASK (NON-DOMINANT HAND) – WEST-BOUND SUBJECTS
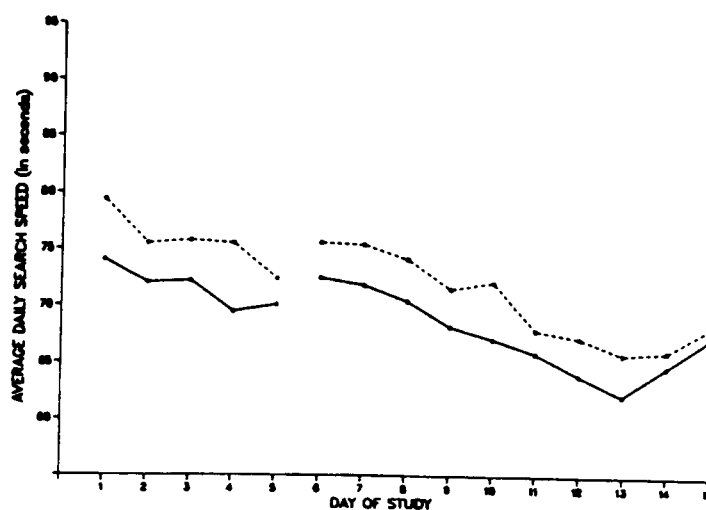
GLOBAL VIGOR – EAST–BOUND SUBJECTS

GLOBAL AFFECT – EAST–BOUND SUBJECTS

MC TASK – EAST–BOUND SUBJECTS

VISUAL SEARCH TASK – EAST–BOUND SUBJECTS

MANUAL DEXTERITY TASK (DOMINANT HAND) – EAST–BOUND SUBJECTS

MANUAL DEXTERITY TASK (NON–DOMINANT HAND) – EAST–BOUND SUBJECTS

GLOBAL VIGOR - WEST-BOUND SUBJECTS
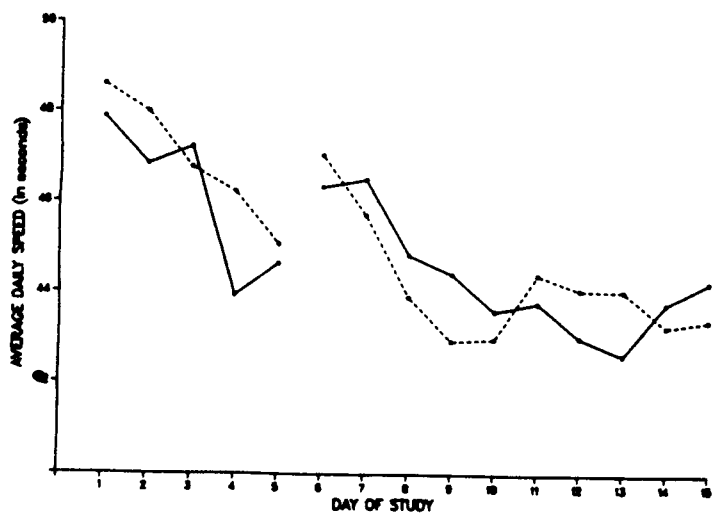
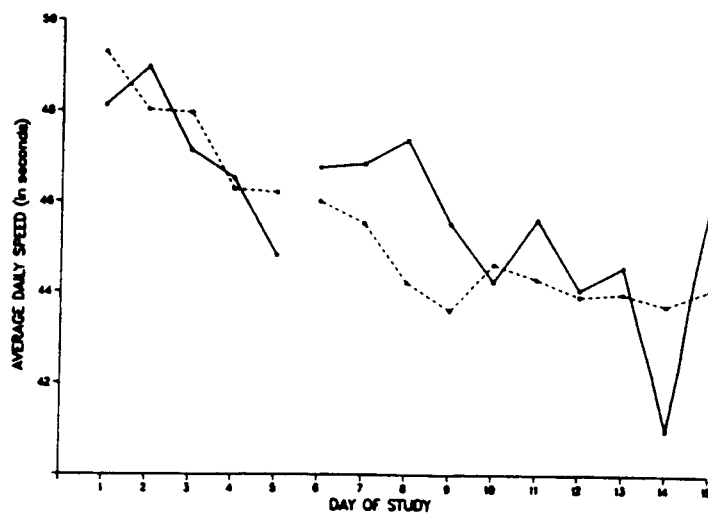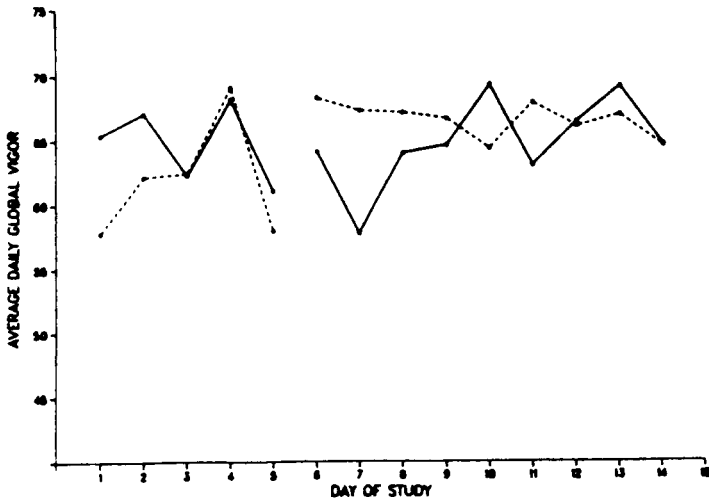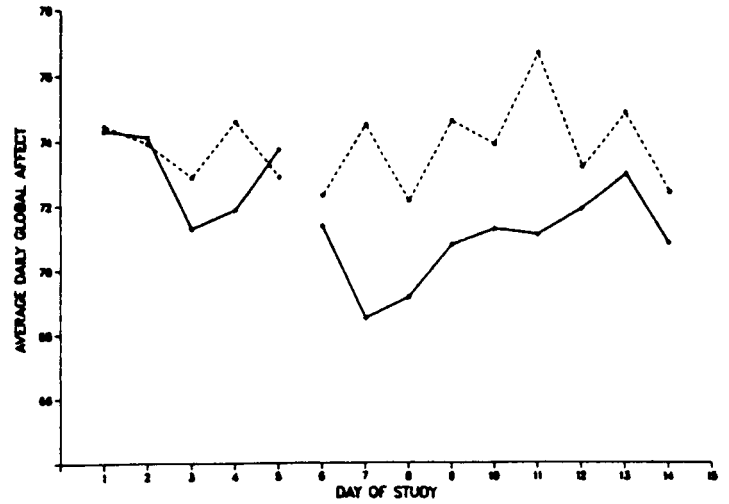GLOBAL AFFECT - WEST-BOUND SUBJECTS

MC TASK - WEST-BOUND SUBJECTS

VISUAL SEARCH TASK - WEST-BOUND SUBJECTS

MANUAL DEXTERITY TASK (DOMINANT HAND) - WEST-BOUND SUBJECTS

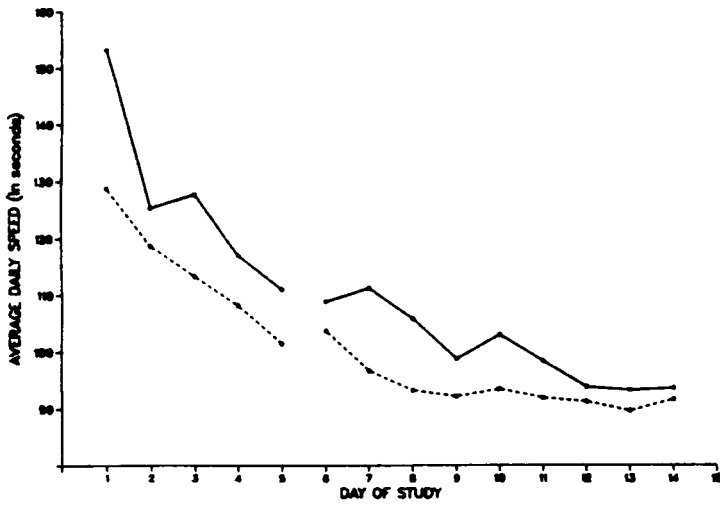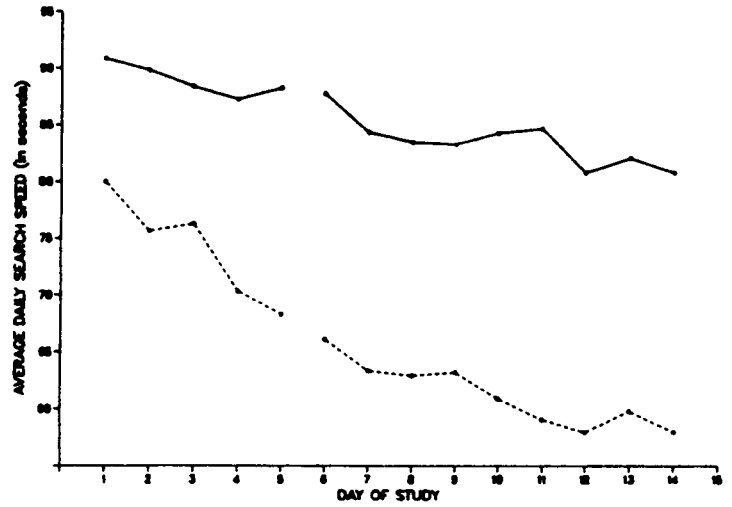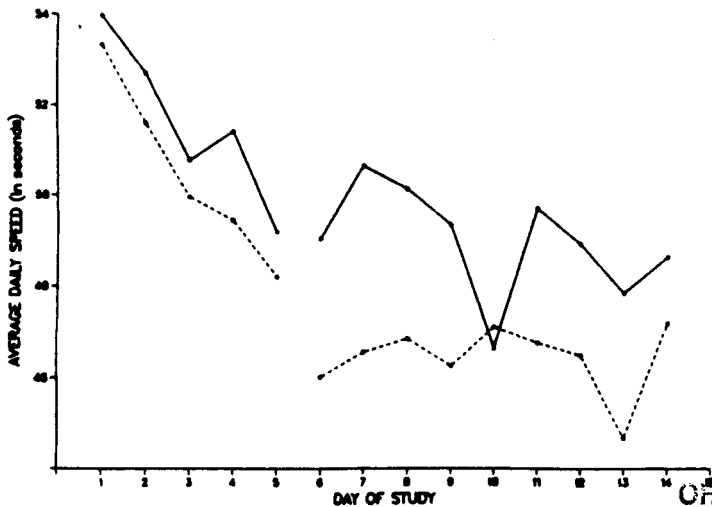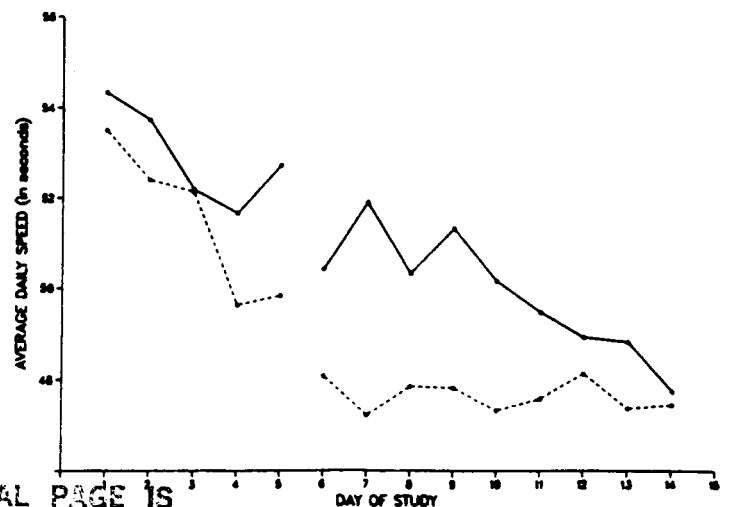MANUAL DEXTERITY TASK (NON-DOMINANT HAND) - WEST-BOUND SUBJECTS

does not support an explanation based solely on the phase advance hypothesis (that depressive symptoms result from an endogenous circadian system that is in a phase advanced state relative to the patient's routine).

Performance measures (Figure P-2) suffered from residual practice effects, despite efforts such as training and prior practice to eradicate them. In the westbound condition there were no performance decrements due to the phase shift, as indicated by the relatively smooth practice curve over the whole study. In the eastbound condition, decrements (slower responding-longer latencies) were observed, especially in the verbal reasoning task and in the dominant hand dexterity task. Thus, when a phase shift is an advance and is associated with sleep loss (as it is on many eastbound transatlantic overnight fights), performance decrements would be expected for the first few days after arrival, especially in measures of cognitive performance. In contrast, westward flights would be expected to produce few performance decrements from the phase shift.

Control Versus Nap Comparisons. Figures P-3 and P-4 illustrate average control (——————) and nap (- - -) condition data from 6 subjects (within subjects design, balanced for practice). Their most remarkable aspect is that when baseline levels were equated, there were no reliable differences whatsoever between control and nap conditions in overall post-shift daily levels of either mood or performance. The apparent differences in P-4 failed to achieve significance. Only when the "afternoon" data of the first two post-shift days were looked at individually was any advantage observed from the nap, and then only in the eastward condition (which involved truncating the previous night's sleep). We thus conclude from our results that unless performance level is critical on the first afternoon after arrival following an eastward night

flight, a siesta nap on the first two days after arrival is probably not help-ful as a jet-lag countermeasure as far as mood and performance are concerned.

REFERENCES

Kupfer, D.J., Monk, T.H., and Barchas, J.D., eds. Biological Rhythms and Mental Disorders. The Guilford Press, New York, 1988.

Monk, T.H. A visual analogue scale technique to measure Global Vigor and Affect (GVA). Psychiatry Research, in press, 1989.

Monk, T.H., Moline, M.L., and Graeber, R.C. Inducing jet lag in the laboratory: Patterns of adjustment to an acute shift in routine. Aviation, Space, and Environmental Medicine, 59, 703-710, 1988.

Monk, T.H., Fookson, J.E., Kream, J., Moline, M.L., Pollak, C.P., and Weitzman, M.B. Circadian factors during sustained performance: Background and methodology. Behavior Research Methods, Instruments and Computers, 17, 19-26, 1985.

Wehr, T.A., and Goodwin, F.K., eds. Circadian Rhythms in Psychiatry. The Boxwood Press, Pacific Grove, CA, 1983.

Publications Resulting from the Co-operative Agreement

The major publication of direct relevance to the co-operative agreement so far has been "Inducing jet-lag in the laboratory: Patterns of adjustment to an acute shift in routine" by T.H. Monk, M.L. Moline and R.C. Graeber (Aviation, Space and Environmental Medicine, 1988, 59:703-710). Also published was an abstract: "Changes in sleep, mood and performance after a 6h advance shift in routine" by T.H. Monk, M.L. Moline, R.C. Graeber, J.K. Lauber and P.H. Gander (Aviation, Space and Environmental Medicine, 57:504, 1986) describing a paper presented at the 1986 meeting of the Aerospace Medical Society (Nashville, TN, 1986). Other aspects of the study are currently in preparation.

Support from the co-operative agreement is also acknowledged in the following publications:

Book

Hours of Work: Temporal factors in work scheduling (S. Folkard and T.H. Monk (eds.)) John Wiley and Sons Ltd, New York, 1985

Refereed Articles

Monk, T.H., Fookson, J.E., Kream, J., Moline, M.L., Pollak, C.P. and Weitzman, E.D. Circadian Factors during Sustains Performance: Background and Methodology. Behavior Research Methods, Instruments, and Computers, 17, 19-26, 1985.

Monk, T.H., Fookson, J.E., Moline, M.L., Pollak, P. Diurnal Variation in Mood and Performance in a Time-Isolated Environment. Chronobiology International, 2 185-193, 1985.

Monk, T.H. and Fookson, J.E. Circadian Rhythm Power Spectra - Is Equal Sampling Necessary? Psychophysiology, 23, 472-479, 1986.

Monk, T.H. Parameters of the Circadian Temperature Rhythm Using Sparse and Irregular Sampling. Psychophysiology, 24, 236-242, 1987.

Monk, T.H. A Visual Analogue Scale Technique to Measure Global Vigor and Affect (GVA). Psychiatry Research (in press).

Monk, T.H. and Moline, M.L. The Timing of Bedtime and Waketime Decisions in Free-Running Subjects. Psychophysiology (in press).