

AD-A173 503

SEDATING AND NONSEDATING SLEEPING AIDS IN AIR
OPERATIONS(U) NAVAL HEALTH RESEARCH CENTER SAN DIEGO CA
C L SPINNEBER 14 JUL 06 NAVHLTHRSCHC-06-18

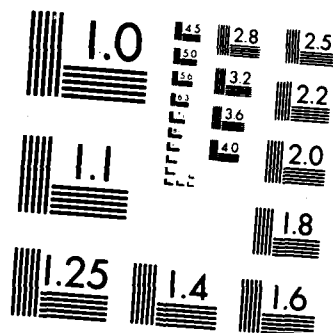
1/1

UNCLASSIFIED

F/8 6/15

NL





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963-A

AD-A173 503

2

SEDATING AND NONSEDATING SLEEPING AIDS IN AIR OPERATIONS

C. L. SPINWEBER

REPORT NO. 86-18

DTIC
ELECTE
OCT 27 1986
S B

DISTRIBUTION STATEMENT A
Approved for public release
Distribution Unlimited

DTIC FILE COPY



NAVAL HEALTH RESEARCH CENTER

P.O. BOX 85122
SAN DIEGO, CALIFORNIA 92138-9174

NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND
BETHESDA, MARYLAND

86 10 27 087

SEDATING AND NONSEDATING SLEEPING AIDS
IN AIR OPERATIONS

Cheryl L. Spinweber, Ph.D.

Naval Health Research Center
P. O. Box 85122
San Diego, California

To expedite communication of our research, this is a preprint of a paper to be published in the Proceedings of the Aerospace Medical Panel Symposium on Biochemical Enhancement of Performance and presented at the NATO Advisory Group for Aerospace Research and Development meeting in Lisbon, Portugal, 30 September-2 October 1986.

Report No. 86-18, was supported by the Naval Medical Research and Development Command, Department of the Navy, under research Work Units MF58528.002-0001 and MR04101.003-0161. The views presented in this paper are those of the author and do not reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U. S. Government. The author wishes to thank the Commanding General, the staff, and personnel of the Marine Corps, Camp Pendleton, California, for their cooperation and help with this study. In addition, the author notes with gratitude the participation of the Commanding Officers and personnel of the 1st Battalion, 5th Marine Division, and the 1st Battalion, 7th Marine Division.

SUMMARY

Both sedating and nonsedating sleeping aids may be appropriate for use in specific operational environments to promote sleep and permit efficient utilization of rest periods. "Sedating" agents, such as the benzodiazepine triazolam, produce an "impairment window" which is a period of time postadministration when performance and responsivity during sleep are impaired. "Nonsedating" agents, such as the amino acid l-tryptophan, enhance sleep but do not alter performance or responsivity at any time postadministration. In a field trial of use of l-tryptophan in U. S. Marines airlifted from California to Okinawa, l-tryptophan increased total sleep time the first night after arrival. This sleep enhancement was associated with significantly faster reaction times the next day, sparing of short-term memory from jet-lag effects, and more rapid recovery of reaction time over the first three days after arrival. Which type of agent to use in support of an air operation will be determined by the nature of the environments in which rest periods will occur and the duration of scheduled sleep times.



Approved for	✓
Signature	
Date	
A-1	

INTRODUCTION

The conduct of military air operations frequently involves transits across multiple time zones, altered work-rest schedules, and sustained performance under conditions of sleep loss. Over the years, the Behavioral Psychopharmacology Department of the Naval Health Research Center (NHRC) has focused on identifying the effects of these mission factors on human performance and has emphasized evaluation of sleeping aids for use in operational settings to promote sleep and permit efficient utilization of rest periods. Our research on sleeping aids is a component of a major research program designed to develop psychopharmacological techniques to enhance and maintain human performance. The approach and philosophy behind this research program were presented at an earlier DRG symposium (Spinweber and Johnson, 1983).

Our laboratory has carefully evaluated the suitability for operational use of the short half-life benzodiazepine triazolam (Halcion®) and the amino acid L-tryptophan, which are, respectively, sedating and nonsedating sleeping aids. From our point of view, the term "sedating sleeping aids" has a data-based definition--it is applied to those agents which, in addition to enhancing sleep through some pharmacological mechanism, produce measurable performance decrements and alter responsivity during sleep for some time period postadministration. This time window can be delineated in the research laboratory by repeated sampling of performance and arousal threshold, according to a standard research protocol. Conversely, "nonsedating" agents enhance sleep but do so without producing an "impairment window", as shown by performance and arousal threshold data which are not statistically different from placebo values.

In recent years, we have conducted several laboratory studies of triazolam (Johnson and Spinweber, 1983, 1984; Johnson et al., 1985; Spinweber and Johnson, 1982; Spinweber et al., 1985). Use of triazolam at the .5 mg dose was found to be associated with performance impairment up to 5 hours postadministration, anterograde amnesia, and elevated arousal thresholds during sleep (Spinweber and Johnson, 1982). The lower .25 mg dose had adequate hypnotic efficacy and was found to produce a smaller but significant performance decrement lasting approximately 4 hours after administration (Spinweber et al., 1985). We recently reported that responsivity to a smoke detector alarm sounded during sleep was strikingly reduced after triazolam administration at bedtime (Johnson et al., 1985). These changes in performance and responsivity during sleep are presumed to be a consequence of the nonspecific CNS depressant effects of benzodiazepine-hypnotics. Depending upon the nature of the operational environment and the mission demands, the acute effects of a short-acting benzodiazepine like triazolam may or may not be problematic: if personnel are scheduled for rest in safe locations with little probability that they will be called back to duty before the dose wears off, then agents such as triazolam may be excellent choices for operational use because of their rapid onset of action and exceptional efficacy in short-term administration. However, during the effective phase of drug action, personnel would be difficult to arouse and would

perform more poorly on reaction time, cognitive, and memory tasks up to 5 hours after drug use.

Because many missions require continuous readiness and are unpredictable in terms of scheduling work and rest periods, our laboratory has also investigated the nonsedating sleeping aid, l-tryptophan (Spinweber et al., 1983; Spinweber, 1980, 1981, 1986). L-tryptophan was considered to be appropriate for use in military operations because these laboratory studies had demonstrated that it did not impair performance at any time postadministration. We and other authors have suggested that its sleep-promoting action is mediated by a serotonergic deactivation of the awake state, thus establishing a preparatory relaxation which permits more rapid sleep onset. This mechanism is nonsedating, as shown by normal task performance, intact memory systems, and unaltered arousal threshold during the effective time period of action (Spinweber, 1986).

An air operation of considerable interest to the U. S. Marines, as well as to other services, is the airlift of large numbers of ground forces from the continental United States to distant locations. Rapid deployment across multiple time zones raises the operational issue of the consequences of the so-called "jet-lag syndrome" on military readiness. Jet-lag effects are hypothesized to result from at least three causes: sleep loss, the discrepancy between environmental and internal clocks, and circadian desynchronization. (For a discussion of these factors, see Spinweber et al., 1986). In the following report, the results of a field trial of the efficacy of l-tryptophan in reducing the sleep-loss component of the jet-lag syndrome are described.

L-tryptophan Field Trial. The U. S. Marine Corps, in its unit deployment concept, currently airlifts whole battalions from Camp Pendleton, California (located approximately 30 miles north of San Diego), to Okinawa, Japan, for 6-month training missions. In a given week, two 747 flights transit from San Diego to Okinawa, and, during the same week, two flights return from Okinawa carrying a second battalion home. This study was conducted on the first westbound flight from San Diego to Okinawa during one of these week-long air operations. The westbound flight is approximately 15 hours air time plus a 2-hour stop in Anchorage, Alaska. Local time in Okinawa is 17 hours ahead of California Pacific Standard Time (PST). In this study, data were obtained before, during, and after the flight to assess acute jet-lag effects and to evaluate the sleep-enhancing efficacy of l-tryptophan in the field.

METHOD

Subjects. Subjects were U. S. Marines stationed at Camp Pendleton, California, who were scheduled for deployment to Okinawa, Japan. Pilot data were collected from 27 Marine volunteers from the 1st Battalion, 5th Marine Division (1/5) (mean age 21.7 +

3.2 years). The operational trial was conducted with 51 Marine volunteers from the 1st Battalion, 7th Marine Division (1/7) (mean age 21.0 ± 2.2 years).

Procedure. The testing schedule for the operational trial is summarized in Table 1. Baseline data were collected 2 weeks prior to deployment on 3 consecutive days (B1, B2, and B3) at 0900 and 1500. On B3, in addition to the 0900 and 1500 batteries, an evening test battery was conducted at 2100. Also on B3, subjects were required to remain awake after the evening test battery until after another battery was conducted at 0300. The 4 test batteries scheduled on B3 provided comparison data for the day of the flight (F). Two days of preflight data (P1, P2) were collected at 0900 and 1500. During flight, only subjective measures and oral temperature were obtained. Arrival at Okinawa was at 1730 local time. An evening test battery was conducted at 2200. Testing on the first 2 full days (O1 and O2) in Okinawa was at 0900, 1500, and 2100. The study ended at 0800 on the third morning.

Table 1.

TEST SCHEDULE

Battery	Study Day	San Diego Time	Okinawa Time
1	B1 ¹	Mon 0900	
2	B1	Mon 1500	
3	B2	Tue 0900	
4	B2	Tue 1500	
5	B3	Wed 0900	
6	B3	Wed 1500	
7	B3	Wed 2100	
8	B3	Thu 0300	
(two weeks intervening time)			
9	P1 ²	Mon 0900	
10	P1	Mon 1500	
11	P2	Tue 0900	
12	P2	Tue 1500	
13 ⁶	F ³	Wed 0900 ⁵	
14 ⁶	F	Wed 1500 ⁵	
15 ⁶	F	Wed 2100 ⁵	
16 ⁷	F ⁴		Thu 2100 ⁵
17	O1 ⁴		Fri 0900 ⁵
18 ⁷	O1		Fri 1500
19 ⁷	O1		Fri 2100
20	O2		Sat 0900
21 ⁷	O2		Sat 1500
22 ⁶	O2		Sat 2100
23 ⁶	O3		Sun 0800

¹ "B" indicates baseline days, 2 weeks prior to departure week.

² "P" indicates days immediately prior to the flight day.

³ "F" indicates day of the flight.

⁴ "O" indicates days immediately following the day of flight.

⁵ Battery was delayed due to other requirements (see text).

⁶ Subjective measures and oral temperature only were obtained.

⁷ L-tryptophan 2 grams administered at the conclusion of the test battery.

Batteries 1-12 were conducted in the battalion mess hall at Camp Pendleton. Batteries 13-15 were conducted aboard the aircraft. Batteries 16-23 were conducted in a classroom at Camp Hansen in Okinawa.

Target shooting performance was assessed one week prior to departure and on O1. Both target shooting sessions occurred at 0800 local time. Stationary targets were used. The target consisted of 3 silhouettes. Subjects were allowed one practice round on the left and right silhouette and permitted to adjust their weapon sights. Then, each subject was allowed 8 rounds on the center silhouette. Accuracy was scored using a bull's-eye scoring system with a total possible accuracy score of 40 points. Each subject used his own M16 rifle on both days. A total of 45 subjects provided target scoring data in both locations.

L-tryptophan 2 g or placebo was administered en route after reboarding at Anchorage and on the first 3 nights in Okinawa at approximately 2200, following the evening test batteries. To maximize sleep during flight, environmental interventions included timing of meals and other inflight activities, avoiding caffeinated beverages, and control of cabin lighting.

Performance and Subjective Mood Measures. Performance measures included a test of reaction time, the Wilkinson 4-Choice Reaction Time Test (RT) (Wilkinson and Houghton, 1975); a decoding task, the Digit Symbol Substitution Test (DSST) (Wechsler, 1955); a test of short-term memory, the Williams Word Memory Test (STM) (Williams and Williams, 1966); and a test involving math calculations, the Wilkinson Addition Test (AT) (Wilkinson et al., 1966; Wilkinson, 1969). All tests chosen were known to be sensitive to sleep deprivation and to drug effects.

Subjective reports of mood were obtained through use of Analogue Mood Scales (AMS) which are a paper-and-pencil version of the computerized Visual Analogue Scales (VAS) developed by Monk et al. (1985), the Profile of Mood States (POMS) (McNair et al., 1971), and the Stanford Sleepiness Scale (SSS) (Hoddes et al., 1973).

Physiological Monitoring. Twelve subjects wore devices for ambulatory monitoring of physiological processes. We used Medilog 9-channel recorders available from Oxford Medilog, Inc. The following physiological parameters were recorded: Left/right EOG, C4 referred to A1, C3 referred to A2, O1 referred to A2, skin temperature from an ancillary placement, EKG from two chest electrodes, and chest impedance. In addition, a time code and an event marker channel were used. Medilog subjects wore the devices continually during waking and during sleep. Cassette tapes and batteries were changed once every 24 hours. For baseline data collection, Medilogs were applied and recordings begun on B1 and removed after the 0300 test session on B3. During the week of flight, Medilog electrodes were attached and recordings begun two days before the flight and Medilogs were removed after the 23rd test battery at the end of the study. Medilog tapes were later played back on the system scanner and scored for the presence of waking or sleep (Stages 2, 3, 4 or REM) by

human scorers. In this report, only the results of analysis of the EEG for total sleep time is described.

Statistical Analyses. A lengthy description of the statistical procedures employed and a detailed summary of results are presented in an NHRC Center Report (Spinweber et al., 1986) which is available by request from the senior author. Only an overview of the statistical procedures is presented here.

One approach to assessment of acute jet-lag effects was to measure and compare data for the same time of day at Camp Pendleton and at Okinawa. Test batteries were scheduled at 0900, 1500, and 2100 on B3 to provide baseline data for comparison with Okinawa data for the same time of day. These comparisons held local time (LT) of day constant and provided information about what kinds of jet-lag effects are to be expected if activities are scheduled according to the local time at destination. Statistically, effects were evaluated by comparing data for B3, O1, and O2 at 0900, 1500 and 2100 LT by ANOVA for repeated measures. Post hoc t-tests were used to isolate sources of significant F values.

A second statistical approach held biological time (BT) of day constant. This approach was used to determine the source of performance and mood changes that were found through the LT approach. The question asked in this approach was whether performance and mood measures were still locked to PST (biological time) and for how long after arrival. Our study design was structured to permit us to compare Okinawa data with Camp Pendleton data that was within an hour of the identical BT as follows: comparisons for the 0900 O1 and O2 batteries were made with the 1600 battery data from B3, the 1500 O1 and O2 batteries with the 2100 B3 data, and the 2100 O1 and O2 batteries with the 0300 battery from B3.

RESULTS

Sleep Management. L-tryptophan subjects obtained significantly more sleep on the first night in Okinawa compared to placebo subjects (274.5 ± 19.9 minutes versus 222.3 ± 44.8 minutes, $t = 2.16$, $p < .0314$). Total nocturnal sleep time was not enhanced on the following 2 nights. En route, control of the aircraft environment dramatically increased sleep compared to total sleep time measured in the pilot study. Pilot study Medilog subjects only obtained 120.0 ± 72 minutes sleep aboard the aircraft. The range was 16 minutes of sleep in one subject to a maximum of 3 hours 52 minutes in another. Total sleep time during the operational trial was 291.3 ± 79.2 minutes for placebo subjects and 324.3 ± 145.9 minutes for l-tryptophan subjects. This 33-minute difference in total sleep time between the 2 groups was not statistically significant. The range of sleep times was 2 to 7 hours.

Acute Effects of Flight. Upon arrival, the l-tryptophan subjects had higher mean self-reported alertness (44.7 ± 28.1 versus 31.3 ± 14.4 , $t(47) = 2.09$, $p < .0425$), and a more positive mean rating of overall mood (44.4 ± 23.2 versus 31.5 ± 17.2 , $t(47) =$

2.20, $p < .0327$) on the AMS. There were no performance differences between the two treatment groups upon arrival.

To determine the acute effects of flight upon performance over all subjects, battery 16 performance data were compared with battery 7 data and, separately, with battery 8 data using t-tests for correlated means. The comparisons with battery 7 provide a LT analysis and, with battery 8, a BT analysis. DSST showed essentially no decrement upon arrival. STM data suggested some slight impairment upon arrival but, comparisons of battery 16 data with battery 7 and battery 8 data showed no statistically significant differences. For AT, performance upon arrival resembled battery 8 performance and, in fact, differed significantly from battery 7. For RT, performance upon arrival was significantly slower than both battery 7 and battery 8 mean reaction times.

Evaluation of the acute effects of flight on subjective mood proceeded similarly. All t-test comparisons between battery 7 and battery 16 were highly significant. Overall, there were fewer significant differences between subjective mood upon arrival and subjective mood reported at 0300 on B3 at Camp Pendleton. Notably, reported alertness, effort required, weariness, sleepiness, and fatigue were similar upon arrival at 2200 to those at 0300 LT at Camp Pendleton. Measures which may reflect more the psychosocial difficulties encountered upon arrival including customs, a drug information lecture, and a rather long bus ride to Camp Hansen, were significantly worse than battery 8 measures. These reports included being more sad, more tense, less calm, having a poorer overall mood, and more depression and anger.

Performance Measures. Mean RT data for the l-tryptophan and placebo groups are presented in Figure 1. L-tryptophan subjects had significantly faster reaction times than placebo subjects at 2100 on O1.

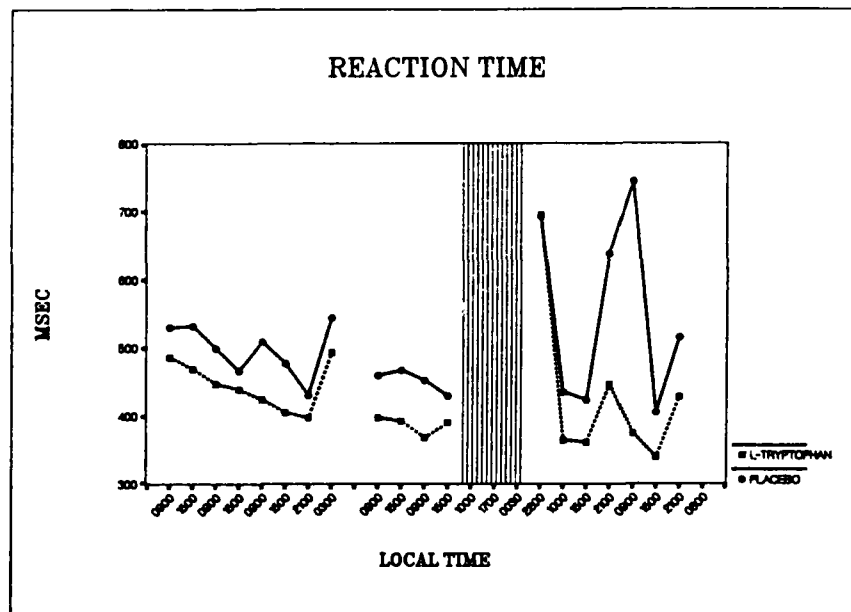
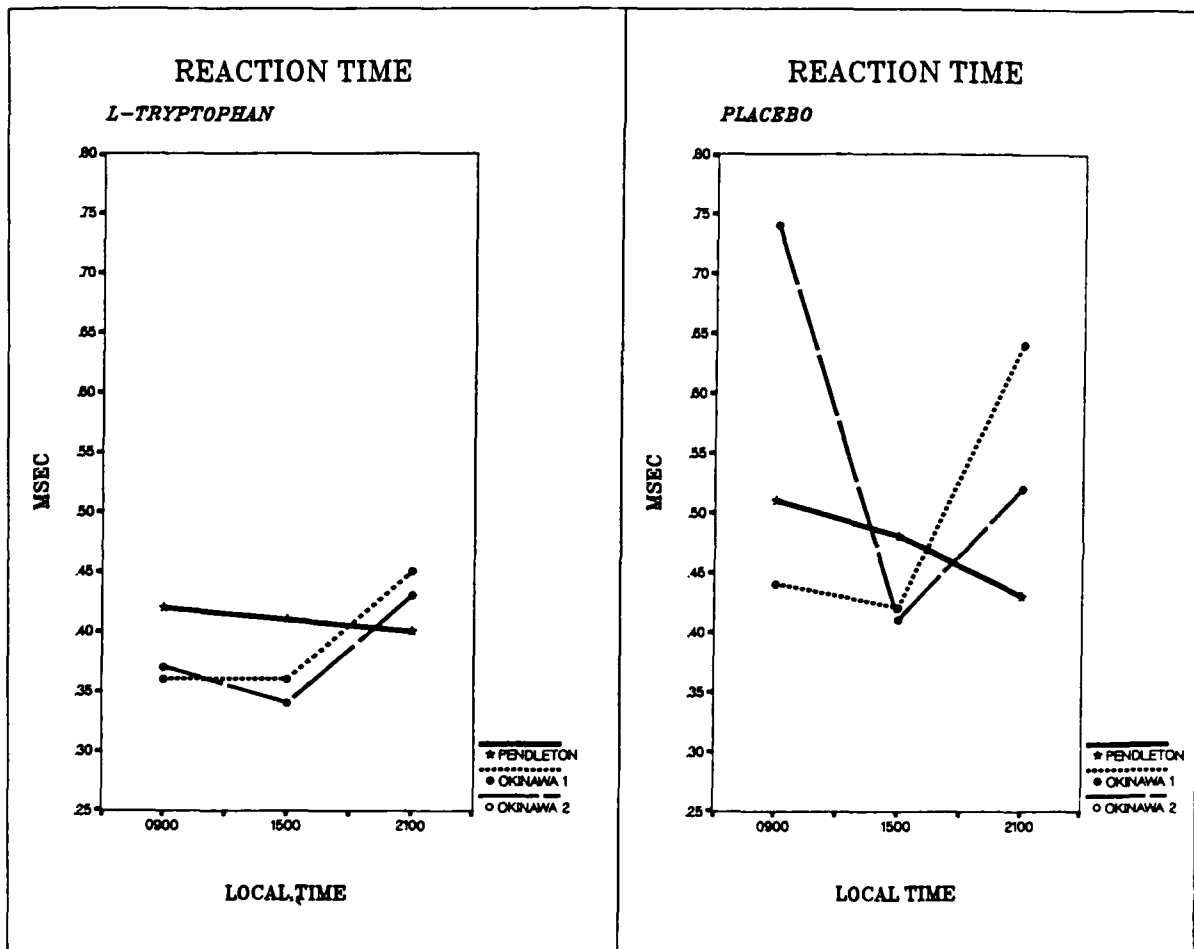


Figure 1. Mean reaction time (RT) on the 4-choice Reaction time Test for the l-tryptophan and placebo groups separately for all test sessions.

Figures 2a and b present RT data for 0900, 1500, and 2100 on B3, O1, and O2 for each treatment group separately. These figures show that the l-tryptophan group's mean RTs show little change over time, while the placebo group showed a slowing at 0900 on O1 as well as at 2100 on O2.



Figures 2a & b. Mean reaction time (RT) on the 4-choice Reaction Time Test at 0900, 1500, and 2100 on study days B3, O1, and O2 for l-tryptophan and placebo groups, separately.

Mean STM data for all performance batteries are presented in Figure 3. The LT analysis showed a significant day-by-treatment group interaction which was due to the fact that, compared to baseline, overall performance in the l-tryptophan group

did not decline on O1 and O2, while performance in the placebo group showed a within-group impairment on both days.

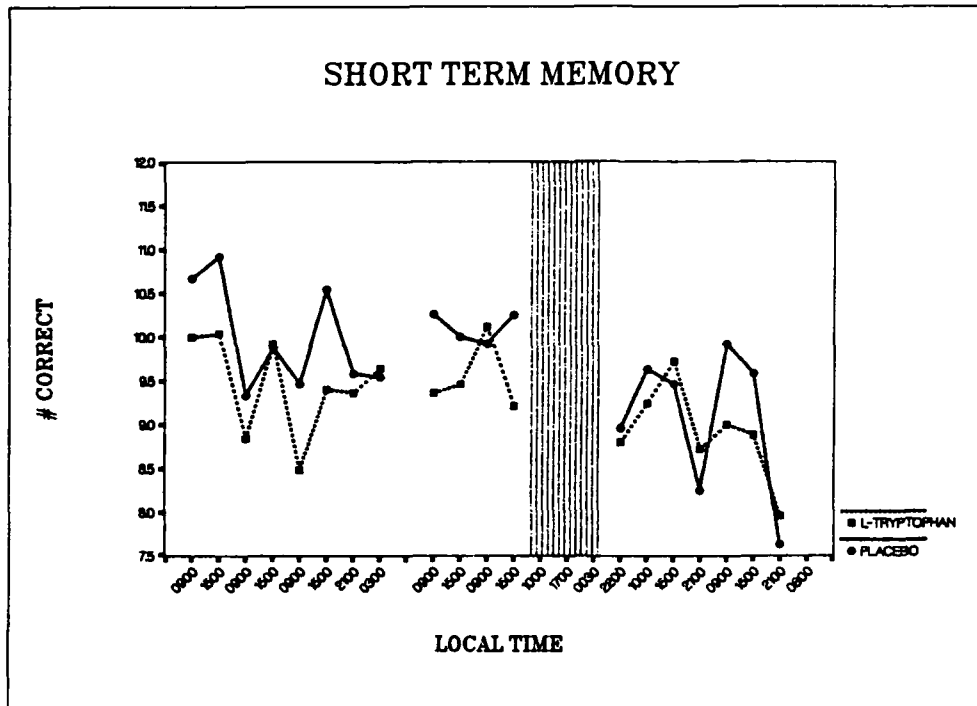
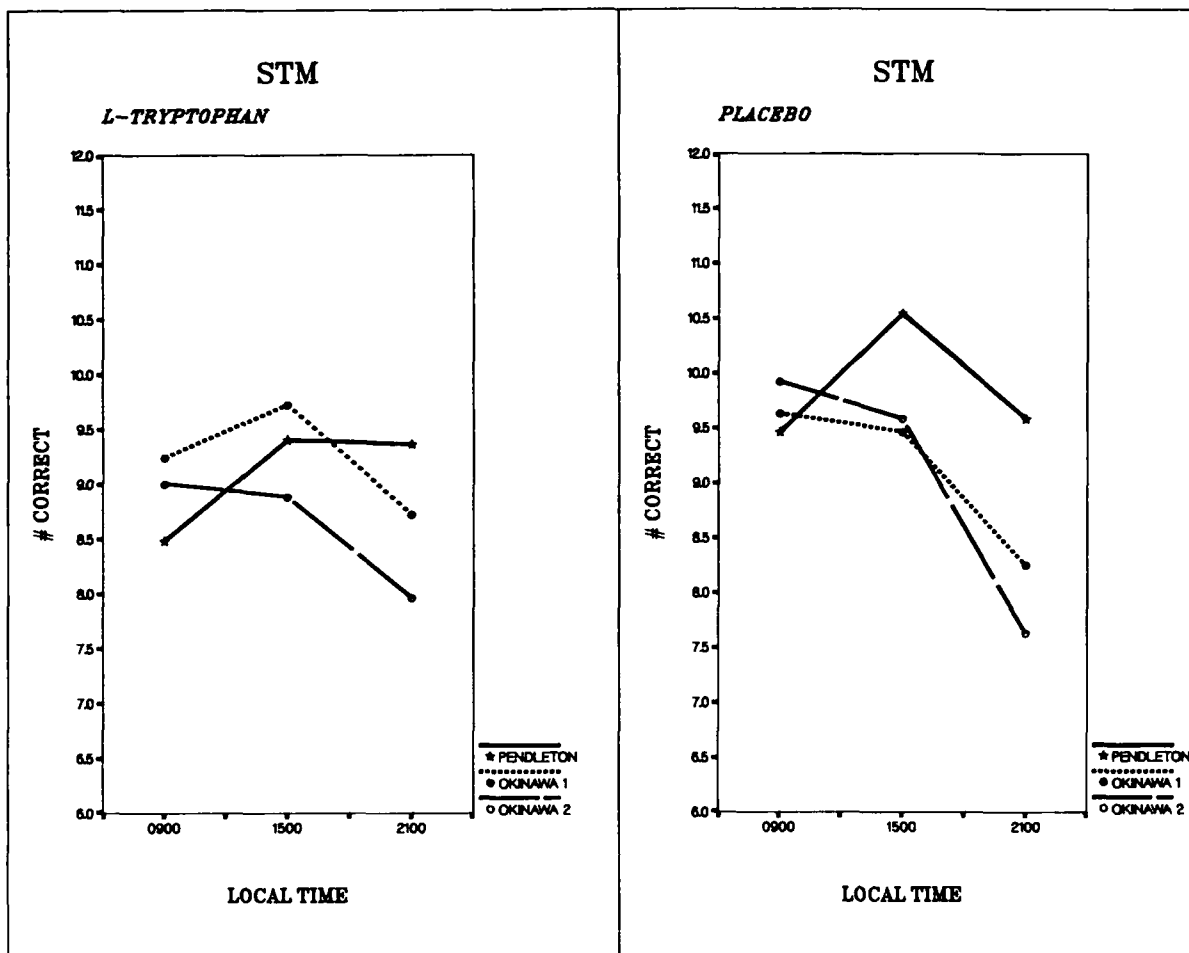


Figure 3. Mean number correct on the Williams Word Memory Test (STM) for the l-tryptophan and placebo groups separately for all test sessions.

As can be seen in Figures 4a and b, in the l-tryptophan group, the evening decrement in STM performance was not present on O1 but did show up on O2. The placebo group curves for O1 and O2 were highly similar to each other, and the evening decrement was present on both days.

The other performance measures AT, DSST, and target shooting accuracy showed jet-lag effects in the LT analyses, but there were no treatment-group differences.



Figures 4a & b. Mean number correct on the Williams Word Memory Test (STM) at 0900, 1500, and 2100 on study days B3, O1, and O2 for l-tryptophan and placebo groups, separately.

In order to quantify the degree of performance loss occurring in the evenings according to LT, the numerical change in mean performance at the time of arrival and on each of the two subsequent evenings was compared to the mean performance obtained during battery 7. Results are presented in Table 2a for the DSST, AT, and STM. The calculations were based on all subjects, collapsed over treatment groups. The target shooting percentage decrement was 33%. For RT, in which treatment-group differences were present, the comparable percentages for the placebo subjects were 61.3%, 48.4%, and 19.9%. For l-tryptophan subjects, the percentage decrements were 72.6%, 12.2%, and 7.7%.

Table 2a.

PERFORMANCE LOSS (PERCENT DECREMENT)

Task	Upon Arrival ¹	After 1 Day ²	After 2 Days ³
DSST	2.1%	4.4%	-8.4% ⁴
AT (attempted)	23.1%	13.9%	3.2%
AT (# correct)	26.0%	14.5%	3.2%
STM	6.3%	10.5%	17.9%

¹ Battery 16 compared to battery 7.² Battery 19 compared to battery 7.³ Battery 22 compared to battery 7.⁴ The negative value indicates that the mean performance score in Okinawa was higher than that of the baseline mean at 2100 on B3.

For comparison, percentage decrement values were also computed using battery 8 data as baseline providing a BT approach by comparing 0300 LT on B3 with the evening test batteries in Okinawa. These results are presented in Table 2b. On RT, for placebo subjects, the percent decrements were 27.4 and 17.3 for the first two nights in Okinawa. RT had recovered by the third night. For l-tryptophan subjects, a 39% decrement was present upon arrival, but RT performance had recovered after the first night of sleep.

Table 2b.

PERFORMANCE LOSS (PERCENT DECREMENT)

Task	Upon Arrival ¹	After 1 Day ²	After 2 Days ³
DSST	1.2%	3.6%	-9.4% ⁴
AT (attempted)	7.1%	-4.1% ⁴	-17.0% ⁴
AT (# correct)	8.8%	-6.1% ⁴	-20.1% ⁴
STM	7.3%	11.5%	18.8%

¹ Battery 16 compared to battery 8.² Battery 19 compared to battery 8.³ Battery 22 compared to battery 8.⁴ The negative values indicate that the mean performance score in Okinawa was higher than that of the baseline mean at 0300 on B3.

Subjective Mood Measures. Because of the large number of subjective variables, an overall review of mood effects will be presented here. As illustrated, mean reported sleepiness on the SSS for the 23 batteries is presented in Figure 5. Mean reported "effort" (that is, "how much of an effort is it to do anything?") for the 23 performance batteries is presented in Figure 6.

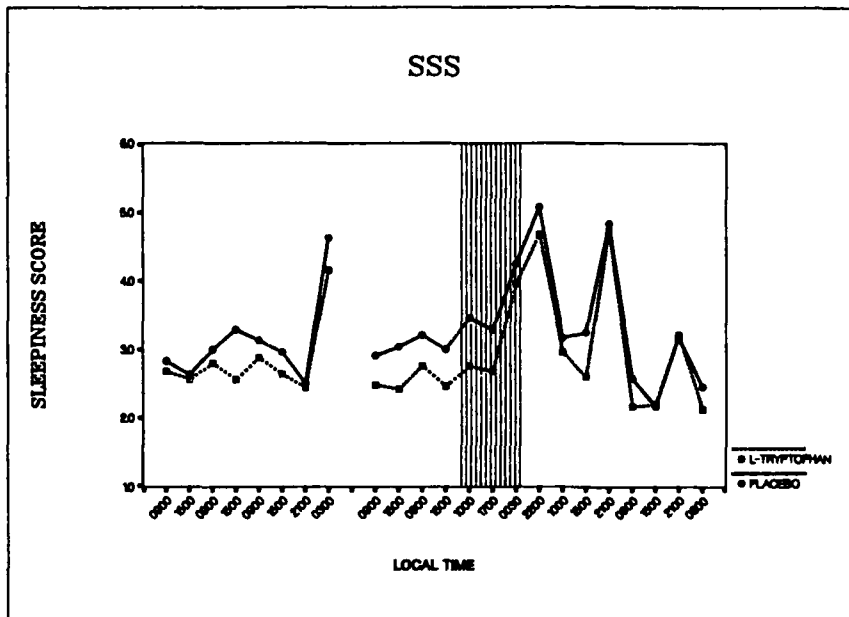


Figure 5. Mean subjective sleepiness on the Stanford Sleepiness Scale (SSS) for the l-tryptophan and placebo groups separately for all test sessions.

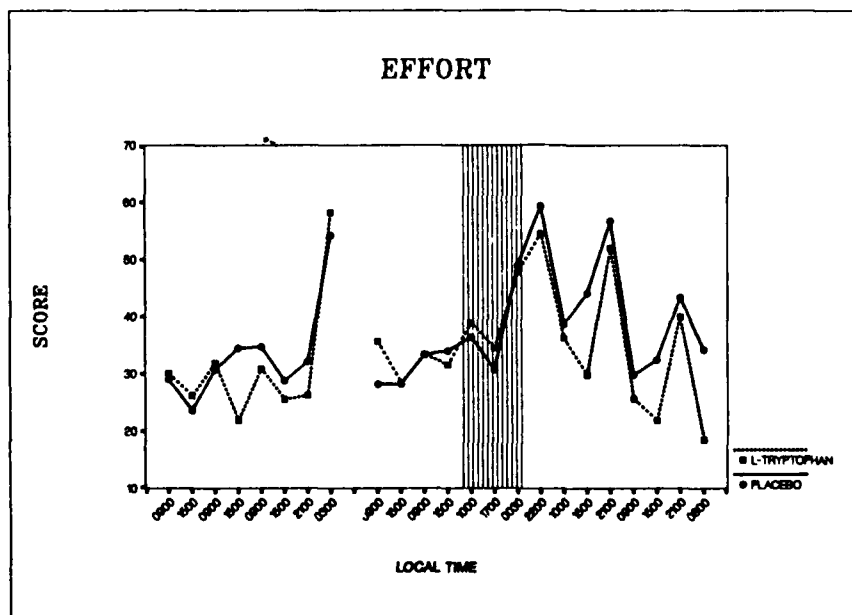


Figure 6. Mean reported "effort" on the Analogue Mood Scales (AMS) for the l-tryptophan and placebo groups separately for all test sessions.

Compared to the same time of day on B3 at Camp Pendleton, all mood measures were significantly worse in the evening at 2100 on O1. Certain measures indicated poorer mood throughout the day on O1: these included more sadness, less happiness, more depression and less vigor. By O2, subjective mood recovered. Overall, mood measures were still worse in the evening on O2, but there were fewer statistically significant comparisons with baseline.

DISCUSSION

L-tryptophan Field Trial. Major goals of this study of transmeridian flight were to document performance and mood changes and to examine the efficacy of two sleep-enhancing interventions in alleviating acute effects of jet lag.

The environmental controls were very effective in increasing the sleep en route, as objectively measured on Medilog subjects in this operational trial, compared to the pilot subjects studied earlier. The elements of those controls were varied and included timing of activities to maximize uninterrupted sleep periods, control of diet, and administration of a "pill". These manipulations alone increased mean sleep time more than 2 3/4 hours compared to mean sleep time of pilot subjects. The l-tryptophan effect aboard the aircraft was not statistically significant, even though the mean increase above placebo was 33 minutes. In laboratory studies of overnight sleep, a mean increase in total sleep time of over 1/2 hour compared to placebo would ordinarily be statistically significant and considered to be substantial. The 52-minute increase in total sleep on the first night in Okinawa was considerable, as well. In this case, the difference between l-tryptophan and placebo groups reached statistical significance. There was no sleep-enhancing effect, though, on subsequent nights. It is important to note that most previous studies reporting positive findings on l-tryptophan emphasized effects on sleep latency rather than total sleep time. In fact, in previous studies, when sleep latency was reported to be reduced, total sleep time was often not statistically increased. In this study in the field, it was impossible to obtain reliable and valid sleep latency measures for individuals and, therefore, we used total sleep time as a measure of sleep-enhancing efficacy. In view of the use of total sleep time rather than sleep-onset time as the dependent measure of efficacy, we were impressed with both the en route and first-night effects.

It may be the case that the absence of sleep-enhancing effects on the second two nights in Okinawa was due to inadequate dose size. On the day of the flight, subjects received two doses of 2 g each, one en route and one after the evening test battery. Our previous sleep laboratory study demonstrating daytime sleep-enhancing effects used a 4-g dose (Spinweber et al., 1983).

Upon arrival, significant between-groups differences were present only on subjective measures; l-tryptophan subjects reported more alertness and more positive overall mood. But, on O1, after having obtained significantly more nocturnal sleep time

(that is, 52 minutes additional nighttime sleep), the l-tryptophan group differed clearly from the placebo group on one important measure, the faster mean reaction time performance at 2100 on the RT. Probably because it is a longer duration test, RT is very sensitive to sleep-loss effects. The difference between groups on RT showed up at the time of maximal performance loss on several tests, so we are confident that this RT difference reflects real treatment differences. There is also an indication that STM performance is spared from "jet-lag" effects in the l-tryptophan group on O1. In addition, these data indicate that RT may recover more quickly in l-tryptophan subjects.

There have been no laboratory studies of sleeping pills and next-day performance which demonstrated enhanced next-day performance in subjects who take the active pill compared with those taking the placebo. (For an extensive review of such studies and a comprehensive discussion of sleeping pills and performance effects, see Johnson and Chernik, 1982). This study is the first demonstration that improving sleep by psychopharmacological means is associated with enhanced performance on any measure of performance the following day. Perhaps of equal importance, in contrast to sedative-hypnotics, l-tryptophan produced no decrement in performance at any time compared to placebo.

Operational Implications. The field trial results have important implications for westward rapid deployments having operational demands similar to those occurring in this troop airlift. First, the importance of sleep enhancement cannot be over-emphasized. By controlling the aircraft environment and administering l-tryptophan 2 g, the company commander can increase total sleep time en route by over 3 hours. L-tryptophan is also effective in enhancing nocturnal sleep after arrival. It is suggested that the appropriate dose for use on the second and third nights after arrival is 4 g.

Second, "jet-lag effects" on performance are problems primarily in the evening and adjustment occurs quickly, for many measures, by the second full day after arrival. Reaction time performance seems to be most sensitive to jet-lag effects and, conversely, to sleep enhancement. If possible, company commanders should avoid nighttime operations on the day of transit and the following day. By the evening of the second full day at destination, the ability to perform calculation quickly and accurately (AT) and decoding performance (DSST) are essentially recovered. Memory performance, though, may continue to deteriorate over the first 3 nights at destination. The protocol did not extend long enough to identify the time at which short-term memory recovers. Additional justifications for the use of l-tryptophan in the field are that its administration appeared to spare memory to some degree and to hasten readjustment of reaction time performance.

Third, mood upon arrival is generally no worse than would be expected in the middle of the night after a small amount of sleep loss. Throughout the first full day after arrival, mood is poorer than predeployment. If possible, operations requiring

positive mood and feelings of alertness and vigor should be scheduled on the second day after arrival.

Extrapolating from both the performance and mood data collected in this study, it appears that military operations would be most effectively conducted in the morning of what would be day 02, the day occurring after 2 nights of sleep and 1 full day at destination. This time frame is consistent with certain U. S. Marine wartime scenarios. Earlier operations would require compensation for performance impairment in the evenings and impaired mood throughout the first day at destination. The above conclusions would probably hold for similar deployments crossing time zones in the westward direction. Results from other published studies suggest impairment following a similar eastward deployment would be greater and persist longer.

Indications for Use of Sedating and Nonsedating Sleeping Aids. As is now known, the RAF aircrews used a sedating sleeping aid, temazepam (Restoril®), in the Falkland conflict in 1982 (Baird et al., 1983). We have not tested temazepam in our own laboratory because the U. S. formulation of the drug currently available is slowly absorbed and has a much longer half-life than the form of temazepam available in Great Britain. In addition, there is a question about the sleep-inducing efficacy of the U. S. version of temazepam (Bixler et al., 1978, Mitler et al., 1979). For the RAF, the critical factors permitting use of a sedating sleeping aid were that rest periods occurred on Ascension Island, away from the scene of conflict, and crews were not scheduled to fly again for at least 6-8 hours (Baird et al., 1983). For similar U. S. operations, triazolam would be a suitable agent for use, based on our laboratory studies.

In the major troop movement by airlift described in this paper, there was a continuing requirement that personnel retain the ability to awaken readily with intact memory and other cognitive and visuomotor skills, both en route and after arrival. When the decision is made that an impairment window is not acceptable, then psychopharmacological support for the mission must involve use of nonsedating sleeping aids.

The decision regarding which pill to employ rests primarily upon consideration of the impairment window (see Table 3). If the environment is safe and the duration of the rest period can be established in advance, then the sedating agent may be the better choice since it acts more rapidly and, perhaps, more consistently than l-tryptophan. (For a discussion, see Spinweber et al., 1983). However, in other operational environments--aboard aircrafts or in dangerous environments--or for use in brief rest periods of undetermined duration, l-tryptophan would be the agent of choice since its sleep-promoting effects are completely reversible and its use is not associated with an impairment window.

Table 3.

Sleeping Aids for Operational Use

	Sedating	Nonsedating
Agent	triazolam	tryptophan
Class	benzodiazepine	amino acid
Dose	.125-.5 mg	1-4 g
Impairment Window	4-5 h	none
Onset of Action	15 min	45-60 min

REFERENCES

- Baird JA, Coles PK, and Nicholson AN. Human factors and air operations in the South Atlantic campaign: discussion paper. J R Soc Med, Vol. 76, No. 11, 1983, 933-937.
- Bixler EO, Kales A, Soldatos CR, Scharf MB, and Kales JD. Effectiveness of temazepam with short-, intermediate-, and long-term use: sleep laboratory evaluation. J Clin Pharmacol, Vol. 18, 1978, 110-118.
- Hoddes E, Zarcone V, Smythe H, Phillips R, and Dement WC. Quantification of sleepiness: a new approach. Psychophysiology, Vol. 10, 1973, 431-436.
- Johnson LC and Chernik DA. Sedative hypnotics and human performance. Psychopharmacology, Vol. 76, 1982, 101-113.
- Johnson LC and Spinweber CL. Benzodiazepine effects on arousal threshold during sleep. Proceedings of the Fourth International Congress on Noise as a Public Health Problem, Turin, Italy, 21-25 June 1983, Centro Ricerche e Studi Amplifon, Milano, Italy, 973-984.
- Johnson LC and Spinweber CL. Benzodiazepine activity: daytime effects and the sleep EEG. Presented at the 14th Collegium Internationale Neuro-Psychopharmacologicum Congress (C.I.N.P.), Florence, Italy, 19-23 June 1984. Clin Neuropharmacol, Vol. 7, Supplement 1, 1984, 820-821.
- Johnson LC, Spinweber CL, Webb SC, and Muzet AM. Dose level effects of triazolam on sleep and response to a smoke detector alarm. Naval Health Research Center, San Diego, CA, Report #85-44, 1985.

- McNair DM, Lorr M, and Droppleman LF. Manual for the POMS. San Diego: Educational And Industrial Testing Service, 1971.
- Mitler MM, Carskadon MA, Phillips RL, Sterling WR, Zarcone VP Jr, Spiegel R, Guilleminault C, and Dement WC. Hypnotic efficacy of temazepam: a long-term sleep laboratory evaluation. Br J Clin Pharmacol, Vol. 8, 1979, 63S-68S.
- Monk TH, Fookson JE, Kream J, Moline ML, Pollak CP, and Weitzman MB. Circadian factors during sustained performance: background and methodology. In JB Sidowski (Ed), Behavior Research Methods, Instruments, & Computers, Vol. 17, No. 1, 1985, 19-26.
- Spinweber CL. Plasma l-tryptophan levels, subjective sleepiness, and daytime sleep. Naval Health Research Center, San Diego, CA, Report #80-25, 1980.
- Spinweber CL. Daytime effects of l-tryptophan. Psychopharmacol Bull, Vol. 17, 1981, 81-82.
- Spinweber CL. L-tryptophan administered to chronic sleep-onset insomniacs: late-appearing reduction of sleep latency. Psychopharmacology, 1986, in press.
- Spinweber CL and Johnson LC. Effects of triazolam (0.5 mg) on sleep, performance, memory, and arousal threshold. Psychopharmacology, Vol. 76, 1982, 5-12.
- Spinweber CL and Johnson LC. Psychopharmacological techniques for optimizing human performance. Proceedings of the 24th DRG Seminar on The Human as a Limiting Element in Military Systems, Toronto, Canada, 2-4 May 1983, Vol. I, 1983, 139-157.
- Spinweber CL, Ursin R, Hilbert RP, and Hilderbrand R. L-tryptophan: effects on daytime sleep latency and the waking EEG. Electroencephalogr Clin Neurophysiol, Vol. 55, 1983, 652-661.
- Spinweber CL, Johnson LC, and Webb SC. Dose level effects of triazolam on memory. Presented at the Benzodiazepines and Memory Conference, San Diego, California, 24-25 January 1985.
- Spinweber CL, Webb SC, and Gillin JC. Jet lag in military operations: field trial of l-tryptophan in reducing sleep-loss effects. Naval Health Research Center, San Diego, CA, Report #86-15, 1986.
- Wechsler D. Manual for the Wechsler Adult Intelligence Scale. New York: Psychological Corp., 1955.
- Wilkinson RT. Sleep deprivation: performance tests for partial and selective sleep deprivation. In L. A. Abt & B. F. Riess (Eds), Progress in Clinical Psychology, Vol. 8. New York: Grune & Stratton, 1969.
- Wilkinson RT and Houghton D. Portable four-choice reaction time test with magnetic tape memory. Behavior Research Methods & Instrumentation, Vol. 7, No. 5, 1975, 441-446.
- Wilkinson RT, Edwards RS, and Haines E. Performance following a night of reduced sleep. Psychonomic Sci, Vol. 5, 1966, 471-472.
- Williams HL and Williams CL. Nocturnal EEG profiles and performance. Psychophysiology, Vol. 3, 1966, 164-175.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM								
1. REPORT NUMBER 86-18	2. GOVT ACCESSION NO. ADA173503	3. RECIPIENT'S CATALOG NUMBER								
4. TITLE (and Subtitle) Sedating and Nonsedating Sleeping Aids in Air Operations		5. TYPE OF REPORT & PERIOD COVERED Interim (Oct 1985 - July 1986)								
		6. PERFORMING ORG. REPORT NUMBER								
7. AUTHOR(s) Cheryl L. Spinweber		8. CONTRACT OR GRANT NUMBER(s)								
9. PERFORMING ORGANIZATION NAME AND ADDRESS Naval Health Research Center P. O. Box 85122 San Diego, CA 92138-9174		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS MR04101.003-0157 MF58528.002-0001								
11. CONTROLLING OFFICE NAME AND ADDRESS Naval Medical Research & Development Command Naval Medical Command, National Capital Region Bethesda, MD 20814		12. REPORT DATE 14 July 1986								
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) Commander, Naval Medical Command Department of the Navy Washington, DC 20372		13. NUMBER OF PAGES								
		15. SECURITY CLASS. (of this report) UNCLASSIFIED								
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE								
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.										
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) Approved for public release; distribution unlimited.										
18. SUPPLEMENTARY NOTES None										
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) <table border="0"> <tr> <td>Jet lag</td> <td>Sedating & nonsedating sleeping aids</td> </tr> <tr> <td>Benzodiazepines</td> <td>Psychopharmacological techniques</td> </tr> <tr> <td>L-tryptophan</td> <td>Sleep</td> </tr> <tr> <td>Performance enhancement</td> <td>Humans</td> </tr> </table>			Jet lag	Sedating & nonsedating sleeping aids	Benzodiazepines	Psychopharmacological techniques	L-tryptophan	Sleep	Performance enhancement	Humans
Jet lag	Sedating & nonsedating sleeping aids									
Benzodiazepines	Psychopharmacological techniques									
L-tryptophan	Sleep									
Performance enhancement	Humans									
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Both sedating and nonsedating sleeping aids may be appropriate for use in specific operational environments to promote sleep and permit efficient utilization of rest periods. "Sedating" agents, such as the benzodiazepine triazolam, produce an "impairment window" which is a period of time post-administration when performance and responsivity during sleep are impaired. "Nonsedating" agents, such as the amino acid l-tryptophan, enhance sleep but do not alter performance or responsivity at any time postadministration. In										

DD FORM 1 JAN 73 1473

EDITION OF 1 NOV 68 IS OBSOLETE

S/N 0102-LF-014-6601

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

a field trial of use of l-tryptophan in U. S. Marines airlifted from California to Okinawa, l-tryptophan increased total sleep time the first night after arrival. This sleep enhancement was associated with significantly faster reaction times the next day, sparing of short-term memory from "jet-lag" effects, and more rapid recovery of reaction time over the first three days after arrival. Which type of agent to use in support of an air operation will be determined by the nature of the environments in which rest periods will occur and the duration of scheduled sleep times.

S/N 0102- LF-014- 6601

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

END

12-86

DTIC