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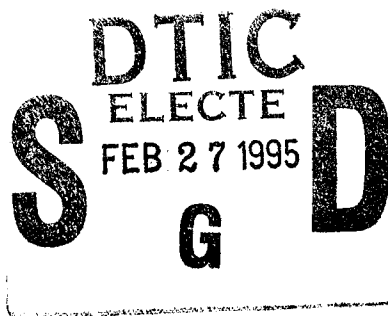
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## *THE EFFECT OF BRIGHT LIGHT AND LEET ON SLEEP AFTER A 10-HOUR PHASE DELAY*

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THE EFFECT OF BRIGHT LIGHT AND LEET ON SLEEP  
AFTER A 10-HOUR PHASE DELAY

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## SUMMARY

### Problem

Disruption of sleep can be a problem for shift workers or with jet lag because of conflicts between internal circadian rhythms and the sleep/wake schedule. Sedative-hypnotic agents have drawbacks, particularly for operational conditions. Controlled bright light exposure can shift circadian rhythms, but its effects on sleep have not been verified polysomnographically, and light exposure can be difficult to control. Low Energy Emission Therapy (LEET) has shown evidence of promoting sleep in insomniac and normal subjects, but has never been tested under shift work or jet lag conditions.

### Objective

The purpose of this study was to verify polysomnographically whether controlled bright light exposure or LEET could improve sleep quality under conditions similar to shift work or jet lag, and to determine whether combining the two interventions led to increased benefits.

### Approach

At the start of the study, subjects slept 2 nights in the laboratory. The first night was to allow adaptation to the laboratory environment, the second night was recorded as baseline sleep data. Subjects then underwent a 10-hr phase delay of the work/rest schedule, accomplished by delaying the onset of the following sleep period by 10 hr. Sleep was recorded during the daytime sleep period on each of the next three days. There were four parallel groups. The Light group received 4 hr of bright (>3500 lux) white light, from 2200 to 0200 each night after the shift, and inactive LEET before the daytime sleep periods. The LEET group was exposed to dim (<300 lux) red light, during the 2200 to 0200 periods, and active LEET before the daytime sleep periods. The Light/LEET group received bright light and active LEET. The Control group received dim light and inactive LEET.

### Result

Total sleep time (TST), Sleep Efficiency (SE), Sleep Latency (SL), and total number of awakenings were similar between the groups at baseline, although exact amounts of Stage 2 sleep and REM sleep varied somewhat. During the first daytime sleep period, both interventions appeared to decrease the total number of awakenings, as compared to the Control group. The effect of bright light was larger, and bright light and LEET effects were not additive. After three nights of treatment, subjects who received bright light had significantly greater TST and higher SE, with no change in SL. While there was a trend for a similar additive effect from LEET (the Light/LEET group slept better than the Light group and the LEET group slept better than the Control group), the LEET effect was not significant, possibly related to the small group sizes.

### Conclusion

Three nights of bright light exposure, timed to promote a phase delay of the endogenous circadian rhythms, improves sleep by helping individuals to remain asleep rather than by helping them to fall asleep more quickly at the start of the sleep period. The effects of LEET are inconclusive.

## INTRODUCTION

Shift work and jet lag have been demonstrated to disrupt sleep.<sup>1,2</sup> Sleep disruption can cause decreased alertness and impaired cognitive performance, as well as subjective discomfort.<sup>1</sup> With shift work, this can be a persistent problem. Even long-term night shift workers rarely show complete adjustment of their circadian rhythms to a reversed sleep-wake cycle,<sup>3,4</sup> and night workers have significantly shorter sleep duration than day workers.<sup>4</sup> Several interventions have been investigated to remedy the problem of circadian desynchronization-related sleep disruption, including sedative-hypnotic agents,<sup>5,6</sup> melatonin,<sup>2</sup> optimization of sleep hygiene (sleep habits and sleeping environment),<sup>7</sup> and controlled timing of bright light exposure.<sup>8,9,10</sup> Sleeping medications can improve daytime sleep,<sup>5</sup> but should not be used chronically.<sup>11</sup> Additionally, such drugs are typically associated with a decrement in performance and alertness for some period after use.<sup>12</sup> This is a drawback in military (and many civilian) environments in which personnel may be required to respond to emergencies. Melatonin may prove to be a superior agent; however, research on the use of melatonin to promote sleep is only in the preliminary stages. Optimization of sleep hygiene is always desirable, but many military situations provide poor sleeping environments (i.e., noisy, too much light, or otherwise uncomfortable) that cannot be altered. Also, changing sleep habits can be a time-consuming and difficult process.

Controlled light exposure can shift circadian rhythms in lower animals,<sup>13</sup> and, if the light is sufficiently bright, in humans.<sup>14</sup> Careful timing of bright light exposure may improve adjustment to shift work.<sup>8</sup> However, we have found no studies of bright light in shift work that included polysomnographically recorded sleep. Light exposure can be difficult to control. Combining bright light with another sleep-promoting intervention might provide superior results.

The idea of using electromagnetic fields to induce or alter sleep has been the focus of a significant amount of research.<sup>15</sup> However, much of this research has been poorly controlled, making the results difficult to interpret. Recent well-designed studies utilizing the Symtonic Low Energy Emission Therapy (LEET) Device (Symtonic SA, Renens, Switzerland) have suggested this device is effective for promoting sleep in normal individuals as well as in patients with insomnia.<sup>16,17,18,19,20,21</sup> The Symtonic LEET device administers very low intensity, amplitude-modulated electromagnetic fields intrabuccally using a mouth-held transmitter. Radio waves at selected frequencies between 0.1 and 10 kHz are spaced in specific pulsed patterns through the 20-min treatment period. The emissions produce no physical sensations and fall within a range that current FDA and international guidelines accept as safe.<sup>22</sup> A detailed description of the LEET device has been published elsewhere.<sup>20</sup>

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The LEET device has not previously been tested for its efficacy in treating shift work or jet lag-related sleep problems. Effects of LEET stimulation on circadian rhythms have not been reported, nor have effects of combining bright light and LEET. Previous work in animals indicated that the circadian phase-shifting effects of light can interact with other phase-shifting interventions.<sup>23</sup> Thus, if LEET does affect circadian rhythms, it might interact with the circadian effects of bright light in humans.

The purpose of this study was to examine the effects of timed bright light exposure and LEET therapy, separately and together, after a 10-hr shift of the work/rest cycle. The focus of this report is on the effects of these interventions on sleep. Other data<sup>a</sup> will be reported elsewhere.

## METHODS

### Subjects

Nonsmoking male volunteers with no history of sleep disorders who followed a normal nighttime sleep schedule were assigned to one of four groups. All subjects provided informed consent. To avoid problems of caffeine withdrawal symptoms,<sup>24</sup> heavy caffeine users (more than 3 cups of coffee, or the equivalent, per day) were excluded and subjects who regularly drank coffee were allowed one 5-oz cup of coffee with breakfast each day. Coffee and other stimulants (tea, caffeinated soft drinks) were otherwise not allowed during the study. No symptoms suggestive of caffeine withdrawal were observed.

Table 1 shows the number and ages of subjects who completed the protocol under each of the four conditions and had complete data to be included in the analysis.

TABLE 1: STUDY GROUPS

Group	LEET	Light	N	Age $\pm$ SD
Control	placebo	dim red	7	27.1 $\pm$ 8.6
LEET	active	dim red	12	24.8 $\pm$ 7.9
Light	placebo	bright white	12	22.5 $\pm$ 3.5
Light/LEET	active	bright white	8	23.6 $\pm$ 4.4

There were no differences in mean ages of the subjects in the different groups.

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<sup>a</sup>Other measures included cognitive performance, body temperature, and urinary excretion of a melatonin metabolite, 6-sulphatoxymelatonin.

## Design

The experimental schedule is summarized in Table 2. The study was designed to measure the utility of bright light and LEET to counteract the effect of an abrupt 10-hr phase delay of the sleep/wake schedule on performance and sleep. The study was double-blinded with regard to LEET. It was not possible to create blinded conditions for the light treatment. However, subjects were only aware that red and white light were being compared. All subjects participating during a single week were matched for light condition. Subjects did not know that white light was brighter than red and had no reason to expect it to be more effective. Therefore, we expect no placebo effect favoring bright light.

Subjects slept in the laboratory Sunday night with a partial EEG hookup (EEG not recorded) to allow adaptation to the laboratory environment and to sleeping with electrodes affixed. On Monday, subjects were trained on the cognitive tasks (data to be presented elsewhere). This was followed by a baseline night of recorded sleep (2200 to 0600). The next day, subjects underwent five sessions of computer-administered cognitive testing during one 9-hr day shift (0800 to 1700). During the following night and the two subsequent nights, they were tested during a 9-hr night shift (1800 to 0300). Background lighting was less than 550 lux (varying depending on where in the laboratory subjects spent their free time) from overhead lights. Between 2200 and 0200 subjects were exposed to either bright (3,500 to 4,300 lux) white or dim (200 to 300 lux) red light. Light boxes were located just above the computer monitors (i.e., in or almost in the field of direct vision). Overhead lights were on during the 2200 to 0200 period for the bright white light groups and off for the red light groups.

We thought it would be safer to keep the bright light exposure at a moderate interval from the usual circadian nadir (0400 to 0600), to avoid any chance of causing phase advances. Exact circadian phase positioning varies among individuals. Additionally, there is some controversy about the direction of phase shift that will result from light exposure very near the circadian temperature nadir. For example, Tzischinsky and Lavie<sup>25</sup> reported phase advances with bright light exposure at times that Deacon and Arendt<sup>26</sup> and others have found it to cause phase delays.

## Data Recording

The sleep period during the night work part of the study (Tuesday to Friday) was 0800 to 1600. Full polysomnographic recordings were performed during the baseline night and all three daytime sleep periods. Leads recorded included left and right central (C3 and C4), left and right occipital (O1 and O2), and left and right electro-oculogram (LEOG, REOG), all referenced to left mastoid (A1) with right mastoid (A2) as a backup if there were problems with the

TABLE 2: STUDY SCHEDULE

	SUN	MON	TUE	WED	THU	FRI
0000				TEST	TEST	TEST
0030						
0100				vs BREAK	vs BREAK	vs BREAK
0130						
0200				TEST	TEST	TEST
0230						
0300						
0330				BREAK	BREAK	BREAK
0400						
0430						
0500				vs DINNER	vs DINNER	vs DINNER
0530						
0600		WAKE U	WAKE U	BREAK U	BREAK U	BREAK U
0630		SHOWER	SHOWER			
0700		BREAKFAST	BREAKFAST			
0730				LEET	LEET	LEET
0800		TRAIN U	TEST U	SLEEP U	SLEEP U	SLEEP U
0830						
0900		vs BREAK	vs BREAK			
0930						
1000		TRAIN	TEST			
1030						
1100		BREAK	BREAK			
1130						
1200		TRAIN	TEST			
1230						
1300		vs LUNCH	vs LUNCH			
1330						
1400		BREAK	TEST			
1430						
1500			BREAK			
1530						
1600		U	TEST U	WAKE U	WAKE U	WAKE U
1630				SHOWER	SHOWER	SHOWER
1700		vs DINNER	vs DINNER	vs BREAKFAST	vs BREAKFAST	BREAKFAST
1730						
1800		BREAK	TEST	TEST	TEST	
1830						
1900			BREAK	BREAK	BREAK	
1930						
2000	CHECK-IN	FULL EEG HOOKUP	TEST	TEST	TEST	
2030						
2100	PARTIAL EEG HOOKUP	vs BREAK	vs BREAK	vs BREAK	vs BREAK	
2130						
2200	SLEEP	SLEEP U	TEST U	TEST U	TEST U	
2230						
2300			SNACK	LUNCH	LUNCH	
2330						

U = Urine collection. vs = Vital Signs. TRAIN = Training on cognitive performance tests. TEST = Cognitive performance testing. Data to be reported elsewhere.

A1 electrode during the night. Additionally, submental electro-myogram (EMG) and electrocardiogram (EKG) were recorded. Sleep staging was performed on all recordings by the same technician using standard criteria.<sup>27</sup> For the 20 min prior to the daytime sleep periods, subjects received either active (LEET and Light/LEET groups) or dummy (Control and Light groups) LEET treatment.

Data Analysis<sup>a</sup>

Sleep measures and abbreviations used are shown in Table 3. All measures are in minutes, except sleep efficiency (percent), number of awakenings, and number of awakenings longer than 2 min.

TABLE 3: SLEEP MEASURES AND ABBREVIATIONS

Measure <sup>b</sup>	Abbreviation
Total Sleep Time	TST
Stage 1 Sleep	S1
Stage 2 Sleep	S2
Slow Wave Sleep	SWS
REM Sleep	REM
Sleep Latency	SL
REM Latency	REML
Wake Time	WAKE
Sleep Efficiency	SE
Number of Awakenings	AWK
Number of Awakenings longer than 2 min	AWK2

One-way Analysis of Variance (ANOVA) between the four groups was done on each baseline night sleep measure to evaluate any group differences prior to exposure to the experimental interventions (Light or LEET). Multivariate analysis of variance (MANOVA) was run for each variable, with Light and LEET as the between-groups factor and Day (baseline night and the 3 day sleep periods) as the within-group factor. For sleep measures showing significant baseline night group differences (S2 and REM) or a near significant ( $0.05 < p < 0.1$ ) trend for group differences (REML) on the one-way ANOVA, a Multivariate Analysis of Covariance (MANCOVA), including the Wald Test, was done with the baseline night value as the covariate. Tukey's HSP *post-hoc* testing was performed where appropriate to define between-group differences. Because AWK and AWK2 had non-normal distributions related to the lower bound effect, nonparametric tests (Kendall Coefficient of Concordance, and Kruskal-Wallis one-way ANOVA) were used for these measures.

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<sup>a</sup>The SPSS statistical package (SPSS, Inc., 1988) was used for all computations except the Wald test, which was from the 5V program of the BMDP statistical package (Dixon, 1992).

<sup>b</sup>Third-of-the-night (Third) values available for TST, SWS, and REM.



## RESULTS

### Baseline Sleep

Baseline sleep measures are shown in the first column of Table 4. All values in Table 4 represent mean plus or minus the standard deviation. Significance levels for group differences at baseline are shown in the first column of Table 5. The groups were not perfectly matched at baseline. There were group effects on ANOVA for S2, REM, and REML, although no two groups differed significantly on Tukey's HSP *post-hoc* testing for any of these measures. There were no Group-by-Third interactions on the baseline night for the three measures having this scoring (TST, REM, and SWS).

### Daytime Sleep

Sleep data for the daytime sleep periods are listed in columns two through four of Table 4. Significance levels are listed under the heading OVERALL (columns 2 through 9) in Table 5. The Wald test confirmed significance of all findings from the MANCOVAs. MANOVA results (MANCOVA for S2, REM, and REML; Kendall Coefficient of Concordance for AWK and AWK2) showed significant effects for Day on TST, SE, SL, REML, S2, and WAKE, and a trend for a Day effect on AWK.

There were no main effects of Light in these analyses, although there were trends ( $.05 < p < .1$ ) for Light effects on TST, WAKE, and SE. There was a significant LEET effect on S1 and a trend for a LEET effect on REM. There was a significant LEET-by-Day interaction for S2. There was a Light-by-LEET interaction and a trend for a Light-by-Day interaction for REM sleep. There were also LEET-by-Third interactions for SWS and REM, and a trend for a Light-by-Third interaction for REM.

Kendall Coefficient of Concordance indicated Light-by-Day and LEET-by-Day interactions on AWK2, and a Light-by-Day and a trend for a LEET-by-Day interaction on AWK. There was a Group-by-Day interaction (Light by LEET by Day in Table 5) on AWK and AWK2. Kruskal-Wallis one-way ANOVAs on the data from this sleep period showed a trend for a Group effect in the first daytime sleep period for AWK.

### Final Day Sleep

The data from the final day sleep period for the most basic sleep measures, TST and SE (neither of which showed any baseline differences among groups), were examined by two way ANOVA with Light and LEET as the between-group factors. Significance levels and F values are shown in the last column of Table 5. Both TST and SE showed a significant main effect for Light. Similar analyses of SL and WAKE showed a significant Light effect for WAKE but not for SL. LEET effects and Light-by-LEET interactions were not significant for any of these variables.

TABLE 4: SLEEP MEASURES

MEASURE	BASELINE			DAY SLEEP 1			DAY SLEEP 2			DAY SLEEP 3							
	CONTROL	LIGHT	LEET	L/L	CONTROL	LIGHT	LEET	L/L	CONTROL	LIGHT	LEET	L/L					
TST	431+24	432+19	425+26	438+16	422+30	432+35	419+53	429+44	393+35	432+29	419+58	414+35	381+55	413+31	394+76	442+22	
S1	18+6	20+8	29+22	24+12	24+16	14+4	26+14	27+14	20+9	21+7	29+18	30+9	27+21	24+23	26+17	40+9	
S2	252+23	229+30	203+50	206+40	215+30	230+33	176+35	195+42	216+20	203+21	189+49	190+40	191+31	178+30	171+42	196+21	
SWS	71+25	107+23	114+57	109+40	106+25	111+38	118+38	109+22	81+24	116+32	104+41	99+23	84+33	109+31	105+56	102+27	
REM	90+17	77+13	76+23	100+25	76+28	77+28	108+33	98+24	77+23	91+22	98+34	95+20	80+38	102+24	91+36	104+13	
SL	15+12	15+9	17+12	19+17	3+2	3+2	3+2	4+2	3+3	4+2	7+7	4+3	6+3	10+10	7+5	5+4	
REML	104+49	116+49	73+31	98+31	73+21	83+71	50+34	70+56	56+18	75+44	46+22	59+10	82+54	65+36	49+19	64+14	
WAKE	41+25	35+15	44+27	30+18	43+29	41+34	52+55	46+46	79+40	37+29	51+61	54+33	90+60	50+23	68+72	30+23	
SE	90+5	90+4	89+5	92+3	90+6	90+7	87+11	89+9	82+7	90+6	88+12	87+7	80+12	87+5	83+15	92+5	
AWK	2+4	4+2	3+2	3+2	6+4	3+2	4+4	2+1	3+3	3+2	4+3	5+3	5+3	3+2	4+1	4+3	
AWK2	2+3	3+2	2+1	1+1	4+2	2+1	3+4	2+1	3+2	2+1	3+3	4+3	4+2	3+1	3+1	3+2	
<u>THIRD OF NIGHT MEASURES</u>																	
TST	1	136+13	140+10	137+13	136+17	144+15	154+4	152+8	155+2	149+6	152+5	151+9	151+5	142+17	145+10	145+9	153+4
	2	149+13	144+12	146+17	155+5	145+12	152+8	147+15	148+17	138+15	146+13	144+22	149+10	138+18	151+8	142+20	154+4
	3	146+25	148+8	142+13	147+9	133+20	126+35	119+36	126+33	106+31	134+26	125+44	114+30	101+37	118+27	107+57	136+18
SWS	1	51+16	68+12	62+26	56+19	66+17	69+17	65+22	71+14	55+21	77+16	66+29	58+20	57+23	77+16	66+29	66+15
	2	16+14	23+14	35+29	37+31	27+12	30+20	41+27	27+12	19+14	18+15	27+19	34+13	20+19	18+17	24+18	30+11
	3	4+8	15+16	14+14	16+13	14+13	12+14	13+12	11+12	7+5	22+18	11+10	8+12	8+6	14+11	15+18	7+13
REM	1	5+3	9+10	12+11	18+19	12+7	16+15	31+10	26+19	16+11	19+15	34+17	32+18	22+14	20+16	29+12	22+11
	2	33+15	32+13	28+14	43+14	23+8	33+16	33+20	41+15	36+10	40+13	31+11	35+14	32+18	52+16	34+10	44+9
	3	51+17	36+12	36+16	38+17	42+32	28+16	35+20	31+15	24+12	33+19	33+19	28+14	25+19	30+15	27+26	38+11

\*Significant Group effect on Baseline Sleep ANOVA

TST=Total Sleep Time, S1=Stage 1 Sleep, S2=Stage 2 Sleep, SWS=Slow Wave Sleep, REM=REM Sleep, SL=Sleep latency, REML=REM Latency, WAKE=Time Awake. All of the preceding are in minutes.

SE=Sleep Efficiency (percent), AWK=Number of Awakenings, AWK2=Number of Awakenings longer than 2 min.

TABLE 5: SIGNIFICANCE LEVELS  
p value

	BASELINE			OVERALL						FINAL DAY
	Day	Light	LEET	Light LEET	Light Day	LEET Day	Light LEET Day	Light Third	LEET Third	Light <sup>a</sup>
TST	0.007	0.08								0.03
S1			0.02							
S2 <sup>b</sup>	0.05	0.004				0.04				
SWS		0.04						0.02		
REM <sup>b</sup>	0.04		0.06	0.02	0.07		0.06	0.03		
SL	<0.001									
REML <sup>b</sup>	0.09									
WAKE		0.09								0.02
SE	0.09									0.02
AWK <sup>c</sup>	0.07				0.02	0.07	0.002			
AWK2 <sup>c</sup>					0.05	0.04	0.04			

<sup>a</sup> Statistics for final day data only performed for TST, WAKE, SE, and SL.

<sup>b</sup> p values from MANCOVA.

<sup>c</sup> Due to non-normal distribution, nonparametric tests used for these variables.

## DISCUSSION

### Baseline Sleep

The Control group had more (46 to 49 min more) Stage 2 sleep than both the LEET and the Light/LEET groups (59 vs. 47% of total sleep time) at baseline. This S2 increase is largely accounted for (40 min of it) by a decrease in SWS. Thus, subjects in the control group may have started out with poorer sleep than either group that received LEET treatment. On the other hand, the Control subjects had slightly (nonsignificant) less Stage 1 sleep at baseline. In any case, the most basic sleep measures (TST, WAKE, SE) were very similar between groups at baseline.

The three third-of-the-night measures showed no significant Group differences at baseline. The pattern of sleep was normal, with decreasing amounts of SWS and increasing amounts of REM across the night. The one exception was the Light/LEET group, which had slightly less REM in the last third of the night than the middle third. This probably can be attributed to being awakened a little earlier (0600) than they might have normally awakened, causing truncation of the final REM period, and it could indicate that this group started out slightly phase-delayed relative to the other groups.

## Day Effects

The Day effects seen on many measures in the overall analyses are not surprising in individuals subjected to a large phase shift, along with a night of sleep deprivation. TST, SE, S2, and NREM dropped progressively over the four sleep periods (TST: from 431 to 407 min, SE: from 90.1 to 85.7%, S2: from 220 to 182 min, and NREM: from 347 to 312 min). SWS increased from 103 to 112 min after the night of sleep deprivation, but then returned to baseline levels for the remainder of the study. Total number of awakenings and awakenings longer than 2 min increased progressively across the sleep periods (from 12 to 16, and from 8 to 13, respectively). Sleep latency decreased markedly after the night of sleep deprivation (from 16.7 to 3.3 min). It increased over the next 2 days (4.7 min and 7.5 min) but remained well below baseline (i.e., subjects could fall asleep quickly but had some difficulty remaining asleep, presumably because they were trying to sleep on the rising limb of the circadian cycle of alertness). REM latency decreased over the first 2 day sleep periods, from 92 to 59 min, and remained stable in the last sleep period.

## Stage 1 and SWS

There was a main effect for LEET on Stage 1 caused by increased Stage 1 sleep in the groups that received LEET. However, since these groups showed a trend for increased Stage 1 at baseline (see first column, upper half of Table 5), it is questionable whether this was really secondary to the LEET. For SWS, there was a LEET-by-Third interaction, with groups that received LEET showing more SWS during the second third of the sleep period. As with Stage 1, this finding appears to be largely explained by the (nonsignificant) trend for a similar difference at baseline (see first column, lower half of Table 4).

## Stage 2 Sleep

There was a LEET-by-Day interaction on amount of Stage 2 sleep. Means for the three daytime sleep periods (adjusted for the baseline group differences) revealed that the subjects that received LEET (LEET and Light/LEET groups) have less Stage 2 during the first daytime sleep period than those who did not (Light and Control groups) ( $188 \pm 35$  vs  $220 \pm 35$  min). Stage 2 remained stable across the next two days in the subjects that received LEET but dropped progressively in the subjects that did not receive LEET (Day 2:  $201 \pm 32$  min, Day 3:  $176 \pm 30$  min). Amount of stage 2 was roughly equal between the subjects who received LEET and those who did not on the last day. It is unclear what the apparent stabilization of amount of Stage 2 among subjects who received LEET might imply in relation to either phase-shifting or sleep quality effects of the intervention. Although MANCOVA was used to adjust for the baseline difference, the different pattern of Stage 2 sleep after the phase shift in subjects who received LEET may relate to

the smaller amounts of Stage 2 at baseline in these subjects.

### REM Sleep

For REM, there was a Light-by-LEET interaction. Adjusted group means (collapsed across days) showed that, in subjects not exposed to bright light, LEET appeared to elevate overall REM (LEET group:  $103 \pm 22$  min, Control group:  $74 \pm 17$  min), but in subjects exposed to bright light, LEET did not have this effect (Light group:  $94 \pm 16$  min, Light/LEET group:  $90 \pm 19$  min). The effect in the LEET group was large enough that there was a trend for main effect for LEET to elevate REM ( $98 \pm 21$  vs.  $87 \pm 19$  min). This appears to have been predominantly a LEET effect in the first daytime sleep period ( $104 \pm 28$  vs.  $78 \pm 28$  min), with decreasing differences between subjects who received LEET and those who did not over the next two days. There was also a significant LEET-by-Third interaction, and third-of-the-night comparisons showed that the REM-elevating effect of LEET was limited to the first third of the sleep period during which subjects who received LEET averaged  $26 \pm 12$  min of REM sleep, as compared to  $15 \pm 9$  min for those who did not receive LEET.

The REM sleep analyses also showed trends for Light-by-Day and Light-by-Third interactions. During the first day sleep period, subjects exposed to dim red light had higher amounts of REM than those who received bright white light ( $97 \pm 7$  vs.  $85 \pm 7$  min). Over the next two days, the dim light subjects had progressively less REM and the bright light subjects had progressively more REM, so that the bright light subjects had more REM than dim light subjects on the final day ( $102 \pm 6$  vs.  $88 \pm 6$  min). Bright light subjects also showed more REM overall than dim light subjects in the second third of the sleep period ( $40 \pm 8$  vs.  $32 \pm 9$  min).

Group mean values for the third-of-the-night REM data for the baseline and the four daytime sleep periods are plotted in Figures 1-4. It appears that the first third-of-the-night increase in REM among the LEET-treated subjects may relate to the similar, but nonsignificant, baseline difference. The tendency for subjects who received bright light treatment to show higher second third-of-the-night REM is a little more convincing. The higher second third-of-the-night as compared to first third-of-the-night REM in subjects treated with bright light might be interpreted as evidence of phase shifting of REM back toward its normal predominance later in the night. However, the relative amounts of third versus second third-of-the-night REM do not support this hypothesis.

The group means for REM for the three daytime sleep periods (adjusted for the baseline differences, so baseline day cannot be shown) are plotted in Figure 5. There was an initial tendency for LEET to elevate REM (LEET group significantly different from Control and Light groups). Thereafter, the Light group showed progressively more REM (significantly more than Control during the

FIGURE 1: BASELINE NIGHT REM SLEEP

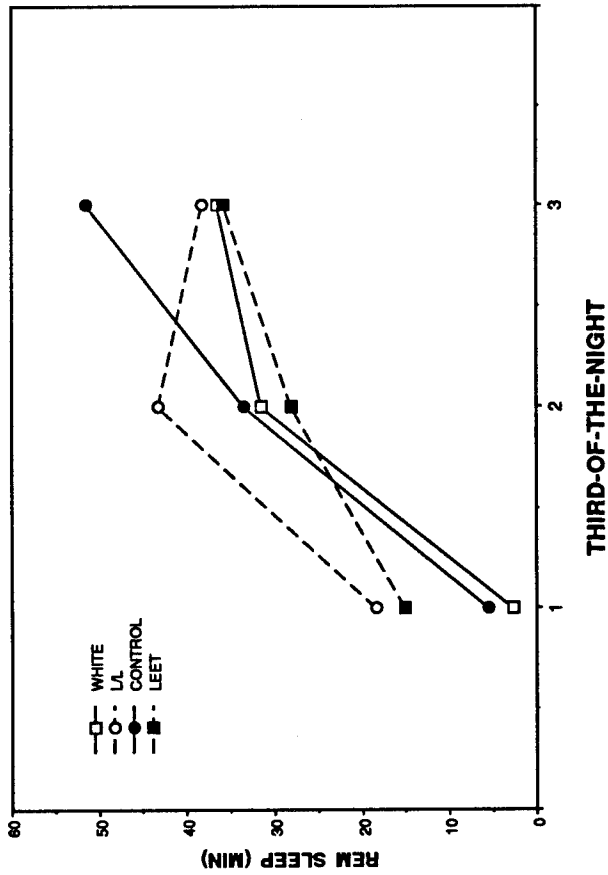


FIGURE 2: FIRST DAYTIME SLEEP PERIOD REM SLEEP

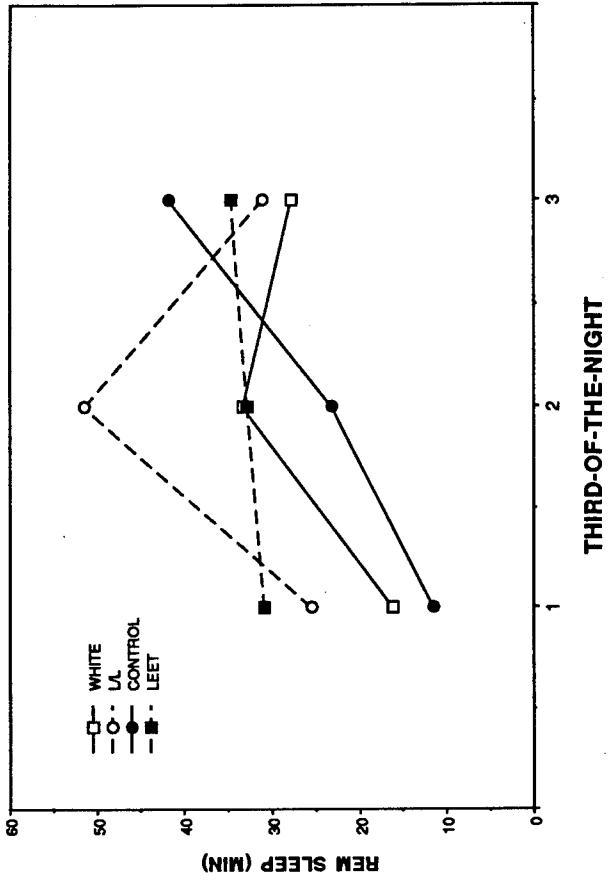


FIGURE 3: SECOND DAYTIME SLEEP PERIOD REM SLEEP

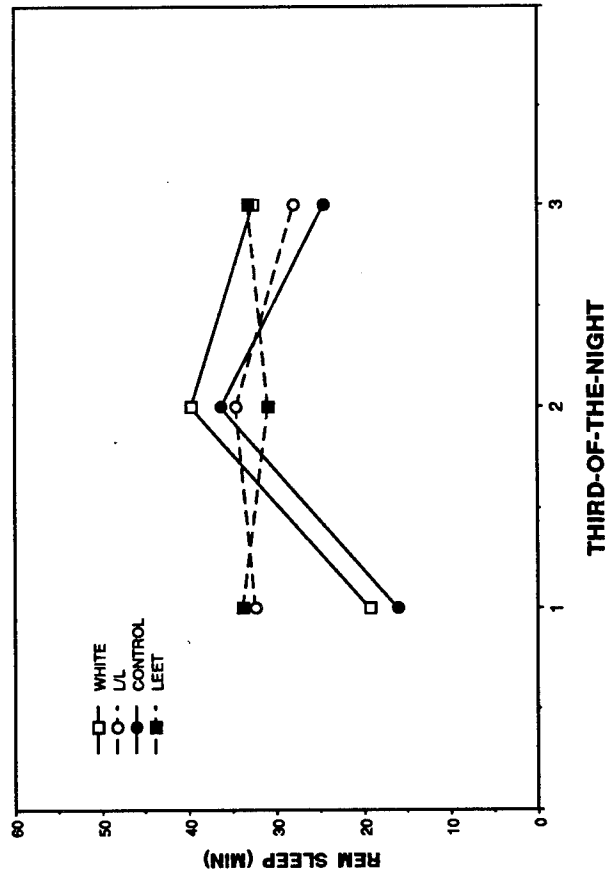
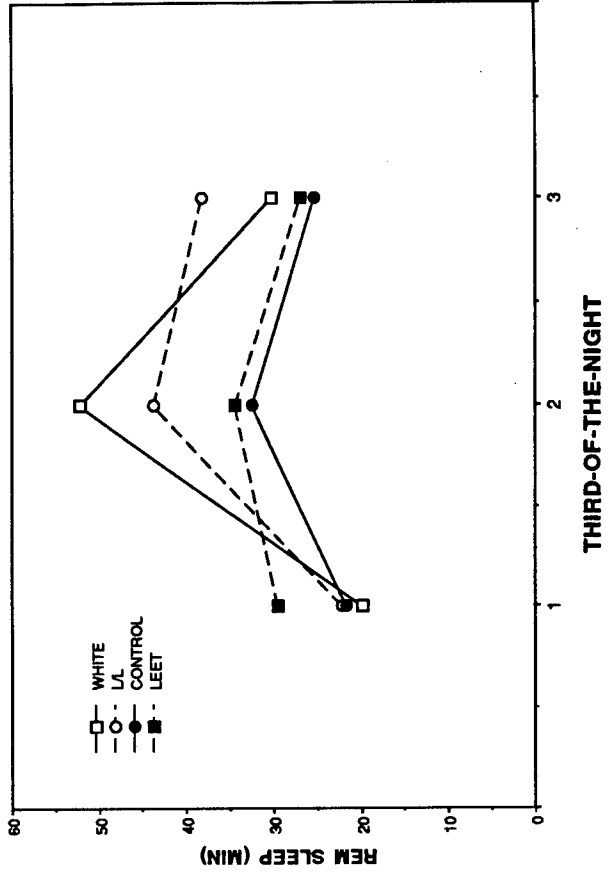


FIGURE 4: THIRD DAYTIME SLEEP PERIOD REM SLEEP



final sleep period) and the LEET group showed progressively less. The Control and Light/LEET groups showed fairly stable amounts of REM across the sleep periods. These findings could be explained by opposing effects of bright light and LEET on REM, which partially cancel each other out in the Light/LEET group.

### Number of Awakenings

Total number of Awakenings and Awakenings Longer Than 2 min are plotted in Figures 6 and 7. The statistical findings on total awakenings (Light-by-Day, LEET-by-Day [trend], and Light-by-LEET-by-Day interactions) appear largely secondary to increased awakenings in the Control group during the first daytime sleep period. Both interventions were associated with fewer awakenings, bright light more so than LEET. However, it should be noted that there was not an associated decrease in amount of wake time, which was very similar between groups during this sleep period.

Despite the almost identical statistical findings, the fluctuations in relative group position on the number of longer awakenings appear more random (Figure 7). Subjects who received LEET showed a relatively high number of awakenings on the second day sleep, as compared to those who did not. Subjects who received bright light showed fewer longer awakenings than those who did not on the first daytime sleep period. The Light group moved from having the most longer awakenings at baseline to having the least during all the daytime sleep periods.

### Amount of Sleep

In the overall analysis, there are trends suggesting Light effects on total sleep time, total wake time, and sleep efficiency. Subjects who received bright light slept more (were awake less), during the sleep periods on the last 2 days. Total sleep time is graphed in Figure 8. ANOVA of the final day sleep period data showed the groups that received bright light (Light and Light/LEET) had significantly greater total sleep time and sleep efficiency than the groups that received dim light (Control and LEET).

By these basic measures, the bright light treatment does appear to have improved sleep. The size of the effect (i.e., a 30- to 60-min increase in total sleep time during an 8-hr sleep period, is comparable to the benefit reported for the hypnotic agent triazolam (@Halcion) under similar conditions (day sleep of night workers).<sup>5</sup> Light treatment appears to have improved subjects' ability to remain asleep rather than ability to fall asleep, since there was no Light effect on sleep latency but there was a significant Light effect for total time awake. This suggests that the effect relates to more rapid phase delay of the circadian rhythm of sleep, since inability to remain asleep is related to the timing of the rising limb of the circadian rhythm of alertness.<sup>28</sup>

FIGURE 5: REM SLEEP ADJUSTED FOR BASELINE NIGHT DIFFERENCES

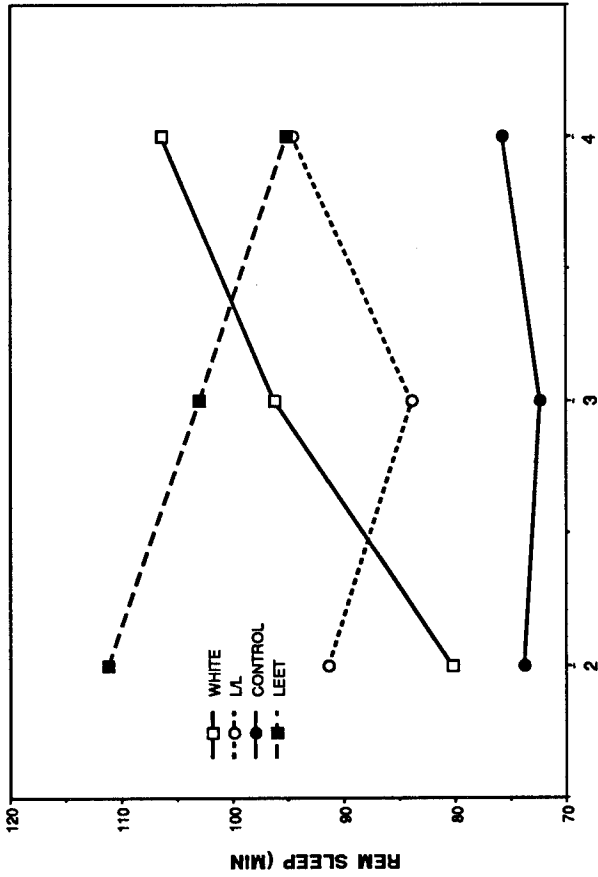


FIGURE 6: TOTAL AWAKENINGS

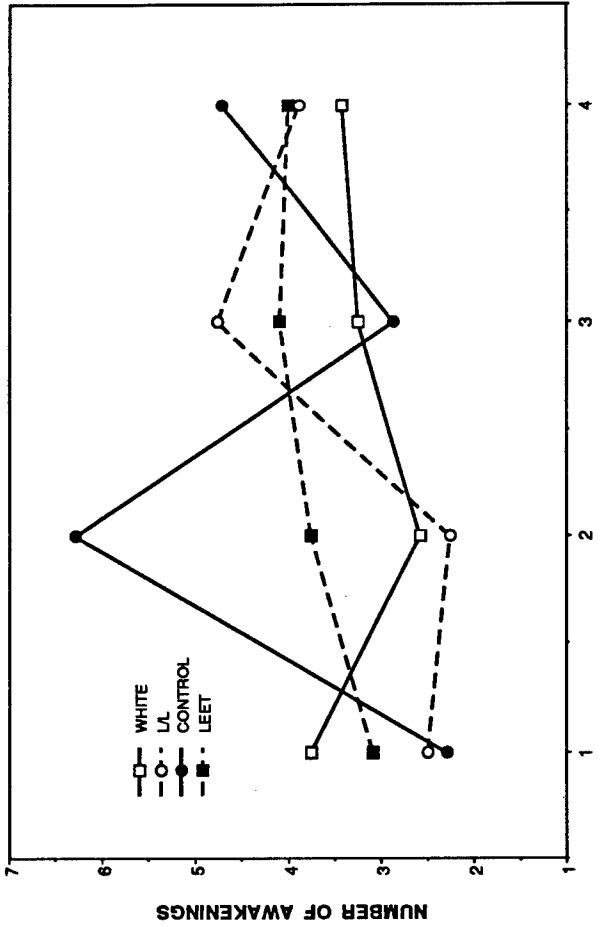


FIGURE 7: AWAKENINGS LONGER THAN 2 MIN

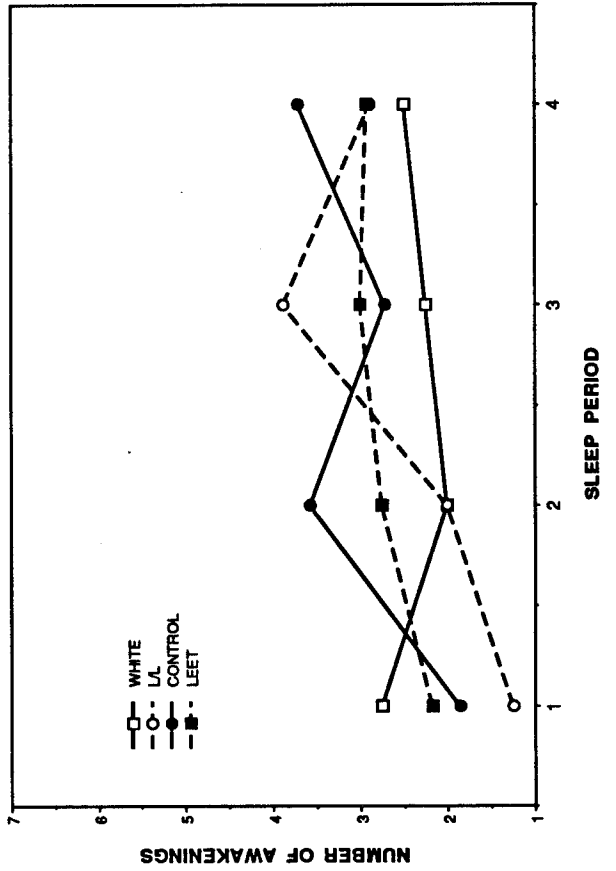
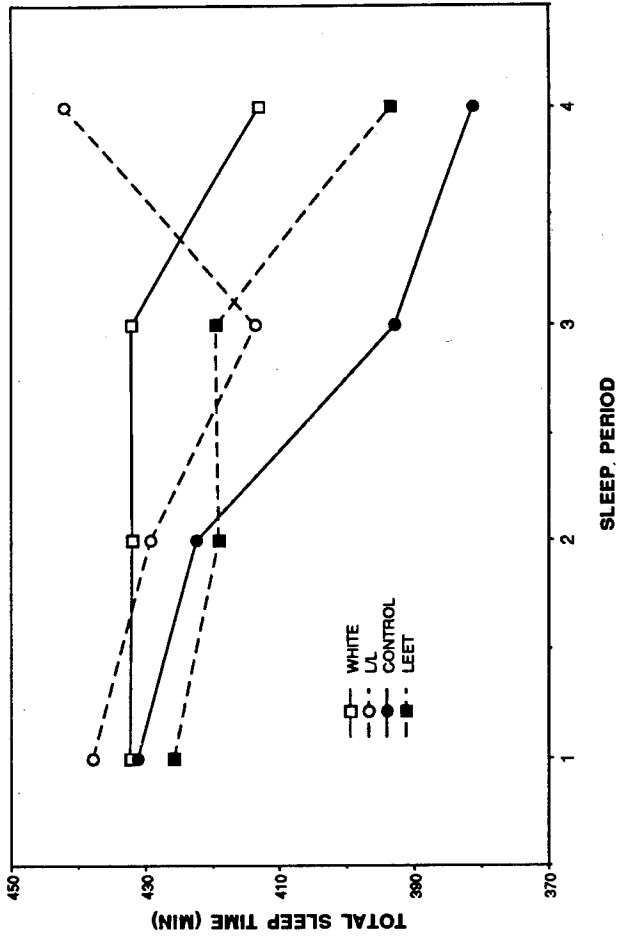


FIGURE 8: TOTAL SLEEP TIME





The LEET group was a little better on each of these measures (total sleep time, sleep efficiency, and total wake time) than the Control group, with the Light/LEET group sleeping the most of all the groups (see Figure 8 and Table 5, last column). This suggests additive beneficial effects of bright light and LEET. However, the LEET effect did not achieve significance on any of these measures, perhaps because of the small group sizes.

#### CONCLUSION

In this study subjects underwent a 10-hr delay in the sleep/wake cycle (entailing an initial 10 hr of sleep deprivation), comparable to the time zone change experienced with travel from California to Egypt. Either timed bright light exposure during the nighttime work period or LEET treatment prior to the daytime sleep period decreased number of awakenings (but not total time awake) during the first daytime sleep period. After three nights of treatment, when the effects of the initial sleep deprivation on sleep would be expected to be least and the cumulative effects of the interventions to be maximal, the subjects who received bright light had greater total sleep time and sleep efficiency and less wake time during the sleep period as compared to those who were exposed to dim light. The quantitative increase in total sleep time is comparable to that seen when triazolam was administered for day sleep in night workers.<sup>5</sup> Subjects who received LEET showed a nonsignificant trend for similar additive benefits.

Effects on sleep structure are less clear, with trends toward baseline group differences making findings uncertain. The initial LEET treatment does appear to elevate REM sleep, with decreasing effects thereafter. LEET also showed evidence of stabilizing the amount of Stage 2 sleep across the sleep periods. Light-treated subjects showed more REM in the final sleep period. Third-of-the-night analyses provided no convincing evidence that either intervention is really normalizing sleep stage organization.

To our knowledge, this is the first study demonstrating polysomnographically that timed bright light can improve sleep within 3 days of such a large phase shift. Based on these data, the use of bright light timed to promote phase readjustment can be recommended to improve sleep in subjects undergoing a large phase delay of the sleep/wake cycle. The effects of using this intervention appear to be similar to those seen with hypnotic drugs, presumably without the risk of side effects inherent in use of such agents. The effects of LEET on sleep after a phase delay are less clear and do not warrant a recommendation at this time.

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