Order Number 9224789

The effects of bright light for the treatment of inadequate sleep in the elderly

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City University of New York, 1992

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THE EFFECTS OF BRIGHT LIGHT FOR THE TREATMENT OF INADEQUATE SLEEP IN THE ELDERLY

by

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A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

1992

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

4/30/92
Date

Chair of Examining Committee

5/1/92
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Abstract

THE EFFECTS OF BRIGHT LIGHT FOR THE TREATMENT OF INADEQUATE SLEEP IN THE ELDERLY

by

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Advisor: Professor Arthur J. Spielman

Three studies of elderly insomnia are presented. In Experiment 1 the effects of bright and dim light on body core temperature, nocturnal sleep and daytime alertness were investigated in sixteen elderly subjects. Subjects exposed to bright light evidence a shift in the body temperature rhythm and an increase in several important measures of sleep quality. Performance and alertness was not significantly effected. In Experiment 2 the relationship between nocturnal sleep variables and sleep tendency was examined in forty-three elderly insomniacs. The results indicated that in this population associations between nocturnal sleep and daytime sleep tendency remain obscured under basal conditions. In Experiment 3 the relationship between daytime alertness and nocturnal sleep variables was examined in the sixteen subjects from Experiment 1. In addition, a post-hoc analysis was carried out between a sub-set of subjects from Experiment 2 who were administered the multiple sleep latency test, and the subjects in Experiment 1 who were administered the repeated test of sustained wakefulness. The repeated test of sustained wakefulness was inversely associated with nocturnal sleep fragmentation, while no significant differences were observed between the two tests when group mean sleep latencies were calculated.

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Many sleep/wake changes accompany aging. Often, elderly people have accepted diminished sleep quality as part of the normal aging process and family practice medicine has not discouraged this point of view. Although many events associated with aging, such as retirement, changes in family structure, death of a spouse, or close friends may affect sleep adversely, it has also been recently recognized that sleep disturbances in the elderly may be related to specific pathophysiological processes (NIH Consensus Statement, 1990). These processes are diverse and include changes in sleep physiology, medical conditions, psychiatric disorders, drug misuse and abuse, and changes in rest/activity cycles. The increased sleep disturbance associated with aging is not a trivial matter, either in terms of the patient's quality of life or in the heightened risk of morbidity and mortality (Kripke, Simons, Garfinkel, & Mammond, 1979; Pollak, Perlick, Linser, Wenston, & Hsieh, 1991). As a result of changing demographic patterns, it is virtually assured that the number of older persons in this country will continue to increase, and many will develop sleep disturbance (Dement, Miles, & Carskadon, 1982; Bixler, Kales, Soldatos, Kales, & Healy, 1979; Fowles, 1989).

Behavioral and Subjective Sleep Characteristics of Older Adults

Estimates of the population prevalence of insomnia in all adults vary depending on the number and types of questions asked. In one study, it was estimated that sleep disturbance affects about one-third of the adult population and seventeen percent considered their insomnia to be serious and the percentage increases with age (Mellinger, Balter, and Uhlenhuth, 1985). From a "representative sample" in the Los Angeles area, it was reported that 32.2% of the adult population had a current complaint of insomnia and the mean duration of the complaint was 10.5 years (Bixler et al., 1979). Here again the incidence of insomnia increased with age, with close to 40% of persons over the age of 50 reporting sleep disturbance. In this older group, 84% described their condition as chronic; that is, lasting longer than the previous year. Age-associated increases in sleep disturbance have also been found in other surveys. For instance, in a sample of non-institutionalized adults, it was observed that 45% of the population between 65 and 79 years of age "had some difficulty with insomnia" during the preceding year and for those individuals using prescription sleeping medications, sixty-nine percent were dispensed to persons between 50 and 79 years of age (Institute of Medicice, 1979).

These results are not unique to America. Of 5,713 Italian adult

respondents, 13.4% reported that they "rarely slept well," and by age 45, gender differences were apparent. Twenty-three percent of the female respondents complained of insomnia at age 45, while only 14.4% of the males did. By age 50, the percentages were 39.7% and 15.3% respectively (Cirignotta, Mondini, Zucconi, Lenzi, & Lugaresi, 1985).

Age-related changes in the temporal distribution of sleep and wakefulness have also been reported. The elderly are inclined to go to bed earlier, wake up earlier, and nap a greater percentage of the time during the day, compared to their younger adults (Tune, 1969a; Gerard, Collins, Dore, & Exton-Smith, 1978; Miles & Dement, 1980; Lieberman, Wurtman, & Teicher, 1989). McGhie and Russell (1962) found that early morning awakenings increase with age, as does the use of hypnotics. The use of hypnotics and the onset of subjectively perceived diminished sleep were not equally distributed between males and females. Forty-five percent of women over the age of 75 said they used hypnotics, while only 28% of male respondents admitted use. Sleep disturbance became manifest earlier in females relative to males; 40% of women complained of light sleep by age 45, whereas light sleep was only reported by 15% of males at this age.

Tune (1969b) found increases in daytime napping and nocturnal

awakenings in subjects over the age of 50 who filled out a daily sleep log for almost nine weeks. He suggested that earlier bedtimes, without a corresponding expectation of earlier waketimes, contributed to the experience of diminished sleep quality in this population. Gerard, Collins, Dore, and Exton-Smith (1978) also observed that, as a group, older subjects had earlier bedtimes and waketimes compared to younger subjects and within the older group, there was an age-related advance of the habitual sleep period. Females reported more early morning awakenings and these behavioral manifestations were borne out by patterns of hypnotic use among women. Forty percent of elderly females reported hypnotic use, while 31% reported that they took these medications *nightly* (Gerard et al., 1978).

Further evidence of an age-related change in sleep and wakefulness patterns comes from a study of 24-hour ambulatory rest/activity measurements. It has been reported that the mean activity acrophase (i.e., the peak in daytime activity) is advanced in older subjects (mean 01:30 p.m.), relative to a young control group (mean 03:30 p.m.) (Lieberman et al., 1989). These findings cannot be attributed to an age-associated decrease in activity, since the mean, levels were not significantly different between the two groups.

In summary, the evidence regarding the behavioral and subjective sleep patterns in the elderly suggests the following. There is a high incidence of self-reported insomnia in the elderly. They tend to have earlier bedtimes, frequent early morning awakenings, and increases in daytime napping. In addition, the complaint of insomnia increases with age and there is some suggestion that a greater number of females are affected. The primary response to this condition is to use sedative-hypnotics. While the use of hypnotic medication by the elderly appears to be alarmingly high, the indiscriminate use of over-the-counter medicines and the proven counter-productive use of alcohol are likely to be even *higher* (Mellinger, Balter, & Uhlenhuth, 1985).

Objective sleep in older adults

Precise definitions of what constitutes "abnormal" sleep, particularly in an older population, are lacking. It must be remembered that insomnia is a symptom (subjective complaint) rather than a sign. 'Old' sleep that is objectively compromised when compared to 'young' sleep, does not always result in a complaint of insomnia (Dement, Richardson, Prinz, Carskadon, Kripke, & Czeisler, 1985). This idea is underscored by the observation that almost every objective sleep study conducted in elderly subjects has found significant sleep fragmentation, yet less than half of these

people complain of sleep disturbance (Feinberg, 1990).

To my knowledge, no controlled studies exist demonstrating differences on objective sleep measures between those elderly that complain of insomnia and those that do not. As Bliwise (1989) has aptly stated, "Whether an aged individual views his or her 75 percent sleep efficiency as insomnia, or merely accepts this as a normal part of aging may depend largely on that individual's perspective on growing old and what that means to him or her" (Bliwise,1989, pp. 24). Nonetheless, complaints of insomnia are substantiated by electroencephalographic (EEG) measures that bear some relationship to the severity of the sleep disturbance (Spielman & Herrera, 1990; Carskadon, Dement, Mitler, Guilleminault, Zarcone, & Spiegel, 1976; Frankel, Coursey, Buchbinder, & Snyder, 1976).

Numerous studies have described the objective sleep of older adults (Kales, Wilson, Kales, Jacobson, Paulson, Kolla, et al., 1967; Bixler, Kales, Jacoby, Soldatos, & Vela, 1984; Feinberg & Carlson, 1968; Feinberg, 1974; Agnew, Webb, & Williams, 1967; Kahn & Fisher, 1969; Webb, 1982; Hayashi & Endo, 1982; Webb & Campbell, 1980). When evaluating the data from these early studies it is important to keep in mind that they were conducted prior to the recognition of the high prevalence of sleep disordered breathing and nocturnal myoclonic events (Bliwise, 1989).

Decreases in sleep efficiency, reductions in the amplitude and amount of slow-wave sleep, the total disappearance of stage 4 sleep and increases in the stage 1 sleep are typically seen in the nocturnal sleep recording of non-complaining older subjects. Total sleep time is not significantly reduced in the elderly and may be because the elderly spend more time in bed trying to obtain sleep (Spiegel, 1981; Dement et al., 1982). Sleep fragmentation, frequent and long awakenings; and more lability within each sleep stage also appear to be age-related. Webb and Campbell (1980) demonstrated that older subjects without sleep disturbance, take longer to fall back to sleep compared to young control subjects after controlled nocturnal awakenings in the laboratory. Other features of aged-sleep are more likely to be associated with the complaint of insomnia in the elderly. These include, frequent early morning awakenings, severe disruptions in sleep continuity, marked decreases in total sleep time, and increases daytime sleepiness (Zepelin, 1983).

Hypnotics and the elderly

By far the most common treatment approach for insomnia in the elderly is hypnotic medication. Due to the considerable side-effects of hypnotics and the build-up of tolerance to them, the development of an effective non-pharmacological treatment for chronic geriatric insomnia is important. The non-institutionalized elderly are

approximately 13 percent of the population, yet they consume almost 30% of the prescribed hypnotics (NIH Consensus Conference, 1990). Similar patterns of hypnotic use have been found in Canada In a convenience sample (i.e., those people enrolled in government prescription programs), Baker and Oleen (1989), found that sixty-two percent of persons over the age of sixty-five were taking triazolam *nightly*, with a substantial portion also taking anti-anxiety drugs during the day.

The chronic use of hypnotics may be both ineffective and potentially dangerous, particularly in the elderly patient. The most commonly prescribed hypnotic, triazolam (HALCION™), can result in significant cognitive impairment. Amnesia, confusion, disorientation, hyperexcitability, hallucinations, feelings of depersonalization, and rebound insomnia have all been reported (Kales, Manfredi, Vgontzas, Bixler, Vela-Bueno, & Fee, 1991). Respiratory depression, impaired motor function, and daytime sleepiness may also result from the use of hypnotics (Carskadon, Seidel, Greenblatt, & Dement, 1982; Mendelson, Garnett, & Gillin, 1981; Church & Johnson, 1979).

The efficacy and safety of long-term hypnotic use has not been established in the elderly. In fact, Oswald reports that when triazolam was first marketed in the USA, only eleven patients over

the age of forty were known to have taken the drug for more than *two weeks* (Oswald, 1989). Subsequent to triazolam's arrival to market, three separate studies conducted in Great Britain found significant daytime side-effects, most prominently anxiety in patients over the age of 40 (Morgan & Oswald, 1982; Bayer, Bayer, Pathy, & Stoker, 1986; Adam & Oswald, 1989).

In this country, results from a study of "spontaneous adverse reports" to the Food and Drug Administration confirmed that triazolam was associated with daytime sedation, agitation, hallucinations, and amnesia, especially in older users (Bixler, Kales., Brubaker, & Kales, 1987). Other studies investigating the neuro-psycho-pharmacological properties of triazolam have observed additional negative side-effects from the use of hypnotics. In controlled studies of triazolam, rebound insomnia (defined as a transient period of insomnia at levels worse than pre-drug administration) has been significant and has been postulated to be intense enough to perpetuate drug use (Greenblatt, Harmatz, Zinny, & Shader, 1987; Kales et al., 1991; Gillin, Spinweber, & Johnson, 1989). Repeated administration of hypnotics produces drug tolerance and the associated problems of dependency and withdrawal reactions. Additionally, elderly patients often are taking at least one other prescibed medication and the possibility of harmful drug interactions

is present. Further, age-related problems of decreased metabolic clearance, reduced kidney and liver function, and an increase in respiratory abnormalities compound the usual problems of hypnotic use in the elderly.

Thus, while it is acknowledged by most sleep researchers that the benzodiazepine hypnotics are of some utility for transient insomnia, their value in the treatment of chronic conditions is limited, particularly in the elderly (Nicholson & Stone, 1986; Nicholson, 1989).

The circadian rhythm of body temperature

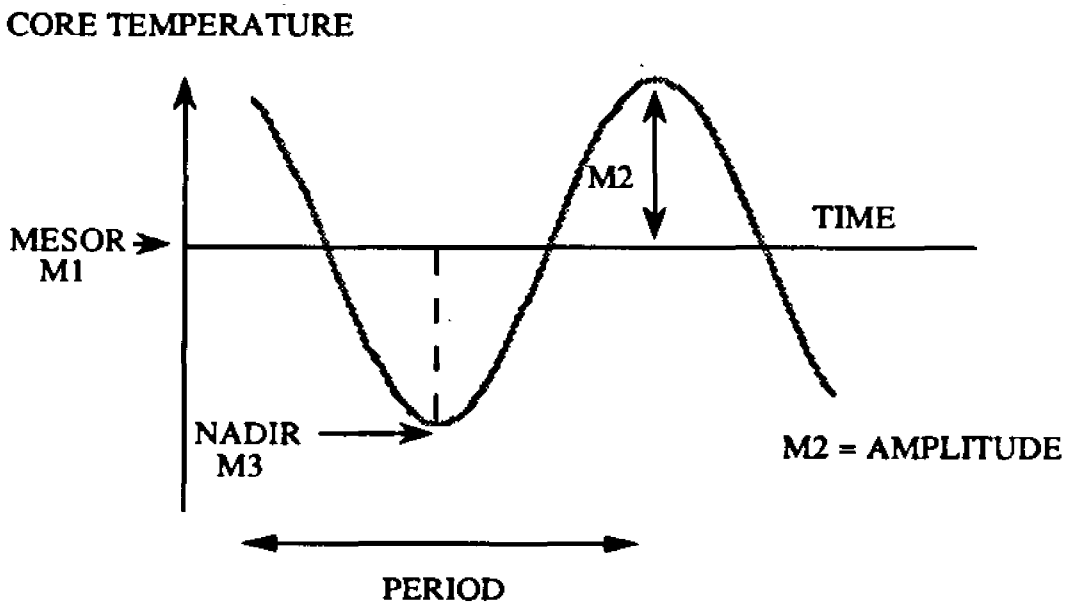
When physiological variables are measured over time, rhythmic changes can be observed, and these changes are referred to as biological rhythms. The time it takes to complete one cycle, known as the *period* of the rhythm, can be relatively short, as in cardiac or respiratory output; it can be relatively long, as exemplified by the female menstrual cycle; or the period can be approximately 24 hours in length, of which the human sleep/wake cycle is the most readily recognizable. Rhythms that manifest period lengths of less than 24 hours are called *ultradian* rhythms, while rhythms with significantly longer period lengths than 24 hours are called *infradian* rhythms (Moore-Ede, Sulzman, & Fuller, 1982). Rhythms with an approximate period length of 24 hours are called *circadian* rhythms,

a term coined by Halberg and derived from the Latin words circa, meaning 'around', and dies, meaning 'a day'. Since the period length of the human body temperature rhythm is close to 24 hours (range 23-27), it is a circadian rhythm. By definition, the frequency of a rhythm is the reciprocal of the period length. For example, the frequency of a circadian rhythm is once every 24 hours, or 1/24 cycles per hour.

Besides derivations of frequency and period length, other basic characteristics that describe biological rhythms are the amplitude, the acrophase and nadir, and circadian phase. The *amplitude* of a rhythm is a measure of the visible change, or range of oscillation over the period length. For example, subtraction of the lowest observed temperature value from the highest observed temperature value is one measure of the amplitude of a rhythm. The *acrophase* and the *nadir* are measures of timing. The acrophase and nadir correspond to points along a hypothetical curve, or a mathematically derived sinusoidal wave-form, marking the maximum and minimum values respectively. Figure 1 depicts the four parmeters of a sinuosoidal rhythm: period, amplitude, acrophase and nadir.

- Figure 1 -

Figure 1: The four parameters of a sinuosoidal rhythm.



The relationship between two or more rhythmic variables is described by their *circadian phase angle*. The circadian phase angle is the temporal difference between reference points of two circadian rhythms. When biological rhythms traverse through peaks (acrophase) and troughs (nadir) with the same frequency, and at the same time, then these rhythms are characterized as being in-phase with each other and their phase angle would be zero. In some situations, the minimum and maximum values of a biological rhythm do not coincide, and these rhythms are characterized as being out-of-phase with each other. Sometimes phase angle differences are described in circadian degrees, where 15^{0} equals one hour, or often for clarity, clock time is used instead.

Synchronous biological rhythms are rhythms which maintain stable phase relationships, or consistent temporal relationships between their respective minima and maxima. Two biological rhythms that are synchronized can have any phase relationship. Synchronized rhythms can be either in-phase or out-of-phase with each other. That is, their phase angle can be minimal or relatively large. For example, if two circadian rhythms were synchronized and in-phase, they have a similar period length of approximately 24 hours, with the peaks and troughs of the rhythm appearing at similar points in time. Synchronized circadian rhythms that are in-phase with each other result in minimal phase angle differences. On the other hand, synchronous rhythms may be out-of-

phase with each other. For example, two biological rhythms may have equivalent period lengths, but their peaks and troughs do not coincide; hence, they are out-of-phase (but still synchronous). When the minimum of variable A always occurs 4 hours prior to the minimum of variable B, the two rhythms are said to be synchronized but out-of-phase with each other. In this example, the phase angle difference would be 4 hours.

In contrast, *desynchronized* rhythms do not share a consistent temporal relationship to each other and, over time, the phase relationship between the two rhythms is constantly changing. This situation can occur when the two biological rhythms under study exhibit substantially different period lengths. For example, in temporal isolation, the human sleep/wake rhythm may oscillate with a frequency of 33 hours, while the body temperature rhythm may oscillate with a frequency of 25 hours. This phenomenon has been termed "internal desynchronization" (Aschoff, Gerecke, & Wever, 1967; Aschoff & Wever, 1976; Wever, 1979). These two rhythms are desynchronous and mostly out-of-phase with each other.

Under conditions of normal, daily life, the human body temperature rhythm exhibits daily variations that manifest a distinctive wave form. In the late evening, prior to the onset of sleep, body temperature begins to fall. During sleep, body temperature remains below daytime levels with a subsequent rise approximately one to two hours prior to getting out of

bed. During the daytime hours, body temperature continues to rise and remains high until the late evening, when it begins its slow decline again (Mills, Minors, & Waterhouse, 1974).

The release of endogenous circadian rhythms from exogenous constraints allows the circadian system to cycle according to its own internally derived impulses, a situation known as "*free-running*." One means of removing the environmental influences from the circadian system is to have subjects live in specially designed temporal isolation environments. Under these conditions, subjects are freed from the demands of everyday life, are isolated from all time cues, and are allowed to sleep and wake when they wish. Along with monitoring the sleep/wake cycle, body core temperature can be monitored frequently in these experiments. Studies of humans in temporal isolation have revealed that the free-running period of the body temperature rhythm lengthens by about 4.1%, from 24 hours to approximately 25 hours (Wever, 1979; Czeisler, Weitzman, Moore-Ede, Zimmerman, & Knauer, 1980). Thus, the human internal clock requires a daily 'setting back' of about one hour in order to keep us 'in time' with our environment. This setting back occurs during the period immediately following awakening in the morning and exposing ourselves to light. The process of period and phase control of a circadian pacemaker by an environmental time cue is known as *entrainment* or *synchronization*.. Environmental stimuli, such

as social contacts, alarm clocks, the light-dark cycle, the sleep-wake cycle itself, or indeed any information that provides a sense of time during the 24-hour day has been postulated to synchronize, or entrain our body clock. This 'data' from the social world has been called a *zeitgeber*, which is German for "time-giver" (Aschoff, 1960).

Changes in activity levels, posture, and the homeostatic response to food and beverages can induce transient changes in mean levels of body temperature. The *constant routine procedure*, developed by Mills and his co-workers, was designed to equally disperse these known confounds on body temperature (Mills, et al. 1974). In the constant routine protocol, levels of illumination are kept constant and subjects are served small hourly snacks. Body movements are limited and sleep is not permitted. Under this procedure, the general shape of the 24-hour temperature curve remains similar to that observed when subjects are recorded under conditions of everyday life. Although there are some differences between the temperature recordings obtained during a normal day and a constant routine day (the overall temperature average is lower and the nadir appears to be advanced in the constant routine), the results clearly show a reliable circadian pattern of temperature oscillation that is not due to environmental events (Mills et al., 1974). Taken together, the increase in period length of the body temperature rhythm observed in isolation and the persistence of this rhythm during the constant routine suggests that it

is driven by an endogenous circadian pacemaker, most likely located in the suprachiasmatic nucleus (SCN) of the hypothalamus (Rusak & Zucker, 1979; Mistleberger & Rusak, 1989).

Figure 2 shows the raw minute-to-minute body temperature data of one human subject during two days of entrainment and during one day of a constant routine protocol. A 24-hour cosinor curve is fitted over the raw data.

- Figure 2 -

Figure 2

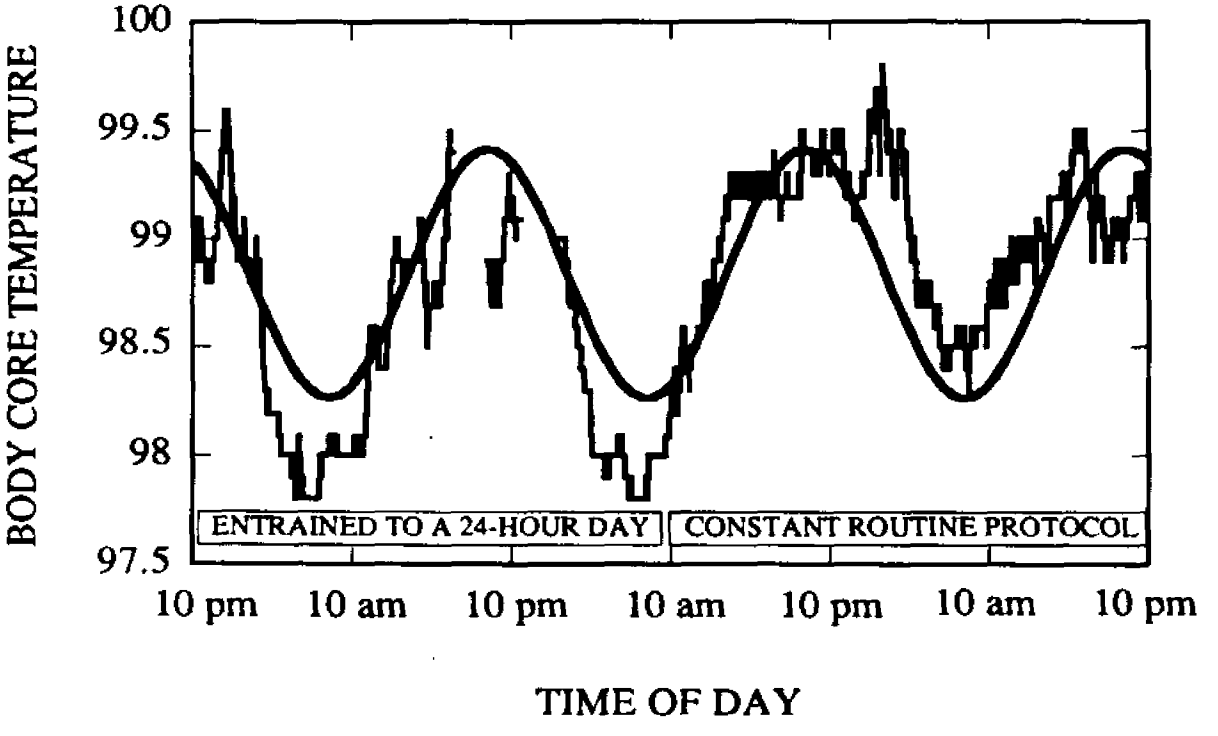


Figure 2. Three consecutive days of minute-by-minute temperature data for a single human subject during entrainment and during a constant routine. A 24-hour cosinor curve is fitted over the raw data. Note the reduction in amplitude during the constant routine.
(Data courtesy of the Institute of Chronobiology).

Even though the evidence suggests that the body temperature rhythm is generated endogenously, clearly exogenous factors such as sleep, activity, exercise, etc., can have a reliable and predictable affect on the shape and mean levels of body temperature (Wever, 1979; Wever, 1985). It is intuitively obvious that periods of inactivity would likely lower mean temperature levels, while periods of heightened activity (changes in posture, exercise) would likely raise it. These reliable and predictable effects of exogenous influences on body temperature have been termed *masking* (Aschoff, 1960). Exogenous factors in the environment not only serve to entrain and synchronize underlying circadian rhythms, but they can also obscure these rhythms.

The relationship between sleep timing and duration and the circadian rhythm of core body temperature in normal subjects

Over the last thirty years, significant relationships have emerged between the sleep/wake cycle and the human body temperature rhythm. It is generally understood that the timing and duration of sleep, as well as subjective sleepiness, REM sleep, and possibly slow wave sleep are dependent on circadian phase relationships (Zulley, 1976; Wever, 1979; Zulley, Wever, & Aschoff, 1981; Czeisler et al., 1980; Akerstedt & Gillberg, 1981; Gillberg & Akerstedt, 1982; Froberg, 1977; Richardson, Carskadon, Orav, & Dement, 1982;

Weitzman, Czeisler, Zimmerman, & Ronda, 1980; Gagnon & Broughton, 1985; Campbell & Zulley, 1989).

A minority of subjects studied under temporal isolation exhibit what has come to be known as *internal desynchronization.* In these instances, the body temperature rhythm continues to have a relatively stable period length of approximately 25.1 hours, whereas the period of the rest/activity cycle is either substantially longer (i.e., > 35 hours), or substantially shorter (i.e., < 21 hours). This divergence in period length results in subjects initiating sleep at all different points along the body temperature curve over the course of the experiment. Dramatic differences in sleep duration result from initiating sleep at different phases of the temperature rhythm. The phenomenon of internal desynchronization is perhaps the most significant and most frequently cited piece of evidence for the existence of multiple oscillators in the human circadian system (Kronauer, Czeisler, Pilato, Moore, & Weitzman, 1982; Wever, 1988). The characterization of this phenomena has recently been challenged and remains controversial. Single oscillator models of the human circadian timing system are capable of accounting for internal desynchronization (Eastmam, 1984). Furthermore, a re-analysis of napping patterns from isolation studies has suggested that internal desynchronization may be an artifact of internal and external behavioral controls on

sleep (Zulley & Campbell, 1985). Regardless of the status of *internal desynchronization*, convergent evidence has shown that the amount, structure, and duration of sleep is, to a significant extent, under circadian control in both free-running and entrained conditions (Czeisler et al., 1980; Zulley et al., 1981; Akerstedt & Gillberg, 1981; Gillberg & Akerstedt, 1982), and that these relationships remain during daytime sleep (Campbell, 1984; Lavie, 1986). Studies where desynchronization does not occur (that is, the periods of the body temperature rhythm and activity rhythm remain similar, and thus maintain a stable phase relationship), can also provide a window to examine the relationship between sleep and temperature.

Results from temporal isolation

The relationship between sleep and temperature can best be examined under constant conditions, in environments free of time cues and social obligations. Subjects in isolation can be entrained to a 24-hour day by a variety of zeitgebers, as if they were living normally in the real world, or they can be allowed to free-run (that is, to choose their own rest/activity patterns). Upon release into free-run, subjects are allowed to sleep and get up when they choose, but they are also asked to adhere to a monophasic sleep pattern (i.e., one major sleep episode per subjective day), and they are encouraged not

to nap.

A short report by Zulley and Schulz provided the first experimental evidence suggesting a relationship between sleep duration and body temperature (Zulley & Schultz, 1980). They studied five young male subjects under entrained (synchronized to a 24-hour day) and free-running conditions. During the entrained condition, subjects were allowed to leave the lab and live a normal life, while during free-running, they lived in an enviroment free of time cues and other social zeitgebers. Electrophysiological recordings (EEG) of sleep were collected along with continuous body temperature data. They found that sleep episodes begun near the temperature minimum and continuing on the rising slope of the temperature curve were shorter in duration than those sleep episodes begun several hours before the body temperature minimum. Sleep episodes initiated before the temperature nadir continued through both the descending and rising portions of the body temperature curve.

Total sleep time per episode was significantly reduced during entrainment compared to free-run. Total sleep time averaged 436.61 (± 46.67) minutes during entrainment and 488.63 (± 110.46) minutes during free-run. The percentages of sleep stages 1, 2, and REM remained similar for the two conditions, while slow-wave sleep was

significantly reduced during free-run. The temporal distribution of REM sleep was altered, although the absolute amount of REM sleep remained unchanged. Onset to REM sleep was advanced significantly during free-run. Latency to REM sleep was 67.9 minutes during free-running conditions compared to 155.0 minutes for the entrained condition. During entrainment, the amount of REM sleep increased from the beginning to the end of the sleep period, whereas during free-run, the greatest amount of REM sleep was observed at the beginning of the night, and decreased during the sleep period.

This report was followed by a larger study by the same group that confirmed and extended these original findings (Zulley, Wever, and Aschoff, 1981). This report concerned studies of 20 subjects drawn from a larger group of subjects conducted over several years. Studies were performed under conditions of temporal isolation and lasted at least one month. Out of these twenty subjects, ten experienced internal desynchronization and another ten did not. Thus, subjects whose rest/activity rhythm varied dramatically (mean 33.4 hours) from their rhythm of body temperature (25.1 hours) initiated sleep at all phases of their temperature cycle during their stay in isolation. Subjects who remain in synchrony are subjects whose sleep/wake cycles and body temperature cycles manifest equal period lengths, and the mean period length for this group of ten was 25.7 hours. Subjects were not permitted

to nap, although some of them did, and sleep episodes designated as naps were excluded from the data analysis.

It was found that subjects who remained in synchrony (sleep/wake rhythms remain coupled to the rhythm of body temperature) initiated sleep most frequently at their temperature minima, while none were observed to be asleep at the temperature acrophase (maximum). The association of body temperature and sleep is further highlighted by the fact that out of 205 sleep episodes "nearly 100%" (no numbers provided) of the subjects were asleep at, or near, their temperature minimum. In slight contrast, the desynchronized subjects (sleep/wake rhythms are uncoupled from the body temperature rhythm, manifesting different period lengths) were asleep at their temperature minima only 80% of the time, and were asleep 10% of the time at their temperature maximum, or acrophase. Although sleep can and did occur at all phases of the temperature cycle, it is also clear that even in subjects who were desynchronized, sleep is not randomly distributed around the entire circadian day (Zulley, Wever, and Aschoff, 1981). It is important to note that, even under conditions of internal desynchronization where the rest/activity cycle has a period length markedly different from that of the body temperature rhythm, the association between the circadian rhythm of body temperature and sleep remains.

These data clearly indicate a robust tendency for subjects to be asleep

around their temperature minimum. Why are most people asleep at this time, and what does the moment of sleep onset have to do with the subsequent duration of sleep?

Sleep initiation in internally synchronized subjects typically occurred approximately 1 hour prior to the temperature minimum, whereas in desynchronized subjects, sleep initiation preferentially was choosen along two points of the temperature curve. These sleep initiation points were located approximately 1 hour and 6.3 hours prior to the temperature minimum. These two points correspond to a) the time when human subjects find it most difficult to be awake (i.e., the temperature minimum)(Akerstedt, 1988), and b) the typical choice of sleep initiation in entrained 24-hour conditions (Broughton, 1990). In both groups of subjects however, sleep termination occured at similar points along the temperature curve. Sleep termination occurred 6.64 hrs. after the temperature minimum in synchronized subjects and 5.10 hrs. after the temperature minimum in desychronized subjects.

These data suggest that sleep timing and duration are not only contingent upon the duration of prior wakefulness. It is remarkable that when subjects are given the opportunity to initiate sleep at their own discretion, sleep onsets would cluster around only two points. Even more striking is the unimodal pattern of sleep termination, suggesting that sleep is no longer possible past a certain point on the temperature curve,

regardless of the previous amount of wakefulness. Thus, sleep episodes initiated approximately 5 hours prior to the temperature minimum would, on average, be 5 hours longer than sleep episodes begun at the temperature minimum, because sleep in both cases is terminated approximately 5 hours after the temperature minimum.

Czeisler, Weitzman, Moore-Ede, Zimmerman, and Knauer (1980) confirmed these relationships between sleep duration and body temperature. In addition to the 24-hour monitoring of body temperature, an assesssment of EEG sleep was conducted along with 24-hour monitoring of various hormones, such as plasma cortisol, and human growth hormone (Czeisler et al., 1980). Data from 12 subjects living in isolation for 16 to 189 days, comprising 562 sleep episodes, have been reported.

In a sub-set of subjects (5) who experienced internal desynchronization, it was suggested that the average length of a self-selected sleep episode was related to the circadian phase of the body temperature rhythm, and not a function of prior wakefulness (provided that at least 14 hours of wakefulness intervened between sleep episodes). Sleep episodes begun near the temperature minimum and continuing on the rising limb of the temperature curve tended to be short (approximately 6-8 hours in length), while sleep episodes begun at the temperature maximum, or slightly after it were much longer in duration,

some lasting as long as 14 hours. The number of self-selected sleep onsets in this group were also firmly centered around the temperature minimum. The influence of the circadian rhythm of body temperature on sleep duration is emphasized by the fact that 86.1% of all sleep episodes were terminated on the rising slope of the temperature curve.

In summary, both of these research groups found that sleep duration was dependent on circadian phase, as indexed by the body temperature minima, and that the influence was particularly pronounced with regard to the termination of sleep. Subjects, studied in isolation, generally experience shorter sleep durations if sleep is initiated close to, or after, the temperature minimum, because sleep episodes occur on the rising slope of the temperature curve. Further evidence that circadian phase modulates sleep duration is based on unusually long sleep episodes obtained in isolation. Since it is intuitive that sleep should comprise approximately 30% of a typical 24-hour day, where 16 hours of wakefulness is followed by 8 hours of sleep, then the finding that sleep durations can be unusually long (up to 14 hours) with only 16 hours of prior wakefulness deserves an explanation. A possible explanation is that subjects in isolation are unaware of time and they may feel sleepy around their temperature maximum, and decide to go to sleep. Even though prior wakefulness may be no greater than a typical 16-hour day, or sometimes even less, the sleep duration reflects the influence of circadian

factors since the sleep episode's probable point of termination is 5-6 hours after the temperature minimum.

The results from free-running studies, in both internally synchronized and internally desynchronized subjects, demonstrate that the initiation of sleep and its subsequent duration is reliably related to the circadian rhythm of body temperature. Further, when internally desynchronized subjects are awake for extended periods of time (i.e., > 35 hours) and sleep is initiated around the temperature minimum, sleep duration is a reflection of its position along the body temperature curve, not the amount of prior wakefulness. That is, sleep is shorter than would be expected. Conversely, if sleep is initiated near the peak of body temperature, regardless of the amount of prior wakefulness, sleep episodes tend to be significantly longer (i.e., 12-14 hours) than those initiated around the temperature minimum. In both states, the most conspicuous evidence that circadian phase relationships govern sleep duration is that the majority of sleep episodes are terminated approximately 5-6 hours after the temperature minimum, in an environment that places no limitations on the decision to get up. Sleep duration is a function of when it is initiated in the circadian cycle.

Sleep displacement experiments

The demonstration in time-free environments of a circadian influence on sleep timing and duration is impressive, and it would be important to

know if similar relationships between sleep and body temperature were borne out in conditions of every day life. For example, are similar relationships between sleep duration and circadian phase apparent when sleep is 'displaced' to various portions of the temperature curve during entrainment to a normal 24-hour day?

The data from sleep displacement experiments moderately supports the thesis that the duration of sleep is influenced by the relationship between the sleep period and the circadian phase. The objective of sleep displacement experiments is to describe the changes in sleep that may result when the sleep period is shifted out of its normal nocturnal location, or when sleep is displaced to various portions of the entrained body temperature curve. An essential feature of experimental sleep displacement is the rapid alteration of the internal phase angle between sleep and body temperature. This allows for inferences to be made about the relative contributions of prior wakefulness and circadian phase relationships on sleep.

Early studies of sleep displacement generally found that when sleep was displaced to the daytime hours, onset to sleep increased, the amount of sleep decreased, and sleep became more fragmented with an increase in "early morning awakening" (Weitzman, Goldmacher, Kripke, MacGregor, Kream, & Hellman, 1968; Webb, Agnew, & Williams, 1971; Weitzman & Kripke, 1981). These results provided

some of the first indications that sleep duration was not only contingent upon prior wakefulness, but instead might depend on its temporal placement within the circadian day.

Convincing evidence of a circadian component in the determination of sleep length in entrained conditions comes from studies conducted by Akerstedt and Gillberg (1981), and Gillberg and Akerstedt (1982).

They studied six subjects in the laboratory over a period of 7 weeks. During the baseline week, all subjects slept in the laboratory from 11 pm to 7 am. Subsequent to baseline evaluations of sleep each week, each subject had their sleep postponed to one of six experimental conditions. For illustrative purposes, let us suppose that a single subject was run in a baseline condition first. Then on each subsequent week in which she returned to the lab, her bedtime was postponed by four hours. Her bedtimes for the seven consecutive weeks would be 11 pm, 3 am, 7 am, 11 am, 3 pm, and 7 pm and 11 pm. Thus, subjects went to sleep with varying amounts of prior wakefulness under each condition. It follows then, starting with the baseline bedtime of 11 pm, subjects went to sleep with 16, 20, 24, 28, 32, 36, and 40 hours of prior wake. There are two important aspects of this design. Subjects were shielded from environmental variables that might interfere with sleep (i.e., noise, light, etc.) and they were

allowed to sleep *ad libitum*. Thus, the termination of the sleep episode was left up to the subjects themselves. It was reasoned that both the effects of prior wakefulness and the effects of circadian phase relationships could be compared.

The circadian influence on the termination of sleep was clearly in evidence. Group mean data for total sleep time revealed the following. At baseline (16 hours of prior wake), subjects slept for an average of 483 minutes. Following 20 hours of prior wake, with bedtime scheduled at 3 am, total sleep time averaged 396 minutes, a decrease of 86 minutes. When bedtimes were scheduled at 7 and 11 am, self-selected sleep durations were 267 and 273 minutes respectively. Thus, over 200 minutes less sleep was obtained compared to baseline with a corresponding increase in prior wakefulness of fifty and seventy-five percent respectively. These results strongly support the suggestion that the temporal placement of sleep is a more reliable determinant of sleep duration than the amount of prior wakefulness because increases in prior wakefulness resulted in decreased total sleep time. When sleep was initiated at 3 pm, sleep durations begin to rise (458 minutes), and continued to increase to 672 minutes when sleep was scheduled to begin at 7 pm (Akerstedt & Gillberg, 1981).

These results suggest that when sleep is initiated substantially

ahead of the temperature minimum (a few hours after the temperature maximum), it will be much longer in duration than if sleep is initiated near, or after the temperature minimum. Finally, the impact of the circadian influence on sleep duration is vividly captured when subjects 'skip' an entire day of sleep. When subjects initiated sleep after 40 hours of prior wakefulness mean sleep durations were 520 minutes, not significantly different from total sleep time values at baseline.

In addition, 34 of 42 sleep episodes were terminated on the rising slope of the body temperature curve. That sleep duration is more reliably associated with its temporal placement in the circadian day as opposed to prior wakefulness is confirmed by the pattern of correlation coefficients. For example, total sleep time was positively correlated with body temperature at bedtime: if body temperature was relatively high, as it is when sleep is initiated hours prior to the temperature trough, then sleep durations were longer. On the other hand, total sleep time was correlated negatively with body temperature at waketime: if temperature was relatively high at wake time, sleep durations were short. If subjects went to sleep at, or slightly after, their temperature minimum, sleep would be short, and temperature would be relatively high upon awakening because it appears that only a limited amount of sleep can be obtained on the

rising portion of the temperature curve, regardless of the amount of prior wakefulness (Akerstedt & Gillberg, 1981; Gillberg & Akerstedt, 1982).

Studies of sleep displacement indicate that the circadian system is an important determinant of sleep length even when prior wakefulness exceeds normal baseline levels. The reduced sleep duration, the placement of the waketimes, and the pattern of correlations between temperature and sleep all suggest that sleep length can be truncated if it is displaced to the rising portion of the circadian temperature curve.

Age and the circadian system

In addition to the previously discussed phase advance of the activity rhythm(and its associated features of earlier bedtimes, early morning awakening, and the subjective report of reduced total sleep time in the elderly), several other physiological measures, such as body temperature (Weitzman, Moline, Czeisler, & Zimmerman, 1982; Richardson et al., 1982), cortisol rhythms (Touitou, 1982), and onset to REM sleep (Reynolds, Kupfer, Taska, Hoch, Spiker, Sewitch et al., 1985), appear to be phase-advanced relative to the habitual sleep period in the elderly as well.

Several theories have been proposed to explain the origins of insomnia conditions. Among them are psychiatric explanations (e.g.,

internal conflict theory) (Kales, Caldwell, Preston, Healy, & Kales, 1976), hyperarousal theories (Monroe, 1967; Freedman & Sattler, 1982; Stepanski, Zorick, Roehrs, Young, & Roth, 1988), genetic predispositional theories (Hauri & Olmstead, 1980), and a myriad of behavioral practices that hinder the normal processess of sleep timing and duration (Bootzin, 1972; Bootzin & Nicassio, 1978; Hauri & Fisher, 1986; Lacks & Rotert, 1986; Spielman, Saskin, & Thorpy, 1987; Weitzman, Czeisler, Coleman, Spielman, Zimmerman, & Dement, 1981). However, these models have been proposed to account for the origin of insomnia in young persons and there is limited evidence to date, that treatment interventions consistent with these hypotheses, are effective in the elderly.

As an alternative to these models of insomnia, it has been proposed that alterations in circadian phase relationships, between body temperature and the sleep/wake cycle, may be linked to nocturnal sleep fragmentation, early morning awakenings, and increased daytime napping that are consistently found in the sleep patterns of the elderly (Weitzman et al., 1982; Czeisler, Kronauer, Mooney, Anderson, & Allan, 1987; Zepelin, 1983; Miles & Dement, 1980; Dement et al., 1985). Specifically, it has been proposed that a shortened circadian period length may alter internal phase relationships between the sleep period and the output of the

endogenous circadian pacemaker. This shortened period could be the result of a specific physiological malfunction of the pacemaker itself, or it could result from a breakdown in the normal entrainment mechanisms responsible for synchronization to environmental cues (Dement et al., 1985). A breakdown in the entrainment mechanism may be caused by changes in social relationships (Aschoff, Fatranska, Giedke, Doerr, Stamm, & Wisser, 1971), or people may engage in behavioral patterns that prevent the normal reception of zeitgeber cues (Campbell, Kripke, Gillin, & Hrubovcak, 1988). Theoretically, entrainment failures could also be caused by a disruption in the retino-hypothalamic-pathways that mediate light effects, or there may be a breakdown in the intrinsic re-setting capacity of the pacemaker itself. It is also possible that changes in internal phase relationships arise from either an abnormally strong phase-advance capacity, or that subjects are resistant to light induced phase-delays (Lewy, Wehr, Goodwin, Newsome, & Markey, 1980; Lewy, 1983; Lewy, Sack, & Singer, 1984; Czeisler, Allan, Strogatz, Ronda, Sanchez, Rios et al., 1986).

What evidence supports the theory that sleep disturbance in the elderly is the result of age-related changes in the circadian pacemaker which result in altered internal phase relationships between sleep and temperature? A brief attempt to answer this question follows.

Animal studies

Pittendrigh and Dann (1974), in a longitudinal design (i.e., animals studied over their entire life span), studied the free-running rhythm of the golden hamster and two types of deer mice and reported age-related reductions of the period length of the rest/activity cycle. They studied rest/activity rhythms for 3 months in all animals, once at 5-7 months and again at 14-16 months. While the magnitude of the effect was small (a reduction in period length from 23.32h to 23.17h for the deer mouse, and 24.35h to 24.02h for the hamster), the association with age was negative ($r = -.673$) and significant ($p < .001$). Frequency analysis revealed that in 8/8 hamsters, and in 16 of 18 deer mice, the period of the rest/activity rhythm was shorter at 14-16 months (Pittendrigh & Daan, 1974).

Welsh, Richardson, and Dement (1986), examined age-related changes in circadian rhythms in the mouse and found that relative to young mice, old mice had smaller circadian amplitudes of wake, activity, NREM, REM sleep and they experimeced greater sleep fragmentation during the rest phase of an imposed 12/12 light-dark cycle. The greater dispersion of sleep episodes around the circadian day, and the increased wakefulness during the habitual sleep periods may be thought of an age-related breakdown in the circadian timing system (Welsh, Nino, Gander, Keenan, & Dement, 1986). Similar

results were obtained by Van Gool and Mirmiran (1983) who found that relative to young rats, old rats manifested significantly more wakefulness, reduced total sleep time, and a reduction in the amount of active sleep (REM) during the sleep period.

Morin (1988) attempted to replicate the finding of Pittendrigh and Dann (1976), while additionally controlling for the effects of prior light exposure, which is thought to confound period measurements in animals. Control over prior photoperiod exposure was achieved by blinding the animals at approximately 5 weeks of age. Animals were then placed in individual wheel-running cages at 7 weeks and remained there until death. The circadian rhythm of wheel-running activity was 24.25 at 15 weeks and by week 30 it had significantly shortened to (24.15) and the period length continued to decline until the animals died.

Taken togther, these animal studies provide some limited support for the following. Rodent circadian rhythms manifest age-related changes reflected by a reduction in period length and a reduction in the amplitude of sleep and wakefulness. Furthermore, these age-related changes in period and amplitude are associated with increased sleep fragmentation and a reduction in total sleep time.

Human studies

Weitzman, Moline, Czeisler, and Zimmerman, (1982) studied six old and six young subjects in temporal isolation under conditions of entrainment (i.e., the rhythms of sleep/wake synchronized to a 24-hour day), and free-running (sleep/wake times self-selected). They reported that compared to young subjects (mean age, 25.3), old subjects (mean age, 50.5), had a significantly shorter (31 minutes) period length in the free-running body temperature rhythm. Temperature amplitude was significantly reduced in the older subjects during both entrained and free-running conditions, and they manifested a higher mean temperature value at sleep onset, midsleep, and waking. The authors implied that these altered phase relationships may be responsible for the reduced sleep efficiency, and increased wakefulness found in the sleep of the aged. Wever (1979), on the other hand, did not observe any differences in circadian period between young and old subjects during conditions of temporal isolation.

Zepelin (1983) concluded that an age-related change in period length may underlie sleep disturbance in the elderly from temperature recordings made exclusively during the nighttime sleep period under entrained conditions (Zepelin, 1983). The upturn in the temperature rhythm during sleep ocurred earlier in an older group of

men and women when compared to a group of younger men and women. The upturn in body temperature occurred approximately 6 hours after sleep onset in the younger group compared to the second hour after sleep onset in the older group. Correlational results support the thesis that altered internal phase relations are associated with the diminished sleep in the elderly. A significant negative correlation was observed between age and the time from sleep onset to the lowest temperature value. Thus, increasing age is associated with an advance of the temperature minimum relative to sleep onset. He also observed a negative correlation between the position of the temperature minimum relative to sleep onset, and the amount of time lying in bed awake. As the temperature nadir moved closer to sleep onset, the amount of wakefulness during the sleep period increased. The older subject's mean values of body temperature during nighttime sleep were lower than those found in the younger group; a result at variance with that reported by Weitzman et. al. (1982), and by Vitiello et. al. (1986).

Zepelin and McDonald (1987) in a later and more extensive report included, in addition to the above mentioned temperature findings, sleep physiology measures and autonomic measures (Zepelin & McDonald, 1987). There were 36 subjects in 4 cells. Nine men and nine women between the ages of 18 to 23 and 57 to 71 served as

subjects. Only two significant differences between young and old were observed with respect to autonomic function; vasocontrictions per minute decreased in the older group, and heart rate increased in the older group. Correlational measures between autonomic function and sleep measures were generally non-significant. This lack of association between autonomic arousal and sleep fragmentation in an older group of subjects was interpreted as disconfirming evidence for the 'hyperarousal theory' of insomnia, leading the authors to reiterate their hypothesis (based on the negative association between the temperature minima and amount of wakefulness), that a phase advance of the body temperature rhythm may underly a substantial portion of the sleep complaints reported by the elderly.

In summary, behavioral data from elderly subjects indicates that increasing age is associated with earlier bedtimes, earlier waketimes and increased diurnal napping. In addition, the subjective complaint of early morning awakening, coupled with an inability to return to sleep, complaints of non-restorative sleep, and complaints of reduced amounts of sleep have all been confirmed by objective measures. There appears to be an advance of several biological rhythms relative to the habitual sleep period; that is, body temperature, REM sleep and rest/activity.

For a sub-set of elderly subjects, it has been suggested that altered

internal phase relations are of pathophysiologic significance. The age-related changes observed in these biological rhythms could be a direct result of a reduction in the output of the endogenous circadian pacemaker itself, or from a breakdown in the processes of entrainment (which could be either physiologically or behaviorally based). The aforementioned studies support the supposition of an age-related change in the circadian timing system.

How does aging affect the SCN and other central nervous system structures that are involved in circadian regulation? First, the eye itself may lose its responsivity to environmental light. It has been demonstrated that glucose utilization is reduced in the retina of older rats and it is speculated that this may be due to cell loss (Shinowara, London, & Rapoport, 1982). Second, age-related processes may reduce the ability of the SCN to transmit photic information accurately. For example, the total number of cells in the rat SCN declines as a function of age (Roozendaal, van, Swaab, Hoogendijk, & Mirmiran, 1987), and this result has been confirmed in humans over the age of 80 (Swaab, Fliers, & Partiman, 1985). Third, partial SCN lesions may be an experimental analog of the aging SCN. Thus, although the diffuse loss of SCN neurons seen in older animals has not yet been experimentally produced in younger animals, partial lesions of the SCN resulted in a significant

shortening of the period of rest/activity rhythm in hamsters (Davis & Gorski, 1984). Similarly, partial lesions of the SCN reduced the amplitude of eating and drinking rhythms in the rat.

Thus, there is a growing body of evidence that suggests that the aging process may alter circadian function, and that this alteration is related to the diminished capacity of the SCN. Altered SCN function may result in a shortening of the intrinsic circadian period. Further investigation of the precise consequences of aging on SCN function may shed some light on the possible neurobiological substrates that underly the suspected pathophysiology of sleep disturbance observed in the elderly.

The Circadian Phase-Shifting Effects of Bright Light: A Possible Method of Intervention for the Treatment of Age-Related Sleep Disturbance in the Elderly Insomniac

Circadian scientists have known for quite sometime that seasonal variations in the photoperiod and the administration of light pulses could act as major synchronizers, and/or entraining agents to the natural 24-hour day in lower organisms and in all mammals except humans (Hastings, Rusak, & Boulos, 1991; Moore-Ede et al., 1982). Humans were thought to be uniquely insensitive to the synchronizing and phase-shifting effects of light because early experimental attempts to do so, failed (Wever, 1974; Aschoff,

1981).

This belief was changed however, when Lewy, Wehr, Goodwin, Newsome, and Markey (1980) demonstrated that bright artificial light could suppress nocturnal melatonin secretion in humans. Melatonin is a hormone that is secreted by the pineal gland during nighttime hours. The onset of melatonin secretion has a circadian periodicity, and has been used as a marker for circadian phase estimates. The onset of melatonin production can be measured in humans through continuous blood sampling. When melatonin levels reach a specific concentration (10 pg/ml), the Dim Light Melatonin Onset, or DLMO is reached. This has been demonstrated to be a reliable marker for estimating circadian phase (Lewy, 1983; Lewy, Sack, Miller, Hoban, Singer, Samples et al., 1986; Lewy, Sack, Miller, & Hoban, 1987).

While the number of subjects studied was small (n=6), the effects of different light intensities on the DLMO were clearly evident in a dose-response manner. Bright light (2500 lux, equivalent to indirect sunlight) significantly decreased nocturnal melatonin secretion between the hours of 2 and 4 am (subjects were awakened from sleep for light administration). Light of less intensity (500 lux, ordinary room light) did not significantly decrease melatonin secretion, and intermediate levels of light (1500

lux) suppressed melatonin to levels in between that of the bright and dim light conditions (Lewy et al., 1980).

As Lewy has repeatedly pointed out this was the "pivotal" study that began the clinical sub-disipline of light treatment for chronobiologic and mood disorders (Lewy, Sack, & Singer, 1990).

As we have seen, the human circadian pacemaker has a free-running period of approximately 25 hours, while our day length is 24 hours. An environmental zeitgeber must correct for the differences in period lengths to compensate, or to maintain stable internal phase relations among a variety of physiologic rhythms within the organism, as well as with the environment. The process of period and phase-control by enviromental zeitgebers is called entrainment (Mistleberger & Rusak, 1989). Light's capacity to entrain or to shift circadian rhythms however, is wholly dependent on the organism's circadian cycle (DeCoursey, 1960).

DeCoursey investigated the phase-shifting effects of bright light pulses in the flying squirrel and reported that light administered early in the subjective night resulted in a phase-delay of the activity rhythm. Light administered late in the subjective night resulted in phase-advances. The plotting of the relationships between the circadian phase of light administration (x-axis) and the amount of

the induced phase-shift (y-axis) results in what is known as the *phase response curve* or PRC (DeCoursey, 1960). Figure 3 graphically illustrates the general schema of this phase response curve to light obtained in the hamster (Takahashi & Zatz, 1982).

- Figure 3 -

Figure 3

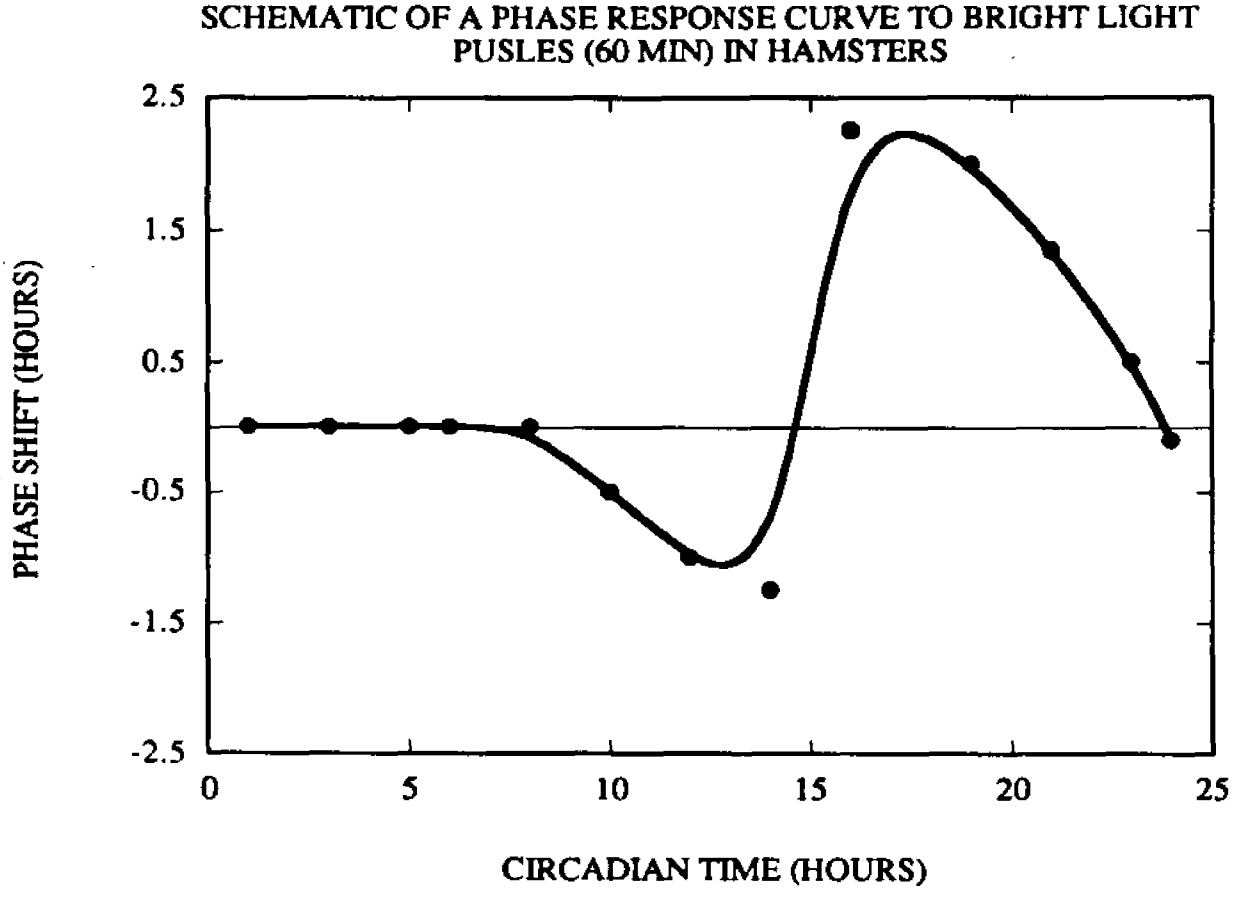


Figure 3. Phase response curve to light in the hamster given at various times relative to the hamsters locomotor activity. Phase-advances are plotted as positive and phase-delays are plotted as negative. The onset of activity is at circadian time 12 (the hamster is active during "subjective night" and inactive during "subjective day"). The graph illustrates the general features of phase response curves to light for all organisms. Light administration early in the subjective evening produces a phase-delay in circadian rhythms, while light administration late in the subjective night produces phase-advances.
(Graph from Takahashi and Zatz, (1982) Science, vol. 17. pp 24-25)

The breadth and depth of this phenomena is remarkable. According to Moore-Ede, Sulzman, and Fuller (1982), and Mistleberger and Rusak (1989), the general PRC to light is similar for virtually all living organisms, from unicellular algae to primates. While a complete human PRC to light has not been mapped out, data collected to date strongly supports Lewy's initial speculations that a human PRC is not likely be to different from that observed in animals (Lewy, Sack, Fredrickson, Reaves, Denney, & Zielske, 1983; Lewy et al., 1984; Lewy et al., 1987). In humans evening bright light administration results in phase-delays, whereas morning light administration results in phase-advances of the circadian rhythm of core body temperature.

By 1983, Wever had demonstrated that bright light (4,000 lux) could increase the range of entrainment beyond 29 hours and Czeisler, Richardson, Zimmerman, Moore-Ede, and Weitzman (1981), had suggested that an absolute light-dark cycle (i.e., subject has no control over when the lights will go on or off, nor access to the lights when they go off), had entrainment properties that had previously been misinterpreted. However, definitive conclusions regarding the circadian effects of light were not possible from these two studies. In both cases, the sleep/wake schedule was allowed to vary along with the scheduled light exposures.

In spite of these criticisms, with the demonstration of the biological effect of bright light by Lewy in 1980, and the possible synchronizing effects of bright light by Wever and Czeisler, the stage was set for someone to demonstrate the phase-shifting effects of light, independent of shifts in the sleep/wake cycle.

This was first achieved by Lewy, Sack, and Singer (1984), who manipulated the length of the photoperiod by either artificially advancing 'dusk', or conversely, by delaying 'dawn'. While holding the sleep/wake schedule constant (sleep period = 11 pm to 6 am) under laboratory conditions for one week, 4 subjects experienced a shorter photoperiod during which dusk-lighting conditions were advanced to 4 pm. This was 2.5 hours earlier than what they were exposed to at baseline. According to Lewy, an advance of dusk is equivalent to removing biologically active light from the phase-delay portion of the human PRC to light. The removal of light from this portion of the phase response curve should result in an advance of human circadian rhythms. These subjects were then exposed to a delay of dawn (subjects were awakened at 6 am but were not exposed to light until 9 am), during which time, light was removed from the phase-advance portion of the phase response curve.

Consistent with phase response curves in animals, the DLMO

was advanced by 2.5 hours when light was removed from the phase-delay portion of the PRC, and the DLMO was delayed when light was removed from the phase-advance portion of the PRC. Both of these results were obtained while the sleep/wake cycle was held constant, and the direction of the phase shifts in response to the removal of biologically active light is consistent with the data obtained in animals (Lewy et al., 1984; Lewy, Sack, & Singer, 1985).

Evidence confirming the phase-shifting effects of bright light independent of the sleep/wake cycle was obtained by Czeisler and associates who used body temperature as a marker for circadian phase (Czeisler et al., 1986b). In a 66-year-old female with an advanced temperature minimum (11:35 pm) and a shortened period of the intrinsic circadian pacemaker (23.7 hours), Czeisler, Allan, Strogatz et. al. successfully delayed her body temperature rhythm by 5.7 hours as a result of 7 days of bright light exposure (7,000-12,000 lux). This phase-delay in body temperature rhythm was apparent after 2 days of light exposure, and was equally reflected in a shift of the cortisol rhythm. Further, the phase-delay of body temperature took place while the sleep period was held constant (0000h-0700h), and the direction of the phase-shift is consistent with phase response curves to light in animals, and with the results

obtained by Lewy, Sack, and Singer (1984). The authors concluded that bright light "must be acting directly on the endogenous circadian pacemaker" (Czeisler, Allan, and Strogatz et al., 1986b, pp. 670).

In 1987, Lewy, Sack, Miller, and Hoban (1987) alternated evening (8 pm to 10 pm), and morning (6 am to 8 am), bright light exposure in both normal control and depressed subjects. Using the DLMO as a marker of circadian phase, and holding the sleep period constant (10 pm to 6 am), these investigators confirmed both their earlier report (1984), and the report of Czeisler, Allan, and Strogatz et al. (1986), that bright light has circadian phase-shifting effects. Light administration in the evening resulted in a phase-delay of melatonin onset, while morning administration resulted in phase-advances. The phase-shifting effects of light were more pronounced in the depressed group, and morning light was associated with a reduction in depressive symptoms, while evening light had little effect. Morning light appears to have had marginal effects on circadian phase in the normal group; however, evening light delayed the onset of melatonin by approximately 2 hours (Lewy et al., 1987).

There are several other studies that have demonstrated either a synchronizing effect of bright light, or a phase re-setting capacity.

Some of these studies have not held the sleep/wake cycle constant, and all of them tend to ignore the results of circadian phase-shifts on sleep measures (Honma, Honma, & Wada, 1987; Eastman & Miescke, 1990; Czeisler, Kronauer, Allan, Duffy, Jewett, Brown et al., 1989; Hoban, Sack, Lewy, Miller, & Singer, 1989; Rosenthal, Joseph-Vanderpool, Levendosky, Johnston, Allen, Kelly et al., 1990).

In this next section, a brief discussion will be presented regarding the phase-shifting effects of bright light and its result on sleep.

Effects of light induced circadian phase-shifts on sleep measures

Results from both temporal isolation and from entrained conditions suggest that sleep duration and quality are affected by the internal phase relationship between body temperature and the sleep period. Sleep becomes lighter, more fragmented, and short when obtained on the rising limb of the temperature curve in entrained conditions. The relationship between the temperature minimum and the sleep period is known as the phase angle. Examples of phase angle relations and the hypothesized effects of sleep are presented in figure 4.

- Figure 4 -

Figure 4.

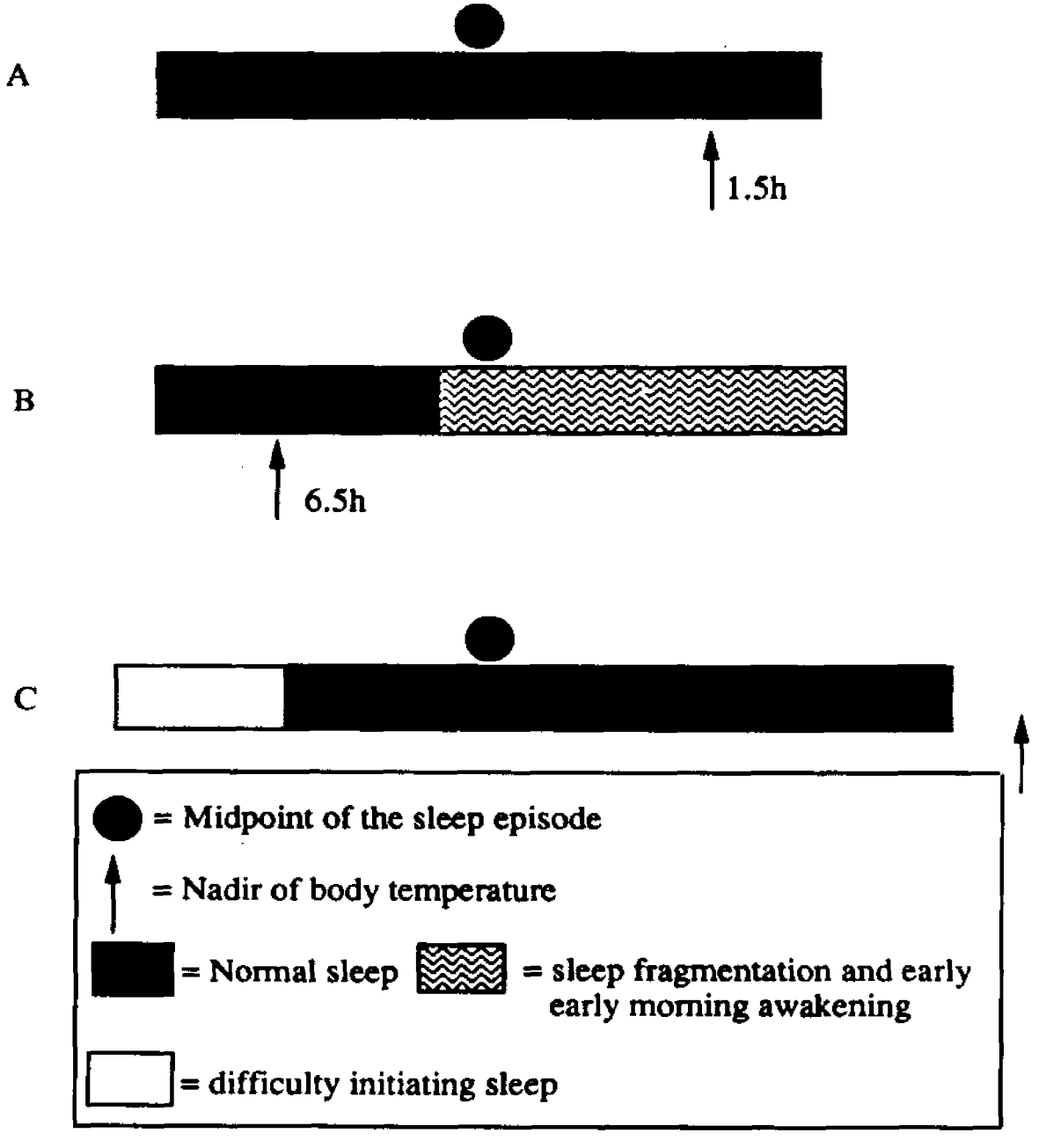


Figure 4 Hypothesize relationships between sleep quality and circadian phase (see text for a description).

In diagram 4A, the temperature minimum occurs approximately 1.5 hours prior to getting out of bed and sleep has occurred primarily on the descending limb of the temperature curve. In diagram 4C, sleep onset is delayed because it is being attempted at a circadian phase known as either a "forbidden zone of sleep" (Lavie, 1986), or the "wake-maintenance-zone" (Strogatz, Kronauer, & Czeisler, 1987). Sleep is artificially truncated, not because of circadian factors, but because the alarm went off and social obligations have to be met. Diagram 4C shows the putative relationships between sleep and body temperature that are thought to underlie the chronobiological disorder called delayed-sleep-phase-syndrome (DSPS) that is most common in adolescents and college students (Weitzman et al., 1981; Thorpy, Korman, Spielman, & Glovinsky, 1988).

In contrast to DSPS, it has been suggested that sleep difficulties in the elderly may be a reflection of breakdown of the circadian timing system. Specifically, a shortened period of the endogenous oscillator, inadequate synchronization as the result of decreased light exposure, or decreases in social cues, or a combination of the above have been proposed as factors that contribute to diminished sleep quality with advancing age (Weitzman et al., 1982; Dement et al., 1985; Czeisler et al., 1986; Campbell, Gillin, Kripke, Erikson,

& Clopton, 1989). Figure 4B is a schematic diagram of the phase angle differences between sleep and body temperature thought to underlie some cases of sleep disturbance in the elderly. This chronobiological sleep disorder has been termed advanced-sleep-phase-syndrome, or ASPS (Kamei, Hughes, Miles, & Dement, 1979). It is worthy to note that the early morning awakening, observed in ASPS, is not associated with mood disturbance, whereas in depression, these two features are strongly associated (Wagner, 1990).

If the proposed relationships between sleep and body temperature are valid, then light-induced alterations of circadian phase should have predictable consequences on sleep quality and duration. Dijk, Visscher, Bloem, Beersma, and Dann (1987) studied 8 males (mean age 23.1) in a cross-over design in which bright (2,000 lux), or dim (1 lux) light was administered after the sleep period (10 p.m. to 6 a.m.) for three hours upon awakening (6 a.m. to 9 a.m.) for three consecutive days. On the fourth night, subjects sat in a darkened room from 6 p.m. to midnight and then sleep was allowed to commence. Dependent measures were standard EEG derived sleep variables, nighttime core body temperature, and measures of EEG power based on spectral analysis which purports to measure sleep intensity, which may

reflect sleep homeostasis (Borbely, 1982; Borbely, Tobler, & Hanagasioglu, 1984).

Subjects were instructed to sleep until they "felt refreshed". Nocturnal sleep latency, and the amount and time course of EEG power were not significantly different between the two conditions. Further, the ten minute interval with the lowest mean body temperature values was not significantly different between the two groups (morning bright = 1:30 am; morning dim = 2:30 am). However, since sleep has a masking affect on the temperature rhythm a second analysis was carried out. The mean nighttime temperature values were calculated for each subject from midnight to 7 a.m. These values were subtracted from the actual values during the night, creating a 'deviation from the mean' temperature curve for both the dim and bright light conditions. Results of this analysis revealed that subjects in the bright light group evidenced a significantly earlier rise in body temperature compared to the dim light control condition. Further, waketimes were significantly advanced (7:44 a.m. v. 8:42 a.m.), total sleep time was significantly reduced (444 minutes. v. 498 minutes), and the accumulation of wakefulness after 7 hours in bed was significantly increased in the morning bright light group. The reduction in total sleep time was the result of significant reductions in REM sleep only (Dijk,

Beersma, Daan, & Lewy, 1989). These results provide some limited support for the thesis that an earlier rise in core body temperature has predictable and detrimental effects on sleep quality when phase relations between sleep and body temperature are altered.

Summary and a proposal for investigation: Experiment 1

Over the last 15 years, evidence has been accumulating from the field of chronobiology that age-related changes in the circadian timing system may underlie sleep disturbance in some elderly patients. Measurements of elderly behavior, sleep patterns, and core body temperature in both isolation and entrained conditions have implicated circadian changes in the etiology of sleep disturbance in the elderly. The phase-shifting capacity of bright light has provided a tool with which to manipulate the human circadian system. Based on the distinctive relations between body core temperature and sleep, it has been suggested that the elderly spend a greater amount of the sleep period on the rising limb of the temperature curve, and with age, the ability to maintain sleep at this time becomes more problematic.

The specific experimental hypotheses to be examined are as follows:

A) Evening bright light administration will delay the body core temperature rhythm, while a dim light placebo will have no effect in a group of elderly chronic insomniacs.

B) As a result of this phase delay in body temperature, several measures of sleep quality will improve in the bright light condition.

C) Daytime alertness and performance will be enhanced in association with bright light treatment, while dim light administration will have no effect.

D) Fine-grained analysis of the changes in the cumulative distribution of wakefulness and sleep will be consistent with changes in shifts of the body temperature rhythm.

Method

A total of sixteen subjects were studied. Subjects were randomly assigned to either a treatment condition with bright light exposure (N=8), or a placebo/control condition with dim red light (N=8) exposure. The experimental group comprised four males and four females with a mean age of 72.0 (sd = 5.0) years. The control group consisted of three males and five females with a mean age of 68.25 (sd = 4.5) years. All subjects were self-described insomniacs, symptomatic for a minimum of one year prior to entering the study. Subjects were recruited through newspaper advertisements and from lectures given by the senior

investigator (SSC) to various senior citizen groups around the greater New York City area. Subjects were paid $300 for completing the study.

All potential subjects went through a screening procedure conducted by the staff physicians at the Sleep-Wake Disorders Center at New York Hospital-Cornell Medical Center in White Plains, New York. A screening consent form was signed by potential subjects before undergoing medical evaluations. If accepted into the study, subjects then completed a study consent form before their first night in the laboratory. Evaluations included a medical history, sleep history, physical exam, blood counts, and chemistry. During the initial interview, subjects were given a tour of the facilities, an explanation of the recording procedures, and a demonstration of the microcomputer system with a trial performance session. Subjects were accepted or rejected for participation in the study based on results of the initial screening evaluation. Every subject who passed the screening was invited to participate and subjects who were not accepted received an explanation for their rejection. Appropriate medical and/or psychiatric referrals were made, if requested.

Apparatus

Electrophysiological variables were monitored using a Bio-Sentry telemetry system. Four channels of electrographic data were collected

including EEG, EOG (eye movements), and EMG (sub-mental tension), and these were transmitted via radio waves to a Microtronics 847 sleep analyzing computer (SAC system, Oxford Medical). Sleep stages were scored visually according to standard criteria (Rechtschaffen & Kales, 1968). Abnormal respiratory events, or period leg movements in sleep were not ruled out by polysomnogram.

Core body temperature was recorded using high impedence, disposable rectal thermistors produced by Yellow Springs Instruments, Inc. (YSI), for use with the Vitalog PMS-8 ambulatory monitoring system. The YSI 4400 series thermistor probe is soft, flexible, and is accurate to 0.1 of a degree between 32-42 centigrade (89.6-107.6 farhenheit). The probe was inserted 8-10 centimeters into the rectum, and was marked by standard surgical tubing to prevent slippage during data collection. Temperature readings were recorded every minute. Temperature monitoring began on the third night in the laboratory at approximately 2200 hours (10 pm), and continued, uninterrupted until the morning following the fourth night. Thus, a total of 36 hours of temperature data was collected for each subject. Subjects were allowed to remove the probe to defecate or shower.

Following the third night of sleep recording, subjects remained in the laboratory to complete a variety of daytime assessment measures. Subjects were offered breakfast, but were not permitted to have

caffeinated beverages. Subjects were allowed to shower if they wished. Technicians re-checked electrode impedences and temperature measurements and made adjustments as necessary. Formal evaluation of daytime functioning began at 10 a.m.

The level of daytime alertness was assessed using the Repeated Test of Sustained Wakefulness (RTSW)(Hartse, Roth, & Zorick, 1982). At two-hour intervals (10, 12, 14, 16, and 18 hundred hours), subjects attempted to remain awake while lying down, with eyes closed, in a quiet, darkened room. Subjects were told before each trial, "Close your eyes and try to remain awake". Each of the five trials continued for 20 minutes, or until the subject fell asleep. Sleep latency was defined as the time from lights out to the first epoch of stage 2 sleep, indicated by the presence of K-complexes of sleep spindles. A trial was terminated after 3 epochs (1.5 minutes) of stage 2 sleep to prevent the accumulation of sleep throughout the day.

Cognitive and psychomotor performance was assessed using items from the computer-based Walter Reed Performance Assessment Battery (PAB) (Thorne, Genser, & Hegge, 1985). Four items from this battery were administered: 1) the Baddeley 3-minute grammatical transformation test (which is an index of grammatical reasoning), 2) the Stroop test 3) Letter cancellation test and 4) the Wilkinson four choice reaction time test (which is an index of pure psychomotor

performance). These tests were chosen because of their short learning curves and their sensitivity to circadian variations in cognitive processes. Practice trials were administered prior to formal assessment.

Light Administration

Illumination was provided by two portable light boxes (Apollo Brite Lite II, Apollo Lite Box Co., Orem, Utah) placed at eye level, one on each side of a television set in the subject's home. At a distance of one meter, subjects were exposed to approximately 4000 lux, in the bright light group, and 250 lux, in the dim red light group. (For a point of reference, illumination equalling 2500 lux is found outdoors within a few minutes of sunrise, while illumination of 100,000 lux is equivalent to that found around noontime in the summer.) The light treatment was self-administered in the subject's home after they had been given detailed instructions. Subjects were told to sit in front of the lights for two hours while maintaining gaze on the television. They were specifically instructed not to read, write, or engage in any activity that would require looking away from the lights. With the exception of the light exposure interval, subjects were encouraged to continue their normal daily activities throughout the treatment period. Bedtimes and waketimes were self-selected, and phone contact was maintained every other day to enocourage compliance and insure the light boxes were

functioning properly

Procedure

The study was divided into three phases: 1) Baseline evaluation, 2) Treatment period, and 3) Post-Treatment evaluation. Subjects completed all three phases of the study without interruption, totaling 25 days. Subjects spent a total of eight nights in the laboratory. The first two baseline nights in the laboratory were considered to be adaptation nights and were not used in the data analysis. The third and fourth nights were averaged into pre-treatment baseline values. Following light exposure subjects returned to the laboratory for four additional nights of sleep recording. Nights five and six were considered as adaptation nights and were not used in the analysis. Nights seven and eight were combined into a post-treatment score and compared to the mean values of nights three and four.

Phase 1. Baseline evaluation

Baseline evaluation lasted for 11 consecutive days. For the first seven days, subjects completed sleep logs in their homes. They then spent four nights in the sleep laboratory and their sleep was electrographically recorded. Bedtimes and wake-up times were self-selected. Following night three, daytime sleep tendency was evaluated using the Repeated Test of Sustained Wakefulness (RTSW). Core body temperature was continuously recorded from 2200 hours (10 p.m.) on

night three until the morning following the fourth night, approximately 0800 hours (8 a.m.).

Phase 2. Treatment period

The treatment period continued for 7 to 10 days, depending on scheduling constraints and subject availability. On the morning following the fourth night of sleep recording at the end of baseline evaluation, subjects were free to leave the laboratory and return home. The assignment of treatment conditions was determined by a coin flip, and less pseudo-random methods were employed later, when necessary, to balance the treatment cells according to sex. Subjects were advised that the treatment would begin in two days and an appointment was made to deliver the light boxes to the subject's homes. Each subject was asked to follow the prescribed schedule of treatment, with either the bright white light (treatment group), or dim red light (control group), until they returned to the laboratory. Both the treatment group and the control group were told that timed exposure to light of different wavelengths has been shown to be effective in ameliorating insomnia, and that the data indicated that the light boxes brought to their homes were best suited for their particular sleep disturbance. Since the primary sleep disturbance in this sample, as hypothesized, was associated with an advance of the circadian timing system, all subjects followed an evening schedule of bright light

exposure (from 8 p.m. to 10 p.m.). One subject, not included in the data analysis, was exposed to morning bright light, since baseline circadian phase estimates indicated a substantial phase delay.

Phase 3. Post-treatment evaluation

Following the treatment period, subjects reported to the laboratory to complete a protocol identical to that described for phase 1. During the four nights in the lab, subjects continued the light treatment. After the data were examined, subjects were re-contacted and an appointment was made to discuss the results.

Data analysis

A Group X Time (pre/post treatment) repeated measures analysis of variance (ANOVA) was performed on the following sleep parameters: bedtimes, waketimes, time in bed (TIB), sleep period times (SPT; TIB minus nocturnal sleep latency), sleep onset to stage 2, total sleep time (TST), awake after sleep onset, sleep efficiency (TST divided by TIB; TST divided by SPT), onset to rapid-eye-movement sleep (REM latency), and percent and minutes of stages 1, 2, 3, 4 and 3+4 combined (slow-wave sleep; SWS), and REM sleep. A total of 8 nights of sleep recordings were obtained. Data from nights 1, 2, 5 and 6 were considered to be adaptation nights and were not analyzed. For all sleep parameters, baseline nights three and four were averaged and compared to post-treatment night averages from nights seven and eight.

Individual nap latencies, from the RTSW were collapsed for each subject and a Group X Time repeated measures ANOVA was performed. To explore the circadian variation in alertness, nap-by-nap comparisons were analyzed separately to explicate interaction effects between condition and time of day.

Temperature data was analyzed in three ways. First, a non-linear least squares algorithm was computed with the software package KaleidaGraph ™ (Synergy Software Co. Reading, PA) on a Macintosh II CI computer ™ (Apple Computer Co., Cupertino, CA.) to determine the theoretical twenty-four hour cosine wave that best fit the raw data for each subject (Bliss, 1970). Three variables were derived from the cosine curve fit; the mesor (M1), the amplitude (M2), and phase (M3) . The mesor is the mean 24-hour temperature. Amplitude is defined as the difference between the maximum-fitted temperature value and the minimum-fitted temperature value. The nadir, or bathophase, is the minimum value of a sine function fitted to the raw data of a rhythm. For all subjects, the goodness of fit (r) was greater than .80. This method will be referred to as the "simple fit" method.

Second, body temperature data was also fitted, using a standard twenty-four hour cosinor fit combined with a 12-hour harmonic, and is labelled as the "complex fit". This fitted curve theoretically provides a somewhat more accurate estimation of circadian phase since

mild inflections in the temperature curve are represented more faithfully.

Third, the raw temperature files were examined and the lowest point determined. When more than one minute defined the temperature minimum the median value was used for the span of minutes which comprised the lowest value. This non-mathematical estimation of circadian phase is presented as an alternative to statistical methods and is similar to that used by Wever (1979), and Drennen, Kripke and Gillin (1989).

A group X time repeated measures ANOVA was performed on the phase estimates, amplitude, and mesors for each of the three methods used to examine the temperature data.

The distribution of wakefulness, SWS, and REM sleep was determined in several ways. To normalize the data set, all calculations were derived from the onset of sleep for each subject. Nights three and four were combined into a baseline value and compared to nights seven and eight, a post-treatment value. Wakefulness data was divided by thirds-of-the-night. SWS and REM measures were compared by thirds- of-the-night only. Analysis of variance procedures were then carried out between baseline and post-treatment values.

To test the association between changes in circadian phase and changes in sleep variables, Spearman's rank-order correlations (rho)

were performed. Changes in circadian phase were correlated with changes in total sleep time, sleep efficiency and WASO.

The course of nighttime body temperature was also analyzed according to the method of Dijk et. al. (1987). The mean nocturnal body temperature was calculated for each subject and then subtracted from each minute of temperature data obtained during the mean group sleep period for each condition. Comparisons were made at baseline and at post-treatment on the basis of light condition.

Correlations between age and sleep parameters for the group as a whole were also performed on baseline data. Mean 'stay awake' values from the baseline RTSW were also correlated with nighttime sleep measures.

Results

Light effects on temperature measures

Circadian phase was determined in three ways. A simple (24-hour fundamental) and complex (24-hour + 12-hour harmonic) least-squares cosinor curve was fitted to each subject's individual raw temperature data. In addition, the time of the absolute temperature minimum was also determined from the subject's data. If the lowest temperature extended over several minutes, the median time was derived. There were essentially no group mean differences among the three methods of circadian phase estimation. Therefore, all further discussion

of temperature results will refer to data derived from the simple 24-hour cosinor fit. Due to technical malfunctions, body temperature data was lost for two placebo subjects during the post-treatment evaluation. Thus, statistical analysis of the temperature data was carried out with 8 subjects in the bright light group and 6 subjects in the placebo group. Treatment effects were analyzed by a condition-by-time repeated measures analysis of variance, and significance values reflect the condition-by-time interaction effect.

At baseline, the fitted nadir in body temperature for all 16 subjects was 4:06 am (1.55 hrs.), the estimated amplitude was 0.75^{o} (.22), and the estimated mesor was 36.79^{o} (.17) Celsius. The temperature minima ranged from 11:05 pm to 6:55 am. Figure 5 depicts a scatterplot of the temperature minima for each subject at baseline.

- Figure 5 -

Figure 5

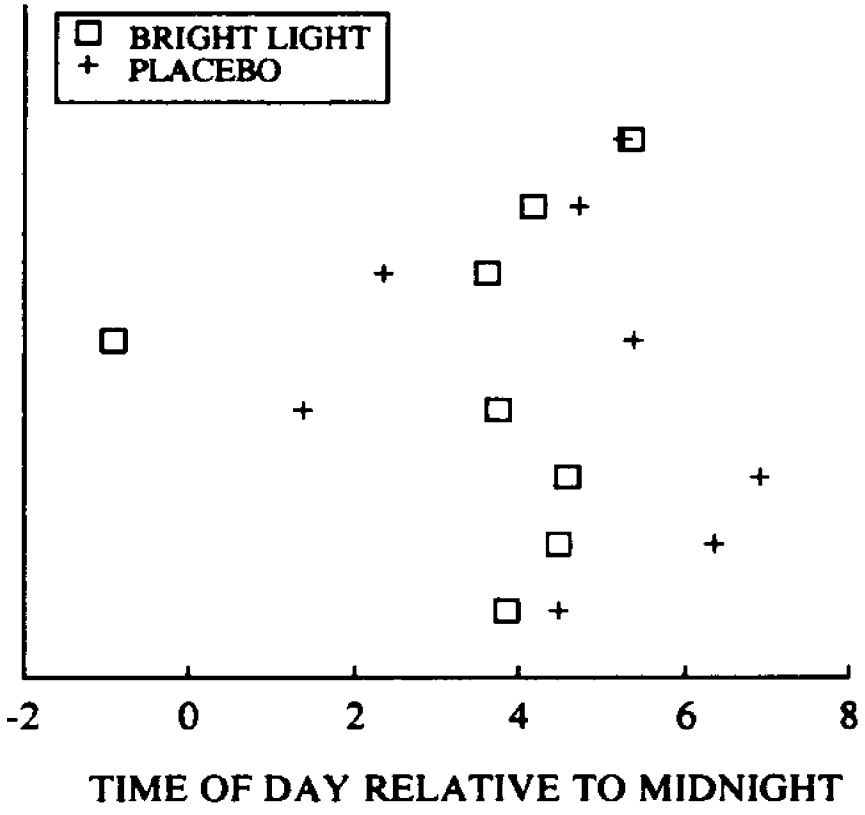

BRIGHT LIGHT
PLACEBO
-2
0
2
4
6
8
TIME OF DAY RELATIVE TO MIDNIGHT

Table 1 shows the mean circadian phase estimates at baseline and post-treatment for the bright light and placebo conditions. The mean temperature (mesor) and the mean amplitude for each condition are also shown. Bright light delayed the body temperature minimum by 187 minutes, from 3:37 am to 6:44 am, while the dim light had no effect on circadian phase estimates $F(1,12) = 60.1$, $p < .0001$. Amplitude was minimally increased in the bright light group from $.67^{o}$ at baseline to $.98^{o}$ at post-treatment, $F(1,12) = 3.9$, $p = .07$. No significant differences were observed between conditions in mean body temperature.

- Table 1 -

Table 1 Mean values of circadian phase, amplitude and mesor.

	ACTIVE		PLACEBO	
PARAMETER	PRE	POST	PRE	POST
(A)				
NADIR**	0337 (1.9)	0644 (1.7)	0415 (1.9)	0423 (1.8)
AMPLITUDE	.67 C^{O} (.24)	.98 C^{O} (.41)	.82 C^{O} (.17)	.76 C^{O} (.20)
MESOR	36.72 C^{O} (.21)	36.89 C^{O} (.34)	36.87 C^{O} (.04)	36.86 C^{O} (.09)
(B)				
NADIR**	0311 (1.8)	0537 (1.8)	0317 (1.8)	0335 (.94)
AMPLITUDE	.59 C^{O} (.26)	.79 C^{O} (.19)	.82 C^{O} (.17)	.76 C^{O} (.20)
MESOR	36.73 C^{O} (.21)	36.69 C^{O} (.26)	36.88 C^{O} (.05)	36.87 C^{O} (.09)
(C)				
NADIR**	0350 (1.8)	0616 (2.3)	0354 (2.8)	0407 (2.4)

** $p < .0001$ Group by time interaction

(A) is simple 24 hour cosinor fit method.

(B) is simple 24 hour cosinor fit method combined with a 12 hour harmonic.

(C) is time of actual body temperature minimum. The median time was computed for subjects whose minimum values extended over several minutes.

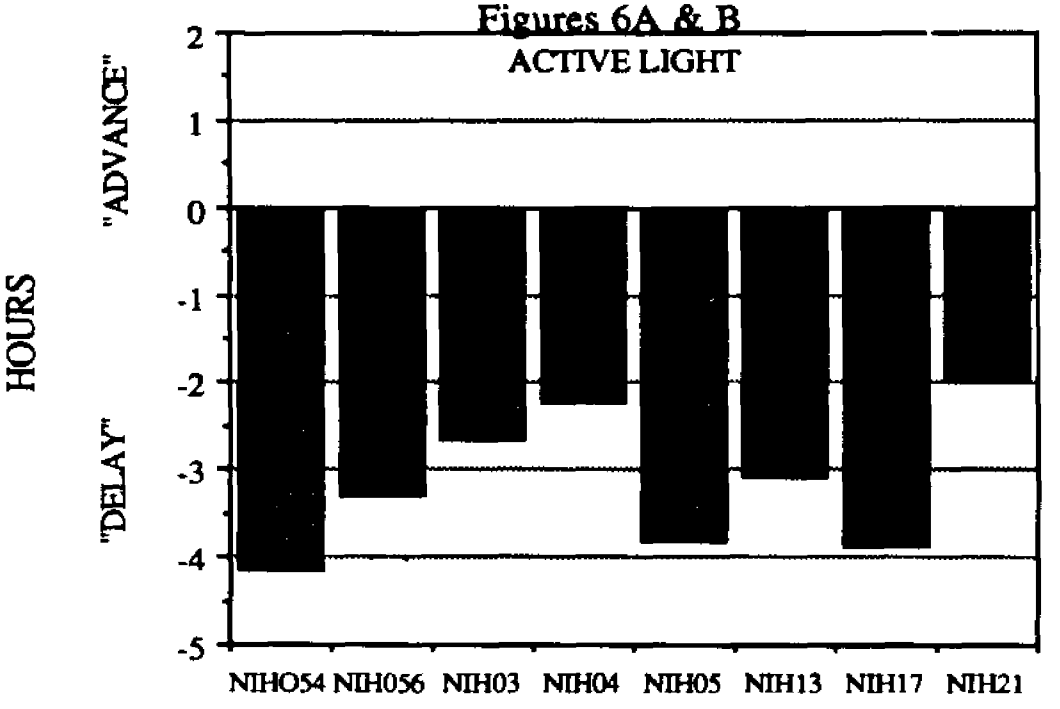
Nadir is the fitted temperature minimum in military time. Amplitude is the peak to trough difference in temperature. Mesor is the mean temperature during data collection.

The net changes in body temperature for each individual subject from the bright light and placebo groups are shown in figure 6. The y-axis is calibrated in hours with positive numbers indicating a phase-advance, while negative numbers indicate a phase-delay. For instance, for subject NIH054 in the bright light group, the fitted-temperature minimum delayed by over 4 hours, from 3:52 am to 8:00 am. Figure 6 also illustrates that the phase delay of the temperature minimum in the bright light group was consistent across subjects. In contrast, phase-shifts in the placebo group were smaller and varied across subjects in amount and direction.

- Figure 6 -

6A

Figures 6A & B



6B

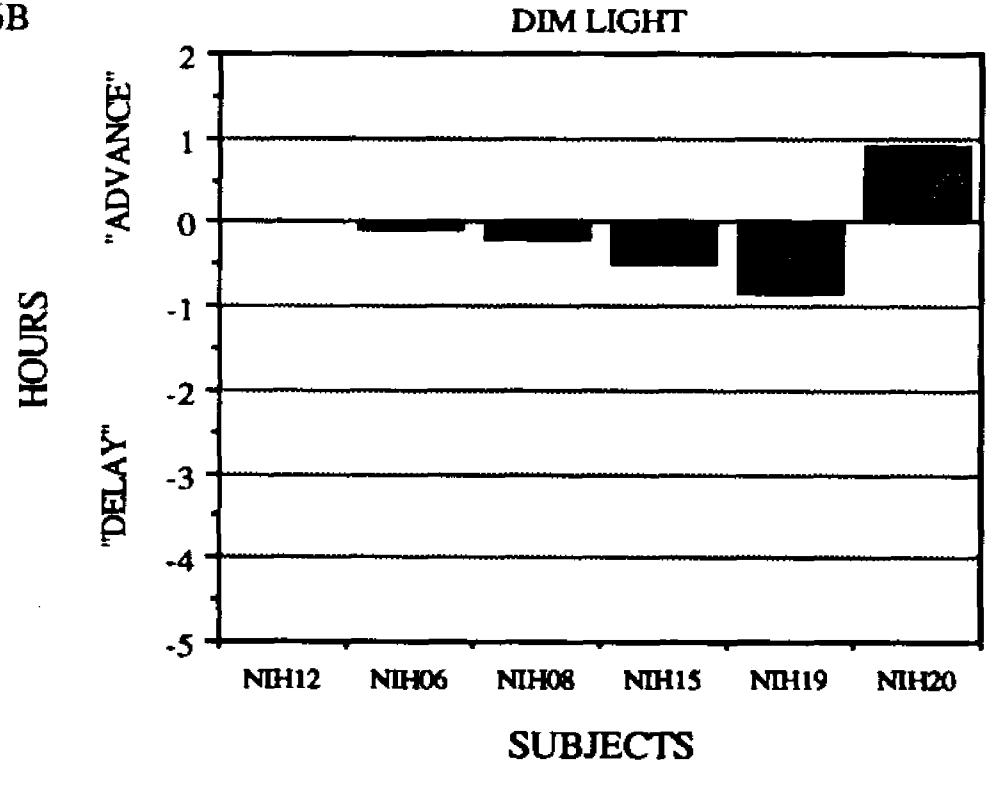


Figure 7 presents a post-treatment comparison between the two conditions for the nocturnal time course of body temperature normalized from sleep onset for each subject. Each subject's mean temperature value was calculated for each of the first seven hours after sleep onset. The individual subject means were then collapsed within group. It can be seen from the figure that after 2:00 am, the two nocturnal temperature curves begin to dissociate. The difference in the shape of the curves is significant, $F(1, 12) = 3.2$ $p < .05$.

- Figure 7 -

Figure 7

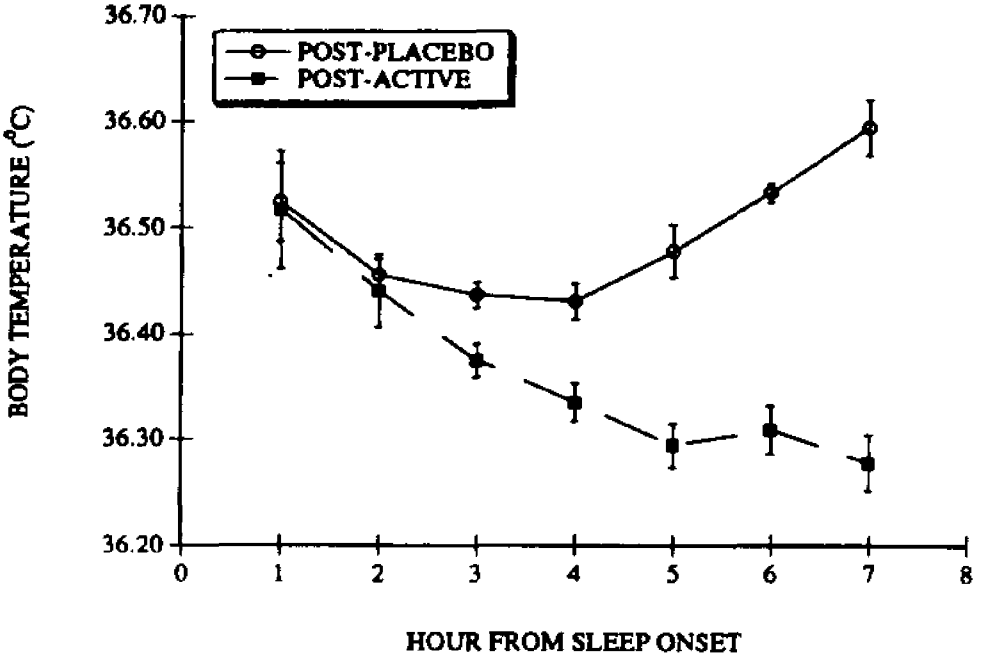
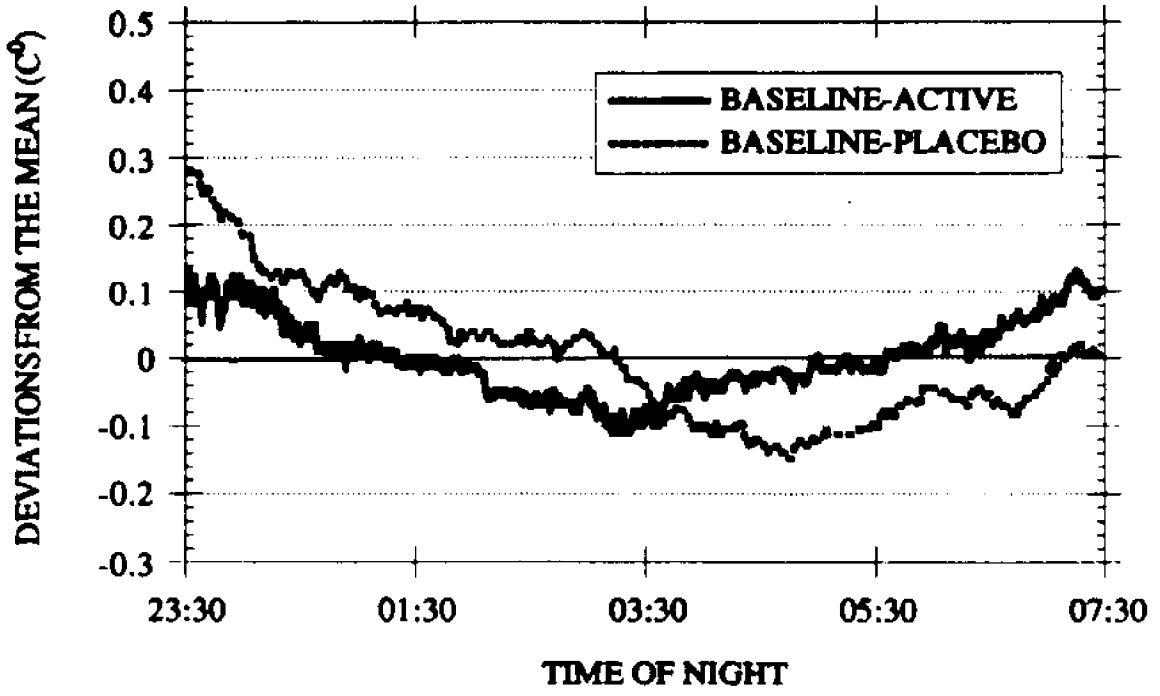
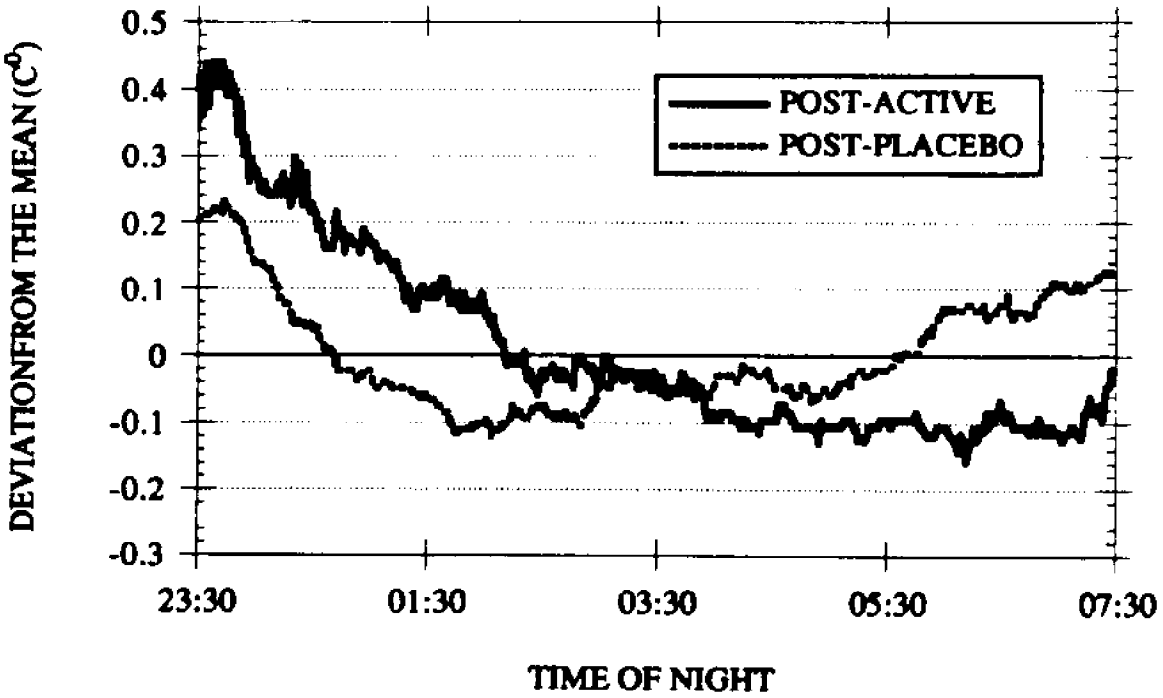

POST-PLACEBO
POST-ACTIVE
BODY TEMPERATURE (°C)
36.70
36.60
36.50
36.40
36.30
36.20
0
1
2
3
4
5
6
7
8
HOUR FROM SLEEP ONSET

Figure 8 illustrates the time course of body temperature in the bright light and placebo groups during baseline and post-treatment. These are expressed as deviations from the mean body temperature between 11:30 pm and 7:30 am. Each subject's mean body temperature between these hours was calculated. For each subject, this value was subtracted from each minute-to-minute (480 minutes total) of temperature recorded between the hours of 11:30 pm and 7:30 am. The deviation from the mean scores were then collapsed within condition (i.e., baseline bright light and placebo; post-treatment bright light and placebo) and plotted with time along the x-axis and deviation from the mean on the y-axis. Viewed in this way, it can be seen that bright light delayed the nocturnal rise in body temperature, while the nocturnal rise in body temperature advanced in the dim light placebo condition from baseline to post-treatment.

- Figure 8 -

Figure 8

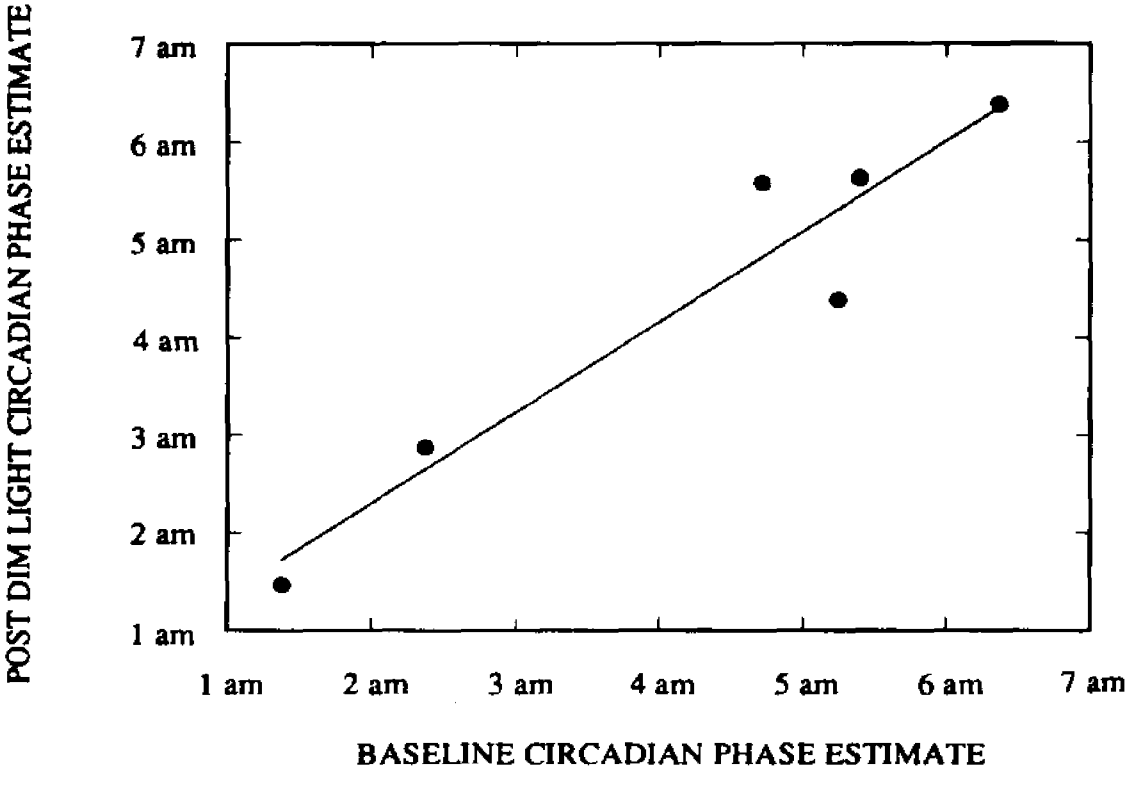

0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
DEVIATIONSFROM THE MEAN (C°)
BASELINE-ACTIVE
BASELINE-PLACEBO
23:30
01:30
03:30
05:30
07:30
TIME OF NIGHT


0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
DEVIATIONFROM THE MEAN (C°)
POST-ACTIVE
POST-PLACEBO
23:30
01:30
03:30
05:30
07:30
TIME OF NIGHT

These results confirm that 10 days of evening bright light exposure can delay circadian phase as indexed by the body temperature minimum in a group of elderly insomniacs. It is also important to note that dim light had virtually no effect on temperature measures. In six subjects, the net change in circadian phase estimate from baseline to post-treatment was 8.4 minutes. Further, an intraclass correlation coefficient between baseline and post-treatment circadian phase estimates in six placebo subjects was significant, $r = .956$ $p < .01$. Figure 9 illustrates this correlation. While conclusions from such a small sample must remain tentative, these results suggest that ambulatory monitoring of human body temperature can provide *reliable* estimates of circadian phase, or the body temperature minimum.

- Figure 9 -

Figure 9



Gigure 9. Scatterplot of baseline and post-treatment circadian phase estimates for the dim light placebo condition.

Light effects on sleep measures

Tables 2 and 3 list the results of baseline and post-treatment sleep recordings. A condition-by-time repeated measures analysis of variance was performed on all sleep measures listed. All reported results are interpreted on the basis of the condition-by-time interaction term. Pre-treatment means are averaged from nights 3 and 4 in the laboratory and are compared to the mean of post-treatment nights 7 and 8 following 10 days of light treatment at home. Several standard sleep variables were significantly augmented in the bright light condition compared to the dim light placebo condition. With time in bed equivalent in both groups, there was a highly significant decrease in wakefulness after sleep onset (WASO) with a corresponding increase in sleep efficiency. Following bright light treatment, wakefulness decreased by over one hour (F (1, 14) = 45.1, $p <$ .001), and sleep efficiency (calculated as total sleep time divided by the time in bed minus sleep latency) increased by 12.6% (F, (1,14) = 54.0 $p <$ .001). Total sleep time increased by 45 minutes in the bright light group. Since sleep time increased by 21 minutes in the placebo group, however, this result did not reach statistical significance.

The number of stage changes, as well as the percent and amount of stage 1 sleep, decreased in the bright light group, while the percent of stage 2 increased from baseline to post-treatment. These improvements in

sleep were significant, $p < .01$. Sleep onset to REM sleep was significantly delayed in the bright light condition, $F(1,14) = 6.8$, $p < .05$, from a baseline mean of 45.2 minutes to a post-treatment mean of 69.5 minutes.

No significant differences were observed between the two groups in measures of slow-wave, or REM sleep, nor in their distribution when divided hour-by-hour, or by thirds-of-the-night.

- Tables 2 & 3 -

Table 2: Baseline and post-treatment parameters the active and dim light conditions

	ACTIVE		PLACEBO	
PARAMETER	PRE	POST	PRE	POST
BEDTIME*	2314 (.58)	2343 (.73)	0027 (1.1)	2358 (.93)
WAKETIME	0706 (.61)	0724 (.86)	0804 (.84)	0753 (.96)
TIME IN BED	473 (38)	461 (32)	457 (47)	475 (45)
SLEEP PERIOD TIME	455 (35)	441 (35)	416 (42)	430 (53)
SLEEP LATENCY	13.5 (8)	12.8 (6)	21.1 (16)	24.5 (20)
TOTAL SLEEP TIME	353 (20)	398 (41)	326 (33)	347 (57)
WAKE AFTER SLEEP ONSET (WASO)	103 (21)	43 (22)	89 (27)	83 (37)**
SLEEP EFFICIENCY [1]**	77.5% (3)	90.1% (5)	79.2 (6)	80.5% (8)
SLEEP EFFICIENCY[2]**	75.1 (2)	88.8 (3)	72.0 (8)	72.8 (9)

* Group by time interaction $p < .01$

** Group by time interaction $p < .001$

Sleep Efficiency [1]: Total sleep time divided by sleep period time.

Sleep Efficiency [2]: Total sleep time divided by time in bed.

Table 3: Baseline and post-treatment values for sleep stage physiology

	ACTIVE		PLACEBO	
PARAMETER	PRE	POST	PRE	POST
STAGE 1%**	11.6 (4)	7.1 (2)	10.4 (4)	10.5 (3)
STAGE 1 min**	54 (20)	32 (10)	42 (17)	45 (18)
STAGE 2%**	42.1 (8)	52.2 (7)	42.5 (8)	42.5 (8)
STAGE 2 min	190 (30)	234 (29)	176 (29)	186 (50)
STAGE 3%	6.2 (2)	7.4 (3)	7.7 (3)	7.2 (4)
STAGE 3 min	29.1 (8)	33 (10)	31 (12)	30 (14)
STAGE 4%	4.0 (2)	5.4 (4)	3.7 (6)	4.2 (4)
STAGE 4 min	18.4 (8)	24 (18)	16 (22)	17 (17)
STAGE 3+4%	10.2 (2)	12.8 (5)	11.4 (8)	11.4 (7)
STAGE 3+4 min	48 (9)	57 (21)	47 (31)	47 (29)
REM %	14.3 (2)	17.9 (4)	14.8 (3)	16.1 (5)
REM min	67 (12)	80 (20)	61 (12)	69 (25)
REM LATENCY*	45.2 (19)	69.5 (22)	54.1 (19)	53.7 (18)
STAGE CHANGES**	170 (26)	118 (19)	151 (34)	160 (34)

* Group by time interaction $p < .05$

** Group by time interaction $p < .01$

The effect of light on sleep stage continuity

The effect of bright light on the continuity of sleep was analyzed by tabulating changes in the number of consecutive epochs of each stage of sleep. This analysis was performed for baseline night three and post-treatment night seven in the bright light condition. For each subject, an occurrence matrix for the number of consecutive epochs of each sleep stage was tabulated. For each sleep stage, the number of epochs with the same stage score is counted until the stage score changes. For instance, in a single subject, the first appearance of REM sleep may continue for seven epochs, which is then followed by a single epoch of stage 1 sleep, followed by three more epochs of stage REM sleep, followed by two epochs of wakefulness, etc. In this brief example, the occurrence matrix for REM sleep would contain one episode consisting of seven consecutive epochs and another consisting of three consecutive epochs. In this way, the frequency of consecutive epochs was tabulated for each stage of sleep. A baseline versus post-cumulative frequency distribution was then derived for all 8 subjects in the bright light condition. The difference between the cumulative frequency distributions was analyzed with the Kolmogorov-Smirnov test for two distributions (Smirnov, 1948).

Figures (10 to13) show the cumulative frequency distributions for stages 1, 2, slow-wave and REM sleep. A shift to the right in the cumulative frequency distribution indicates improved sleep continuity

within a specific stage of sleep. Cumulative percent is presented on the y-axis and the number of consecutive epochs are presented on the x-axis. Sleep continuity was significantly improved from baseline to post-treatment for stage 2 sleep, $p < .05$, and a trend was observed in the direction of improved sleep continuity for both REM and slow-wave sleep, $p < .10$. Stage 1 sleep showed no change.

- Figures 10-13 -

Figure 10

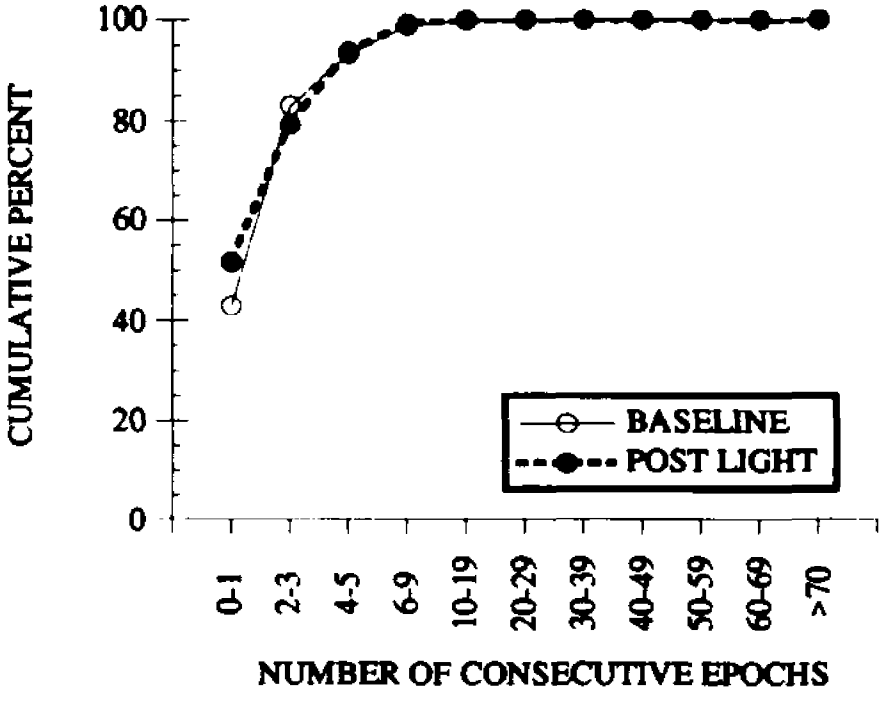

100
80
60
40
20
0
CUMULATIVE PERCENT
BASELINE
POST LIGHT
0-1
2-3
4-5
6-9
10-19
20-29
30-39
40-49
50-59
60-69
>70
NUMBER OF CONSECUTIVE EPOCHS

Figure 11

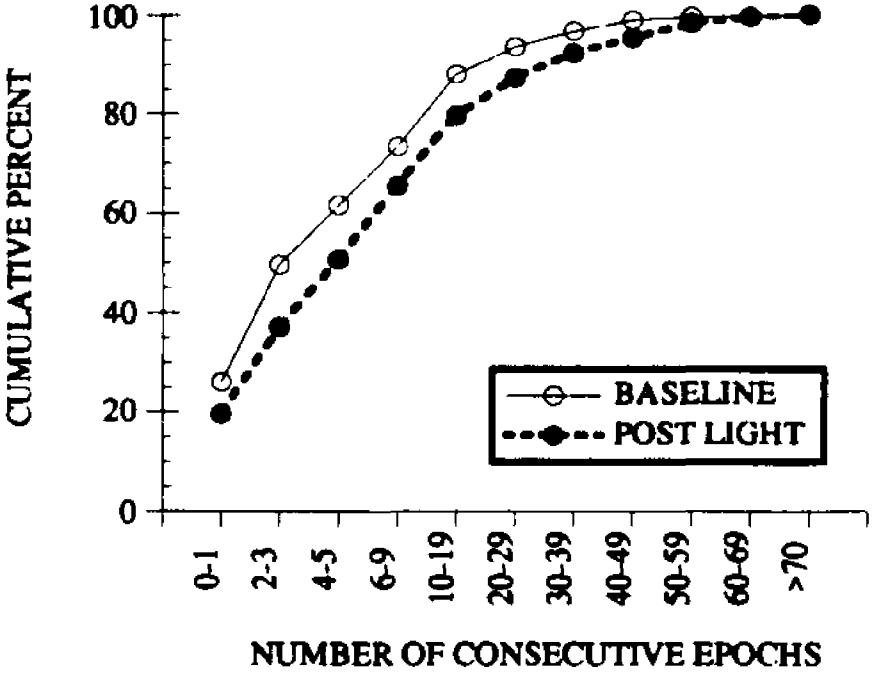

CUMULATIVE PERCENT
100
80
60
40
20
0
BASELINE
POST LIGHT
0-1
2-3
4-5
6-9
10-19
20-29
30-39
40-49
50-59
60-69
>70
NUMBER OF CONSECUTIVE EPOCHS

Figure 12

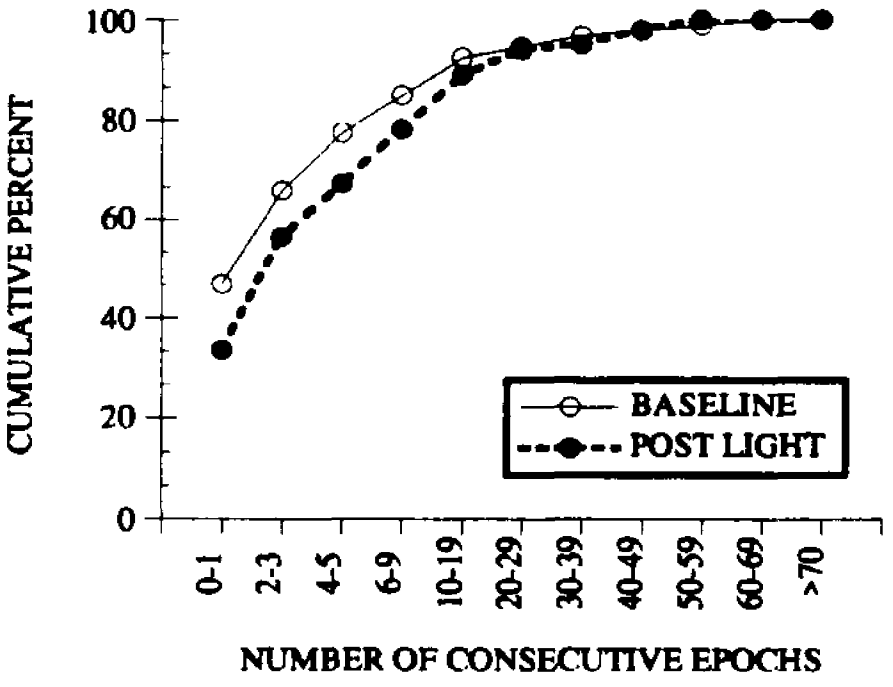
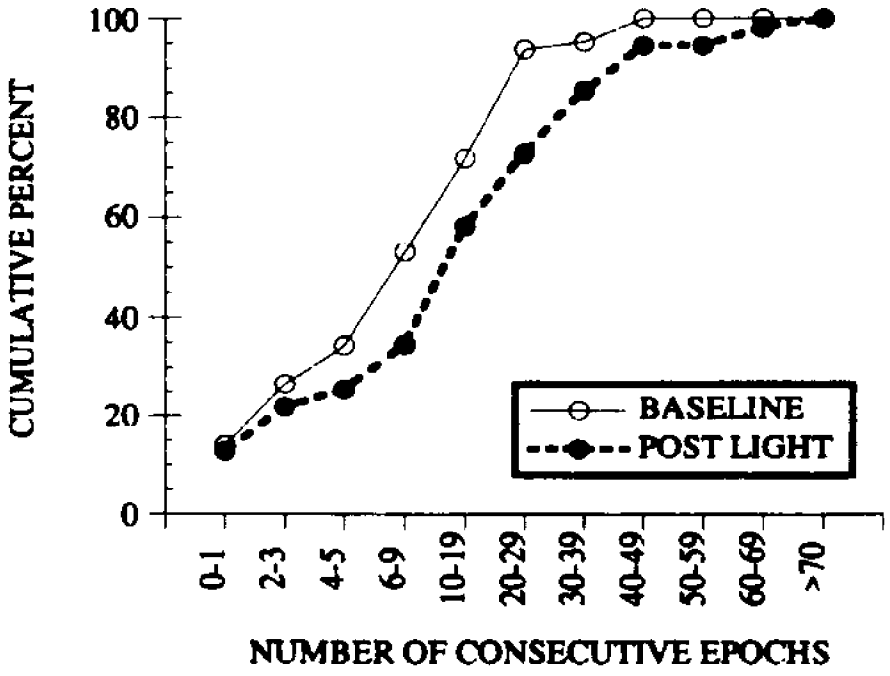

100
80
60
40
20
0
CUMULATIVE PERCENT
BASELINE
POST LIGHT
0-1
2-3
4-5
6-9
10-19
20-29
30-39
40-49
50-59
60-69
>70
NUMBER OF CONSECUTIVE EPOCHS

Figure 13


100
80
60
40
20
0
CUMULATIVE PERCENT
BASELINE
POST LIGHT
0-1
2-3
4-5
6-9
10-19
20-29
30-39
40-49
50-59
60-69
>70
NUMBER OF CONSECUTIVE EPOCHS

Because the data had to be normalized into a cumulative frequency distribution for statistical analysis, it may appear that the improvement in sleep continuity within stage 2, slow-wave and REM sleep is not particularly robust. However, cumulative frequency distributions can obscure some important differences that were apparent in the raw data. For example, for stage 1 sleep at baseline, the total of isolated single epochs of stage 1 sleep episodes was 138. There were 129 episodes of stage 1 sleep that lasted for 2-3 epochs, and 33 that lasted for 4-5 epochs. At baseline, episodes of stage 1 sleep that lasted from 1-5 epochs comprised 93.45% of all stage 1 sleep. Subsequent to bright light treatment, the number of stage 1 sleep episodes in these first three categories (i. e., 0-1, 2-3, and 4-5 epochs) were 75, 40 and 21 respectively, which is a reduction of 169 epochs. Yet, following bright light treatment, stage 1 sleep episodes of less than 6 epochs in length comprised 93.79% of all stage 1 sleep, almost identical to the baseline percentage. While the statistical analysis of the cumulative frequency changes did indicate a modest improvement in sleep continuity within stage 2, slow-wave and REM sleep, an examination of the actual raw data is necessary to fully appreciate these alterations. Thus, the raw data for the change in consecutive epochs of stages 2, REM and slow- wave sleep are presented below.

Sum total of consecutive epochs for 8 subjects before and after bright light treatment.

-Number of occurrences within each epoch range-

Epoch Range	Stage 2		Stage REM		Slow-wave sleep	
	pre	post	pre	post	pre	post
0-1	81	46	9	7	44	34
2-3	73	41	8	5	18	23
4-5	38	32	5	2	11	11
6-9	36	35	12	5	7	11
10-19	46	33	12	13	7	11
20-29	17	18	14	8	2	5
30-39	10	12	1	7	1	2
40-49	3	7	0	0	1	3
50-59	2	3	3	5	1	2
60-69	0	1	0	2	0	1
> 70	1	6	0	1	0	0

It is important to point out that following bright light treatment, the number of short episodes, within each stage of sleep, decreased; the number of relatively long episodes of sleep, within each stage, increased. For stage 2 sleep, the number of sleep episodes less than 19 epochs in length decreased by 87 occurrences, while the number of sleep episodes greater than 20 epochs in length increased by 14 occurrences. The improvement in sleep continuity is further underscored by the finding that the number of episodes over 70 consecutive epochs of stage 2 sleep

increased from 1 at baseline to 6 following light treatment. Similar improvements in sleep continuity within slow-wave and REM sleep can also be observed.

While the foregoing analysis is largely descriptive, it modestly indicates that bright light, in addition to reducing wakefulness during the night, also results in longer bouts of sleep within each sleep stage.

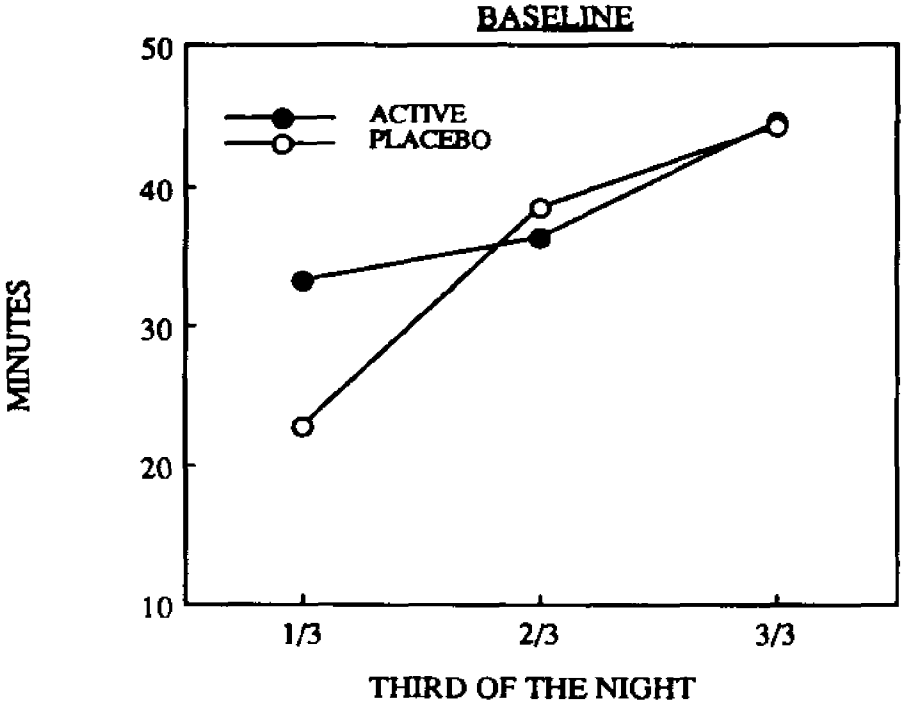
Analysis of wakefulness during sleep

Wakefulness decreased from 103 minutes to 43 minutes following bright light treatment. A more detailed analysis of the nocturnal distribution of wakefulness and a description of the changes in the duration of arousals was also undertaken. Figures 14A and 14B show the differential distribution of wakefulness expressed by thirds of the night. A repeated measures analysis of variance indicated that the linear distribution of wakefulness between the two groups was significantly different, F (1, 14) = 3.74, $p < .05$. Post-hoc comparisons (Wilcoxon Test) revealed that the amount of wakefulness was significantly different between the bright light group and the dim light placebo group during the middle and last third-of-the-night, $p < .05$. Minutes of wakefulness decreased from 32.6 minutes to 13.2 minutes during the middle third-of-the-night and from 48.4 minutes to 14.7 minutes during the last third-of-the-night in the bright light group. Neither the distribution, nor the amount of wakefulness was altered in the placebo group.

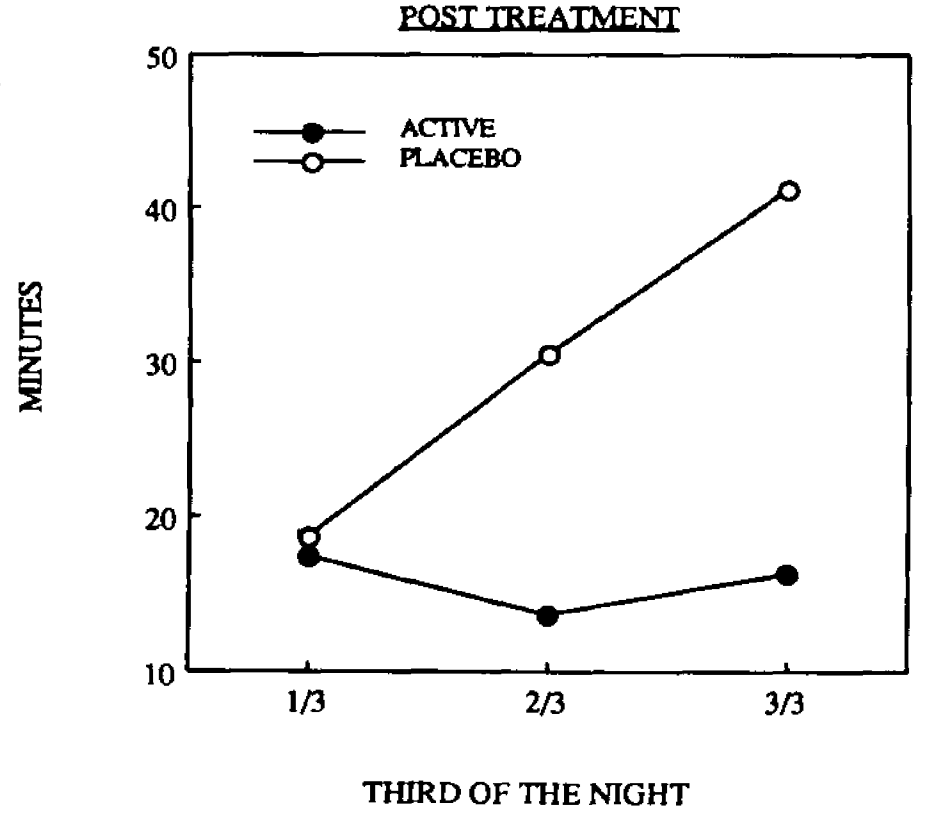
- Figures 14 A & B -

Figures 14 A & 14B. Minutes of wakefulness expressed by thirds of the night.

14A



14B

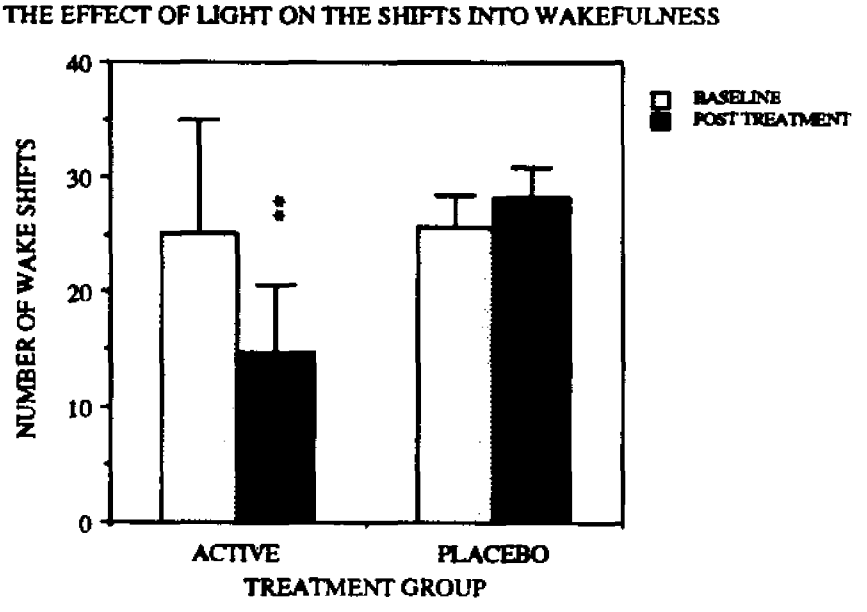


The number of shifts into wakefulness was significantly reduced in the bright light condition, F (1,14) = 11.2, $p < .01$, while there was no change in the duration of the longest waking episode. Compared to the dim light placebo condition, bright light significantly reduced the number of awakenings that lasted for less than 5 minutes, F, (1,14) = 6.38, $p < .05$, as well as those that lasted for greater than 5 minutes, F (1,14) = 13.38, $p < .01$.

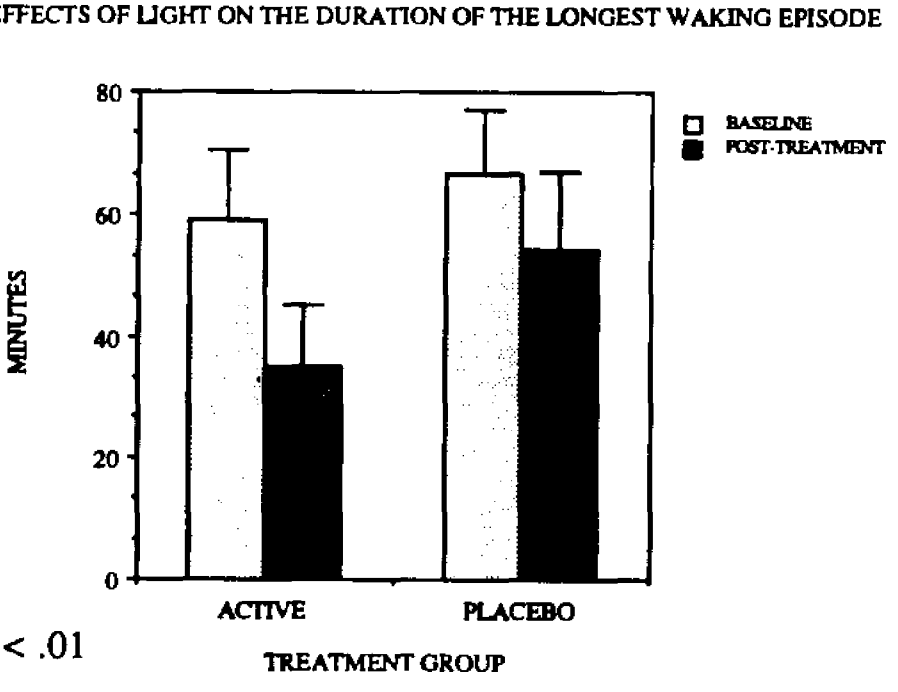
- Figures 15 A & B and 16 A & B -

Figure 15 A & B

A

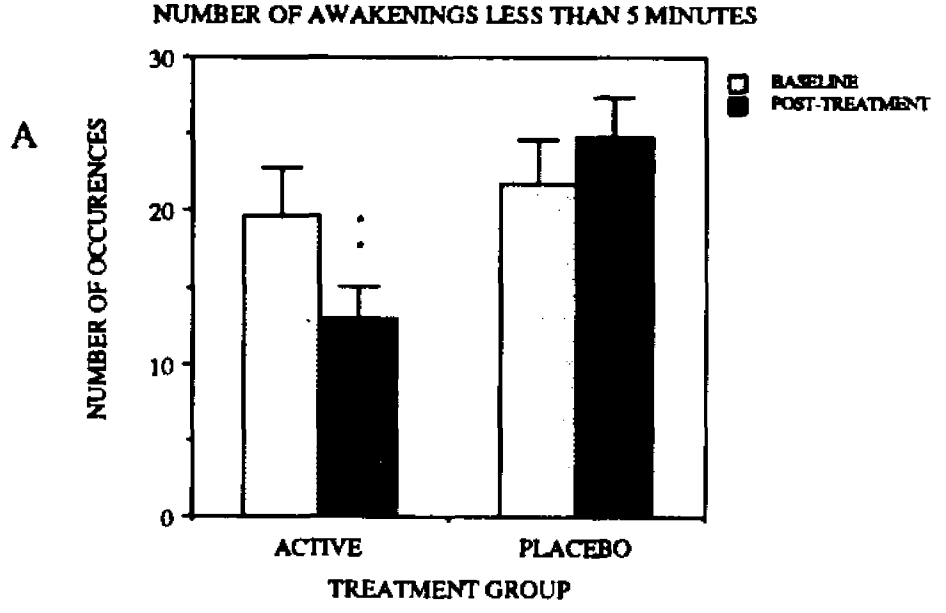


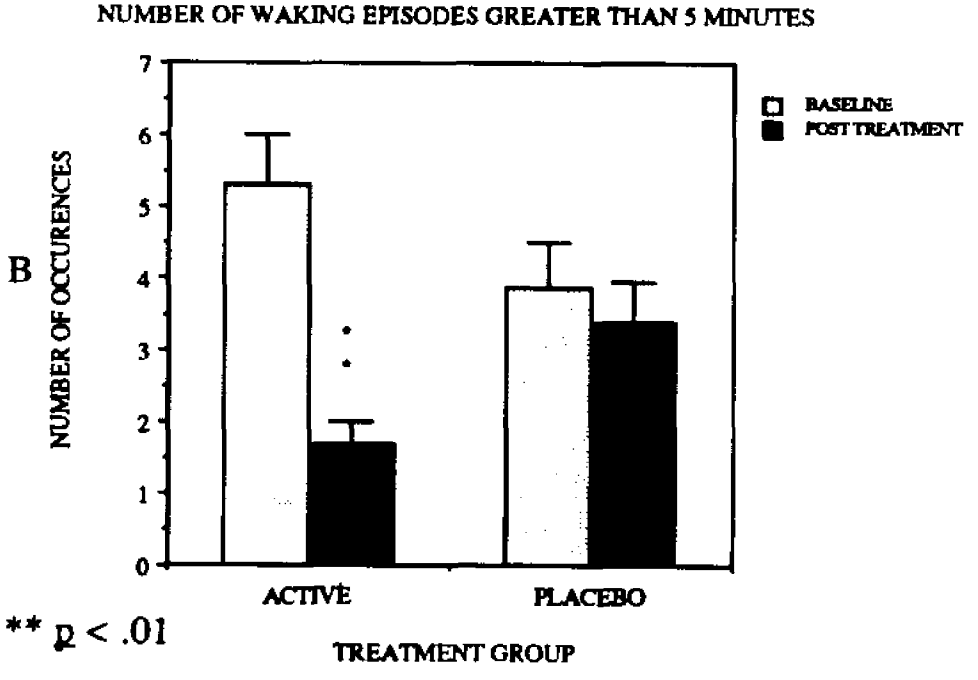
B



** $p < .01$

Figure 16 A & B


NUMBER OF AWAKENINGS LESS THAN 5 MINUTES
A
NUMBER OF OCCURENCES
30
20
10
0
BASELINE
POST-TREATMENT
ACTIVE
PLACEBO
TREATMENT GROUP


NUMBER OF WAKING EPISODES GREATER THAN 5 MINUTES
B
NUMBER OF OCCURENCES
7
6
5
4
3
2
1
0
BASELINE
POST TREATMENT
ACTIVE
PLACEBO
TREATMENT GROUP
** p < .01

The effect of light on daytime alertness

The ability to sustain alertness as measured by the RTSW increased from 15.1 minutes to 17.4 minutes in the bright light group and decreased from 15.5 minutes to 14.8 minutes in the dim light placebo group. This finding did not reach statistical significance, F (1,13) = 2.36, p = .14. Table 4 lists the means and standard deviations for each nap trial for each condition separately. When individual naps were analyzed separately, the bright light group was significantly more alert during Nap 1. However, this interaction effect is more likely to be the result of a relatively large decrease in alertness in the placebo group, rather than a substantial increase in the bright light group. Figure 17 shows the change in alertness from baseline to post-treatment for the bright light condition. It can be seen that alertness is slightly elevated from baseline to post-treatment, although the result was not significant.

Age was not significantly associated with RTSW mean sleep latencies. Significant relationships between nocturnal sleep parameters and RTSW mean sleep latencies were not found. The highest correlation between the RTSW and sleep parameters was rho, = -.355, NS for the number of stage changes.

The number of sleep onsets were calculated for each condition at baseline and post-treatment. No significant difference was observed between the two groups according to Chi-square analysis. However, in

both conditions a large percentage of the sleep onsets were accounted for by only a sub-set of subjects. For example, at baseline in the bright light group, 15 of 20 sleep onsets were accounted for by three subjects, and in the placebo group, three subjects accounted for 12 out of 16 sleep onsets. The number of sleep onsets was reduced from 20 to 13 following light treatment. However, the same three subjects, who accounted for 75% of the sleep onsets at baseline, now accounted for 12 of 13 of the sleep onsets, or 92.3% following treatment.

- Table 4 -

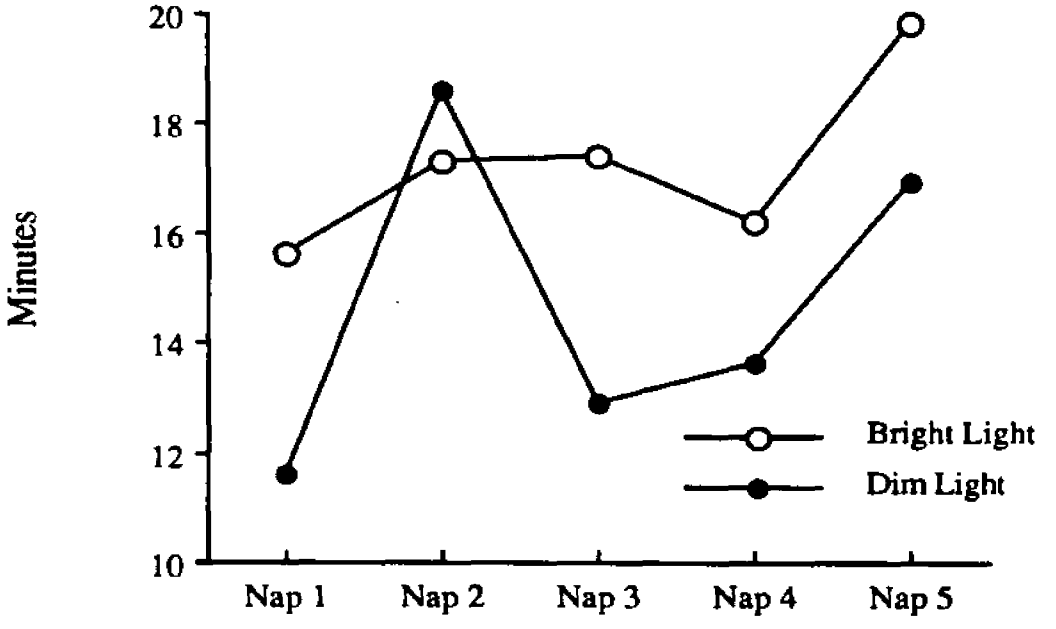
- Figure 17 -

Table 4 Mean RTSW sleep latency

	ACTIVE		PLACEBO	
PARAMETER	PRE	POST	PRE	POST
NAP 1	13.7 (6.5)	15.6 (6.9)	18.4 (3.3)	11.6 * (4.7)
NAP 2	13.9 (6.6)	17.3 (5.1)	19.7 (.49)	18.6 (3.0)
NAP 3	15.8 (6.2)	17.4 (5.6)	12.2 (7.5)	12.9 (7.2)
NAP 4	16.1 (5.6)	16.2 (6.0)	11.7 (6.7)	13.6 (6.9)
NAP 5	15.9 (5.2)	19.8 (.71)	16.0 (6.7)	16.9 (3.9)
NAPS 1-5	15.1 (5.3)	17.4 (3.9)	15.5 (3.8)	14.8 (3.7)

*Group by time interaction $p < .01$

Mean RTSW Sleep Latencies following twelve days of bright or dim light treatment



Performance assessment

Performance data were available for all eight subjects in the bright light group and 5 subjects in the dim light placebo group. Eight dependent measures were used for each of the four tests. Dependent measures were classified into two groups; those measuring accuracy and those measuring speed. No significant differences were observed between the two conditions for any of the four tests administered. Further, on seven of the eight tests subjects in both conditions improved their performance from the baseline to post-treatment evaluation. This strongly indicates a practice effect and it is possible that these elderly subjects required a greater number of practice trials in order to reach criterion levels of performance.

There were no associations between baseline performance measures and age, or daytimealertness as assessed with the RTSW. One hundred eighty correlations were performed between measures of speed and accuracy, with sleep parameters at baseline. Speed on the two-letter cancellation test was negatively associated with the percent of stage 1 sleep, rho = -.57 $p < .05$, and was positively associated with slow-wave sleep, rho = .68 $p < .05$.

Discussion

Scores of studies describe the subjective and objective characteristics of sleep in younger insomniacs. There are descriptions of their psychological conflicts (Kales, Caldwell, Preston, Healy, & Kales, 1976), their behavioral practices (Lacks & Rotert, 1986; Spielman, Saskin, & Thorpy, 1987), their medical conditions (Wooten, 1989), their family history (Hauri & Olmstead, 1980), their response to stress (Borkovec & Hennings, 1978), their body temperature (Monroe, 1967; Zepelin & McDonald, 1987; Morris, Lack, & Dawson, 1990), and their socioeconomic status (Cirignotta, Mondini, Zucconi, Lenzi, & Lugaresi, 1985). Correspondingly, a number of papers describe treatment modalities from "paradoxical intention" to "take two of these." Many of these treatments remain unvalidated. Many treatment studies rely on self-report measures and often lack control groups. A recent analysis of the insomnia scientific data base by the DSM-IV work group on sleep disorders has reported that, over the last twenty years, only twenty-seven studies concerning either the diagnosis or treatment of insomnia meet minimal scientific standards (Reynolds, Kupfer, Buysse, Coble, & Yeager, 1991). None of these studies included older people as subjects.

This report is one of the first controlled studies to investigate a non-pharmacological intervention for the treatment of insomnia in the elderly that includes the objective measurement of sleep parameters. The results

demonstrate that sleep maintenance insomnia in elderly subjects can be effectively treated with timed exposure to bright light: sleep efficiency can be increased without decreasing total sleep time.

Other measures of sleep quality improved in the subjects exposed to bright light. At the post-treatment evaluation, stage 2 sleep appears to have replaced both stage 1 sleep and wakefulness during the sleep period. There was a significant decrease in wakefulness, particularly during the later two-thirds of the night, a time when most elderly persons experience multiple nocturnal awakenings. Total sleep time increased by 46 minutes, although the result did not reach statistical significance.

Recent experiments that have tested behavioral treatments for elderly insomnia have relied, to some degree, on reducing time in bed (Anderson et al., 1988; Morin & Azrin, 1988; Hoelscher & Edinger, 1988; Friedman, Bliwise, Yesavage, & Salom, 1991). While sleep efficiency generally shows modest improvements, self-report measures indicate that total sleep time never exceeds six hours per night. Only one study used polysomnography; in this study, following six to eight weeks of treatment, objective measures of sleep efficiency increased by 5% while total sleep time decreased by 28 minutes in 33 subjects over the age of sixty (Anderson et al., 1988). In the present study, objective sleep efficiency was increased to over 90% and total sleep time increased to almost 6.75 hours without altering time in bed.

The most consistent age-related change in sleep (measured polygraphically) is an increase in the number of awakenings, particularly during the last half of the sleep period (Feinberg et al., 1967; Agnew et al., 1967; Webb & Campbell, 1980). The present study was extremely effective in reducing several measures of wakefulness. Particularly impressive is that bright light significantly reduced the number of very short waking episodes (i.e., less than one minute), as well as the number of waking episodes greater than 15 minutes.

In addition to reducing sleep fragmentation, the continuity of sleep within stages of sleep was improved. Subjects treated with bright light spent more continuous time in stage 2 sleep once they entered this stage. There was also a trend for a similar effect on slow-wave sleep and REM sleep. Whether a reduction in the number of awakenings leads to improved sleep continuity, or whether improved sleep continuity leads to a reduction in the number of awakenings cannot be determined. Nonetheless, these findings suggest that the quality, in addition to the quantity, of sleep can be improved with the use of bright light.

Daytime function

While the bright light group did not evidence a significant increase in daytime alertness from baseline to post-treatment, an overall mean increase of 2.3 minutes was observed; the increase was consistent across all 5 RTSW nap trials. There are no published studies using the RTSW in

elderly people with insomnia. Therefore, it may be instructive to compare alertness in elderly subjects treated with bright light to those who have been treated with sleep restriction therapy, or stimulus control instructions who were evaluated with the multiple sleep latency test (MSLT) (Anderson et al., 1988).

While these comparisons are only descriptive, it may be possible to gain a sense of the differences in changes in daytime alertness produced by these two behavioral treatments and treatment with bright light. Following the first ten days to two weeks of either sleep restriction therapy or stimulus control instructions, elderly insomniacs returned to the laboratory for one day of MSLT testing that included 5 nap trials. A comparison of the mean latencies are presented below. Means and standard deviations are presented in minutes.

		Sleep Latency	
Treatment study	Test	Baseline	During treatment
Sleep restriction	MSLT	11.3 (±5.7)	7.9 (±5.6)
(N = 22)			
Anderson et al., (1988)			
Stimulus Control	MSLT	13.9 (± 5.4)	11.4 (±5.4)
(N = 11)			
Anderson et al., (1988)			
Bright Light	RTSW	15.1 (±5.3)	17.4 (±3.9)
(N = 16)			

This descriptive comparison, while providing little in the way of scientific proof, does suggest that subjects treated with bright light experience no decrements in daytime alertness as a result of treatment. In elderly subjects with insomnia who also show signs of daytime sleepiness, the use of bright light may be a preferable treatment intervention because it does not produce daytime sleepiness.

Twelve days of evening bright light exposure significantly delayed the group mean estimate of circadian nadir in excess of three hours. The observed phase-shifting effect of bright light on the human body temperature rhythm is consistent with previous reports (Czeisler et al., 1986; Czeisler et al., 1989; Drennan et al., 1989; Campbell & Dawson, 1991; Dawson & Campbell, 1991). It has been suggested that the diminished sleep quality observed in older adults may be a consequence of changes in the circadian timing system (Weitzman et al., 1982; Zepelin, 1983; Dement et al., 1985; Campbell et al., 1989). Specifically, it has been proposed that the internal phase angle between the sleep period and the circadian rhythm of body temperature is altered. In this formulation, the temperature minima is advanced in the elderly and they spend a greater portion of the sleep period on the rising slope of the temperature curve. In entrained conditions, when sleep is experimentally displaced to the rising slope of the temperature curve, it becomes fragmented and is usually short (Webb et al., 1971; Weitzman & Kripke, 1981; Akerstedt &

Gillberg, 1981).

To substantiate the claim that changes in the internal phase angle underlie age-related sleep disturbance in the elderly, it would first be reasonable to see if any age-related changes were present in the data. In the current study, age was inversely correlated with sleep efficiency (rho = -.73, $p < .005$), and positively correlated with wakefulness after sleep onset (rho = .75, $p < .005$). The oldest subjects may compensate for their diminished sleep by increasing their time in bed. This finding is supported by the significant positive correlation between sleep period time and age rho = .52 $p < .05$).

An inspection of the bedtimes and waketimes of subjects at baseline suggests that the rest/activity cycle was not phase-advanced in these subjects, relative to solar time as was hypothesized. The mean bedtime at baseline was 11:50 pm and the mean waketime was 7:35 a.m. In healthy normal subjects during entrained conditions, body temperature typically begins to rise 1-3 hours prior to the habitual waketime (Mills et al., 1974; Broughton et al., 1990). In the present study, the upturn in body temperature occurred at 4:22 a.m.; 4.5 hours after bedtime and 3.2 hours prior to waketime. The interval between the temperature upturn and the habitual waketime is almost 2 hours greater than that reported for young, normal subjects and suggests a modest alteration in the circadian phase angle (Czeisler, Brown, Ronda, Kronauer, Richardson, & Freitag, 1985).

However, two studies of the entrained temperature rhythm in healthy, elderly subjects without a complaint of insomnia have found similar group mean circadian phase positions. Campbell, Gillin, Kripke, Erikson, and Clopton (1989) observed a mean acrophase at 3:09 p.m. in 22 non-complaining, elderly subjects with a mean age 69.3 years. Since the the acrophase is precisely 12 hours out of phase with the nadir, or temperature minimum, an acrophase of 3:09 p.m. is equivalent to a temperature minimum of 3:09 a.m. Similarly, Moe, Prinz, Vitiello, Marks, and Larsen (1991) found an estimated temperature minimum of 4:00 a.m. in 31 healthy, elderly subjects (mean age = 67.0 years). Neither study obtained measures of objective sleep; as in the present study, these two studies recorded body temperature while subjects were ambulatory. Thus, the baseline entrained temperature rhythms in the present study indicate that they are moderately advanced compared to young normals, yet not significantly different from elderly subjects who do not complain of sleep disturbance. Since studies of healthy elderly have found temperature nadirs similar to those in our elderly insomniac subjects the sleep disturbance in our subjects cannot be entirely accounted for by the phase angle differences form healthy young subjects. Yet, paradoxically, an intervention which affected the phase angle (in such a way as to delay it relative to healthy elderly), improved objective measures of sleep. So the question arises do healthy elderly have a similar sleep disturbance and just

don't complain, or is there "actually" a sleep disturbance in current subjects relative to healthy elderly?

The relationship between phase of the temperature rhythm and sleep was investigated in the following post-hoc analysis of pre-treatment data. The median estimate of circadian phase was 4:28 a.m. Subjects were divided into two groups based on the time of their temperature minima. The eight subjects with the earliest temperature minima had a group mean of 2:50 a.m. (± 1 hour and 49 minutes), while the eight subjects with the later temperature minima had a group mean of 5:23 a.m. (± 52 minutes). One-way ANOVAs performed with group as the independent variable (earlier/later) revealed that the subjects with the earlier temperature minima had significantly earlier bedtimes (11:19 p.m. vs. 00:22 a.m.) and significantly more awakenings greater than 5 minutes (5.7 vs. 3.5) than the later group.

Experimental alterations of the phase angle between sleep and temperature in normal subjects with bright light administration does not produce a sleep disturbance equal to that seen in the elderly (Dijk et al., 1987; Campbell & Dawson, 1991). By advancing the temperature minimum in young subjects with morning bright light exposure, sleep efficiency is significantly reduced and wakefulness is increased, particularly in the last hour of the sleep period. However, sleep efficiencies remain above 90%. In the study of seven healthy, young

subjects by Campbell and Dawson (1991) the sleep period was held constant from 11 p.m. to 7 a.m. and the temperature minima was centered at 4:42 a.m. during baseline. Baseline sleep efficiency was 97.6%. After morning light administration the temperature minimum advanced to 3:05 a.m., and sleep efficiency was reduced to 93.6%. Much earlier temperature minima were observed in the study by Dijk and his associates (1987). In eight young subjects, the 10-minute interval containing the lowest body temperature values was advanced from 2:30 a.m. at baseline to 1:30 a.m. following three days of morning light exposure. The reported changes in sleep parameters were an advance of spontaneous termination of sleep (8:42 am to 7:44 am) and a reduction in total sleep time (498 minutes to 444 minutes). However, the "diminished" sleep in these subjects was clearly not as severe as that observed in the elderly.

These observations have led Campbell and Dawson to speculate that the relationship between sleep and the circadian rhythm of body temperature is characterized more accurately by degrees of *phase tolerance* (Campbell & Dawson, 1991; Dawson & Campbell, 1991). A shift in emphasis is made from the well-known circadian influences on sleep duration, to one that highlights the ability of some subjects (particularly young subjects) to obtain continuous and adequate amounts of sleep even when it is displaced, or occurs on the rising slope of the temperature curve.

What may occur in older subjects who complain of insomnia is not a fundamental breakdown of the circadian timing system per se, but rather a contraction of that portion of the temperature curve during which they can obtain an adequate amount of sleep. Thus, while the actual temperature minima of the elderly subjects in the present study is not radically different from either young normals, or non-complaining elderly, it may be that disturbed sleep is the result of a decrease in phase tolerance. Or in otherwords elderly insomniacs may have decreased phase tolerance relative to healthy elderly.

At baseline, the temperature upturn occurred 210 minutes prior to waketime in the bright light group. Following treatment, the temperature upturn occurred a mere 40 minutes prior to waketime. In the dim light condition, the upturn occurred 229 minutes prior to waketime at baseline and 210 minutes prior to waketime at the post-treatment evaluation. Thus, the elderly subjects who were treated with bright light were phase-delayed to a point that exceeds that of entrained, healthy, college students (Czeisler et al., 1985; Dijk et al., 1987; Campbell & Dawson, 1991; Dawson & Campbell, 1991). Therefore, the shift in emphasis is critical, and the notion of phase tolerance can help explain this phenomena. Phase tolerance introduces the concept of relativity regarding the relationships between sleep and body temperature and may be particularly salient in understanding the sleep disturbance in the elderly. A phase angle that will

not disrupt the sleep of young adults might cause increasing sleep disruption with age. It has been demonstrated in the present study that an induced phase-delay of the temperature minima, to a point almost out of the sleep period, results in substantial improvements in sleep quality in elderly insomniacs. It is possible that the difference between subjects who complain versus those who don't complain of sleep disturbance can be attributed to individual variations in the amount of phase tolerance within the circadian system. Nevertheless these elderly insomniacs seem to have a disproportionate amount of sleep disturbance relative to the slight advance of the circadian nadir. To test this notion of phase tolerance, one could expose elderly subjects without sleep disturbance to a single four-hour pulse of morning light in an effort to advance the circadian system. If phase tolerance theories are correct, one would predict that these subjects would develop objective sleep disturbance.

It has been advocated, primarily by Czeisler and his colleagues, that accurate and reliable determination of circadian phase can only be achieved with the constant-routine protocol. This protocol purports to eliminate the evoked effects of sleep, exercise, activity, meals, etc., on the body temperature rhythm. Czeisler's group has reported a correlation of .998 between sequential estimates of circadian phase in constant routine studies (Czeisler et al., 1989). The present study employed ambulatory monitory techniques to record core body temperature. Therefore, it is

appropriate to briefly address issues of validity and reliability.

The six subjects in the dim light placebo condition provide data with which to assess the reliability of ambulatory monitoring techniques. That ambulatory monitoring techniques can provide reliable estimates of circadian phase and is supported by the high intraclass correlation (r = .956) between the baseline and post-treatment evaluations (Figure 9). These subjects measured two weeks apart, who adhered to normal daily routines and self-selected bedtimes and waketimes shifted as a group 8 minutes from baseline to post-treatment evaluation.

Are the phase shifts reported here valid? If ambulatory recordings were reliable for six subjects in the placebo group, there is no reason to think that the reliability for the bright light group would be grossly different. Subjects in each condition received precisely the same instructions regarding behavior during the treatment phase of the experiment. In a repeated measures experimental design, the masking and behavioral effects on body temperature are present under both conditions and during each phase of the study. Thus, while there is reason to believe that ambulatory monitoring techniques may not provide the most precise representation of the underlying temperature rhythm, in repeated measures designs, the experimental noise is distributed equally. The stability of the circadian phase position in the placebo group combined with the observed phase-delay in the light group suggest that the effect of

light on the human body temperature rhythm can be assessed with ambulatory recording techniques.

The issue of validity also can be addressed by comparing data from Czeisler et al. (1985), who made circadian phase estimates in 13 elderly subjects (mean age 70.6) during a forty-hour constant routine protocol. In these elderly subjects, the temperature minimum was estimated to be 4:22 am with a standard deviation of 40 minutes. In the present study, the fitted temperature minima for all 16 subjects at baseline was 4:06 am, a difference of 16 minutes. However, the standard deviation in the present study was twice as large (93 minutes) as that observed by Czeisler et al., (1985). Perhaps a more impressive finding is that the mean temperature upturn in the present study was *identical* (4:22 am ±164 minutes) to the fitted temperature minimum obtained by Cziesler et al., (1985) using the constant routine protocol. While the standard deviations are larger in the present study, these results raise doubts about the necessity of exposing elderly subjects to such a rigorous protocol, if less demanding methods produce comparable results. In the future researchers will have to decide if the increased resolution of the constant routine protocol (evidenced only by lower standard deviations when compared to data from this study) is worth the extra effort.

A number of studies have described the objective nocturnal sleep parameters of healthy, aged-adults, but only two previous reports have

described the sleep of elderly subjects who complain of insomnia (Anderson, et al., 1988; Edinger, Marsh, McCall, Erwin, & Lininger, 1991). Below, the present study of 16 elderly insomniacs is compared with the two mentioned reports. Following that, is a presentation of four studies that have examined the sleep of healthy-aged subjects on three sleep variables: nocturnal sleep latency (SOL), total sleep time (TST), and sleep efficiency (SE%). SOL, and TST values are in minutes, and SE% is indicated by the amount of time spent sleeping while in bed.

Studies of elderly insomnia

Authors	N	Mean Age	SOL	TST	SE%
Current Study	16	70.2	17.3	339.4	73.3
			(13.2)	(29.8)	(5.9)
Edinger et al. (1989)	20	62.3	13.5	363.0	79.7
			(10.6)	(44.7)	(8.7)
Anderson et. al. (1988)	43	62.5	11.5	367.4	79.6
			(12.0)	(66.5)	(12)

Studies of elderly normals

Authors	N	Mean Age	SOL	TST	SE%
Kales et al. (1967)	10	75.0	18.0	346	81.9
Feinberg et al. (1967)	15	77.0	18.5	384.4	83.3
			(11.1)	(36.5)	(6.1)

Kahn et al. (1969,70)*	26	77.5	31.5	374.4	72.7
			(17.2)	(51.1)	(8.7)

*Combined data from 2 studies that reported the results of males and females separately.

Polygraphic results from both normal and elderly insomniacs shed little light on objective differences between the two groups. The range in sleep latency is 20 minutes, the range in total sleep time is 45 minutes and the range of sleep efficiencies is less than 10%. Further, the normal, elderly subjects in the studies of Kahn et al., (1969, 1970) have the lowest values on measures of sleep latency and sleep efficiency, while the subjects in the present study have the lowest total sleep times. These findings underscore the difficulty in conceptualizing insomnia by objective measures alone. The substantial overlap between elderly normals and elderly insomniacs has also been observed between younger normals and insomniacs (Carskadon, Dement, Mitler, Guilleminault, Zarcone, & Spiegel, 1976).

Clearly, the data in the present study indicate that timed exposure to bright light improves the ability to sustain sleep in a small group of

elderly subjects with the complaint of insomnia. Improvements in sleep were primarily reflected in measures of sleep continuity, and sleep efficiency. Early morning awakenings were dramatically reduced, as was the amount of light stage 1 sleep. Brief (i.e., less than 1 minute) and longer (greater than 15 minutes) episodes of waking were significantly reduced. It has been suggested that these brief episodes of arousal may contribute to the subjective perception of unrefreshing sleep in older subjects (Carskadon et al., 1982). The number of long episodes of wakefulness during the night was also decreased. A reduction in the number of long waking episodes reduces the time available for cognitive ruminations that often lead to arousal and shortened sleep (Webb and Campbell, 1980; Spielman et al., 1987).

It was hypothesized that an underlying phase-advance of the circadian system may be responsible for some of the features of sleep disturbance in the elderly. While the sleep of these older insomniacs was objectively disturbed to healthy young adults, as a group, the body temperature rhythm was not extremely advanced relative to the sleep period. The notion of phase-tolerance was introduced to account for the objective improvement in sleep quality associated with the robust phase-delay of the body temperature rhythm in the bright light group.

Unfortunately, we cannot infer from the improvement in objective sleep parameters that the subject's *insomnia* was resolved. Since insomnia is

defined as a complaint, the resolution of an insomnia is contingent upon the subject's response to the treatment. Dement and Seidel (1982) have stated that there are three goals in the treatement of insomnia: 1) to improve objective sleep parameters, 2) to relieve the nocturnal sleep complaint, and 3) to relieve the daytime sleepiness complaint. The present study successfully addressed issue number one, while objective improvements in daytime alertness were not found. Changes in the subjective perceptions of either nighttime sleep or daytime function associated with either treatment were not measured. For example, when, if ever, did the bright light group begin to perceive an improvement in sleep quality ? If they did perceive an improvement in sleep quality, was it consistent across nights, or did they still have that occasional terrible night of sleep? What if subjects in the dim light condition perceived an improvement in their sleep that was equal to, if not greater than, that in the bright light condition?

Obviously, one study cannot answer all questions, particularly in the area of elderly insomnia. The present study is another important step in an effort to develop non-pharmacological interventions for the widespread complaint of disturbed sleep in the elderly. Follow-up studies may focus on the objective changes of sleep in response to bright light treatment and its corresponding relationship to a subject's subjective assessment.

THE RELATIONSHIP BETWEEN TOTAL SLEEP TIME AND THE MULTIPLE SLEEP LATENCY TEST IN ELDERLY INSOMNIACS

It is common to see older people "dozing off" at social events, in the living room, and after supper. These episodes of daytime sleepiness are not viewed with alarm by either general practice medicine or the public-at-large. Typically, they are viewed as age-related; a consequence of growing old and "slowing down" (Carskadon, 1990).

However, an increasing body of evidence suggests that the daytime sleepiness observed in some elderly subjects may not simply be a reflection of the normal aging processes, but rather, is a result of increased nocturnal sleep fragmentation (Carskadon, Brown, & Dement, 1982). Other reports suggest that the disturbed nocturnal sleep associated with the complaint of insomnia does not result in increased daytime sleepiness (Seidel, Ball, Cohen, Patterson, Yost, & Dement, 1984; Stepanski, Zorick, Roehrs, Young, & Roth, 1988).

Experiment 2 concerns the relationship between nocturnal sleep parameters and daytime sleepiness in elderly insomniacs.

Several factors that influence daytime sleepiness have been identified. These include the amount of prior sleep (or sleep deprivation), the consolidation of sleep (or sleep fragmentation), the time of day (or circadian variations), and age (or maturation). In addition, alcohol, other drugs, central nervous system pathology, and the presence of pain may also effect the expression of daytime sleepiness (Roth,

Roehrs, Carskadon, & Dement, 1989). Unless defined otherwise, "daytime sleepiness" refers to sleepiness measured polygraphically in two or three standard protocols.

The multiple sleep latency test (MSLT) is the most widely-used technique for evaluating daytime sleepiness. Sleepiness has been formally defined as the tendency to fall asleep in controlled laboratory conditions (Carskadon & Dement, 1987). The MSLT has been proposed as an objective measure of sleepiness, or a direct measure of physiological sleep tendency. Objective measures of sleepiness are not necessarily reflected in elicited subjective reports, especially in patients with excessive daytime sleepiness (Dement, Carskadon, & Richardson, 1975). However, when normal subjects have their nocturnal sleep curtailed (i.e., sleep deprivation), an increase in objective sleepiness is mirrored by increases in subjective sleepiness.

Since both subjective and objective sleepiness are influenced by factors that may either mask or unmask the underlying sleepiness, there can be quite dramatic dissociations between subjective and objective sleepiness evaluations. Environmental factors that may serve to mask a high level of physiological sleep tendency would be the excitement of participating in a political campaign, or the intense involvement in putting together a play. In these cases, people may obtain far less sleep than normal over the course of their involvement, yet deny being sleepy. However, the data

derived from 15 years of study with the MSLT would suggest that physiological sleep tendency in these people is high, but masked. It would be predicted that under controlled conditions in the laboratory, these people would fall asleep more rapidly than when they were adhering to their regular sleep schedule. Environments besides the laboratory which unmask sleepiness, such as a long car ride, would be expected to produce similar results.

Associations between total sleep time and the daytime sleepiness

In normal, healthy, non-complaining adults there are significant associations between age, nocturnal total sleep time, and sleepiness as assessed with the MSLT. From a review of a large series of studies conducted over 10 years (262 subjects, age range, 7 to 79), Carskadon (1989) has reported the following associations. The relationship between total sleep time and the MSLT is positive; higher amounts of sleep are associated with higher MSLT scores across normal subjects over the entire range of ages studied (i.e., 7 to 79 years) (Carskadon, 1989). Age is inversely related to total sleep time; older subjects obtain less sleep under controlled laboratory conditions than younger subjects. Similarly, age is inversely associated with daytime sleep latency as assessed by the MSLT. Older subjects fall asleep more quickly on the MSLT than younger subjects. An age-related increase in daytime sleepiness in the elderly is supported by the finding that 90% of subjects between the ages of 62

and 77 years had one nap latency of less than five minutes, while sleep onsets below five minutes were observed in only 33% of subjects between the ages of 17 and 25 years.

Others have observed a somewhat different pattern of results. Levine, Roehrs, Zorick and Roth (1988) found that younger subjects were sleepier than older subjects, and Seidel, Ball, Cohen, Patterson et al. (1984) found a small, but significant inverse relationship between total sleep time and the MSLT (rho = -.23), in 89 normal, young adults (mean 26.5 years). These two findings suggested to the respective investigators a pattern of chronic sleep debt that is not fully paid off during their laboratory protocols (Levine, Roehrs, Zorick, & Roth, 1988; Seidel, Ball, Cohen, Peterson, Yost, & Dement, 1984). They reasoned that a negative correlation between total sleep time and the MSLT would be obtained if chronically sleep-deprived individuals have recovery sleep (high total sleep time) on the night before they manifest their sleepiness during the day (i.e., low sleep latencies on the MSLT). One night of recovery sleep would be insufficient to settle the postulated chronic sleep debt, since it has been shown that sleep debt accumulates (Carskadon and Dement, 1981) and that sleepiness persists on the day following recovery sleep (Carskadon and Dement, 1979). Recent sleep history is, therefore, a determinant of sleepiness and must be taken into account when sleepiness is evaluated.

Not all of the daytime sleepiness observed in healthy, older adults is explained by age and total sleep time alone. In healthy subjects over the age of 60, the relationship between total sleep time and MSLT scores becomes non-significant (Carskadon et al., 1982). In this age range, transient arousals (i.e., arousals lasting less than 15 seconds), respiratory events, shifts into Stage 1 sleep, and shifts into wakefulness are all inversely correlated with the MSLT, while total sleep time is not. An experimental analog of sleep fragmentation has been produced in the laboratory in healthy, young sleepers with similar results. Stepanski, Lamphere, Roehrs, Zorick, and Roth (1987) administered arousing, auditory stimuli to sleeping subjects and found that 8-9 arousals per hour significantly increased daytime sleepiness, while total sleep time remained unchanged. This descriptive and experimental work, taken together, suggests that increased sleep fragmentation in the elderly may become a more salient factor in producing sleepiness than reductions in total sleep time in the course of aging (Miles and Dement, 1980).

While the overall relationships between total sleep time, age, and the MSLT are reasonably robust, the studies above suggest that within a restricted age range (i.e., the elderly), these relationships begin to become less apparent. It has also been reported that the relationship between the MSLT and total sleep time, in people with insomnia, is the reverse of the relationship in healthy adults. For example, Stepanski, Zorick, Roehrs,

Young, and Roth (1988) have observed a negative correlation between total sleep time on one night and the MSLT the following day within diagnostic sub-groups of insomniac patients. Additionally, mean sleep latency on the MSLT was significantly higher in the insomniac group compared to a control group of asymptomatic sleepers. A negative relationship between total sleep time and the MSLT was also observed by Hauri and Wisby (1990), who, in addition, reported a wide variation of mean MSLT values in young insomniacs. Some insomniacs were pathologically sleepy, manifesting sleep latencies below 5.5 minutes, while others appeared to be reasonably alert, with sleep latencies over 10 minutes (Hauri & Wisby, 1990). Seidel et al. (1984) found no relationship between MSLT sleep latency and total sleep time in 138 insomniacs with a mean age of 54.5 years.

These results are consistent with those initially reported by Dement and Seidel (1982), who found that 7% of insomniac patients were pathologically sleepy, while 41% were "surprisingly alert". In a follow-up report, this group found that 14% of 138 insomniac subjects evidenced no daytime sleepiness on the MSLT (i.e., they did not fall asleep within 20 minutes on any nap), while only 2% of 89 normal subjects did (Seidel et al., 1984). Comparisons between the insomniacs who did not fall asleep on any nap and those with a mean sleep latency between 5 to 17 minutes on measures of nocturnal sleep, daytime performance, subjective

sleepiness, mood, and personality measures failed to reveal any significant differences.

Thus, several investigators have found that the relationship between nocturnal sleep (as measured by total sleep time) and daytime sleepiness (as measured by the MSLT) seems to differ in two groups from that in healthy, young adults; the elderly, and people with insomnia. The group of people with both characteristics (i.e., elderly insomniacs) may show a unique relationship between these two parameters and deserves study. Prior studies demonstrate that longitudinal assessment of sleep history (i.e., assessment of more than one night preceding the day of study) and measures of sleep fragmentation are important methodological concerns. The present study is an attempt to address these issues.

Method

A total of 43 insomniac subjects (14 males, 29 females) participating in a study of behavioral treatments at the City College of New York (CCNY) were recruited through the media. Prospective subjects were free from gross psychopathology and significant cognitive deficits. Subjects taking hypnotic medications were removed from medication under the supervision of a physician with training in sleep disorders medicine.

Subjects ranged in age from 50 to 84 years (mean 62.5 years ± 9.3). The mean duration of sleep complaint was 15.8 years (± 15.35), and the

range was from 6 months to 55 years. Each subject had a pre-treatment evaluation which included three nights of sleep recording followed by the multiple sleep latency test (MSLT). Nocturnal sleep recordings were made on a Grass Model 78D polygraph. Night one consisted of a full screening polysomnogram, including measurements of sleep, respiratory airflow and effort, and leg movement potentials. Baseline sleep recordings consisted of three consecutive nights in the laboratory. During the second and third nights, a standard brief sleep recording montage (i.e., central and occipital EEG, left and right electro-oculogram, chin electromyogram, and a sleep electrocardiogram) was used. Sleep records were scored according to standard criteria (Rechtschaffen & Kales, 1968).

Subjects were strongly encouraged to adhere to a bedtime and waketime schedule that was calculated as an average from the two-week sleep log filled out prior to the laboratory study. Following the third baseline night of sleep recording, subjects remained in the laboratory for the MSLT. MSLT sleep latency was determined by averaging values across 5 naps. The first nap began two hours after subjects arose, and naps were initiated every two hours thereafter, for a total of 5 naps. Sleep onset was defined as 3 consecutive epochs of Stage 1 sleep, or a single epoch of any other

stage of sleep. Naps were terminated following sleep onset to prevent

accumulation of sleep during the day. Subjects remained in the room for a maximum of 20 minutes. If no sleep occurred, a value of 20 minutes was assigned to the nap.

Pearson correlation coefficients were computed between MSLT mean sleep latency scores and several nocturnal sleep variables for individual nights and for combinations of nights 1, 2, and 3. For further analysis, subjects were sub-divided into two groups based on the basal level of sleepiness (i.e., sleepy, normal, alert), or by age (i.e., subjects younger and older than the median age). The number of stage changes, wake-shifts and Stage 1 shifts were calculated. Wake-shifts were defined as a transition from sleep to wakefulness (excluding transitions from Stage 1 to wake). Stage 1 shifts were defined as shifts into Stage 1 sleep (excluding shifts from wake to Stage 1). Instead of analyzing apnea events, and leg movement events separately, these two variables were combined into one index. This was done because a few subjects had either low levels of sleep-disordered breathing or periodic leg movements, and it was thought a combined-event index would enhance our ability to detect the relationship between occult events in sleep and daytime sleepiness. The respiration and periodic movement index will be referred to as the "event index."

Results

Table 5 lists the nocturnal sleep variables for 43 elderly insomniac

subjects during the third baseline night of sleep recording. While the mean values listed in Table 5 indicate a moderate level of sleep disturbance, the range for many of the sleep parameters is striking. In particular, sleep latency to Stage 2, time in bed, total sleep time, minutes of slow-wave sleep, and the event index show a high degree of variability.

Mean sleep latency collapsed across all naps of the MSLT was 12.9 ± 5.5 minutes (range 3.1 to 20.0 minutes). The mean sleep latencies in minutes and standard deviations for naps one through five were as follows: Nap 1 = 13.4 ± 7; Nap 2 = 11.1 ± 6.8; Nap 3 = 10.3 ± 6.6; Nap 4 = 12.0 ± 7; Nap 5 = 13.0 ± 7.2.

All Pearson correlations performed between the MSLT and nocturnal sleep variables were non-significant (Table 6). Correlations between the MSLT and total sleep time minus Stage 1 sleep for all nights singly, and for various combinations of nights, were also non-significant.

- Tables 5 and 6 -

Table 5

Nocturnal Sleep Characteristics in 43 Elderly Insomniacs

Parameter	Mean	Standard Deviation	Range
Sleep Latency (stage 1)	14.2	18.5	1.0 - 93.5
Sleep Latency (stage 2)	22.8	27.2	1.0 - 110.0
Time in Bed	467.7	53.1	336.0 - 623.5
Wakefulness After Sleep Onset	73.0	57.1	21.5 - 232.0
Sleep Efficiency (%)	80.0	13.0	53.2 - 97.3
Total Sleep Time	374.0	6.6	222.5 - 482.0
Stage 1	62.4	30.9	31.5 - 158.0
Stage 2	206.3	51.6	99.5 - 330.5
Slow Wave Sleep	36.9	31.8	0.0 - 138.5
REM Sleep	68.3	20.1	10.0 -114.0
REM Latency	75.0	36.9	35.1 - 166.5
Stage 1 (%)	17.0	8.0	4.5 - 38.6
Stage 2(%)	53.8	11.6	30.9 - 70.5
Slow Wave Sleep (%)	9.8	8.0	0.0 - 30.5
Wake Shifts (number)	20.8	9.0	5.0 - 47.0
Stage 1 Shifts (number)	19.9	9.6	4.0 - 46.0
Respiration and Periodic Movement Index (number)	16.0	26.8	0.0 - 134.5

Note: All values in minutes unless otherwise indicated by percent (%) or number.

Table 6

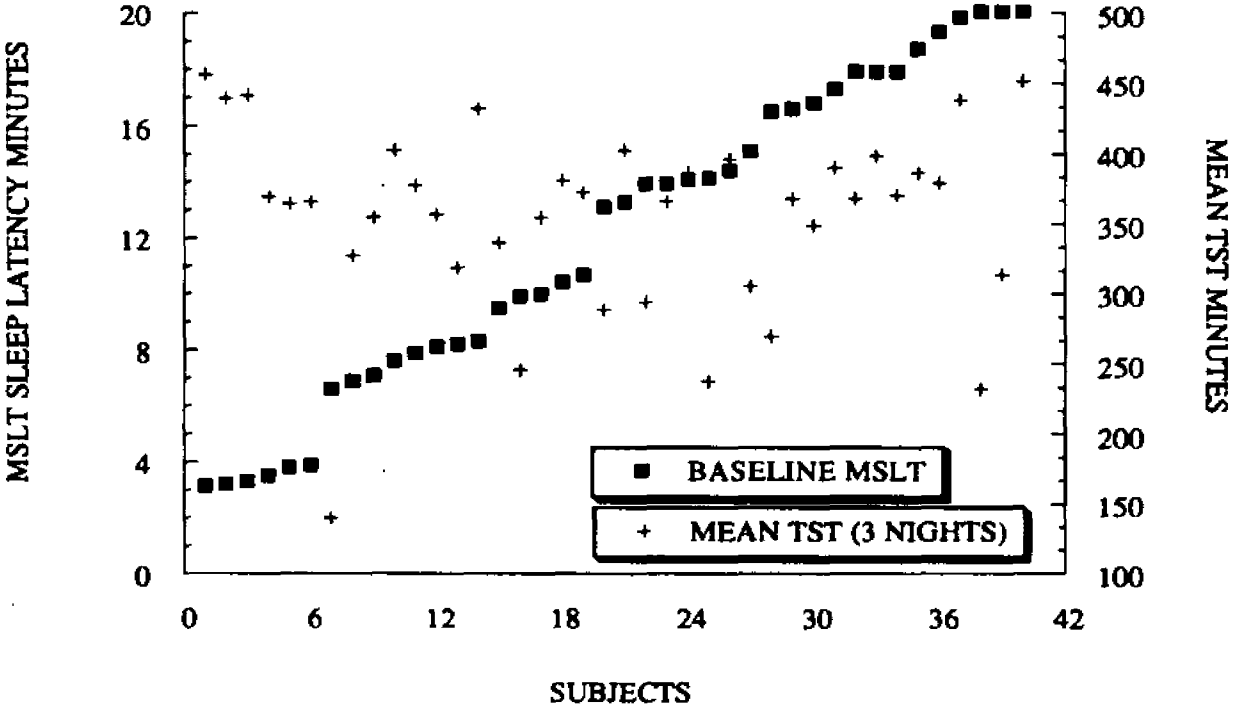
Correlation of Sleep Parameters With Mean MSLT Sleep Latency

Nocturnal Sleep Parameter	Correlation Coefficient	Significance
Nocturnal Sleep Latency (Stage 1)	.280	NS
Nocturnal Sleep Efficiency	.007	NS
Total Sleep Time (Night 3)	.176	NS
Total Sleep Time (Night 2)	.140	NS
Total Sleep Time (Night 1)	.192	NS
Total Sleep Time (Nights 2+3)	.175	NS
Total Sleep Time (Nights 1+2+3)	.177	NS
Wake Shifts (number)	-.073	NS
Stage 1 Shifts (number)	-.141	NS
Respiratory and Periodic Movement Index (number)	.145	NS

To graphically illustrate the lack of significant association between total sleep time and MSLT sleep latency in this population (r = .177, NS), each subject's mean values for both variables were plotted. Figure 18 depicts a double-y plot of individual, ascending MSLT scores and the individual total sleep time values. Each individual subject is plotted along the X-axis.

- Figure 18 -

Figure 18



Double-y plot of ascending MSLT scores and the mean total sleep time averaged from three consecutive nights in the laboratory. Each individual subject is plotted along the x-axis.

As seen in Table 5, the event index is not significantly associated with MSLT sleep latency (r = .145, NS). Inspecting the data for the 12 subjects with the lowest MSLT scores is illustrative. Out of the 12 subjects with the lowest MSLT scores (located on the X-axis from left to right), the second, seventh and eleventh subjects had event indices greater than twenty. Each of the other nine subjects with low MSLT scores had zero events in sleep. The mean number of wake-shifts for these 12 subjects was 23.2 (± 10.2), and the mean number of Stage 1 shifts was 20.8 (± 9.8). The mean values of these two variables for the other 31 subjects were 20.4 and 19.5 respectively.

To further investigate the impact of occult nocturnal events on daytime sleepiness, the following analysis was performed. Subjects were divided into two groups: twenty-two subjects who had the lowest MSLT scores were categorized as sleepy, and twenty-one subjects who had the highest sleep latencies were categorized as alert. A one-way ANOVA with group as the independent variable (sleepy/alert), and event index as the dependent variable was non-significant. Furthermore, while the difference was not significant, the mean values were counter to what was predicted. The *alert group* had a mean event index of 21.3 (15.6), whereas the sleepy group's event index was 8.8 (33.3).

To further explore the relationship between total sleep time and MSLT sleep latency, three sub-groups were formed based on MSLT scores. The

sleepy group included subjects with MSLT scores less than 10 minutes, the normal group included subjects with scores between 10 and 15 minutes, and the alert group included subjects with scores greater than 15 minutes. The characteristics of each group are listed below. The mean MSLT values, the range and total sleep time (TST) are in minutes and parentheses indicate standard deviations.

Group	N	Mean MSLT	Range	TST	Age
Sleepy	17	6.3 (2.4)	3.1 - 9.9	357 (86)	64.4
Normal	11	12.9 (1.7)	10.0 - 14.4	379 (57)	62.8
Alert	15	18.1 (1.5)	15.1 - 20.0	392 (42)	60.6

Correlations between the MSLT and total sleep time within each sub-group were non-significant. A one-way ANOVA performed with group (sleepy/normal/alert) as the independent variable and total sleep time as the dependent variable was also non-significant, $F(2, 40) = 1.17$, NS, further de-emphasizing the importance of total sleep time in predicting daytime alertness in this population.

A similar strategy was used to assess the effect of age. The subjects were divided into two groups: a young group comprising the 21 youngest subjects and an old group comprising the 22 oldest subjects. Below are the characteristics of each group.

Group	N	Mean MSLT	Range	TST	Age
Young	21	12.3 (6.1)	3.1 - 20	399 (43.5)	54.5
Old	22	11.9 (5.1)	3.2 - 20	354 (54.2)	70.1

Correlations between the MSLT and total sleep time within each age group were non-significant. A one-way ANOVA revealed no significant differences with age as the indenpendent variable (young/old) and the MSLT as the dependent variable. However, a one-way ANOVA with age (young/old) as the independent variable and total sleep time as the dependent variable revealed a significant difference in total sleep time, $F(1, 41) = 4.96$, $p < .05$.

Discussion

In this sample of 43 middle-aged and elderly insomniacs, none of the measured nocturnal sleep variables were associated with mean sleep latency on the MSLT, including total sleep time, wake-shifts, Stage 1 shifts and event indices. The non-significant relationship between total sleep time and the MSLT is consistent with a previous study by Carskadon, Brown and Dement (1982), who reported on 24 non-complaining elderly subjects (mean age 72.85 yrs.). However, this group reported that sleep fragmentation (defined as respiration events and transient arousals, i.e., the appearance of an alpha rhythm not long enough to result in a stage change) was inversely related to the MSLT (Carskadon, Brown, &

Dement, 1982). Increased sleep fragmentation was associated with lower MSLT values across subjects. Unfortunately, transient arousals were not measured in the present study. Other measures of sleep fragmentation, however, such as wake-shifts, Stage 1 shifts, and the event index, were not significantly associated with the MSLT in this study.

One possible reason for the different findings in the two studies is that subjects spent much less time in bed in the present study. Time in bed (TIB) was scheduled according to the subject's own habitual bedtime. The mean TIB was 467.68 minutes with a range of almost 300 minutes (336 to 623). In contrast, Carskadon and her colleagues scheduled TIB between 2200 and 0800 hours for all subjects. Thus, subjects in their study spent, on average, over 2 hours longer in bed than subjects in the present study. Although these data were not reported, it seems reasonable to speculate that in the Carskadon study, there may have been an increase in Stage 1 shifts and wake-shifts near the end of the sleep period.

Below is an abbreviated comparison of selected nocturnal sleep variables from the Carskadon, Brown, and Dement study (1982, pp. 323) and the present one.

Variable	Anderson	Carskadon et al.
Sleep latency	22.8 min	19.0 min
Stage 1%	17%	18%
Stage 2%	53.8%	39.4%
SWS%	9.73%	8.00%
Stage REM%	18.20%	13.1%

These nocturnal sleep variables are reasonably similar and are not necessarily directly influenced by increases in TIB. However, the variables presented below are quite distinct and it is possible that the increased time in bed is responsible.

Variable	Anderson	Carskadon et al.
Total sleep time (minutes)	374.0	426.0
Sleep efficiency	80.0%	72.0%
WASO (minutes)	73.0	148.0
Wake-shifts (number)	20.8	41.0
Stage 1 shifts (number)	19.9	75.0

Thus, it is possible, that by increasing TIB for these elderly subjects (whose sleep was already likely to be fragile), Carskadon and her colleagues produced an increase in sleep fragmentation, particularly in the last 2-3 hours of sleep. This could have resulted in marked increases in wake-shifts, Stage 1 shifts, and in wakefulness after sleep onset (Spielman, Saskin, & Thorpy, 1987). It is easy to imagine that when elderly subjects are confined to bed for 10 hours, the last 2-3 hours are spent drifting in and out of Stage 1 sleep.

While an increase in TIB may increase sleep fragmentation, it does not explain the inverse correlation between sleep fragmentation and the MSLT in their study. To explain this inverse correlation, one might consider the interaction between the circadian rhythm of body temperature and the imposed ten hour TIB. Campbell, Dawson, and Anderson (1992) found that the average temperature minimum for 16 elderly insomniacs was around 4:00 a.m.. It is likely that some of the subjects in Carskadon's study had similar temperature rhythms.

In phase-advanced subjects, an extended TIB might result in relatively small increases in sleep, because sleep becomes more difficult on the rising portion of the temperature curve (Akerstedt and Gillberg, 1981; Gillberg and Akerstedt, 1982). Thus, phase-advanced subjects may have experienced relatively large increases in sleep fragmentation during the last 2-3 hours of the night and relatively small increases in sleep and were

sleepy on the MSLT. Conversely, other elderly subjects may not have been phase-advanced and these subjects could have benefited from the increased TIB by obtaining more sleep and less fragmented sleep. Thus, the less fragmented their sleep, the higher their sleep latencies on the MSLT. This logic does not deny that increased nocturnal sleep fragmentation is inversely related to MSLT latency. Instead, it suggests that individual differences in phase-relationships between sleep and temperature underlie differences in sleep fragmentation. The influence of the circadian rhythm of body temperature might be magnified by increases in TIB, especially by extensions at the end of the sleep period. It seems plausible then, that our failure to observe a negative correlation between measures of sleep fragmentation and MSLT sleep latency may be due to protocol differences. In the present study, subjects adhered to their regular schedules. Average time of arising in the present study was 6:42 a.m. In support of this position, Seidel and his colleagues failed to observe an inverse correlation between MSLT scores and the number of awakenings greater than 15 seconds in a group of 138 insomniacs with a mean age of 54.5 years (Seidel, Ball, Cohen, Patterson, Yost, & Dement, 1984). In this study, time in bed was scheduled, but typically only for 8 hours. This group also failed to observe a correlation between total sleep time and MSLT sleep latency in insomniacs.

Further comparisons can be made between the present study and that of Seidel et al. (1984). Fourteen percent of their insomniac subjects did not fall asleep on the MSLT in spite of having the same amount of total sleep time as those with lower MSLT scores. In the present study, ten subjects (23%) had sleep latency values between 18 and 20 minutes. Total sleep time for these subjects was 396 minutes; an amount of sleep not significantly different from the group mean of 374 minutes. Thus, regardless of the lack of association between total sleep time and the MSLT in the present study and the one by Seidel, Ball, Cohen et al. (1984), it appears that a sub-group of insomniacs do not fall asleep on the MSLT during the day, despite their objectively verified, disturbed sleep (i.e., in this study significant differences were found between insomniac subjects and normal controls in: nocturnal sleep latency, total sleep time, and sleep efficiency).

The minimal sleep tendency of some insomniacs has been suggested to be the result of an abnormal response to sleep loss, or simply a reflection of a reduced need for sleep (Seidel et al., 1984). It has also been suggested that a common attribute underlying all insomnia conditions is a tendency toward physiological (autonomic) hyperarousal, that is a necessary (but not sufficient), cause of insomnia (Stepanski, Zorick, Roehrs, Young, & Roth, 1988). An alternative explanation may be found in conditioning models of sleep behavior. Stimulus control instructions

have been developed to strengthen the bedroom as a cue for sleep, while simultaneously weakening its power to lead to anxiety and arousal (Bootzin & Nicassio, 1978). Although stimulus control instructions were designed for the treatment of sleep onset insomnia, the principles of conditioning have recently been examined in the context of daytime sleepiness (Spielman, 1987).

Speculations that the ability to fall asleep during the daytime could be conditioned in accord with the principles of classical conditioning theory were given a minimal amount of credence based on pilot data from four subjects. Spielman, Caruso, and Glovinsky (1987) demonstrated that a previously neutral stimuli, in this case a 200 hertz tone, could become a discriminative cue for sleep after it had been paired with hypnotic medication during the day. In other words, a conditioned response had been developed to the 200 hertz tone, resulting in a 27% reduction in daytime sleep latency after the daytime drug administration had been discontinued. Based on these findings, as well as a large animal literature that deals with classical conditioning of behavior, these authors suggested that the MSLT may reflect a conditioning component, in addition to physiological sleep tendency (Spielman, 1987). It is plausible that the minimal daytime sleep tendency observed in some insomniacs may reflect a classically conditioned response to the sleep environment rather than an abnormal response to sleep loss, or physiological hyperarousal. By

adding a conditioning component to the interpretation of MSLT values, an explanation is provided for subjects who appear extremely sleepy on the MSLT, yet do not complain of daytime sleepiness (Anderson, Zendell, Rosa, Rubinstein, Herrera, Simons et al., 1988). Some subjects may be favorably conditioned to fall asleep rapidly, without necessarily being pathologically sleepy. In the elderly especially, the ability to fall asleep is typically not the primary sleep problem, but rather, it is the inability to maintain sleep. In the present study, 6 subjects had sleep latencies of less than 5 minutes, and another 12 subjects had latencies between 5 and 10 minutes. As Figure 18 shows, the differences in sleepiness in these 18 subjects are not explained by total sleep time, nor do any other measured variables adequately account for the wide range in MSLT scores. It is possible that individual differences in response to environmental cues associated with sleep may be important. Subjects may respond to an environment in both favorable (sleep enhancing) and unfavorable (arousing) ways.

The lack of association between total sleep time and the MSLT may also be a consequence of the experimental design and the statistics employed to assess these relationships. In normal subjects of all ages, cumulative sleep loss results in an increase in sleep tendency (Carskadon & Dement, 1979; Carskadon & Dement, 1981; Carskadon, Seidel, Greenblatt, & Dement, 1982; Carskadon & Dement, 1985; Brendel,

Reynolds, Jennings, Hoch, Monk, Berman et al., 1990). There is also evidence to suggest that sleep extension reduces sleep tendency in normal subjects (Roehrs, Timms, Zwyghuizen, & Roth, 1989). Thus, in studies using within-subject designs, predictable and reliable relationships between total sleep time and sleep tendency are manifested.

Perhaps the reason total sleep time does not correlate with the MSLT in this study, as well as others, is because the individual variation in both total sleep time and sleep tendency is too great under basal conditions. For example, given the insomniac's high night-to-night variability in sleep quality (Karacan, Williams, Littel, & Salis, 1973), it is plausible that a number of the subjects arrived for the baseline sleep recordings after a series of bad nights, while others arrived after a series of good nights.

This argument would apply to the actual nights in the laboratory as well. Consider the elderly subject who has slept poorly for seven consecutive nights, obtaining only 3 hours of sleep or less on each night. Then, on the night prior to the MSLT, this subject experiences a recovery night and sleeps 7.5 hours. Will sleep tendency reflect only the prior night of sleep, or will the cumulative effects of sleep loss be apparent? The data in normal subjects suggests that the sleep loss has a cumulative effect on daytime sleep tendency (Carskadon & Dement, 1981; Carskadon, 1989). The same principle can also work in the opposite direction with a subject who sleeps very well for a few consecutive nights and then, on the

night prior to the MSLT, experiences a poor night of sleep. In these cases, rather than recording a night typical of the past week's sleep, an unusual night is recorded.

In part, this question was addressed in the present study; three consecutive nights were combined and correlations were performed between total sleep time and the MSLT. The relationship between total sleep time and the MSLT remained non-significant. Thus, three consecutive nights in the laboratory were not enough to precipitate out a relationship between total sleep time and the MSLT in this sample of elderly insomniacs. Nonetheless, concerns about between-subject analysis may still be relevant in the present study.

To further investigate this question, additional data were analyzed. Following baseline evaluation, subjects in this study were assigned to one of three treatment groups that ostensibly produced mild sleep loss. A fourth group received no treatment instructions, thereby serving as a control group. These forty-three subjects were evaluated six weeks subsequent to their baseline evaluation. The mean total sleep time was significantly reduced from 375 minutes at baseline to 352 minutes following treatment, t (42) = 2.7 $p < .02$. The correlation between total sleep time and the MSLT at this time was positive and significant, $r = .36$, $p < .05$. Thus, when sleep time is manipulated and the variability reduced through experimental instructions, the predicted relationships hold, even

in a between-subject comparison: total sleep time is positively related to the MSLT. Across subjects, more sleep was associated with increased alertness, as assessed with the MSLT.

The positive relationship between total sleep time and the MSLT was also observed within-subjects. For instance, the correlation between the change in total sleep time from baseline to post-treatment with the change in MSLT scores from baseline to post-treatment was significant and positive, $r = .32$, $p < .05$. Increases in total sleep time resulted in increases in alertness, while decreases in total sleep time from baseline to post-treatment resulted in decreases in alertness. Thus, the non-significant correlations between total sleep time and the MSLT in elderly insomniacs and in non-complaining elderly may be a consequence of the extreme between-subject variability in sleep tendency. This may obscure the relationship between sleep and daytime function when first evaluated in the laboratory.

Heretofore, the discussion has focused on the lack of association between total sleep time and the MSLT observed in this study. This lack of an observed relationship is consistent with previous reports in elderly subjects without sleep disturbance and with results from a group of middle-aged insomniacs (Carskadon et al., 1982; Seidel et al., 1984).

Other studies have compared daytime sleepiness between insomniacs and normals and found no differences. Seidel and his colleagues reported

that there were no significant differences in daytime sleepiness between 138 insomniac patients and 89 normal control subjects. The mean MSLT value for the insomniac group was 12.4 minutes and the mean values for the control group was 12.9 minutes. Three other published studies also failed to observe significant differences between insomniac subjects and normal controls on the basis of MSLT scores (Mendelson, Garnett, Gillin, & Weingartner, 1984; Stepanski, Lamphere, Badia, Zorick, & Roth, 1984; Sugarman, Stern, & Walsh, 1985).

Recently, however, Stepanski and his colleagues in Detroit have suggested that insomniacs are not only more alert than normal controls, but that among diagnostic sub-groups, there is a significant inverse relationship between total sleep time and the MSLT (Stepanski, Zorick, Roehrs, Young, & Roth, 1988). Within a group of insomniac patients, higher daytime sleep latencies were associated with less total sleep time on one night preceding the daytime evaluation. The authors interpret this finding to mean *"the greater the sleep loss, the greater the daytime alertness"* (sic) (Stepanski, Zorick, Roehrs, Young, and Roth, 1988, pp. 58).

Since this counter-intuitive finding has attracted wide attention and is often cited, a brief discussion of the differences between the present study and that of Stepanski et al. (1988) is warranted. The subjects in the present experiment differed from those studied by Stepanski. Subjects in

the present study were approximately 15 years older (mean age CCNY = 62.5; mean age Detroit = 46.7), and were free of hypnotic medication. Stepanski et al. (1988) studied seventy insomnia patients who were referred to the sleep clinic. It is unclear if they were studied while on hypnotic medication. In addition to the insomniac patients, forty-five normal, asymptomatic control subjects were studied (mean age 50.4). The MSLT was administered subsequent to one night of sleep that included recordings of respiration and leg movements. It is traditional not to include data from the first night in the laboratory because of the well-documented, first-night effect (Agnew, Webb, & Williams, 1966; Mendels & Hawkins, 1967; Webb & Campbell, 1979). It is possible that some insomniacs and some normal subjects experienced a relatively poor night of sleep. The suggestion that normal subjects slept more poorly than usual is supported by the observation that the normal subjects had 18.1% of Stage 1 sleep, an unusually large amount. In the present study, the MSLT was administered following the third consecutive night of sleep recording.

The amount of daytime sleep that was allowed differed between the two studies as well. In the present study, MSLT nap trials were terminated following 1.5 minutes of Stage one sleep, or after a single epoch of any other stage. This was done to limit the accumulation of daytime sleep. In the Stepanski et al. (1988) study, MSLT nap trials were

terminated after 15 minutes of sleep. Perhaps, compared to healthy, normal sleepers, alertness levels in insomniac patients are differentially enhanced by these short daytime sleep episodes.

Additional comments concern the nature of the differences between MSLT values in insomniacs and control subjects. The mean values for both the insomniac patients and the controls are centered firmly within the normal range of sleepiness and alertness (insomniac = 14.7 minutes; normal 12.2) (Roehrs, Zorick, McLenagan, Sickelsteel, Lamphere, & Wittig, 1984). The conclusion that insomniacs are hyperalert rests on the fact that they had significantly less sleep, and significantly higher MSLT sleep latencies than the controls. However, an alternative explanation may be that insomniacs benefited more from the accumulation of daytime sleep, up to a maximum of 60 minutes, than did the normal control subjects. Thus, in the insomniac group, each successive 15-minute daytime nap could have had a larger impact on sleep tendency compared to normals.

The most important finding from the Stepanski et al. (1988) study, an inverse relationship between total sleep time and mean MSLT sleep latency in the insomniac group, was derived in the following way. Sixty-three subjects were diagnosed according to the Association of Sleep Disorders Centers Criteria (ASDA, 1979), and categorized into 8 separate sub-groups. Not surprisingly, an unequal number of subjects

fell into each category. The following is a breakdown of the diagnoses: Psychiatric (affective), n = 15; Psychophysiological insomnia, n = 11; No objective findings, n = 11; Psychiatric (anxiety), n = 7; Insomnia (not otherwise specified), n = 7; Medical, Toxic, and Environmental, n = 5; Periodic Leg Movements, n = 4; Restless Legs Syndrome, n = 3. Group mean total sleep time and MSLT values were calculated separately for each sub-group. A correlation was then performed (test not specified) between total sleep time and the MSLT for these eight sub-diagnostic groups. The reported correlation was -.67, $p < .05$, with 7 degrees of freedom. On the basis of this observation, as quoted above, the authors suggested that sleep loss is associated with greater daytime alertness. This data analytic method is flawed since the assumption of equal weight for each data point has been violated. This particular analysis does not compare insomniacs to normal controls, nor does it achieve a within subject comparison. A data point representing 15 or 11 subjects is treated statistically the same as a data point that represents only 3 or 4 subjects. At best, the results are misleading, particularly because no correlations were made with each subject serving as one data point.

For example, in four of the eight insomnia diagnostic sub-groups (restless legs, periodic movements in sleep, medical and toxic insomnia, and alcoholism), nocturnal sleep fragmentation is common (Montplaisir & Godbout, 1989; Wooten, 1989; Zarcone, 1982). There are two extreme

end points to any correlation. Stepanski has emphasized only one end of the negative correlation. It may be true that some insomnia patients, such as those with anxiety disorders or psychophysiological insomnia, have elevated MSLT scores and relatively low total sleep time. It is also likely that the subjects diagnosed with restless legs syndrome, period leg movements in sleep, alcoholism, or a medical disorder that interferes with sleep, have low MSLT scores and more sleep than those with anxiety or psychophysiological insomnia. When sub-groups such as these are combined, an inverse relationship between the MSLT and total sleep time will naturally result. To suggest that sleep loss results in greater alertness is not supported (or justified) by these data. That some insomniacs sleep more and are sleepier may be due to occult sleep disturbance which disrupts the continuity of their sleep and results in the complaint of insomnia.

In summary, two previous reports have failed to observe a relationship between total sleep time and the MSLT; one in non-complaining elderly and one in insomnia subjects (Carskadon et al., 1982; Seidel et al., 1984). The present study yielded similar findings in elderly insomniacs. It was suggested that either a conditioning effect, or large between-subject variations in either cumulative sleep loss, or improved sleep in the laboratory may be responsible for the observed non-significant findings.

The theory that insomniacs who sleep less are more alert

rests on experimental data from one study that is seriously flawed, both in design and in statistical treatment of the data. Nonetheless, in this study, relative to normal controls, insomniacs have less sleep and higher MSLT values. The difference is small. This result is not easily accounted for by simple cause-effect relationships between total sleep time and daytime alertness (Stepanski et al., 1988).

It is the conclusion of the author that the data in the present study more accurately represents the varied nature of daytime function in insomnia conditions in the elderly. A re-inspection of Figure 18 emphasizes the smooth linear distribution of daytime sleepiness in these elderly insomniacs. The relationship between sleep time and the MSLT is not counter-intuitive in insomnia conditions; rather, it is obscured by the enormous night-to-night variability in sleep quality, both within a single subject and between subjects. A single snapshot of a night and day in the life of an insomniac is unlikely to produce the most accurate picture of the relationship between nighttime sleep variables and daytime sleep latency as assessed with the MSLT.

THE EFFECT OF INSTRUCTION ON SLEEPINESS AND ALERTNESS IN ELDERLY INSOMNIA

An unexpected finding from Experiment 2 was that nocturnal sleep variables, including measures of nocturnal sleep fragmentation, did not correlate with the mean sleep latency on the MSLT. Although used infrequently, other tests of daytime sleep latency have been developed. These include the repeated-test-of-sustained-wakefulness (RTSW) (Hartse, Roth, Zorick, & Zammit, 1980); the maintenance-of- wakefulness-test (MWT) (Mitler, Gujavarty, & Browman, 1982); and the modified-assessment-of-sleepiness-test (MAST) (Erman, Beckham, & Gardner, 1987). A common feature of all of these tests is that during the "nap administrations" subjects are instructed to try and remain awake, instead of being asked to try and fall asleep. The change in protocol instructions results in longer mean latencies in patients complaining of excessive daytime sleepiness, but they still appear less alert when compared to normal control subjects.

In the present study, the results of the daytime testing carried out in Experiment 1 are more thoroughly analyzed, and then compared to a similar population of subjects who were administered the MSLT. In Experiment 2, an association between MSLT sleep latency and nocturnal sleep parameters observed in previous studies were not confirmed. The first analysis in the present experiment is a post-hoc replication of Experiment 2, using subjects from Experiment 1 who were administered the RTSW. The second objective of the present experiment was to assess the effect of instruction on daytime sleep latency by comparing two

independent groups of age-matched subjects who were administered either the MSLT or RTSW. A sub-set of subjects administered the MSLT in Experiment 2 are compared to all sixteen subjects who were administered the RTSW in Experiment 1.

The RTSW is a multiple daytime nap test that was developed to assess improvements in alertness in patients treated for excessive daytime sleepiness (Hartse, Roth, & Zorick, 1982). The protocol of the RTSW is identical to that of the MSLT, except the instructions differ. Every two hours in the laboratory, subjects are put into a darkened room, asked to lie down and told, "Close your eyes and try to remain awake." The RTSW is the flip side of the MSLT. Instead of measuring sleep propensity, this test purports to measure "wake propensity" (Hartse et al., 1982).

Comparisons between the RTSW and the MSLT have been reported for normal subjects after a night of normal sleep and after a night of total sleep deprivation (Hartse, et al., 1982). Twenty subjects between the ages of 24 and 70 years were administered the MSLT and the RTSW after normal nights of sleep approximately two weeks apart. Nap trials in each condition lasted for 30 minutes and sleep was allowed to accrue for 15 minutes before each trial was terminated. Four nap trials were administered in each condition. Collapsed across all 4 trials, the RTSW mean sleep latency value was significantly higher (mean = 16.95) than the MSLT mean (mean = 12.6) . In a second study, 12 subjects were studied after a night of total sleep deprivation (seven of them had

participated in the first study). Subequent to a night without sleep, latency to stage 1 sleep was 7.05 minutes in the RTSW condition, and 6.7 minutes for the MSLT condition, a non-significant difference (Hartse et al., 1982). A post-treatment comparison between the RTSW and the MSLT in a group of narcoleptic patients treated with stimulants revealed no significant difference in latency values between the two tests (Hartse et al., 1982). On the other hand, a slightly different daytime assessment protocol can produce differences in sleep latencies in this clinical population. Mitler and associates (1982) found that improvements in the alertness level of treated narcoleptics could be detected with the MWT and similar results have recently been reported for patients treated with nasal CPAP devices for obstructive sleep apnea (Poceta, Timms, Jeong, Ho, Erman, & Mitler, 1992). In contrast to the RTSW, subjects administered the MWT are not asked to lie down, or to close their eyes during the assessment trial. Instead, subjects are seated in a comfortable chair in a dark room and told to try and remain awake.

The effect of subject motivation (operationally defined as financial incentive), on daytime sleep latency has been investigated in normal subjects on the RTSW after one night of sleep deprivation. In addition measuring sleep latency, measures of reaction time and subjective sleepiness were obtained. Alexander, Blagrove and Horne (1991) found that the introduction of monetary compensation could boost daytime sleep latency, while having little effect on subjective sleepiness or reaction time.

Thus, in addition to instruction, it appears that subjects can rally some resource to maintain wakefulness in response to an instrumental stimulus.

Clodore, Benoit, Foret, and Bouard (1990) compared 11 normal, young subjects (mean age 22.1) on the RTSW and the MSLT and found no differences in sleep latency between the two tests, although the number of sleep onsets was significantly reduced in the RTSW group (Clodore, Benoit, Foret, & Bouard, 1990). However, the trials in which sleep was not initiated for both tests were excluded from the data analysis. Because a greater number of sleep onsets occurred in the MSLT group compared to the RTSW group (59% of all trials v. 34% of all trials respectively) these results are difficult to interpret, particularly since the mean sleep latency was lower in the RTSW group compared to the MSLT group (11.86 min v. 12.55 min).

To assess the effects of a 4-hour afternoon nap versus a no-nap condition on nighttime sleepiness and alertness, Sugarman and Walsh (1989) compared performance on the RTSW, MWT and MSLT between 9:30 p.m. and 7:30 a.m. in seven young (mean age 21.3 years) subjects. The results suggested that the RTSW and the MWT more reliably reflected the benefits of an afternoon nap, because significant differences were observed between the nap/no-nap condition during the RTSW and MWT administrations, but not for the MSLT administrations. However, all three tests were highly influenced by the circadian propensity for sleep, as sleep latencies declined in a linear fashion for all tests in all three conditions

(Sugarman & Walsh, 1989).

The purpose of this study is to assess the association between nighttime sleep parameters and daytime alertness as reflected by the ability to remain awake, rather than the ability to fall asleep in a sample of elderly insomniacs. A second objective is to compare two independent groups of elderly insomniacs on two tests of daytime sleep latency in order to answer the following question: Do differences between the MSLT and RTSW test instructions significantly affect sleep latency values in two independent groups of elderly insomniacs?

Method

Subjects

Fifteen insomniacs (10 Females, 5 Males) participating in a study of behavioral treatments at the City College of New York Sleep Disorders Center were compared to 16 insomniacs (10 F, 6 M) participating in a study of bright light treatment at the Institute of Chronobiology. Subjects in both groups were recruited from newspaper advertisements and from talks to various senior citizen groups in the greater New York metropolitan area. The subjects studied at The City College of New York (CCNY) underwent MSLT testing, whereas subjects studied at the Institute for Chronobiology (IOC), New York Hospital/Cornell Medical Center, White Plains, NY, underwent testing with the RTSW. Subjects were self-described insomniacs who complained of insomnia reportedly lasting a minimum of 6 months. The CCNY subjects were a sub-set, drawn from

the 43 subjects studied in Experiment 2. All CCNY MSLT sleep score sheets were located at the college. While the criteria for nap termination in Experiment 2 was three consecutive epochs of Stage 1 sleep, often subjects obtained a single epoch of Stage 2 sleep. The author re-examined all previously scored MSLTs and selected 15 records that contained Stage 2 sleep. The mean age of the CCNY subjects in this sample was 72.5 (±5) years, compared to 70 (±5) years for the IOC sample. Subjects were not taking hypnotic medications and all subjects were screened for medical and psychiatric illness by a physician prior to entering the study. Although formal psychological diagnoses were not made, an effort was made to insure that potential subjects were not suffering from a current major depressive disorder or significant cognitive impairment.

Procedure

The data reported here were collected prior to treatment, during the baseline evaluation phase of each study. Protocols at the two laboratories were similar. During baseline, subjects slept in the laboratory for three or four consecutive nights. On the day following the third night, daytime alertness was measured with either the MSLT or RTSW. CCNY subjects had a full screening polysomnogram on the first night in the laboratory, while the IOC subjects did not. Bedtimes and waketimes for the CCNY subjects were scheduled according to data obtained from the subject's sleep log filled out two weeks prior to laboratory study. IOC subjects were allowed to freely choose their own bedtime and waketime for each night

in the lab. Nocturnal and daytime sleep was scored according to standard criteria (Rechtschaffen & Kales, 1968). Sleep onset for both groups was defined as the first epoch of stage 2 sleep characterized by the presence of K-complexes and/or sleep spindles. Naps were terminated upon sleep onset to prevent the accumulation of sleep throughout the day. Subjects at CCNY were administered the MSLT according to standard criteria (Carskadon, Dement, Mitler, Roth, Westbrook, & Keenan, 1986). Subjects were put in a darkened room, told to get comfortable, relax, and "try to fall asleep." Naps were begun every two hours, and there were a total of five. The first nap began two hours after wake time. Subjects were allowed to read, watch television, and have meals at their discretion. Caffeinated beverages were not permitted. All 15 subjects completed five nap opportunities. Nap attempts were terminated after twenty minutes if no sleep occurred and a value of twenty minutes was assigned to these naps.

The 16 subjects at the IOC were administered the RTSW at five set times spaced two hours apart during the day (1000, 1200, 1400, 1600, and 1800 hours). At these times, subjects went into a darkened room, were told to get comfortable, lie down, close their eyes and "try and remain awake." Testing was terminated after twenty minutes if no sleep occurred and a value of twenty minutes was assigned to that nap. Sleep onset was defined as the presence of a single epoch of Stage 2 sleep. In practice, subjects usually had 2 to 3 unquestionable epochs of Stage 2 sleep so that

naps were not terminated prematurely.

Data Analysis

All data analyses are post-hoc. Sleep latencies from individual subject RTSW trials were collapsed across 5 naps into a single mean value. To assess the influence of nighttime sleep parameters on the ability to sustain wakefulness, Spearman rank order correlations were performed between several nocturnal sleep variables derived from the third night of sleep recording and sleep latency on the RTSW.

To assess the difference in mean daytime sleep latency between the RTSW condition and the MSLT condition, a non-parametric Mann-Whitney-U-test was employed because the sleep latency data were not normally distributed. To assess whether the groups had similar nocturnal sleep, one-way analysis of variance procedures were performed for objective total sleep time, nocturnal sleep latency, wake after sleep onset (WASO), and sleep efficiency (total sleep time divided by time in bed). The number of trials in which sleep was initiated was tabulated for each group and a Chi-Square analysis was performed. This was done to explore possible differences in the two tests regarding mean latency values versus number of sleep onsets.

Results

The associations between the ability to sustain wakefulness and nocturnal sleep parameters are presented in Table 7. Two measures of sleep continuity were inversely correlated with the ability to sustain

wakefulness on the RTSW. In these subjects a relatively high number of shifts into wakefulness and a high number of waking episodes less than 5 minutes each were associated with a diminished capacity to remain awake. In addition, the number of stage changes was inversely correlated with the ability to remain awake, although the result failed to reach statistical significance. Once again, as in Experiment 2, total sleep time is unrelated to a measure of daytime alertness/sleepiness.

- Table 7 -

Table 7

Correlations Between Sleep Parameters and RTSW Sleep Latency

Sleep Parameter	Correlation Coefficient	p<
Sleep Latency	-.01	NS
Total Sleep Time	.15	NS
Sleep Efficiency % (tst/tib)	-.25	NS
Sleep Efficiency % (tst/spt)	-.13	NS
Intermittent Wake	.18	NS
Stage 0%	-.17	NS
Stage 1%	-.27	NS
Stage 2%	.09	NS
Stage 3%	-.27	NS
Stage 4%	-.38	NS
Stage REM %	.01	NS
Stage Changes	-.43	p=.10
Wake shifts	-.54	$p < .05$
Number of Stage 0 < 5 minutes	-.61	$p < .05$
Number of Stage 0 > 5 minutes	-.08	NS

Results of the comparisons between the MSLT and RTSW

One-way ANOVA's performed on nocturnal sleep latency, nocturnal total sleep time, wakefulness after sleep onset (WASO), and sleep efficiency (SE%) revealed no significant differences between the RTSW and MSLT groups. Below are the means and standard deviations for these nocturnal sleep parameters for each group:

Variable	MSLT group	RTSW group
Sleep latency (minutes)	26 (30)	18 (21)
Total sleep time (minutes)	341 (93)	330 (58)
WASO (minutes)	109 (82)	103 (46)
SE% (percent)	73 (16)	71.5 (12)

A Mann-Whitney-U-test was performed to test the difference in mean sleep latency for each nap separately, and for the grand mean for all five trials. All comparisons were non-significant. The overall mean sleep latency for the MSLT condition was 12.7 minutes (±4.7) and the median was 12.0 minutes. The overall mean sleep latency in the RTSW condition was 15.6 minutes (±4.3) and the median was 16.5 minutes. The nap-by-nap comparisons can be seen in Figure 19.

- Figure 19 -

Figure 19

RTSW and MSLT sleep latency in elderly insomniac subjects.

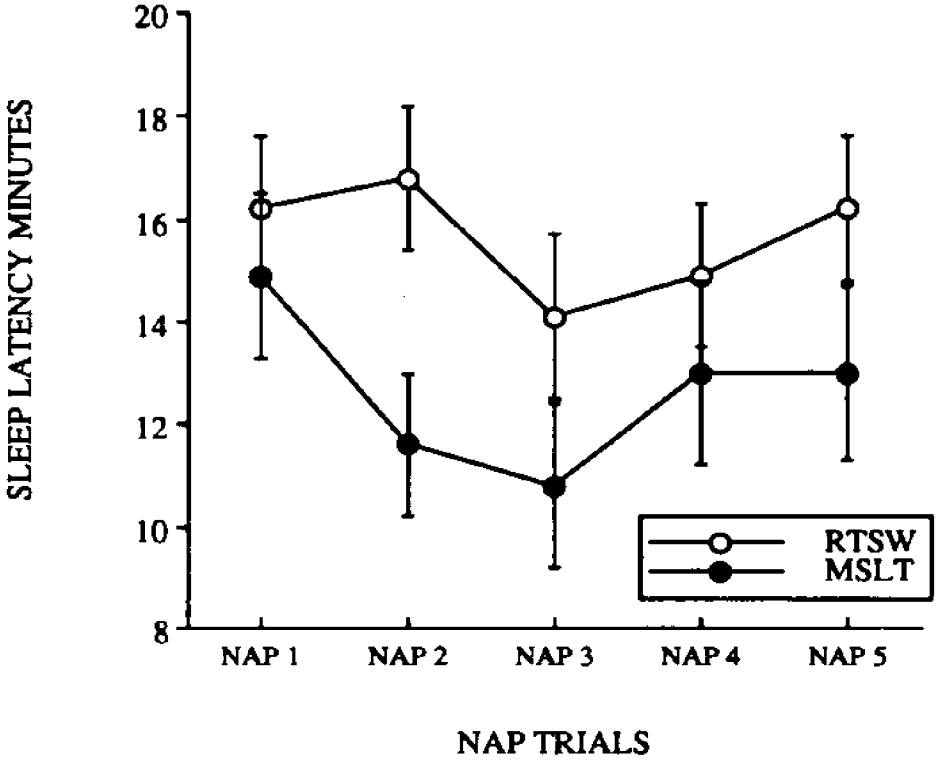
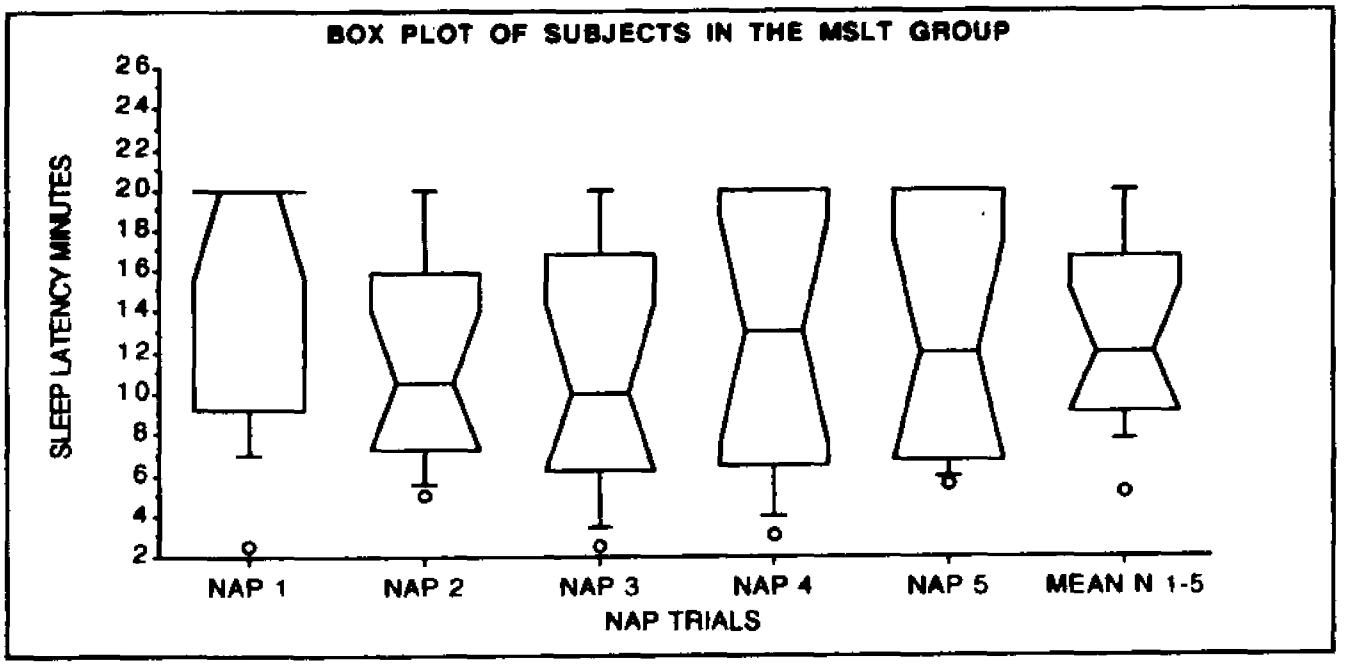
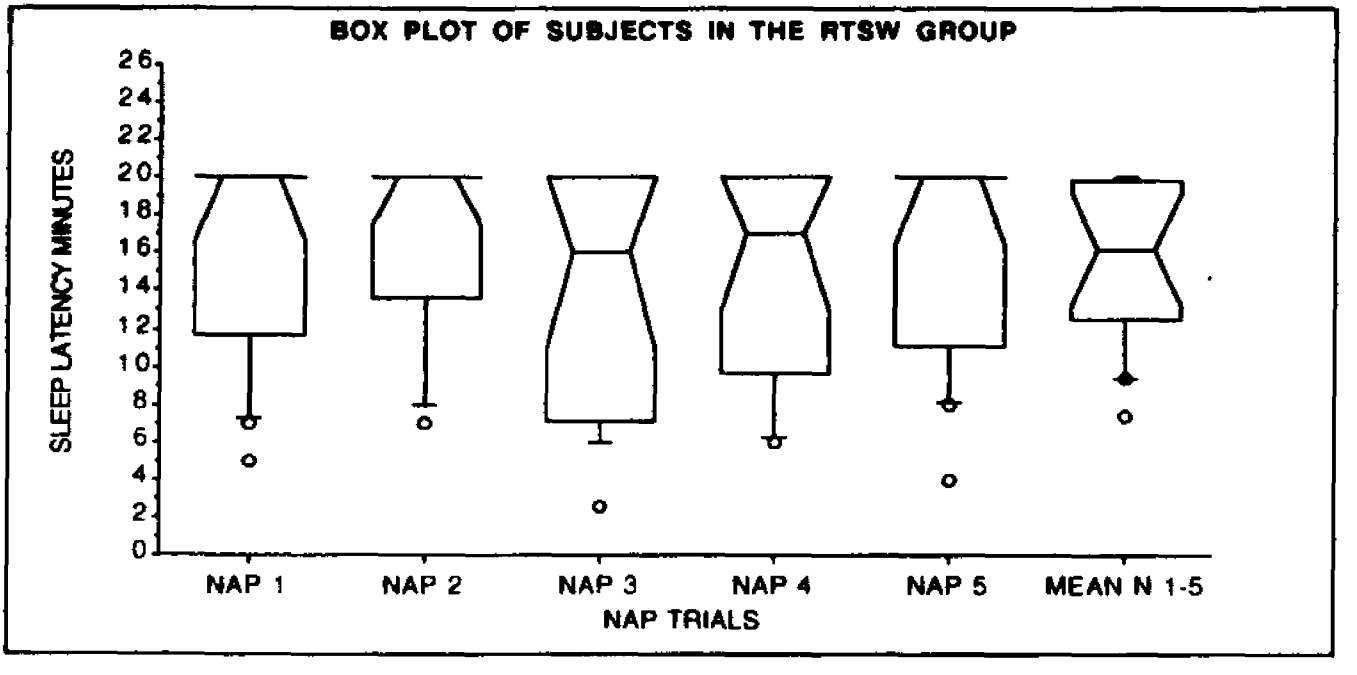


Figure 20 A and B shows the sleep latency data presented as box plots in order to highlight the presence of a ceiling effect in the RTSW condition. The box represents 50% of the distribution and the horizontal line indicates the median values. Four subjects in the RTSW condition did not fall asleep on any trial, while two more had only one trial in which sleep was initiated. The sleep latency value for these two trials was 18 minutes for one subject and 19 minutes for the other. In three of the five trials (naps 1,2, and 5) the median value in the RTSW condition is at the upper limit of 20 minutes, while this occurs only on nap trial 1 in the MSLT condition.

- Figures 20 A and B -

Figures 20 A & B





Three subjects in the RTSW group had mean sleep latencies of less than 10 minutes, while one subject in the MSLT group had a mean sleep latency of less than 5 minutes. Since these values fall into the pathological range these data were excluded and the group data were re-analyzed with 14 subjects in the MSLT condition and 13 subjects in the RTSW condition. Again a Mann-Whitney-U-test was employed. In this analysis instruction had a significant effect on mean sleep latency for nap trials 2, 3 and 5 with RTSW latencies being significantly longer. In addition, the grand mean for all five nap trials in the RTSW condition of 17.2 minutes was significantly longer than the mean observed in the MSLT condition (13.2 minutes). The individual nap means for the RTSW condition and the MSLT condition are presented below.

	Nap 1	Nap 2	Nap 3	Nap 4	Nap 5
MSLT	15.4	12.1	11.4	13.7	13.5
RTSW	17.7	18.0*	16.2*	16.4	17.9*

Mean sleep latency values are in minutes. * $p < .05$ Mann-Whitney-U.

The number of naps in which sleep was initiated was tabulated for each group and a Chi-Square analysis was performed. This was done in order to identify differences in the number of sleep episodes initiated between the two groups. The result ($X^2 = 4.5$) was not significant. The mean

number of sleep onsets per subject in the MSLT group was 3.3 (1.8) and the mean number of sleep onsets for the RTSW group was 2.2 (1.9). Mean sleep latencies were then calculated for each group from trials in which sleep was initiated. The mean sleep latency of 8.8 minutes for the MSLT group is the average of 45 trials in which subjects actually went to sleep; and the mean sleep latency for the RTSW group (10.8 minutes) was similarly derived. Nap trials in both groups that did not contain sleep were discarded.

While significant differences between the MSLT and RTSW were not observed on measures of sleep initiation, an inspection of Table 8 reveals a trend in the expected direction. Across several different methods of analyzing the data MSLT subjects appear to fall asleep more often and more quickly than do subjects who are administered the RTSW.

- Table 8 -

Table 8 MSLT and RTSW values for two groups of elderly insomniacs

	Number of sleep onsets per S.	Number of sleep onsets per trial	Mean latency	Number of sleep onsets (a) and mean latency to sleep onset (b) as a function of time of day				
				N^1	N^2	N^3	N^4	N^5
MSLT								
	3.3 (1.8)	45/75 65.3%	8.8 (4.1)	a) 7	12	12	9	9
				b) 9.1 (4.3)	9.5 (3.8)	8.5 (4.7)	8.3 (4.8)	8.3 (3.5)
RTSW								
	2.2 (1.9)	38/80 47.5%	10.8 (4.8)	a) 7	6	9	9	7
				b) 11.4 (5)	11.5 (5.8)	9.5 (5.1)	10.9 (4.1)	11.3 (5.3)

Discussion

In Experiment 2, nocturnal sleep variables were not associated with daytime sleep tendency in a sample of 43 elderly insomniacs who were administered the MSLT. In a much smaller sample, the present study indicates that nocturnal sleep fragmentation is inversely correlated with the ability to sustain wakefulness. Prior studies with which to compare the present results are lacking. Nonetheless, this result consistent with studies that have examined the effect of sleep fragmentation on daytime alertness using the MSLT protocol (Carskadon, Brown, & Dement, 1982; Stepanski, Lamphere, Badia, Zorick, & Roth, 1984; Stepanski, Lamphere, Roehrs, Zorick, & Roth, 1987). Perhaps in elderly insomnia, alertness, conceptualized as the ability to maintain wakefulness is compromised to a greater extent than sleep tendency.

When all subjects are included in the analysis, instruction had no effect on sleep latency in these two independent samples of elderly insomniac subjects. These results cannot be attributed to differences in age, or total sleep time on the night preceeding daytime testing. Similar results have been observed in narcoleptic patients, normal subjects after a night of sleep deprivation, and in normal subjects whose data were examined exclusively for the number of sleep onsets produced on the MSLT and RTSW (Harste et al., 1982; Clodore et al., 1990).

Four subjects were then excluded from the data analysis based on their extremely low daytime alertness scores. It is possible that the three

subjects in the RTSW condition who had mean sleep latencies below ten minutes also had nocturnal sleep pathology (these subjects were not screened polygraphically for occult sleep disturbance). For example, Mitler et al. (1982) observed MWT sleep latencies of approximately 10 minutes in untreated narcoleptic subjects and Poceta, Timms, Jeong (1992) reported that 40 minute MWT trials yielded a mean sleep latency of 26 minutes in 322 obstructive sleep apnea patients. The sleepiest subject in the MSLT condition had a periodic leg movement index of 22.3 per hour.

When these subjects were excluded, the mean difference of 4 minutes between the two tests was significant and consistent with the difference seen in normal sleepers. Sleep latency is thus influenced by instruction in this population.

Are elderly insomniacs sleepy?

It would not be unreasonable to predict that the reported chronic sleep loss associated with the complaint of insomnia should result in diminished daytime alertness when measured objectively with our current tools of daytime assessment. However, the results of this study do not indicate that the complaint of insomnia is associated with either an increase in sleep tendency, or a diminished capacity to maintain wakefulness. In the present study, the mean MSLT value for 15 elderly insomniacs was 12.7 minutes and the median was 12.0 minutes. Roehrs, Zorick, McLenaghan et al. (1984), observed a mean MSLT score of 9.2 minutes in a sample of normal sleeping subjects between 50 and 59 years of age. Recored total

sleep time for these subjects was 402 minutes. Recorded total sleep time in the present study was an hour less, yet MSLT sleep latency is 3.5 minutes longer. Carskadon (1989) has reported a median MSLT score of 13 minutes in non-complaining elderly subjects between the ages of 60 and 69 years, and a median score of 11.5 minutes in subjects between the ages of 70-79 years. These MSLT sleep latency scores are also consistent with the present results. The mean RTSW score for 16 elderly insomniacs was 15.6 minutes and the median was 16.5 minutes. A grand mean of 16.95 minutes has been observed in non-complaining, young subjects (Hartse et al., 1982). The present results do not indicate that elderly insomniacs are any sleepier than non-complaining elderly, nor do they appear sleepier than normal, young subjects.

These data provide some support for the theory that some individuals with the complaint of insomnia are "short sleepers" who are able to satisfy their biological sleep need with less total sleep during the nocturnal sleep period (Seidel & Dement, 1982). For example, Seidel and Dement (1982) found that 41% of chronic insomniacs had mean MSLT sleep latencies greater than 15 minutes. In an analysis of daytime performance, Bonnet (1985) compared 12 normal and 12 insomniac subjects between the ages of 55 and 71 years and found no differences between the two groups at baseline, or after 64 hours of sleep deprivation on any dependent variable. This observation led Bonnet to suggest that "...a sub-set of older individuals have a decrease need for sleep which is behaviorally

demonstrated as an inability to maintain sleep, but...is defined by the individual as insomnia" (Bonnet, 1985: pp. 332). Support for the theory that the elderly may have a reduced need for sleep, or that they need less sleep to maintain daytime levels of alertness that are within the normal range, comes from a study of subjects in the ninth decade of life. In a group of ten non-complaining subjects between the ages of 80 and 89 years, Brendel, Reynolds, Jennings et al. (1990), found that MSLT sleep latencies were significantly higher in this older group of subjects at baseline and following 24-hours of total sleep deprivation when compared to a control group of 20-year-old subjects. According to the author's, the assumption that older individuals need more sleep than they attain may be overstated. These non-complaining elderly subjects obtained 395 minutes of sleep on nights two and three in the laboratory with a sleep efficiency of 80.8%. MSLT sleep latency was 16.52 minutes.

In the present study, the combination of low sleep efficiencies, the complaint of insomnia, and the lack of daytime sleepiness, suggests that if the primary complaint of the patient revolves around the distress of nocturnal and early morning awakening, then modest sleep restriction may be a viable non-pharmacological intervention in this population (Spielman, Saskin, and Thorpy, 1987). On the other hand, in subjects with diminished alertness, interventions that rely on curtailments of time in bed will likely be counter-productive. Unfortunately, an interesting question that cannot be answered by the present study is the extent to which the complaint of insomnia was based on nighttime sleep disturbance or

daytime consequences.

Perhaps a larger question raised by the present study is the issue of the measurement of daytime sleepiness itself. Neither instrument has been validated in this population and it remains a possibility that these subjects do suffer decrements in daytime alertness, but they are not reliably detected in this population. For example, unpredicted results have recently been found in patients with obstructive sleep apnea (another group of patients who should manifest high levels of objective daytime sleepiness). In patients administered the MWT, a sub-set of patients with extremely high indices of respiratory disturbance (i.e., 40 to 60 per hour), had latencies within normal limits, while others, with much lower indices (i.e., 5 to 10 per hour), were severely sleepy (Poceta et al., 1992). Sangal, Thomas, and Mitler (1992) administered the MSLT and MWT to 258 patients with the complaint of excessive daytime sleepiness, including patients with sleep apnea, narcolepsy, depressive disorders, and subjective complaints without objective findings. While as predicted, many subjects exhibited pathological levels of daytime sleepiness on both tests, some subjects were observed to be *discordant* on the two tests. For instance, some subjects were able to follow instructions: when asked to fall asleep they were able to do so rapidly, and when asked to maintain wakefulness they were able to do so at levels corresponding to normal control values. In this situation are you measuring sleepiness/alertness, or some behavioral or psychological trait that motivates patients to follow the

experimental instructions? Conversely, some patients were unable to follow instructions: when asked to fall asleep they were unable to do so rapidly and they were unable to maintain wakefulness for longer than 10 minutes. Here again it is unclear as to what is actually being measured. Is it physiology or psychology? It is extremely hard to believe that the MSLT only measures physiological sleep tendency, if some obstructive sleep apnea patients, who complain of severe daytime sleepiness, cannot fall asleep rapidly when asked to do so.

Why this discordance exists is not explained by the authors, except for the speculation that "various diagnostic entities may differentially affect brain mechanisms of sleep tendency and maintenance of wakefulness" (Sangal, Thomas, and Mitler, 1992; pp. 901). Data from the present experiment does not allow us to address this question because subjects were only administered one or the other daytime tests. However, the observation of discordance in a large sample of subjectively sleepy patients leaves open the possibility than our current tools of assessing daytime sleepiness, or alertness are "impure" measures. In otherwords these tests measure more than the brains readiness to fall asleep, or it's ability to maintain consciousness. Perhaps in some of the elderly subjects studied here, daytime levels of alertness, would be characterized as reflecting discordance. Some may be sleepy, yet possess an ability to remain awake if asked to do so, or some may be sleepy yet have difficulty falling asleep on the MSLT

The present post-hoc analysis must be considered to be preliminary. Future studies that are designed to evaluate daytime function may well consider increasing the upper limit of testing to 40 minutes in order to eliminate the observed ceiling effect. Many patients with obstructive sleep apnea have can stay awake for 20 minutes, while reporting profound levels of daytime sleepiness (Poceta et al., 1992). Differences in daytime sleep latency may become more apparent in this population in a parallel design that assesses both the ability to fall asleep and the ability to maintain wakefulness. The response to sleep deprivation and the reponse to recovery sleep may also provide further clues to the nature of daytime sleepiness and alertness in elderly subjects who complain of sleep disturbance.

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