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Is the Nap Zone Controlled by a Light Sensitive Circadian Arousal Process?

by Susanne Krupa

**Thesis submitted to the Faculty of Graduate Studies
and Postdoctoral Studies of the University of Ottawa in
partial fulfillment of the requirements for the Doctoral of
Philosophy Degree, in Clinical Psychology (Neuroscience
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Abstract

This study attempts to identify the mechanism of the so-called afternoon nap zone. More specifically, it investigates a recent proposal that the afternoon nap zone represents the point in time after morning awakening when process-S has increased to a sufficiently high level to facilitate sleep onset, while at the same time an SCN-controlled circadian arousal process has not yet risen high enough to reverse this increased sleepiness.

Eight normal male subjects aged 20-30 years, were monitored on two separate occasions under low ambient light (150 lux). Night sleep hours were maintained at 23:00-06:00h. PSG monitoring included EEG (C3-A2, O2-A1), right EOG-M1, left EOG-M2, submental EMG and core body temperature recorded continuously by a combination of the Oxford Medilog 9000 8-channel ambulatory recorder and the Minilogger temperature monitoring system. Following a baseline 24-hour day, bright light stimulation (10,000 lux) was given on two consecutive days either in the evening (20:00–22:00h) or morning (06:00–08:00h) in counter-balanced fashion with a 30 day washout periods between. Other than during a period of bright light stimulation, the level of daytime arousal was assessed every 60 min by quantified EEG spectral power followed by a 10 min duration simple reaction time test.

In the baseline condition both the performance and Q-EEG variables confirmed the presence of a transitory afternoon nap zone as indexed by the

timing of poorest performance and of greatest spectral power in a number of Q-EEG measures. Evening bright light treatment phase delayed these nap zone measures. Conversely, morning bright light phase advanced these measures.

The finding that the timing of poorest performance and of the Q-EEG determined nap zone can be phase delayed by evening light and phase advanced by morning light supports the hypothesis tested, as well as supporting the existence of an SCN- dependent circadian arousal system in humans similar to that described by Edgar et al. (1993) in sub-human primates.

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Is the Nap Zone Controlled by a Light Sensitive Circadian Arousal Process?

Disregarded until the late 1970's, excessive daytime sleepiness (EDS) has more recently been brought to the forefront of scientific and public awareness. Books, articles and television programs have focused on related concerns with increasing frequency. Industrialization has led to around the clock work schedules that few can entirely escape during their working lives. In the United States this trend has doubled in the past 20 years. Society is becoming more and more aware of the risks that sleepy people pose at work, on the roads and even at home.

Over the past several decades there have been some major industrial catastrophes that have been associated with worker fatigue and excessive sleepiness. The Chernobyl nuclear disaster, the worst in history, occurred at 01:25. Human error, later attributed to fatigue and sleepiness, led to highly radioactive materials drifting across Europe spreading contamination. The total count of those killed or injured will never be known.

A similar incident occurred in the United States at the Three Mile Island facility in Pennsylvania, between the hours of 04:00 and 06:00 when workers who just that day had rotated from the day shift to the night shift, failed to notice that a valve was stuck (Mittler, 1988). A major loss of core

coolant water resulted leading to the near melt down of the reactor, which was only narrowly averted. These examples demonstrate what a high price society may have to pay for pushing workers beyond their human biological limitations in regards to sleep.

Perhaps the most devastating result of sleep loss is its subtle effect on vigilance. Drowsy people make mistakes and miss things which they would never do if alert. Fatigue and sleep deprivation are commonly associated with human errors that result in transportation accidents. According to the U.S. Congress Office of Technology Assessment (1991), an average of between 4000 and 5000 fatalities occur each year in accidents involving tractor-trailer trucks. Of the fatalities due to heavy truck accidents, about 80% of those killed are pedestrians or occupants of other vehicles (U.S. Congress, Office of Technology Assessment 1988). The National Transportation Safety Board (NTSB) says that sleepiness is the most frequently cited (31%) apparent probable cause of death in heavy truck accidents that were fatal to the driver (National Transportation Safety Board, 1990).

As Dement and Carskadon (1982) have stated: "Alertness is one of the most important dimensions of human function." It has become of crucial importance to better predict those periods at risk for undesired sleepiness or overt sleep attacks. The present study addresses the little understood transitory period of afternoon sleepiness, the so-called afternoon "nap zone."

Chapter I will consider performance fluctuations during the day, the means available for assessing alertness/sleepiness levels, circadian rhythms and light stimulation, circadian models of sleep/wake regulation, and evidence for an endogenous origin of, and proposed mechanisms for, the afternoon nap zone. It concludes with a statement of the theoretical hypotheses of the study. Chapter II describes the method by which one of these hypotheses has been tested. Chapter III presents the results. These are then discussed in Chapter IV.

CHAPTER I

REVIEW OF THE LITERATURE

When following the usual pattern of nocturnal sleep, we regularly experience a temporary period of increased sleepiness in the mid-afternoon. This period is most commonly referred to as the "nap zone" and throughout the discussion will be referred to as such.

Decreased Performance Occurs at Certain Times of Day

It has been shown that, whether or not we have adequate prior night sleep, there is an increased sleep tendency and a diminished capacity to function at certain times of the day. For example, errors at work have shown two peaks, one in the middle of the night and the second in the mid-afternoon

(Bjerner, Holmes, & Swenson, 1955; Browne, 1949; Hildebrandt, Rohmert, & Rutenfranz, 1974). Studies of single vehicle car accidents that have been judged as fatigue related have been shown to peak at certain times. A major peak occurs between 12:00 midnight and 07:00 , and a secondary one occurs between the hours of 01:00 and 04:00 pm (Lavie, Wollman, & Pollack, 1986).

It has also been shown that the nap zone involves a transitory decrease in performance for measures sensitive to sleepiness (Hockey & Colquhoun, 1972). The possibility that food intake causes this so-called "post-lunch dip" in performance of Blake (1967) has not been supported. Blake varied both the time of lunch and of performance testing and found no difference in performance when lunch was delayed by as much as two hours from the usual food intake.

Similar decreases in mid-afternoon performance have been reported in other studies. Browne (1967), for example, found that the time taken to detect a light signal presented in a car driver's rear view mirror varied with time of day in much the same way as in the majority of Blake's experiments.

It has become evident over the years that certain problems are inherent in research into alertness in human performance. Blake (1971) was able to demonstrate this clearly when subjects were given a letter cancellation task. He found that the introduction of an incentive greatly reduced the normal variation in performance over the day. A technique which was particularly effective was to announce the scores of each subject immediately after the

task was completed. This produced a spirit of competition and increased the subject's interest in the task. As a result the usual mean time- of- day variation in performance was reduced to a non-significant level. In order to circumvent this problem, Wilkinson (1961, 1969) successfully demonstrated that tasks become increasingly sensitive to periods of decreased arousal as a function of the number of times they are administered across the test day. Presumably, the effect of repetition either leads to a decrease in efficiency ("fatigue") or removes the challenge by fostering habituation to the familiar event or situation.

Not only should all aspects of the testing situation be such as to minimize the effects of motivation, but the tasks themselves should also be as devoid as possible of interest value. This was demonstrated in a study by Wilkinson (1964) showing that after 50 hours of sleep deprivation, subjects could perform for an hour without degradation on complex and interesting tasks such as a "battle game". Whereas performance suffered increasingly with greater complexity on other tasks involving choice, the stimulating nature of the battle simulation offset these effects. Summarizing his findings, Wilkinson (1969) concluded that in order for the effects of sleepiness to become evident, performance tasks must not be stimulating in nature and that, optimally, the tasks should last for at least thirty minutes and preferably one hour, be monotonous, and lack in incentive.

Following these initial pioneering performance studies, it has been found that certain tests of quite short duration can be sensitive to the effects of sleepiness. These tests were also developed by Wilkinson at the Applied Psychology Unit, Cambridge, and include the four choice serial reaction time test and a simple visual reaction time test. These tests have been shown to reflect deterioration in performance within 5 minutes on task (Wilkinson & Houghton, 1975). More recently, such work has led to the appearance of relatively brief (approximately 10 min), portable and computer based performance measures, including both the simple and choice reaction tests (Glenville, Broughton, Wing, & Wilkinson, 1978; Godbout & Montplaisir, 1986). Simple reaction time tests have a more rapid learning curve than do the complex tests, and so they are better suited for repeated testing. Both tests have proven to be sensitive detectors of sleepiness (Glenville et al. 1978; Herscovitch & Broughton, 1981).

Quantitative EEG: An Objective Measure of Vigilance

Visual analysis of the EEG is a sensitive measure of alertness/drowsiness levels in wakefulness and has been traditionally used for sleep staging. EEG waves are commonly divided into four groups or bands by frequency: delta, theta, alpha, and beta. Alpha is defined as 8-12 Hz activity. The alpha rhythm is a posteriorly and often relatively symmetrically distributed sinusoidal rhythm with a typical amplitude of 20-50 μ V in awake normal

individuals after the age of 10 years. Alpha is seen most clearly while the individual is comfortably resting awake with eyes closed; and it "blocks" (attenuates) with eye opening. The alpha rhythm is usually maximum over both occipital head regions with a field distribution usually extending to parietal and posterior temporal areas, often with somewhat greater amplitude on the right side. Beta defines the frequency band above 13 Hz and its amplitude is usually below 15-20 μ V. Beta activity is typically symmetrically distributed over frontal and central areas. Theta activity defines the frequency band of 4 to 8 Hz and its amplitude is normally less than 20-30 μ V. Theta appears in, or is increased in, drowsy normal subjects as the alpha rhythm disappears. Delta is activity of less than 4 Hz and can be of high amplitude. During slow wave sleep stage 3 and 4 sleep, delta becomes the most prominent frequency.

The EEG component of polysomnographic recordings is traditionally derived from a single central scalp electrode referred to a relatively inactive location (ear-lobe, mastoid) as recommended in the standard sleep staging manual of Rechtschaffen and Kales (1968). However, variations and additions to this single electrode montage have appeared intermittently in the literature and are usually made for practical reasons or to monitor unique aspects of brain wave activity that are not present at the central lead. For instance, ambulant recordings often include the contralateral central electrode, which is frequently used as a backup for the designated lead should it become loose in the field (Broughton, Dunham, Newman, Lutley, Duschesne, & Rivers, 1988;

Sharpley, Solomon, & Cowen, 1988). With respect to the prior physiological considerations, studies involving transitional sleep states, such as sleep onset and arousal phenomena, have often included an occipital lead in order to monitor fluctuations of the EEG alpha rhythm (Broughton, Dunham, Weisskopf, & Rivers, 1994; Corsi-Cabrera, Ramos, Arce, Guevara, Ponce-de Leon, & Lorenzo, 1992; Gastaut & Broughton, 1965; Johnson, Lubin, Naitoh, Nute, & Austin, 1968; Matousek & Petersen, 1983; Torsvall & Akerstedt, 1987).

The ability to detect subtle changes in EEG can be accomplished by using computer quantification techniques. Quantitative EEG is the mathematical processing of digitally recorded EEG in order to analyze specific waveform components, transform the EEG into a format or domain that elucidates relevant information, and produce numerical results of various EEG parameters for subsequent review or comparison. During recent years power spectral analysis has become the most frequent means to study quantified EEG changes in drowsiness and alertness (Belyavin & Wright 1987; Matousek & Petersen 1983, Torvall & Akerstedt 1987).

The appearance of the computer equipped with physiological data entry and storage capacities enabling laboratory processing, as well as the introduction of the Fast Fourier Transform (FFT), have made it possible to analyze diverse kinds of EEG data. FFT is a mathematical transformation procedure designed to evaluate stationary processes in a time series of data

by generating a sine/cosine decomposition of the time series. It assumes that a complex wave can be accurately described by a series of sine/cosine statements or values that vary in magnitude and phase and thus combine to create the signal data. Power changes in a specific frequency range can reflect changes in abundance and even in frequency of events within the constituent frequency bands. For example, the alpha frequency band ranges from 8-12 Hz. If the alpha rhythm becomes slower, as can occur in drowsiness, and its peak frequency goes below the alpha range, the spectral power in the alpha band will decrease. In power spectral analysis, each of the chosen frequency bands is given a power value, which is the square of the voltage amplitude provided by the FFT. The resulting spectral power is expressed typically in μV^2 and is integrated and averaged across the frequency ranges of interest for selected EEG epochs. Spectral analysis provides an efficient quantification of overall broadband rhythms present in an EEG epoch.

A need to assess the alertness/sleepiness level of a subject often arises in different types of studies. Subjective estimation is frequently unreliable because feelings like alertness or sleepiness are poorly defined. Subjective estimation is accordingly of limited value, if different situations, or different subjects, are to be compared.

Furthermore, sleep latency tests such as the Multiple Sleep Latency Test (MSLT) do not measure alertness but rather the propensity to fall asleep,

which itself reflects a combination of sleep pressure and ability to fall asleep. The MSLT is based on the assumption that "those individuals who are sleepy will fall asleep more quickly than those who are not" (Hartse, Roth, & Zorick, 1982). This might be true in general, but there are several exceptions. For example, after head injury the ability to fall asleep may be impaired and may cause an increase in sleep latency (Manseau & Broughton, 1990). The level of anxiety in sleep deprived insomniacs can also lead to prolonged sleep latencies (Stepanski, Zorick, Roehrs, Young, & Roth, 1988). In some rested normal subjects learning/conditioning factors facilitating sleep onset may lead to unusually short sleep latencies (Broughton, 1994)

Quantified EEG, on the other hand, appears to provide a direct and "pure" measure of alertness (i.e., one unaffected by motivation). Borbély, Bauman, Brandeis, Strauch and Lehmann (1981) found that following one night of sleep deprivation the spectral power using an ipsilateral fronto-occipital bipolar increased in all bands with the exception of beta (15-17Hz). Corsi-Cabrera, Ramos, Guevara, Ponce-de Leon, Lorenzo, (1992) found that after sleep deprivation the awake EEG shows an increase in spectral power for theta, alpha and beta frequency bands recorded from C3, C4, T3, T4, P3, P4, and O1 derivations in both the eyes open and eyes closed conditions. Brunner, Dijk, & Borbély, (1993) reported that after sleep deprivation significant changes in the delta and alpha ranges were obtained from the C3 and C4 derivations in both the eyes open (while fixating) and eyes closed

conditions. Power densities in their high delta band (3.75-4.5 Hz) were significantly increased and in the alpha range (9.25-10 Hz) were decreased. Studies in our laboratory (Yan, Rivers, Boucher, & Broughton, 1998) found that sleep deprivation in normal subjects mainly increased absolute power in the theta range of the waking EEG and to a lesser extent in the high delta band, changes which correlated negatively with sleep latency on MSLT.

In a more recent study the EEG of eight normal subjects was recorded from several electrode sites (FC1, FC2, CP1, CP2, PO1, PO2, CZ, C3) with both eyes open and eyes closed every three hours over 40 hours of prolonged wakefulness (Finelli, Baumann, Borbély & Achermann, 2000). All subjects in this study showed an increase in theta with a maximum increase at FZ and a minimum at CP2. Furthermore a strong negative correlation between subjective alertness and theta was found over the 40-hour trial. Finelli et al., (2000) also found changes in other frequency ranges which correlated negatively with subjective alertness but to a lesser extent than did the theta frequency range.

Other studies have suggested that EEG power density increases in theta and alpha frequencies across prolonged periods of wakefulness (Akerstedt & Gillberg 1990; Akerstedt, Kecklund & Knutson, 1991; Torsvall & Akerstedt 1987). For example, Akerstedt and colleagues analyzed either the Cz or O2 electrode sites using a 4-channel Medilog recorder; all subjects were normal workers, working under real-life conditions. They found that the

spectral power in the theta and low alpha bands were the most sensitive EEG measures reflecting diminished alertness, proneness to accidents and decreased performance (Akerstedt & Gillberg 1990; Akerstedt et al. 1991; Torsvall & Akerstedt, 1987). Similar quantified EEG changes have been described in patients with excessive daytime sleepiness (Matousek, 1988).

Cacot, Tesolin, and Sebban (1995) studied 9 non- sleep deprived subjects during the daytime. They analyzed 16 electrode sites averaged for anterior frontal, fronto-temporal, posterior-temporal, occipital, sagittal, and central locations, with both eyes open and closed in 1 Hz frequency bands from 1-30 Hz. They showed a temporary increase of spectral power in all frequency bands during the afternoon, followed by a reduction in the late afternoon-early evening period, with again an increase occurring shortly prior to sleep onset. The maximum overall power was reported from the central sites.

Lafrance and Dumont (2000) studied 16 non- sleep deprived subjects during the day. EEG was recorded from, C4, C3, O1, O2, every two hours with eyes open. They found a negative correlation between the theta band and subjective alertness scores. In other words as subjective alertness decreased spectral power in the theta band increased. Furthermore they showed that subjective alertness and sleep latencies decreased in the middle of the day with an associated increase in theta at approximately the same time of day. Inversely, Niedermeyer (1993) states that increasing alertness within

wakefulness induces a reduction of theta and alpha frequency activities leading at times to a "low voltage fast" EEG.

Several studies have examined changes in EEG over a 40-hour period of prolonged wakefulness using a constant routine protocol, which minimizes factors that mask the endogenous rhythm (Aeschbach, Matthews, Postolache, Jackson, Giesen, & Wehr, 1999; Cajochen, Brunner, Krauchi, Graw, & Wirz-Justice, 1995; Dumont, Macchi, Carrier, Lafrance & Hébert, 1999).

Recording from the C3 and C4 derivations with eyes open and fixated Cajochen, et al., (1995) reported that the spectral power value for theta and alpha frequency bands increased during sustained wakefulness at 3 hrs, 10hrs, 34hrs, and 37hrs. They further reported a temporary peaking in spectral power occurring mid-afternoon, which decreased prior to the time of evening sleep onset. Aeschbach, et al., (1999) examined the EEG recorded from the C3 and C4 derivations with eyes open in 19 subjects during prolonged wakefulness. In order to more clearly interpret the wake-dependent and circadian processes they fitted both a 24-hour cosinor curve-fit and a saturating exponential component to the power densities. They found significant changes in the theta range reflecting both a circadian and a wake dependent process, whereas in the high alpha range only a circadian component was present.

Dumont, et. al., (1999) in a similar protocol of prolonged wakefulness examined the EEG recorded from the C3, C4, O1, and O2 sites with eyes

open and fixated for four minutes every two hours throughout the trial. These researchers chose non-traditional frequency bands and divided the 1 Hz frequency bands into five separate clusters based on their time course and compared these clusters to subjective sleepiness. Cluster 1 (2.00-7.75 Hz), Cluster II (8.00-10.75 Hz), Cluster III (11.00-14.75 Hz), Cluster IV (15.00-17.75 Hz), Cluster V (18.00-24.75 Hz). Comparable time courses were noted for Cluster I and Cluster III: both increased throughout the trial with a mid-afternoon peak and a dip in the middle of the night. Cluster II also showed an increase in the mid-afternoon with a decrease in the middle of the night. Cluster V was most strongly correlated with subjective sleepiness. Cluster I and Cluster III were the next most highly correlated and, like Cluster V, showed positive correlations.

Circadian Rhythms and Light Stimulation

Circadian rhythms are endogenously generated oscillations with a period of approximately 24 hours. In respect to sleep/wake status and core body temperature these biological oscillations are normally entrained (synchronized) mainly by the environmental light-dark cycle. This entrainment is critical for the circadian system responsible for generating these oscillations to function adaptively as a time-keeping system for the organism.

Researchers recognized the close connection between light stimuli and animal behavior decades ago. The physiology of vision is also well

understood. Light enters the eyes and stimulating the retina. From the retina signals are transmitted to the visual relay nuclei and cortex of the brain, thereby producing sight. Some neural signals are also transmitted from the retina to the hypothalamus with most, but not all, terminating in the suprachiasmatic nuclei (SCN) (Klein, Smoot, Weller, Higa, Markey, & Greed, 1983; Moore, 1983; Pickard & Silverman, 1981). Research has demonstrated that the SCN complex is a fundamental component of the biological clock, and is an endogenous oscillator which contributes to the regulation of the body's physiological and behavioral rhythms (for reviews, see Meijer & Rietveld, 1989; Rusak & Zucker, 1979). Light has been clearly shown to be the primary stimulus in the regulation of the circadian system. Other stimuli such as temperature, food intake, environmental sound, social cues and activity levels also contribute to the body's rhythms (Czeisler, Allan, Strogatz, Ronda, Sanchez, Rios, & Freitag, et al., 1986; Lewy, Sack, Miller, & Hoban, 1987; Minors, Waterhouse, & Wirz-Justice, 1991).

The means by which the SCN exerts its influence over circadian rhythms has been clarified by research which demonstrates that the retinal information is relayed directly to many of the body's major systems (Moore, 1983). Non-visual photic information has been shown to be transmitted by a neural pathway from the SCN complex to the pineal gland with connections being made consecutively to the paraventricular hypothalamus, the upper thoracic intermediolateral cell column, and the superior cervical ganglion (Klein

et al., 1983; Moore, 1983). Dark and light cycles are transmitted by the retina to the SCN and control the rhythmic secretion of melatonin by the pineal gland. In mammals high levels of melatonin are secreted during darkness and low levels during the light (Lynch, Jimmerson, Ozaki, Post, Bunney, & Wurtman, 1978; Reiter, 1981; Vaughan, Bell, & De La Pena, 1979; Wetterberg, 1978). It has also been shown that exposing the retina to light even during the dark cycle can substantially reduce the secretion of melatonin (Klein & Weller, 1972).

Initially studies on humans failed to demonstrate the sharp suppression of melatonin production by light which earlier had been demonstrated in other mammals. Despite previous negative findings, Lewy, Wehr, Goodwin, Newsome and Markey (1980) conducted a study using 6 normal volunteers who were exposed to 2,500 lux of light during the night. They found that melatonin decreased within the first 10 to 20 minutes following light exposure and reduced to daytime levels within 60 minutes. On the other hand melatonin levels remained relatively constant when subjects were exposed to 500 lux of light during the same time of the night. They concluded that light has a suppressive effect on human melatonin levels, if the intensity is increased to a substantially higher level than that needed to suppress melatonin in other mammals.

The 1980 study by Lewy et al., (1980) led to further important research into the biological responses of humans to bright artificial light including those

of Czeisler, et al., 1986; Czeisler, Johnson, Duffy, Brown, Ronda, & Kronauer, 1990; Eastman, 1990; Lewy, et al., 1987; Minors, et al., 1991. These studies demonstrated that bright light (>2500 lux) also provides a potent stimulus for other elements of the circadian system. For example, a further finding was that timed exposure to bright light could shift the phase position of the circadian system (K. Honma, S. Honma, & Wada, 1987; Wever, Polasek, & Wildgruber, 1983).

The magnitude and direction of these phase shifts, however, are dependent on a number of factors. Firstly, change can be augmented by the intensity or duration of light exposure: secondly the phase shifts can be enhanced by the timing of the light exposure on the circadian phase. This interaction is termed the phase response curve (PRC). Czeisler, Richard, Kronauer, Allan, Duffy, Jewell, Brown, Ronda, (1989) using a constant routine protocol and exposing fourteen subjects to five hours of bright light (7000-12000 lux) constructed the first human phase response curve equivalent to that which had been documented in other animals (Daan & Pittendrigh, 1976). They found that the greatest shift occurred when light exposure was close to the temperature minimum. Light exposure after the minimum produced a phase advance and light exposure before the minimum produced a phase delay. They reported that the smallest shifts occurred when light exposure was administered 180° from the temperature minimum.

Phase shift using bright light has now been widely documented in human studies. For example, Drennan, Kripke and Gillin (1989) induced a three hour phase delay in nine healthy volunteers by exposing them to five hours of bright light (3,800-6,000 lux) on three consecutive evenings starting at 18:00 and ending at 23:00 hours. Lack and Wright (1993) phased delayed the circadian core temperature by two to four hours in insomniacs with early morning awakening and delayed their wake up time by one hour. In their protocol they exposed their patients to four hours of bright light (2,500 lux) from 20:00-24:00 hours on two successive evenings.

Dijk, Beersma, Daan, & Lewy, (1989) induced a one hour advance in eight healthy male subjects. In their study the eight subjects were exposed to three hours of bright light (2,000 lux) on three consecutive mornings between the hours of 06:00 and 09:00. Rosenthal, Vanderpool, Levendosky, Johnston, Allen, Kelly, Souetre, Schultz, et al., (1990) phase advanced the circadian core body temperature by two hours in delayed sleep phase syndrome (DSPS) patients. In their protocol the DSPS patients were exposed to bright light (2,500 lux) for two hours in the morning between the hours of 6:00 and 9:00 for a period of two weeks. Czeisler, et al., (1988) demonstrated that 3 mornings of light exposure at about 10,000 lux for 4 to 5 hours resulted in a phase advance of 3 hours in a patient with delayed phase sleep syndrome.

Campbell and Murphy (1998) suggested that bright light exposure to body areas other than the retina may also influence circadian rhythms. These

authors used light exposure behind the knee. However, in a study attempting to replicate these findings, Wright and Czeisler (2002) found that, when no light was permitted to enter the eyes, exposing the posterior knee area to light had no effect.

Investigation of the effect of bright light therapy on the human circadian rhythm requires accurate and complete assessment. Trials carried out in humans to assess initial and final rhythm states have looked at a number of additional variables to those of sleep such as core body temperature, cortisol, and melatonin levels. Core body temperature has been recognized as the most accurate marker of the endogenous circadian oscillator (Czeisler et al., 1986, 1989; Wever, 1979). However, the reliability of this indicator is weakened by other significant factors that ordinarily affect ("mask") core temperature such as sleep, activity, food intake, and postural changes (Barret, Lack, & Morris, 1993; Kleitman & Doktorsky, 1933).

A constant routine protocol can expose the underlying endogenous rhythm by lessening or removing some of these factors that mask this rhythm (Czeisler, Brown, Ronda, Kronauer, Richardson, & Freitag, 1985). In this protocol subjects are placed in bed in a semi reclined position and kept awake for approximately 36 hours. Light exposure is kept constant and dim at approximately 150 lux, and food intake is taken in evenly by dividing meals into small hourly snacks (Czeisler et al., 1989, 1990). This method permits

accurate assessment of circadian phase and amplitude (Brown & Czeisler, 1992).

Nevertheless, some prudence may be justified when interpreting the results, taking into account that subjects are required to abstain from sleep for 36 hours. Another technique has been used to even better reveal the nature of the endogenous circadian rhythm which is called "forced desynchronization". This technique involves subjects following a sleep/wake cycle which is outside of the period range of entrainment of the circadian rhythm (Wever, 1979). The protocol requires that subjects live in the laboratory for an extended period of time with no external time cues and low levels of light. In a common version of the protocol subjects follow a 28-hour sleep/wake cycle staying in bed to sleep for approximately 9 hours (i.e., one third of the 28-hour "day") and then staying awake for the remaining 19 hours. As the period of the circadian rhythm remains at or near the 24-hrs, over time this places sleep/wake states across all points of the circadian rhythm and helps unmask the latter. Circadian phase is assessed after three baseline days and again at the end of the protocol. The protocol also enables the assessment of the circadian variation of alertness and performance measures across the wake portion of the circadian rhythm without the powerful interfering effects of sleep deprivation that are present, for example, in the constant routine paradigm.

Does Bright Light Exposure Interfere with Subsequent Sleep?

That light has an alerting effect has long been recognized and dates back to the use of bright light treatment for seasonal affective disorders (Rosenthal, Sack, Gillin, Lewy, Goodwin, Davenport, Mueller, et al., 1984). Bright light exposure, by increasing alertness, might be expected to have harmful effects on quality of subsequent sleep. However, in a number of studies following bright light exposure, subsequent sleep remained unchanged or actually improved. For example, Campbell and Dawson (1990) exposed subjects to bright light throughout the night from 23:00 to 07:00 and found that subjects exposed to bright light performed better on a performance battery than subjects in the dim light condition while their subsequent sleep remained unaffected. Czeisler, et al., (1990) also found that bright light exposure improved both shift workers' alertness at night and their sleep quality during the day. Matsumoto, Kamata, & Muto, (1995) noted an increase in sleep propensity following all night bright light exposure in five healthy young males.

Similar results were reported in studies involving partial night exposure to bright light. For example, Thessing et al., (1994) found that following four hours of bright light, performance improved in all subjects whereas their sleep remained unaffected. However, no effect was noted on either measure following only two hours of bright light exposure. Badia, Myers, Boecker and Harsh (1991) found that exposing subjects to bright light during part of the

night improved subjects' performance whereas later sleep remained unaffected.

In general comparable results have been reported in studies that exposed subjects to bright light prior to sleep onset. For example Bunnell et al., (1989) exposed five subjects to two hours of bright light (2,500 lux) just prior to sleep onset. They found that sleep latencies were not significantly delayed after two consecutive evenings of light exposure. On the other hand, Dijks, Cajochen and Borbely, (1991) reported that sleep latencies were delayed by an average of 4 to 20 minutes in subjects exposed to three hours of bright light (also 2500 lux) versus subjects in the dim light control group.

Finally in nursing home studies where sleep difficulties are prominent, the main contributing factor seems to be a lack of light. This is supported by a number of studies which have shown that increasing the illumination levels improves sleep quality. For example Shochat, Martin, Marler and Ancoli-Israel (2000) monitored the light exposure in 77 institutionalized elderly individuals and found that patients with more time exposed to greater than 1000 lux of light had fewer awakenings at night. Furthermore Mishima, Okawa, Hishikawa, Hozumi, Hori and Takahashi, (1994) exposed elderly patients with behavioral disorders to four weeks of light therapy and found that both sleep and behavior improved following light exposure. Satlin, Volicer, Ross, Herz and Campbell (1992) reported similar improvement in inpatients with Alzheimer's disease.

In summary, bright light in general seems to have an overall beneficial rather than detrimental effect on sleep, behavior and performance.

Models of Circadian Sleep/Wake Regulation

Currently mathematical models of sleep/wake regulation exist that account for the patterning of the major sleep episodes observed during temporal isolation (Borbély, 1982; Daan, Beersma, & Borbély, 1984; Kronauer, Czeisler, Pilato, Moore-Ede, & Weitzman, 1982). In general these models have neglected to incorporate the nap zone which is the focus of this thesis. For example, the Borbély-Daan-Beersma 2-process model of sleep/wake regulation combines a homeostasis sleep process (process-S) with a circadian process (process-C) (Borbély, 1982; Daan & Beersma, 1983; Daan et al., 1984). In this model process-S is said to increase exponentially with accumulating wakefulness across the daytime and decrease exponentially across the night sleep period. The homeostatic component is believed to be reflected in the spectral power of NREM sleep slow wave (0.75-4.5 Hz) EEG activity, and would increase across wakefulness and decrease during sleep. Process-C in this model reflects a clock-like mechanism expressed as the alternation of cyclic periods of high and low sleep propensity which, exists independently of prior sleep and waking. The circadian component is believed to be indexed by the core body temperature with increased sleep propensity occurring at times of lowered body temperature and visa versa.

Dijk and Czeisler (1995) clearly demonstrated the interaction of process S and process C. They studied 8 subjects for a period of 33-36 days. During the first three days of the protocol subjects were permitted to sleep at their regular time. Immediately following the third night subjects followed a 40-hour constant routine protocol, which was repeated just prior to the end of the study. During the 26-29 day interval between the two constant routines subjects followed a 28-hour day of forced desynchrony. Temperature and EEG were recorded throughout the protocol. The authors analyzed the temperature data using three different techniques to accurately determine circadian phase. Only the sleep data from the desynchronized portion of the protocol was analyzed. To assess process-S, the data was aligned at 28 hours (onset of the major sleep period); and to assess process-C it was aligned by the nadir of circadian core temperature variation.

The latter allowed the authors to describe more clearly the shape and time course of the circadian rhythm of sleep propensity. For instance they noted that waking episodes were unlikely when sleep began near the temperature minimum but increased approximately two hours following the temperature minimum. As the core body temperature rose sleep episodes were less likely but increased again when the temperature started to decline. As a function of time asleep they noted that waking was unlikely during the first two hours of sleep and increase progressively thereafter. The initial two hours of sleep seemed unaffected by circadian phase however, as sleep

duration increased and wakefulness increased so did the influence of circadian phase. Approximately 5.5 to 7.5 hours after sleep onset wakefulness further increased in parallel with the rise in body temperature and only after a peak was reached did wakefulness decrease again which coincided with 15-17 hours after the temperature minimum. Additionally the authors reported that wakefulness increased approximately 4 hours after the temperature minimum and peaked on the rising temperature.

In this study of Dijk and Czeisler (1995) sleep dependent and circadian changes were also documented for REM sleep, NREM sleep and sleep spindles. For example they reported that REM sleep was highly influenced by circadian phase with REM gradually increasing during sleep and the highest portion occurring after the temperature minimum. NREM sleep was found to be influenced by both sleep dependent and circadian processes with the greatest proportion occurring at approximately 22:00 hours following the temperature peak and then decreasing throughout sleep and at its minimum just after the temperature minimum. Sigma was also shown to be influenced by both processes by showing an increase just after the temperature peak and progressing through the night with its maximum increase as temperature rose in the early hours of the morning.

A second model, proposed by Kronauer et al. (1982), was initially developed to explain the data obtained from temporal isolation studies. This model consists of two oscillators. The first oscillator, referred to as (X),

controls the central body temperature. The second oscillator, the weaker of the two, is referred to as (Y) and controls the sleep/wake state. The two oscillators differ in their period range and intrinsic period stability. For instance, in temporal isolation conditions initially x and y rhythms are synchronized then, as the period of y lengthens, an internal phase drift sets in. Ultimately, there is a phase independence that signals the transition from synchrony to desynchrony. Unlike the 2-process model this model does not account for the homeostatic aspects of sleep. Both of the models, however, have, contributed to our understanding of the monophasic sleep pattern in which no napping occurs.

Some Weaknesses of the 2-Process Model

The 2-process model of sleep regulation (Borbély, 1982; Daan & Beersma 1983; Daan & Borbély, 1984), as currently defined, is unable to account for a number of experimental findings. Firstly, the model postulates that process-S, a homeostatic process, is reflected in the spectral power of low delta sleep EEG frequencies. Process-S is believed to increase progressively across the daytime and decrease exponentially across the night. Sleep deprivation would therefore be predicted to increase the spectral power in the delta range in the recovery sleep EEG, which has been experimentally, confirmed (Borbély, Baumann, Brandeis, Strauch, & Lehman, 1981; Dijk, Beersma, & Daan, 1987).

One might also expect that sleep deprivation would increase the spectral power of EEG slow wave activities in the awake daytime. However, studies of sleep deprivation have generally not shown an increase in waking low delta power as an index of process-S. For instance, Corsi-Cabrera et al. (1992) found significantly higher spectral power for theta (3.66-7.32 Hz), alpha-2 (9.77-12.45 Hz) and beta (12.7-25.15 Hz) following one night of total sleep deprivation. Brunner, et al. (1993) analyzed the C3 and C4 electrode sites and found that the power density across the high delta and low theta bands (3.75-4.5 Hz) increased after four nights of partial sleep deprivation. As mentioned earlier, a study carried out in our laboratory was also unable to confirm the expectation that sleep deprivation leads mainly to an increase in the spectral power in the low delta range of the waking EEG. This study found little, if any, change in this band but showed a strong increase in both absolute and relative power in low theta (4-6 Hz) and high theta (6-8 Hz) frequency bands (Yan, et al., 1998). This study was unique in that it measured slow eye movement indices (related to drowsiness) to confirm that the EEG sampled after sleep deprivation did not have more drowsiness than did samples in the baseline rested state.

Some recent studies have reported a transitory daytime peaking of spectral power in these frequency bands around the time of the afternoon nap zone, a phenomenon that the model does not predict. Cajochen, et.al., (1995) reported that the spectral power value for theta and alpha frequency bands

increased during sustained wakefulness with a peaking of spectral power occurring mid-afternoon which then decreased prior to the time of evening sleep onset. Moreover, Cacot, Tesolin, and Sebban (1995) showed a temporary increase of spectral power in all frequency bands during the afternoon, followed by a reduction in the late afternoon-early evening period, with again an increase occurring shortly prior to sleep onset. Similar results were found by Sterman (personal communication)

A second weakness in the model relates to process-C and involves the assumption that sleep propensity only correlates with periods of lowered core body temperature. Temporal isolation studies have shown that minor sleep periods equivalent to the nap zone cluster near the maximum, rather than the minimum, core body temperature (Campbell & Zulley, 1989a).

A final weakness in the model involves the method used to analyze the circadian temperature data which is traditionally curve fitted by cosinor analysis. Such curve fitting produces a sine wave fit that does not necessarily represent the true circadian temperature curve. Broughton, Campbell, and Dunham, (1993) used polynomial regression as an alternative approach to analyze 10 subjects' temperature data. They found that the polynomial regression, when compared to analysis by the cosinor approach, accounted for much more of the variance and more closely approximated visual analysis of the raw data. They found that the portion of the variance explained by different techniques was as follows: the cosinor technique (mean .58, range

.20-.83), the 3rd order polynomial regression (mean .70, range .46-.88) and for the 10th order polynomial regression (mean .81, range .69-.95)

Broughton (1998) has shown that the average normal circadian temperature curve in the typical entrained state is far from sinusoidal. The (mainly nocturnal) portion of the curve below the mean is both considerably shorter and of greater magnitude than the (mainly daytime) portion above the mean. Cosinor curve-fitting therefore necessarily and predictably distorts the empirical mean data, as it regularly generates a sine wave in which the minimum (nadir) is later and smaller and the maximum (acrophase) is earlier and larger than in the data. For similar reasons Lack's group in Australia has also opted for polynomial regression curve-fitting for circadian temperature data (Lack & Lushington, 1996; Lushington, Dawson & Lack, 2000).

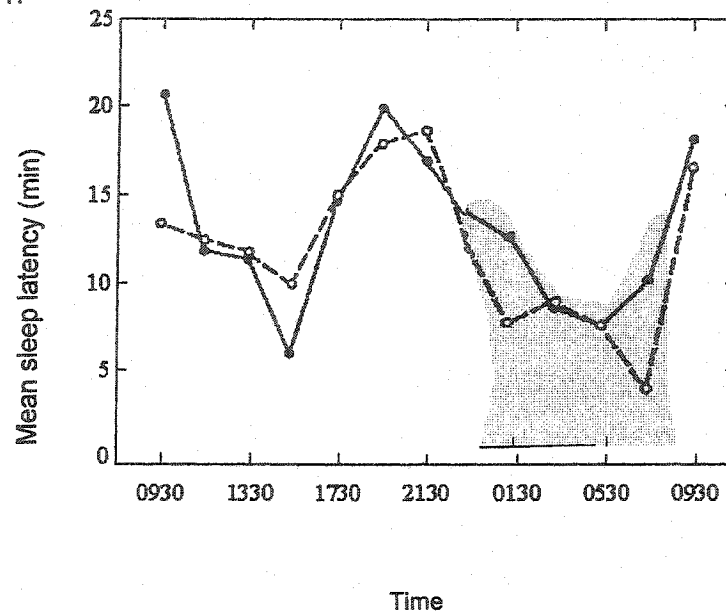
Further Evidence for the Nap Zone and its Endogenous Origin

There are two factors that influence sleep propensity over time: the amount of prior wakefulness and the circadian rhythm (Borbély, 1980). Sleep propensity can be tested using sensitive measures at short regular intervals over the 24 hours. This has revealed a circadian variation of sleep propensity. Lavie and Scherson (1981) tested sleep propensity every 20 minutes using an ultrashort sleep paradigm with 15 minutes for wakefulness and 5 minutes for sleep over a period of 24 hours. They then graphed the amount of sleep in each 5 minute time slot to obtain the "sleep propensity function". The plotted

data demonstrated two periods of high sleep propensity one occurring between midnight and 7 a.m., and another occurring in the mid-afternoon. Also shown was a period of minimal sleep propensity in the late afternoon/early evening (which they referred to as the "forbidden zone" for sleep) and in which little or no sleep occurred during the sleep trials (Lavie, 1985).

A number of other researchers, using other approaches, have also documented 2 strong peaks of sleep facilitation per 24 hours. For instance a transitory shortening of sleep latency (SL) during the mid- afternoon has been found for both the MSLT (Richardson, Carskadon, Flagg, Van den Hoed, Dement, & Mitler, 1978) and the maintenance of wakefulness test (MWT) (Mitler, Gujavarty, & Brownman, 1982). Another period with short sleep latencies exists at night, as reported by Richardson, Carskadon, Orav, and Dement (1982), who assessed sleep propensity in two groups of adults. In this study eight young adults and ten elderly adults were assessed every two hours with the MSLT over a 24-hour period. In both groups there were two peaks of heightened sleep propensity, one occurring at night between 01:30 – 07:30 hrs and the other peaking in the mid-afternoon at 15:30 hrs. Moreover, sleep onset was almost as rapid in the mid-afternoon as in the middle of the night, as is seen in Figure1.

Figure 1.



Mean Sleep latency in minutes for young (open circles, $n=8$) and old (filled circles $n=10$) subjects as a function of time of day. Shaded area demarks nocturnal sleep period. (from Richardson et al., 1982)

Similar 2 per day sleep/wake and rest/activity patterns have been reported in animal studies (Aschoff, 1966). Primates display a 2 per day sleep pattern in the wild and under laboratory conditions (Tobler, 1989). McNew, Burson, Hoshizaki, and Adey, (1972) reported a detailed study of the sleep patterns of an adolescent chimpanzee under entrained and temporal isolation conditions. They found a consistent pattern of a major (nocturnal) sleep period combined with a single (midday) nap; the latter averaged 1.1 hours in duration and occurred on 29 out of 30 days.

Borbély and Achermann (1992) suggested that the habit of eating three meals per day might have contributed to the establishment of the pattern of 2 peaks per day of sleep propensity. In the previously mentioned study of Lavie and Scherson (1981) these authors managed to circumvent this possibility by spreading food intake into light snacks distributed equally throughout the 24-hours. Despite this, the 2 peaks per day remained clearly present. Carskadon and Dement (1992) reported similar findings for SL in subjects following the constant routine protocol, which controls for potential masking factors including large meals. Dijk and Czeisler (1995) using a forced desynchronization of a 28 -hour "day" over a one month period and found that the secondary peak persisted.

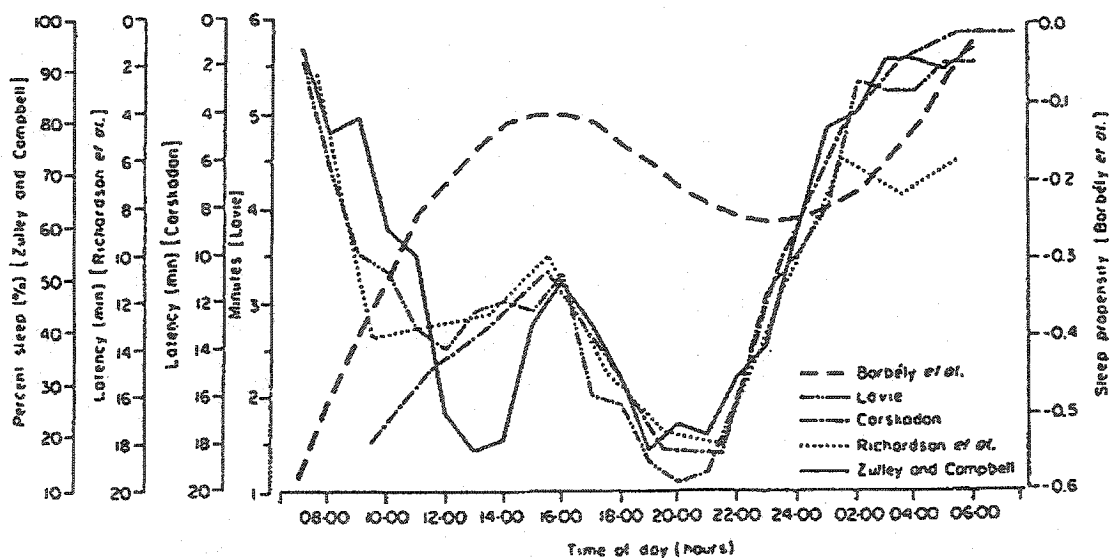
Temporal isolation studies confirm the proposal (Broughton, 1975) that the 2 peak per day pattern of sleep propensity is endogenous in nature and suggest that it is linked with the circadian rhythm of body temperature (Zulley & Campbell 1985, Campbell & Zulley 1989a,b). These studies were carried out with young adults, no external time cues were permitted, and the subjects could choose when to eat, sleep or be active. Under such conditions minor sleep episodes still occurred and were clustered around the time of maximum core body temperature, whereas the onset of the major episodes equivalent to night sleep were associated with minimum core temperature.

When comparable data were superimposed from studies carried out on normal young adults studied by a number of totally different paradigms

including MSLT, the 7:13 ultra short sleep schedule, the constant routine and temporal isolation conditions, the consistent 2 peak per day of sleep facilitation become clearly evident, as shown in Figure 2 from Broughton and Mullington (1992). However, when sleep propensity as predicted by the 2-process model (Borbély, Achermann, Trachsel & Tobler, 1989) was superimposed (dashed line in Figure 2), it failed to explain the 2 per day pattern and did not accurately predict the empirical laboratory data.

Figure 2

R. Broughton and J. Mullington (1992)



Why is the Nap Zone so Infrequently Followed in Industrialized Societies?

With so much research supporting the existence and the endogenous CNS origin of the afternoon nap zone of sleep facilitation, one may wonder

why more individuals don't nap. Moreover, one may question why industrialized society has not taken this important information into account and adjusted work schedules accordingly. There are, however, several explanations.

Experimental data shows that in humans the magnitude of sleep propensity in the afternoon nap zone is only 20%-25% of that for the major nocturnal sleep period (see Figure. 2 from Broughton & Mullington, 1992). Furthermore, most individuals achieve a sufficient amount of sleep during their nocturnal sleep period to meet their 24-hour need and therefore do not require a nap in this secondary period of sleep facilitation. Finally, the nap zone is followed by a major sustained period of arousal and sleepy individuals learn that, if they stay awake, sleepiness will diminish later in the day.

Although in industrialized societies napping is rare, there are some groups such as the elderly and students that are not bound by the usual work conventions and who do nap and feel better for it. Daytime napping is particularly common in certain cultures, where siesta time is allowed. Although midday heat has been postulated to be associated with afternoon napping, this custom appears to be independent of seasonal variations in ambient temperature (Taub, 1971).

Unlike the nocturnal sleep period, voluntary napping can be readily suppressed, if desired but no opportunity is available. Requirements of the workplace most likely account for the infrequency of daytime napping in non-

siesta cultures rather than an inability to nap. When these limitations are removed and social restrictions lifted, napping increases (Webb & Dinges, 1989). In a large study of both young and old adults, Tune (1969) found that quantity of naps taken in an eight week period increased with age. He documented that on average the young group (aged 20 to 30) napped once during the eight-week period and the old group (aged 70 to 80) napped on average 14 times in the same time period. Taub, (1971) also reported increased napping with age in a study conducted in a siesta culture (Mexico).

Finally, Dinges, M. Orne, E. Orne, and Evans, (1980) studied students with flexible hours and found that they were frequent afternoon nappers. Furthermore, students that did not nap reported that they would like to nap but that the need to both work and attend school prevented them from so doing.

In summary, all of these studies point to the fact that in industrialized societies napping is suppressed by social constraints. When these are reduced or removed, napping increases.

Potential Mechanisms of the Nap Zone

Several proposals have been put forward to explain this transient secondary increase in sleep propensity. The earliest proposal (Broughton, 1975) was that the major sleep period, which has a circadian distribution, also shows a super harmonic expressing an endogenous brain rhythm providing a twice daily increase in sleep propensity. Zulley and Campbell (1985) validated

the endogenous nature of the rhythm by means of time-free studies in which subjects were free to choose when to eat and sleep, as discussed above. It was also noted by Broughton (1975) that the major and minor sleep periods are about 180° degrees apart. Using 7:13 ultrashort sleep/wake protocol, Lavie (1989) was able to demonstrate that at approximately 180° in phase after the middle of the major sleep period there existed, a "secondary sleep gate" of sleep facilitation.

Broughton (1975) and Aschoff and Gerkema (1985) hypothesized that the secondary period of sleep facilitation might denote a super-harmonic of the fundamental 24-hour circadian rhythm. Some support for this hypothesis comes from two different studies. Dinges (1989) studied sleep logs of habitual nappers who reported that, when they delayed their nocturnal sleep by one hour on the weekend, their naps the following days were also delayed by approximately one hour. Similarly, our own pilot data in habitual nappers support this mechanism. Acute 4- hour phase delay of night sleep in habitual nappers instructed to nap when they felt sleepest led to a similar delay of the afternoon nap (Broughton, 1995) (personal communication).

It was also suggested in the original article (Broughton, 1975) that the afternoon sleep tendency might reflect pressure for slow wave sleep (SWS) as part of an approximately 12-hour bimodal SWS biorhythm. It has subsequently been shown that, if sleep is extended beyond 12 hr, a second increase in SWS appears in the afternoon (Gagnon and DeKoninck, 1984).

These authors found that the mean interval from the onset of the first SWS pulse to that of the much later one was 12.4 hr.

More recently, Broughton (1989) raised the possibility that the twice a day periodicity of sleep propensity is not one of sleep, but rather one of arousal with sleep being facilitated during periods of lowered arousal. When the level of arousal drops below a certain threshold, sleep is facilitated. Broughton noted that during states of heightened arousal sleep can be suppressed for several days with sleep again becoming possible when the level of arousal drops below a certain threshold. He also noted that in healthy individuals prolonged sleep cannot suppress wakefulness to the same extent that prolonged wakefulness and stimulation can suppress sleep. Experimental evidence for a circadian arousal process emerged later from primate research. Edgar, Dement, and Fuller (1993) demonstrated that destruction of the SCN nuclei of the hypothalamus in squirrel monkeys led to a loss of circadian periodicity controlling activity/inactivity and was also associated with a significant increase in amount of sleep per 24 hrs. This latter finding indicated involvement of an active circadian arousal process.

A more specific later proposal suggested that the nap zone might reflect the coupled effects of increasing sleep pressure (process-S) across the daytime and an opposing circadian system (process-C) (Broughton, 1994; Webb, 1994). Broughton (1994, 1998) further proposed that the afternoon nap zone would be initiated by the increasing sleep propensity with

accumulating wakefulness after morning wake-up and be reversed and terminated by the circadian arousal process which peaks later in the day, typically in the evening (see Broughton and Mullington, 1992).

In summary the mid-afternoon transient increase in sleepiness, although well documented experimentally, is not well understood. Several models have been proposed to try to explain sleepiness in general, and the mid-afternoon increase in particular. Most of the modeling involves process-S and process-C. The research of this thesis tests the proposal that the nap zone occurs when increasing sleep pressure from prior wakefulness (process-S in Borbély's model of sleep regulation) is terminated by a light-sensitive circadian arousal process. In this conceptualization it is a combination of the clock hours of prior wake plus the circadian arousal process, which times the daytime period of increased sleep propensity.

Hypotheses

The present study attempts to identify the mechanism of the afternoon nap zone. More specifically, it investigates the recent proposal that the afternoon nap zone represents the point in time after morning awakening when process-S has increased to a sufficiently high level to facilitate sleep onset, while at the same time the SCN-controlled circadian arousal process has not yet risen high enough to counteract this sleepiness.

It is predicted that exposure to morning bright light stimulation will phase advance the circadian arousal process by about 1-2 hours so that the peak level of daytime somnolence (nap zone) will be both earlier and smaller (earlier intercept with increasing process-S). Evening bright light stimulation, on the other hand, will phase delay the circadian arousal process by about 1-2 hours so that the peak level of daytime somnolence (nap zone) will be both later and somewhat larger (later intercept with a higher level of process-S).

To test the hypothesis requires three preconditions: that the state of the SCN circadian arousal pacemaker be accurately measured, that it be reliably manipulated, and that a sensitive and essentially pure measure of daytime arousal level be employed to document the timing of the afternoon "nap zone".

Based on the previous studies cited, the assumption can be made that the associated circadian core body temperature curve accurately reflects the circadian arousal process and that the latter can be phase shifted by exposure to bright light without significantly altering nocturnal sleep. The specific hypothesis were:

- I. Following two nights of evening bright light exposure (phase delay condition), the temperature minima will be delayed by one to two hours. Exposure to morning bright light (phase advance condition) on two consecutive mornings will advance the temperature minima by one to two hours.

To assess daytime alertness/sleepiness levels, both the simple reaction time test and quantified EEG were chosen. The simple reaction time test has been shown to be a sensitive measure of arousal without significant learning effects and thereby provides a back-up in the case that the quantified EEG is insufficiently sensitive. Q- EEG is considered a "pure" measure because no learning or motivational factors are involved.

Regarding performance on the simple reaction time task, it was hypothesized that:

- II. During the baseline condition, poorest daytime performance (longest mean reaction times and/or greatest RT variability) will occur around the time of the nap zone. Following the evening light stimulation, poorest performance will be delayed by about 1-2 hours, while morning light stimulation will advance the time of poorest performance by a similar amount.

Regarding quantified EEG measures it was hypothesized that:

- III. During the baseline condition, lowest daytime arousal indexed by increased spectral power in lower frequency bands, and will occur around the time of the nap zone. Following evening light exposure, the lowest arousal level by Q- EEG will be phase delayed by about 1-2 hours, while for morning light it will phase advance by a similar amount.

CHAPTER II

METHOD

Subjects

Eight normal male subjects aged 20-30 years were selected consecutively having met all inclusion/exclusion criteria to participate in the study. The subjects were informed about the nature and purpose of the experiment (Appendix A) and were paid for their participation. Signed informed consent was obtained from all subjects (Appendix B) for the protocol which, had been accepted by the appropriate Human Ethics Committee.

Prior to acceptance into the study, all subjects were screened by a standard sleep questionnaire (Appendix C) for nocturnal sleep of 6.5-8.0 hours duration, (group mean = 7.23), no abnormal sleep habits, no habitual nappers, no medication affecting central nervous system arousal levels, and no health problems. All subjects were non-smokers and all but one subject, who was a light social drinker did not drink alcoholic beverages. The Horne-Ostberg (1977) Morning/Eveningness Questionnaire was used to ensure that all subjects were neither extreme morning nor extreme evening types; subject scores were as follows 49, 49, 51, 52, 52, 53, 58 and 58 (Appendix D). Additionally, overnight polysomnographic recordings (PSG) were performed to exclude subjects with significant sleep apnea (apnea index > 5 per hour or apnea plus hypopnea index > 10 per hour), periodic leg movements (over > 5 per hour) or excessive sleepiness on the MSLT (mean SL > 12 min).

Procedure

Subjects were asked to abstain from alcohol and drug ingestion for at least two weeks prior to, and for the duration of, the experiment. Caffeinated beverages were discouraged but permitted up to a maximum of one cup per day. During the two weeks prior to the commencement of the experiment, subjects maintained a consistent sleep/wake schedule with bedtimes from 23:00-06:00 hours, which was confirmed by wrist actigraphy.

All subjects were then monitored for a total of nine days in the laboratory, which was divided into two separate sessions of four days in the evening light condition, and five days in the morning light condition. Each session was followed by thirty days at home away from the laboratory with continued regularization of bedtimes monitored. The order of conditions was counterbalanced across subjects and 2 subjects were studied simultaneously.

While they were in the laboratory subjects lived under constant dim indoor ambient light (approximately 150 lux) with no external time cues permitted. They maintained night bed hours of 23:00-06:00 hours. Meals were small hourly snacks with intake monitored. EEG was recorded using 8 channel Medilog (Oxford Medical Systems, Inc., Abingdon, U.K.) cassette tape recorders with a montage of C4- A1, C3-A2, O2-A1, right EOG-M1, left EOG-M2, and submental EMG. Core body temperature was also recorded throughout the trial by rectal probe (Mini Mitter Co., Inc., Oregon, U.S.A.) using a Mini-Logger Series 2000 system.

The protocol is schematized in Figure 3, and was as follows. In both the morning light and evening light stimulation conditions two baseline days were collected. Days 1 and 2 in the morning light stimulation condition were baseline sessions, and days 2 and 3 were for evening light stimulation. On days 3 and 4 half the subjects were exposed to two hours of bright light (10,000 lux) by a commercial light stimulator (Apollo Bright Light 3 Stimulator, Apollo Light Systems, Utah, U.S.A.) from 06:00-08:00, and the other half of subjects from 21:00-23:00. Light intensity was monitored by a light meter (United Detector System S351 Photometer, Graseby Optronics, Florida., U.S.A.).

During bright light stimulation, subjects watched television programs or videotapes with the monitor placed just above the light boxes, as in Lack and Wright (1993). This was in order to ensure that the full intensity of light was received throughout the entire photic period as recommended by Dawson and Campbell (1991).

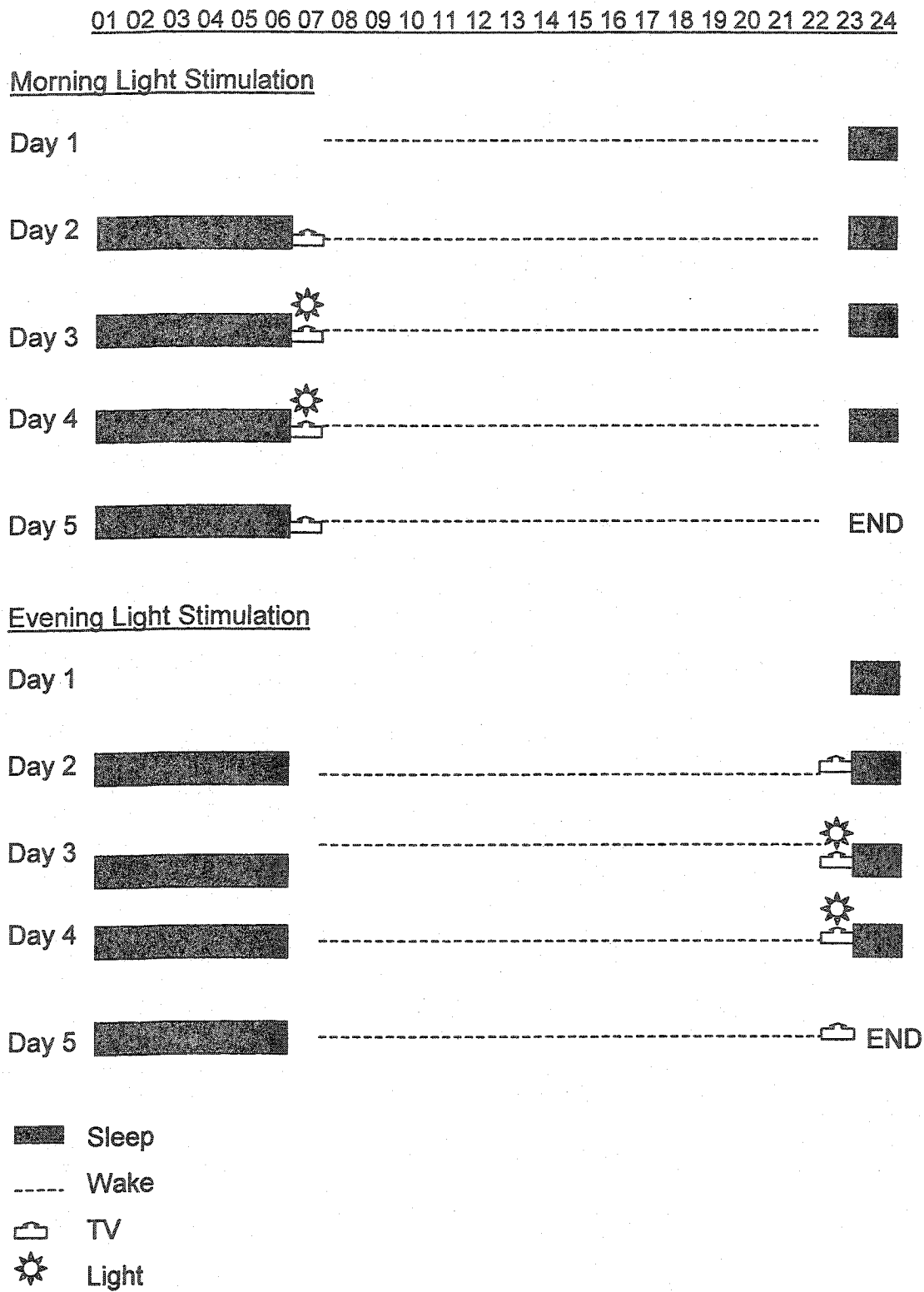
In order to eliminate the possible confounding effects of television stimulation on the two treatment days, subjects continued to watch two hours of television on baseline days. During the rest of the day, subjects read or did other non-strenuous activities in the laboratory area except during the repeated samplings of EEG and Simple Reaction Time (SRT) testing, described below. Recordings terminated at the end of day 5 depending on the light stimulation schedule (see Figure 3).

Other than during hours of bright light stimulation, the level of daytime arousal was assessed every 60 minutes by quantified EEG followed by a simple reaction time test. For each EEG sample, subjects were requested to return to, and relax in, a comfortable chair for two minutes with eyes opened fixated and two minutes with eyes closed. The onset and termination of these sampling sessions were noted by an event marker.

Two minutes after the two EEG samples, the subjects moved to a table located in the same room and sat down in front of a blank screen computer. They then typed their initials on the keyboard, pressed enter and the reaction time task began. This ten minute task involved a small peripheral black box with a small red light in one corner. Subjects were instructed to press the button as quickly as possible, when the red light was illuminated. A one second response delay caused the computer to beep and it continued to beep until the subject responded. The light illuminated between one to ten second intervals following each response in random fashion.

Core body temperature sampled every minute throughout the trial was divided into 24-hour segments starting and ending at 22:00 hours.

Figure 3



Data Processing and Analysis

The .05 level of significance was used for all statistical comparisons. Day two was selected as the baseline, since the subjects were considered to have been acclimatizing to the lab environment on day one. The baseline was compared with the post-stimulation day for all variables including those of temperature, simple reaction time, and Q-EEG, measures.

Circadian Core Body Temperature

As recommended by Broughton et al., (1993) and for the advantages described in the introduction a polynomial least squared regression was used to fit the raw temperature data (using 1 minute samples). This was done separately for all eight subjects in both baseline and treatment conditions. The curve-fit employed the polynomial regression software inherent in Excel (Microsoft Systems, Seattle, WA) with the criteria of using at least the 5th order regression needed to fit a bimodal distribution as explained by others using this curve-fit approach for circadian temperature data (Lack and Lushington, 1996).

The curve fitted times of temperature minimum ("nadirs") for baseline and post stimulation, evening light (phase delay) and morning light (phase advance) conditions, were taken as the circadian temperature rhythm phase markers. In order to establish that bright light exposure induced a circadian phase shift, each subjects' temperature minima were compared for baseline

versus post light conditions using a repeated-measures t-test; one for the phase advance and one for the phase delay conditions.

Performance Simple Reaction Time

The Simple Reaction Time task provided the following dependent measures: number of gaps (RTs >1000 msec), overall mean reaction time and standard deviation of reaction time. Number of gaps was not analyzed due to their rare occurrence: there was a total of only 284 gaps out of approximately 158,400 reaction times.

In order to establish whether bright light exposure induced a circadian phase shift, each subject's performance nadir (the timing of maximum mean and standard deviation of reaction time) was compared for baseline versus post light data using a repeated-measures t-test; one for the phase advance and one for the phase delay conditions.

Circadian Core Body Temperature versus Performance

In order to test whether these variables covaried directly (i.e., whether resetting the circadian clock similarly reset the time of performance and temperature minima), a regression analysis was performed on scores of difference between pre and post treatment for the phase shift of temperature and performance.

Quantified EEG

The EEG derivations (C3-A2, C4 -A2 and O2-A1), the two electrooculograms and the submental electromyograms were collected continuously using Oxford Medilog 9000 8 channel ambulatory recorders. The high pass and low pass filter settings of the Medilog amplifiers were 0.5Hz and 40Hz, respectively. For each test session, two minutes each of eyes opened and eyes closed EEG data were fed in parallel (by interface cable) from the Medilog recorders to a data collection computer and acquired at a sampling rate of 240Hz onto hard disk using the Melville Sandman Sleep System which also permitted online data visualization to ensure minimization of artifacts. The latter was aided by coached relaxation of the jaw and scalp muscles. For each session and for all subjects, a minimum of 15 artifact-free two-second mini-epochs was selected for both the eyes opened and eyes closed conditions.

Each two-second mini-epoch was subjected to spectral analysis by FFT. The resultant absolute power spectra (in μV^2) covered the frequency range of 0.5 - 15.5 Hz in 0.5Hz increments. The >15 individual power spectra for each test session were averaged to produce the data representing the session. The values of adjacent frequency bands were then collapsed into the following bins: delta-1 (1.0-1.5Hz), delta-2 (2.0-3.5), theta-1 (4.0-5.5), theta-2 (6.0-7.5), alpha-1 (8.0-9.5), alpha-2 (10.0-11.5) and sigma (12.0-15.5). Higher

frequencies were not analysed due to concern for artefact of EMG, mainlines or other origin. As the literature indicated that decreased alertness was associated with increases in spectral power of frequencies in the delta, theta and alpha bands, emphasis was on the global Q-EEG power from 0.5-15.5 Hz.

Since inter-individual differences in spectral EEG power were considerable, a normalized absolute power was derived for each subject. Each band's normalized power was calculated dividing the band's absolute power value by its corresponding baseline power. The band's baseline power was computed by averaging the band's absolute power for the 11 hourly sessions in the baseline condition.

As in Dijk, Brunner, Domien, & Borbély, (1990), for the analysis the C3-A2, and O2-A1 leads were both used unless the quality of the signal was unsatisfactory. All analyses were conducted separately for eyes open and eyes closed conditions at each of the two electrode sites. One of the eight subjects was a non-responder to morning light, (i.e., no temperature phase advance) and was dropped from subsequent EEG analysis.

From a statistical perspective, because of the increased Type I error rate relating to a violation of assumptions inherent in repeated measures designs, it is appropriate to use a Greenhouse-Geisser or Huynh-Feldt correction. As in Lafrance and Dumont (2000), the probabilities presented have been corrected by using the Huynh-Feldt method to reduce the degrees

of freedom. The uncorrected degrees of freedom are given together with the Huynh-Feldt probability levels.

Adjustments for multiple comparisons are not made because changes in frequency bands were only interpreted when the expected spectral pattern occurred at certain times over several days. Therefore significant tests in the predicted direction are unlikely to have occurred by random chance and adjustments for the number of tests performed in these analyses would result in overly conservative confidence levels. Visual analysis examining patterns of significance were employed in lieu of multiple comparison adjustment.

To examine for changes in EEG comparing baseline versus post light exposure conditions, a three way analysis of variance with repeated measures (or subjects- design) was applied to either eyes opened or eyes closed across 11 trials and 7 bands ($2 \times 11 \times 7$).

A post hoc analysis of individual frequency bands was also performed and is in the appendix E-L.

CHAPTER III

RESULTS

Circadian Core Body Temperature

For both the morning (phase advance) and evening (phase delay) bright light conditions, a sixth order polynomial regression was applied to the baseline and post- stimulation 24-hour temperature data. The sixth order regression explained 94% of the variance ($r^2=0.94$) in the evening light condition and 92 % of the variance ($r^2=0.92$) in the morning light condition, for the data averaged for all eight subjects.

Figures 4 and 5 show both the raw rectal temperature data and curve fits before and after evening light stimulation for all subjects. Phase shift measures were based on the fitted curves. Phase delays in minimum temperature values are evident in the curves for all subjects. Figures 6 and 7 show rectal temperature data and curve fits before and after morning light stimulation. Phase advances in temperature minimas occurred in all subjects with the exception of subject 2 (see Figure 6).

After bright light treatment, the temperature minima occurred on average 1:46 hours (i.e., 1h 46 min) later ($t= -5.85$, $df=7$ $p< 0.001$) in the averaged evening light stimulation data and 0:53 minutes earlier ($t= 3.94$, $df=7$ $p< 0.01$) in the morning light stimulation data. All changes from baseline in timing of temperature were significant at $p < 0.01$ or better, as can be seen in Table 1. Perusal of the individual fitted curves suggests that with phase delay

the duration (breadth) of the nadir increased, and that with phase advance it decreased.

Simple Reaction Time Test

Both mean and standard deviation of reaction time increased in the mid-afternoon period for all subjects in the baseline condition. The time of occurrence of this nadir in performance were identical for both the mean and standard deviation of reaction time: therefore only the standard deviation results are displayed in Figures 4, 5, 6, and 7.

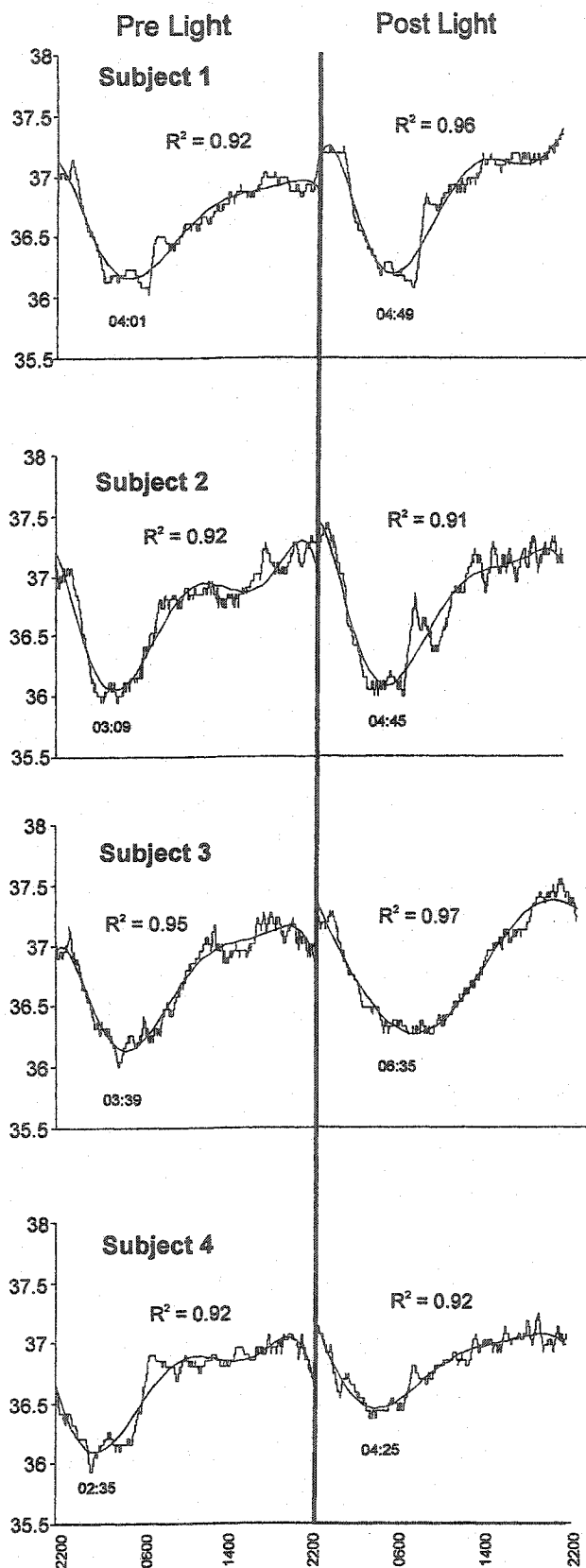
Following evening bright light exposure, phase delays in poorest performance were observed in all subjects (see Figures 4 and 5). In the morning light condition, phase advances in poorest performance were obtained for seven out of the eight subjects (see Figures 6 and 7). As can be seen for both the temperature and performance data in Figure 6, subject 2 did not respond to morning bright light exposure.

After bright light treatment, the maxima in mean and standard deviation of reaction time occurred on average 1: 54 hours later ($t=-6.29$, $df=7$ $p<0.001$) with the evening light stimulation data and 1: 03 hours earlier ($t=5.21$, $df=7$ $p<0.01$) with morning light stimulation. The results for the mean and standard deviation of reaction time are provided in Table 2. All changes from baseline in timing of peak standard deviation of reaction time were significant at $p < 0.01$ or better.

Figure 4

Evening Light

Temperature (C°)



Performance (SD, msec)

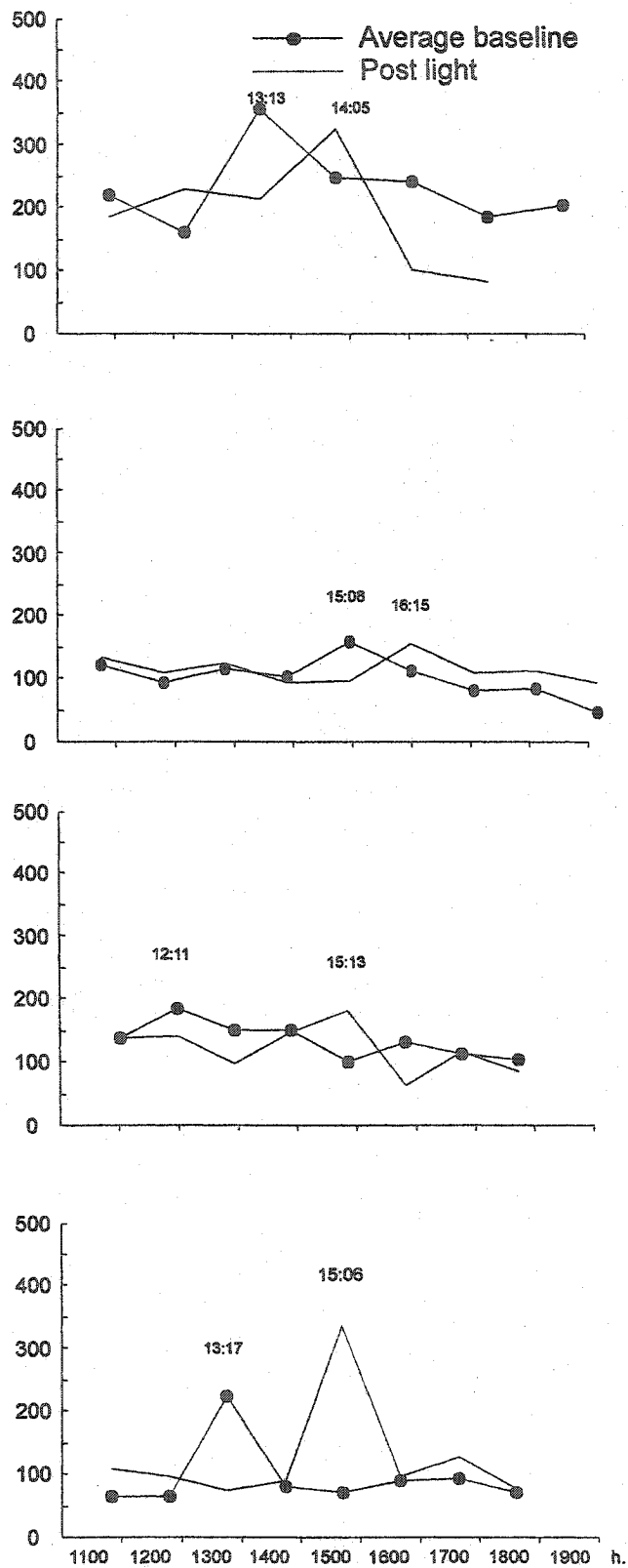


Figure 5

Evening Light

Temperature (C°)

Performance (SD, msec)

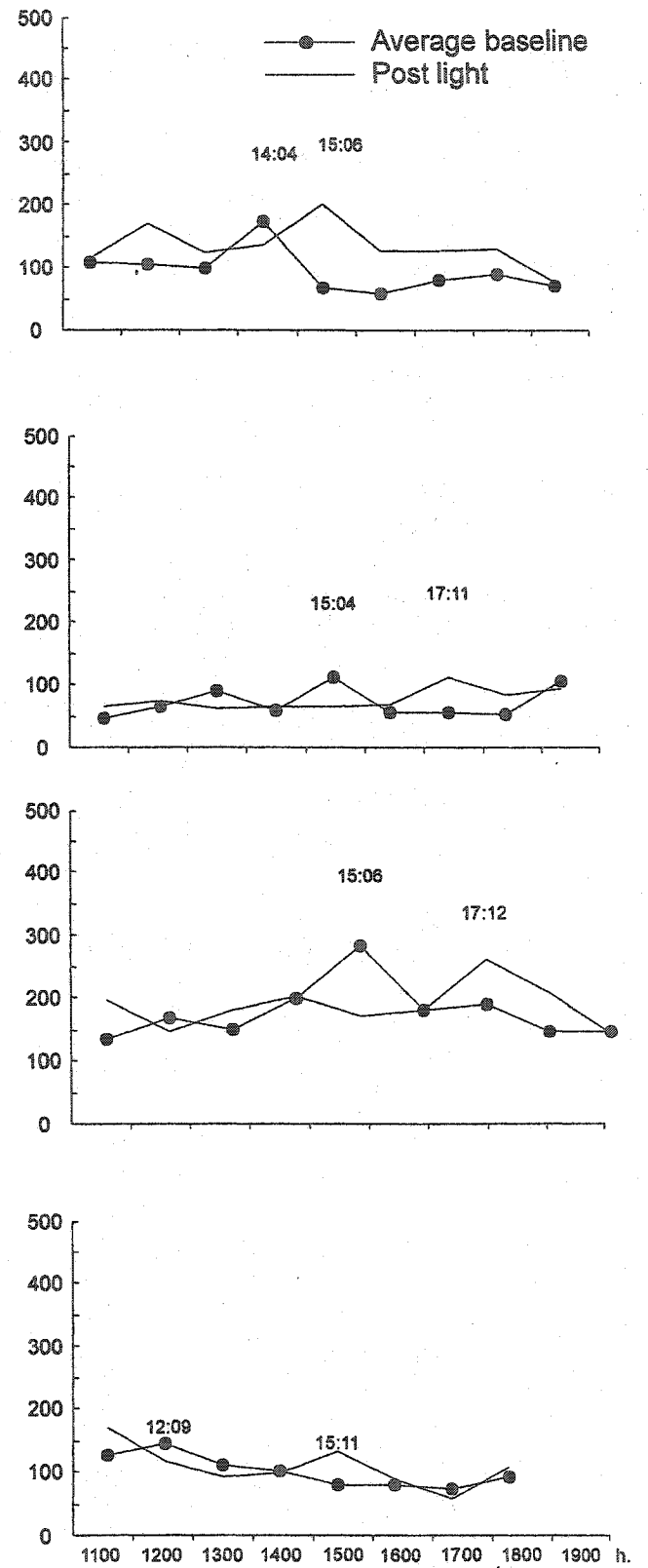
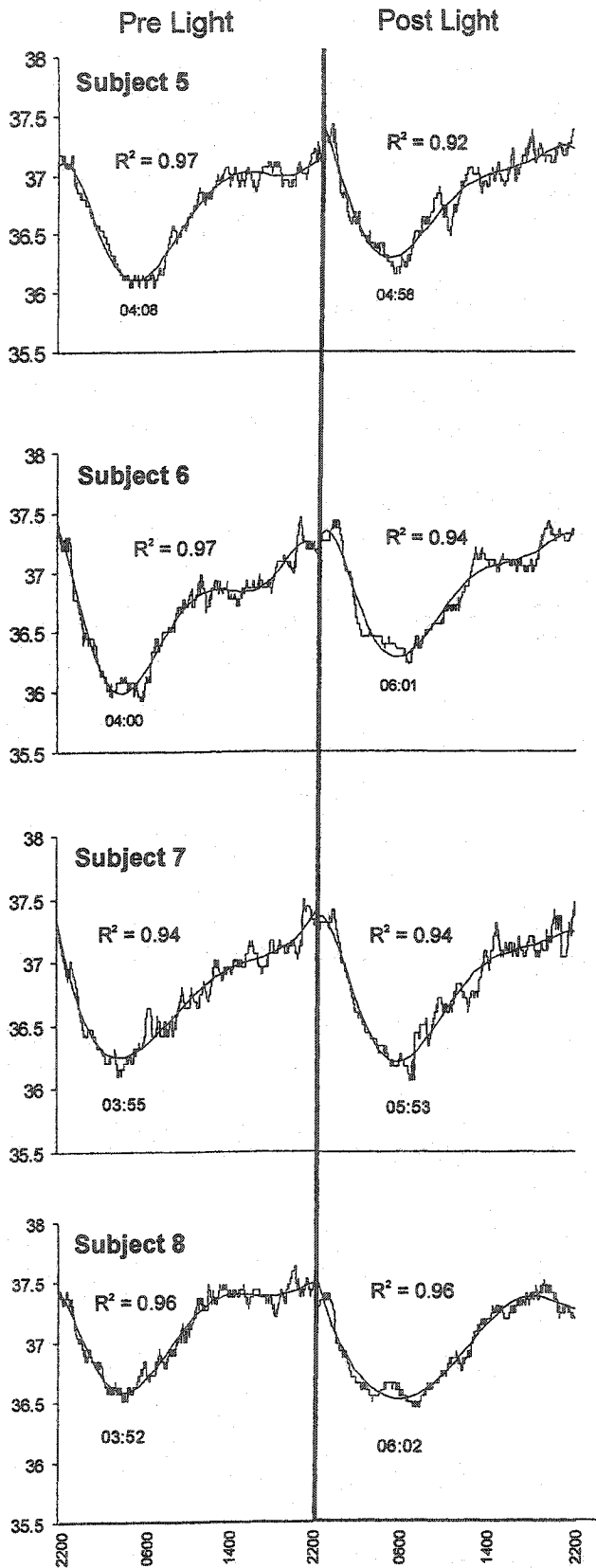


Figure 6

Morning Light

57

Temperature (C°)

Performance (SD, msec)

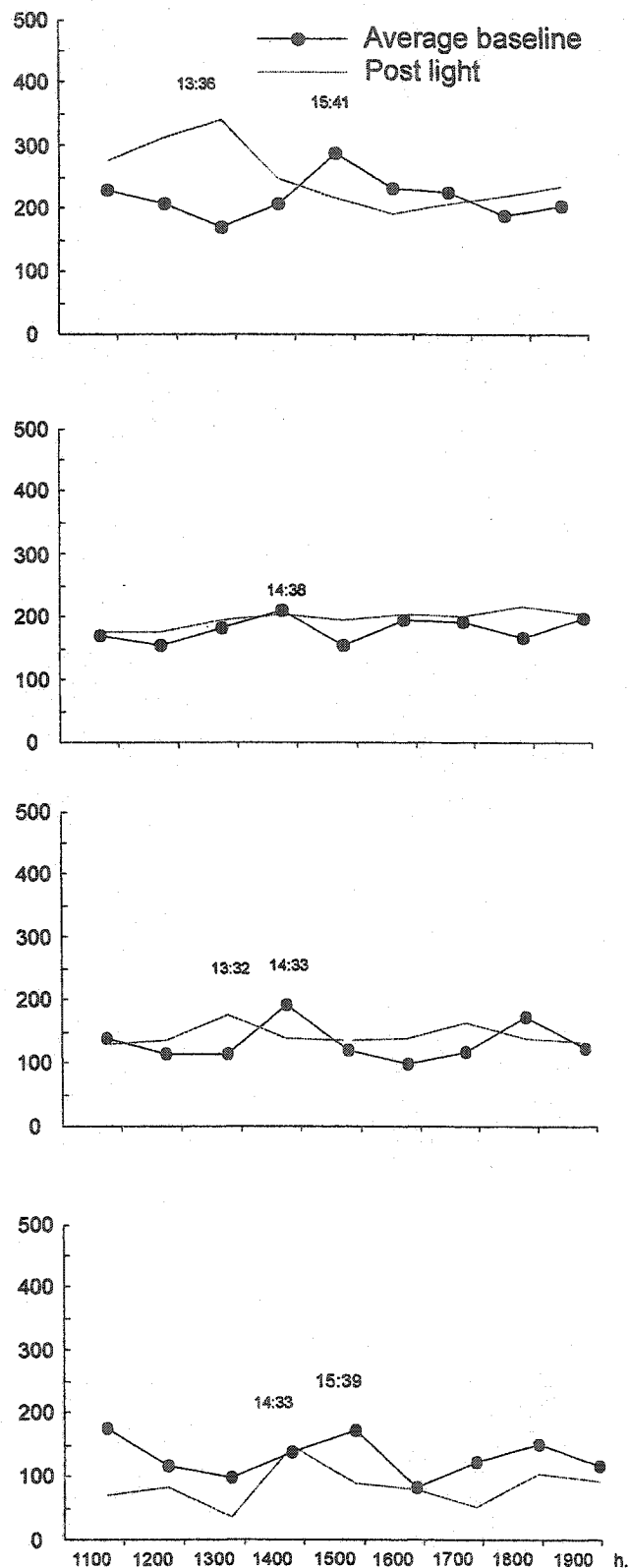
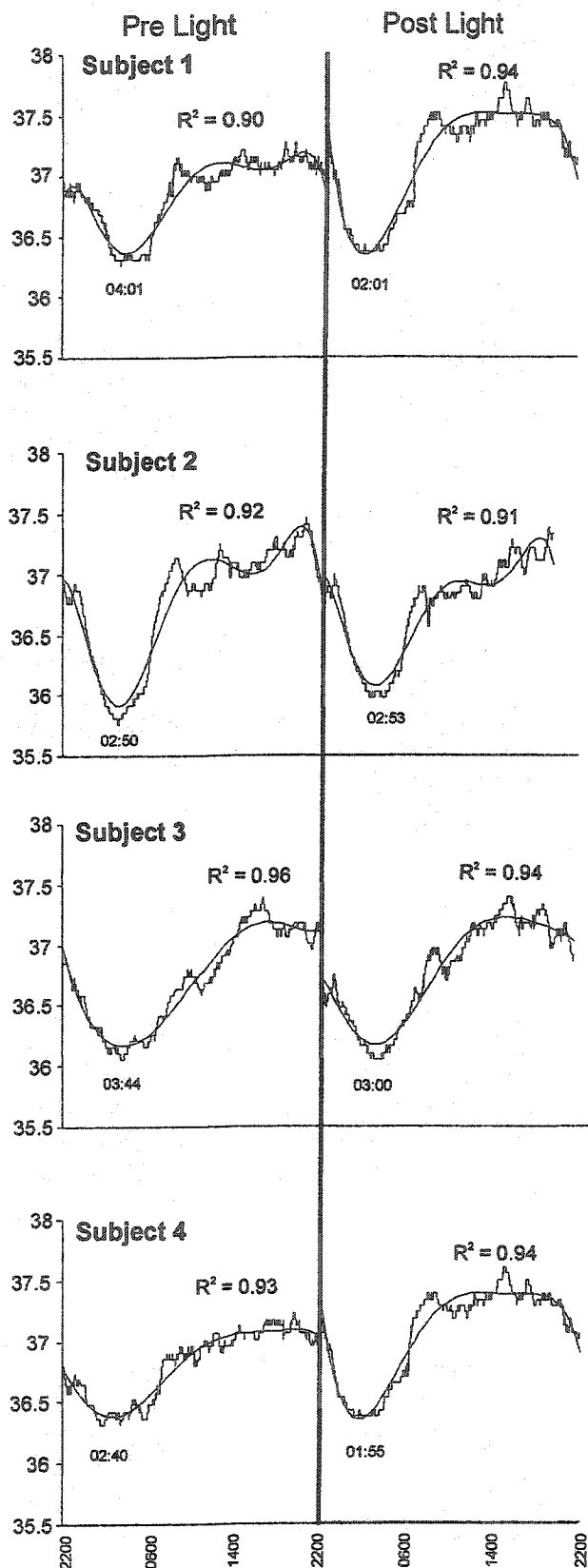


Figure 7

Morning Light

58

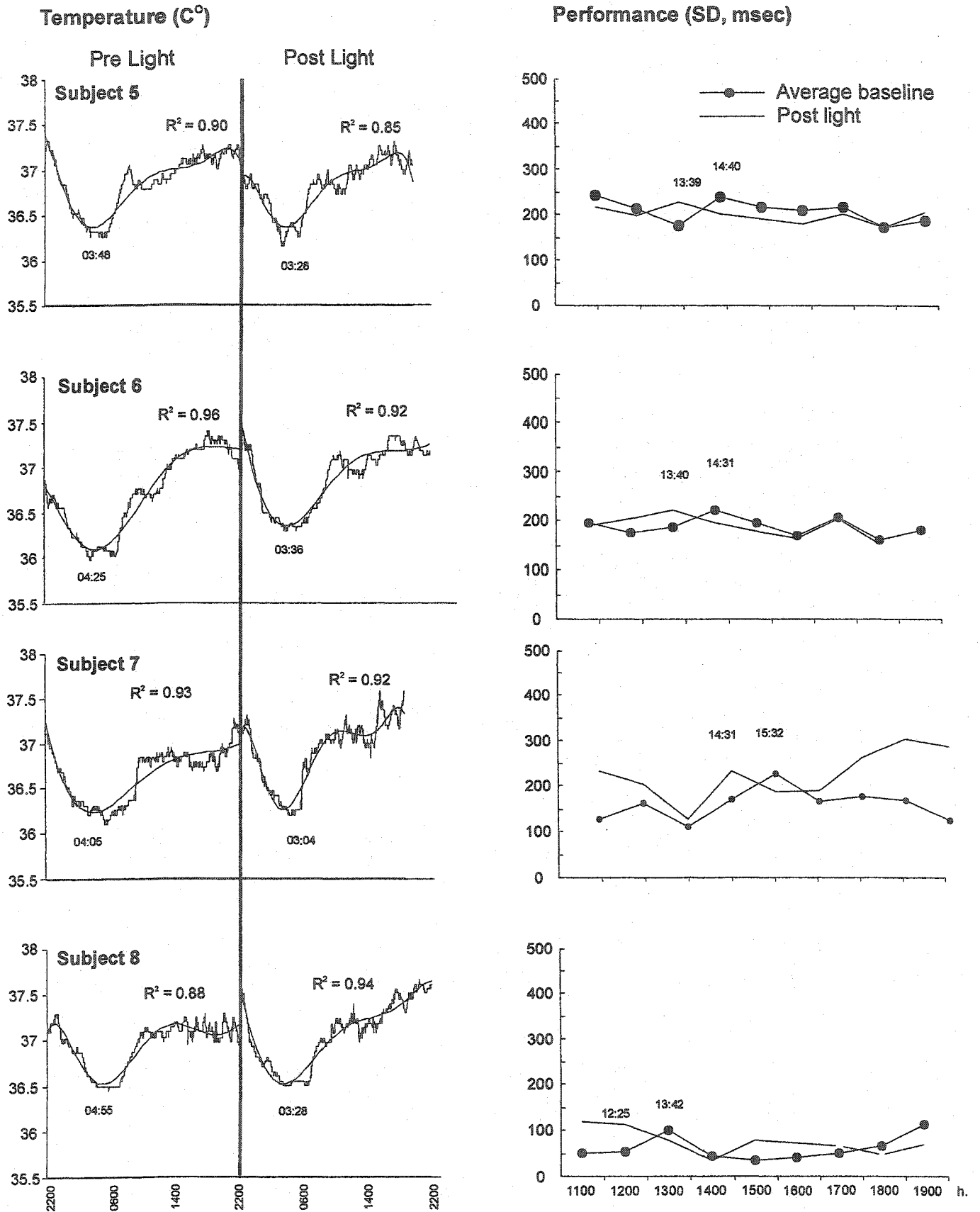


Table 1

Temperature Phase Shifts Following Bright Light Exposure.

		<u>Before Light Exposure</u>		<u>After Light Exposure</u>		Difference (h:m)
		Mean time (h:m)	SD (h:m)	Mean time (h:m)	SD (h:m)	
Evening Light (phase delay)	03:40	0:32	05:26	0:47	+ 1:46 ***	
Morning Light (phase advance)	03:48	0:45	02:55	0:38	- 0:53 **	

Note. h = hours; m = minutes

** p < 0.01 *** p < 0.001

Table 2

Performance Phase Shifts Following Bright Light Exposure.

		<u>Before Light Exposure</u>		<u>After Light Exposure</u>		Difference (h:m)
		Mean time (h:m)	SD (h:m)	Mean time (h:m)	SD (h:m)	
Evening Light (phase delay)						
(Mean SRT)	13:46	1:15	15:40	1:06	+ 1:54 ***	
(SD SRT)	13:46	1:15	15:40	1:06	+ 1:54 ***	
Morning Light (phase advance)						
(Mean SRT)	14:52	0:41	13:49	0:44	- 1:03 **	
(SD SRT)	14:52	0:41	13:49	0:44	- 1:03 **	

Note. h = hours; m = minutes, SD = standard deviation, SRT = simple reaction time

** p < 0.01, *** p < 0.001

Circadian Core Body Temperature and Performance

A regression analysis performed on scores of difference between pre and post treatment for temperature and performance data phase shifts, found that they were highly related both for the evening light $r^2 = 0.82$ ($r = 0.90$ $p < 0.01$) and for morning light $r^2 = 0.82$ ($r = 0.90$ $p < 0.01$) conditions. Figure 8 shows the rectal temperature and performance shifts for eight subjects following evening light exposure along with a fitted regression line. Figure 9 shows the same measures following morning light exposure for all 8 subjects, including the non-responder.

Quantified EEG: Evening Light Stimulation

From the $2 \times 11 \times 7$ (Condition by Hour by Frequency) completely within-subjects ANOVA performed on the evening light condition, for data with eyes closed at 02, the Condition by Hour by Frequency was non-significant. However, the Condition by Hour interaction was highly significant, $F(10, 70) = 5.40$, $p < 0.001$ (see Table 3). In order to interpret the interaction, the simple main effects of condition at each level of hour were analyzed (see Table 4). Four tests were significant: Condition at 16:00h, $F(1,7) = 6.04$, $p < .05$; Condition at 17:00h, $F(1,7) = 8.76$, $p < .05$; Condition at 18:00h, $F(1,7) = 8.99$, $p < .05$; and Condition at 19:00h, $F(1,7) = 7.50$, $p < .05$. An increase in the mean spectral power can be seen following evening bright light exposure in the late-afternoon.

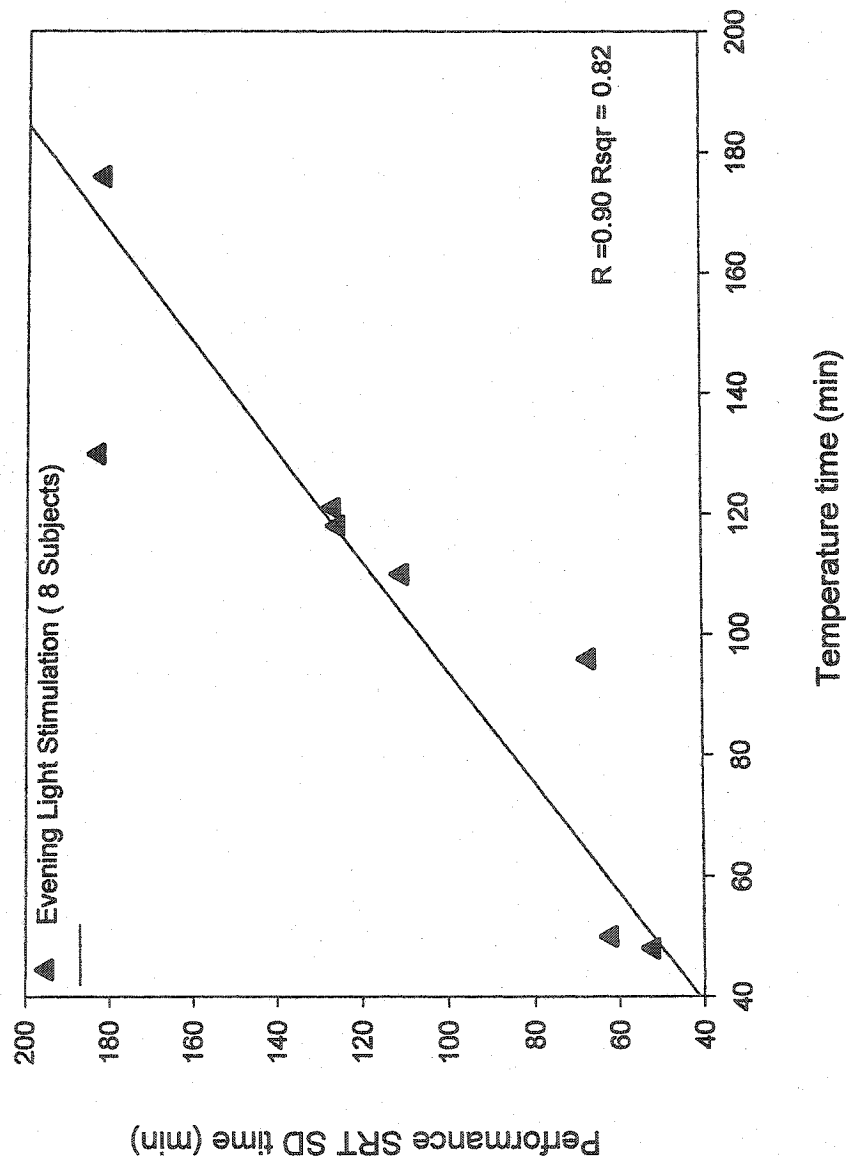


Figure 8. Regression plot of temperature and performance phase shifts following evening light exposure.

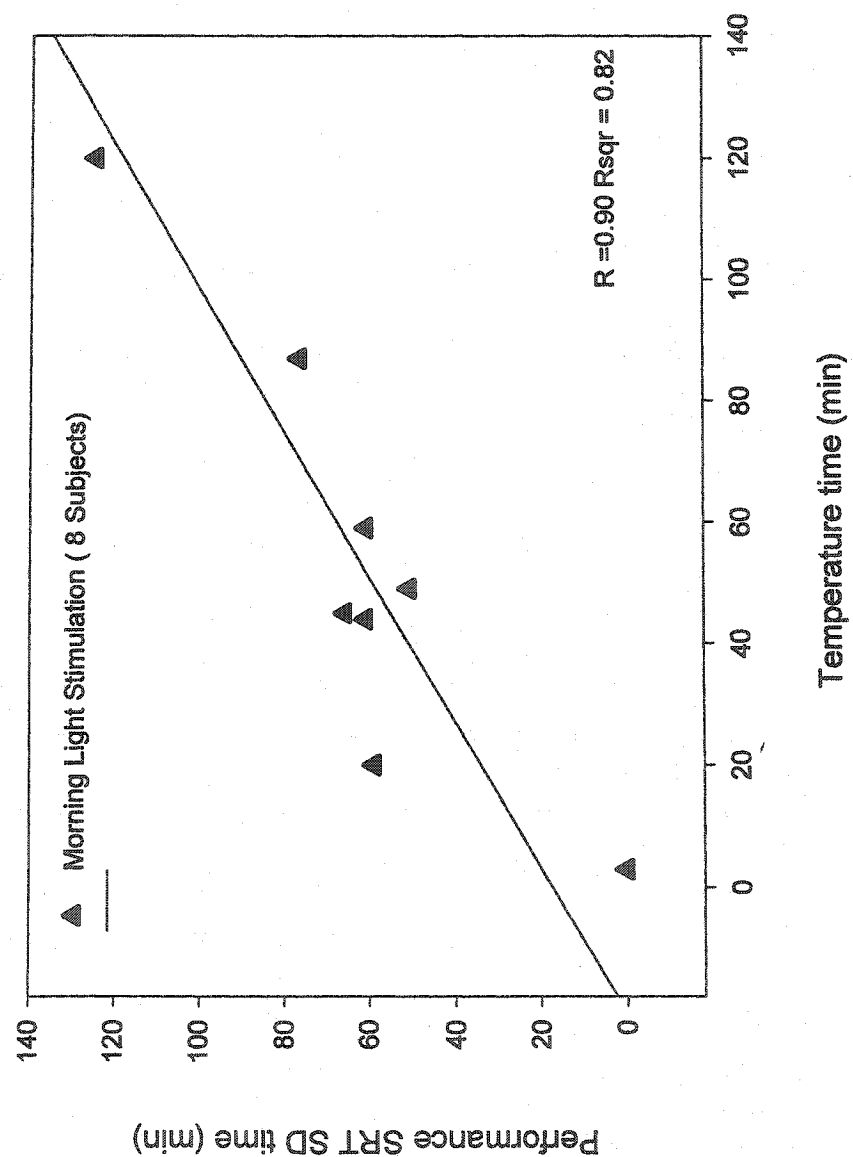


Figure 9. Regression plot of temperature and performance phase shifts following morning light exposure.

Table 3

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at 02, eyes closed, for evening light exposure (phase delay).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EC, 02	A (Condition)	1.42	1,7	0.27	0.27
	B (Hour)	2.51	10,70	0.01	0.06
	C (Frequency)	0.42	6,42	0.86	0.72
	A x B	5.40	10,70	0.000	0.000 ***
	A x C	0.63	6,42	0.70	0.57
	B x C	1.62	60,420	0.00	0.06
	A x B x C	1.42	60,420	0.03	0.15

Note. EC = eye closed; 02 = electrode site

*** $p < 0.001$

Table 4

Simple main effects of condition at each level of hour at 02 eyes closed, for evening light (phase delay)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	1.03	(1.55)	0.89	(1.58)	0.14
11:00	0.92	(1.56)	0.90	(1.56)	0.02
12:00	1.03	(1.62)	0.90	(1.57)	0.13
13:00	1.15	(1.59)	0.92	(1.59)	0.23
14:00	1.12	(1.59)	1.02	(1.60)	0.11
15:00	1.14	(1.54)	1.25	(1.62)	-0.11
16:00	0.94	(1.55)	1.30	(1.62)	-0.36 *
17:00	0.87	(1.55)	1.38	(1.66)	-0.51 *
18:00	0.92	(1.56)	1.26	(1.62)	-0.34 *
19:00	0.88	(1.56)	1.08	(1.59)	-0.20 *
20:00	0.96	(1.56)	1.05	(1.60)	-0.09

Note. Peak increases in EEG spectral power are in bold text* $p < 0.05$

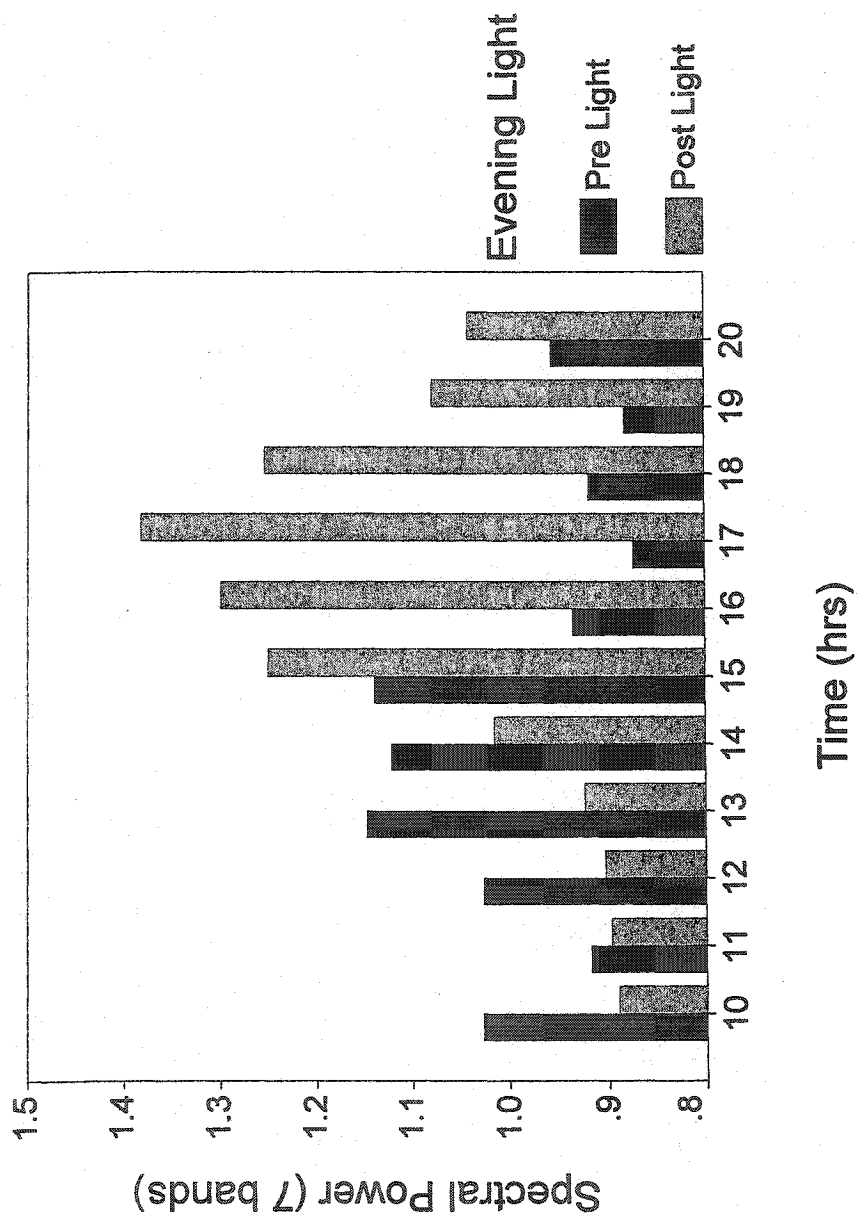


Figure 10. Group mean values for all bands with eyes closed at O2

Both the Condition by Frequency and the Hour by Frequency interactions were non-significant. Figure 10 shows the group means for all frequency bands before and after evening bright light exposure. As can be seen in Figure 10 the spectral power in all bands both increased and were phase delayed by several hours.

Often in the literature, changes in frequency bands are examined individually. Therefore the individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma are provided in Appendix E.

Similar results were obtained for evening light exposure with eyes open at 02: that is the Condition by Hour by Frequency was non-significant. The Condition by Hour interaction was highly significant, $F(10, 70) = 6.23$, $p < 0.001$ (see Table 5). The simple main effects tests which were associated with this interaction are shown in Table 6. Three tests were significant: Condition at 16:00h, $F(1,7) = 6.37$, $p < .05$; Condition at 17:00h, $F(1,7) = 8.91$, $p < .05$; and Condition at 18:00h, $F(1,7) = 7.19$, $p < .05$. An increase in the mean spectral power can be seen from 16:00 to 18:00h following evening bright light exposure.

The Condition by Frequency and the Hour by Frequency interactions were non-significant, as was true for the three main effects. In Figure 11 the group mean values for all frequency bands are displayed. The results with eyes opened essentially mirrored the phase delay as well as the increased spectral power changes seen with eyes closed, at 02. The individual mean

Table 5

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at 02, eyes open, for evening light (phase delay).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
E0, 02	A (Condition)	0.33	1,7	0.59	0.59
	B (Hour)	1.56	10,70	0.14	0.15
	C (Frequency)	0.51	6,42	0.80	0.71
	A x B	6.23	10,70	0.000	0.000 ***
	A x C	0.63	6,42	0.71	0.66
	B x C	1.26	60,420	0.10	0.23
	A x B x C	1.41	60,420	0.03	0.14

Note. EO = eye open; 02 = electrode site

*** $p < 0.001$

Table 6

Simple main effect of condition α at each level of hour at 02 eyes open, for evening light (phase delay)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	1.03	(1.56)	0.93	(1.60)	0.10
11:00	1.02	(1.55)	0.93	(1.58)	0.09
12:00	0.97	(1.56)	0.94	(1.58)	0.03
13:00	1.09	(1.62)	0.96	(1.57)	0.13
14:00	1.13	(1.58)	0.97	(1.58)	0.16
15:00	1.15	(1.60)	1.02	(1.59)	0.13
16:00	0.90	(1.55)	1.41	(1.72)	-0.51 *
17:00	0.87	(1.57)	1.31	(1.68)	-0.44 *
18:00	0.89	(1.56)	1.14	(1.57)	-0.25 *
19:00	0.90	(1.55)	1.02	(1.57)	-0.12
20:00	0.91	(1.56)	0.96	(1.55)	-0.05

Note. Peak increases in EEG spectral power are in bold text* $p < 0.05$

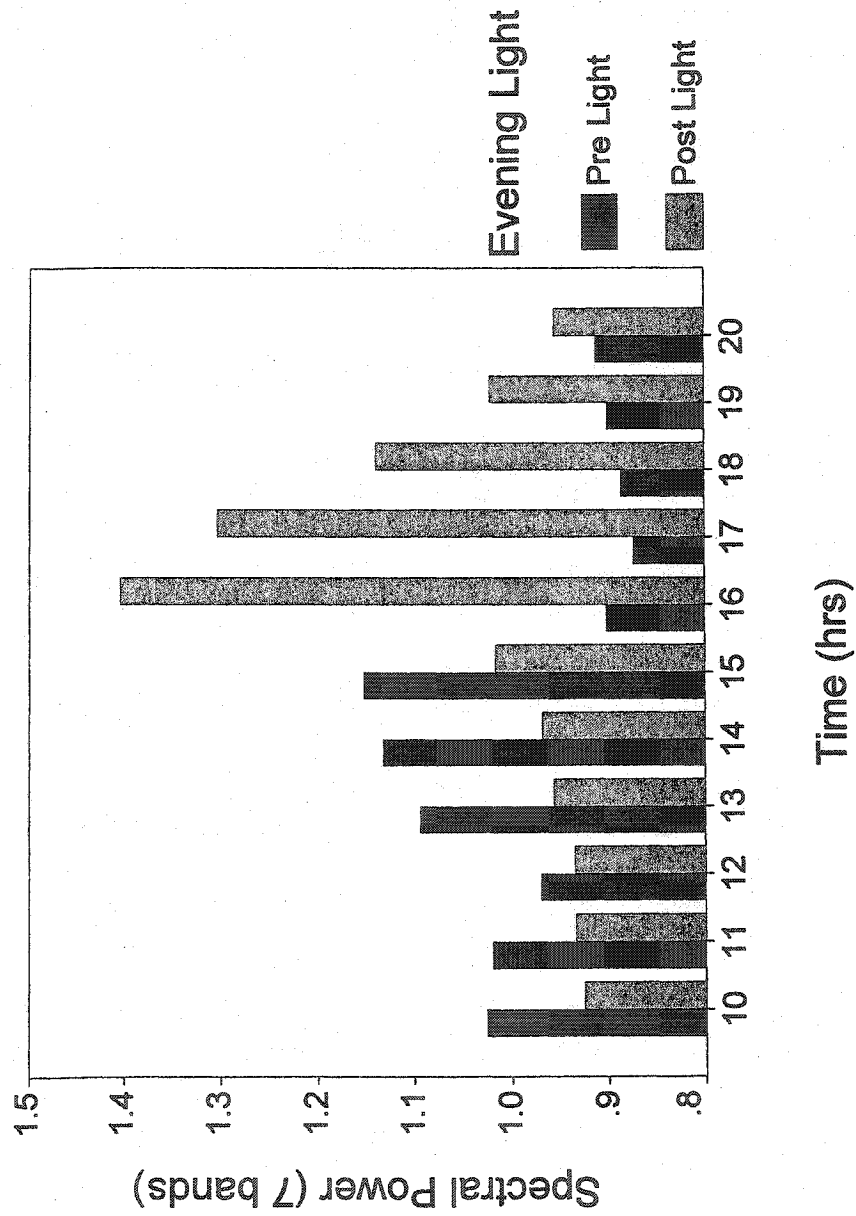


Figure 11. Group mean values for all bands with eyes open at 02

values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma are provided in Appendix F.

In the evening light condition, with eyes closed at C3, Condition by Hour by Frequency was non-significant. The Hour by Frequency interaction was significant $F(60, 420) = 1.43, p < 0.05$ (see Table 7). In order to interpret the interaction the simple main effects of hour at each level of frequency were analyzed with the spectral power collapsed across the pre-treatment and post treatment conditions. Two tests were significant: delta-2, $F(10, 70) = 2.27, p < 0.05$; and theta-1, $F(10, 70) = 4.12, p < 0.000$.

Finally pairwise comparisons were conducted. Among the pairwise comparisons for delta-2, three sample hours were significant: 12:00 - 13:00h, $F(1, 7) = 7.00, p < 0.05$; 16:00 - 17:00h $F(1, 7) = 7.93, p < 0.05$; and 17:00 - 18:00h $F(1, 7) = 6.29, p < 0.05$. For theta-1 only two comparisons were significant the 14:00 - 15:00h $F(1, 7) = 11.57, p < 0.05$; 15:00 - 16:00h $F(1, 7) = 7.18, p < 0.05$. The mean values for all normalized absolute spectral power for all bands across hour can be seen in Table 8.

The Condition by Hour interaction approached significance $F(10, 70) = 2.40, p = 0.07$ (see Table 7). The change in spectral power pre versus post evening light was less pronounced, but was clearly phase delayed by several hours (see Figure 12).

The Condition by Frequency interaction was non-significant. The main effect of Hour associated with this interaction was significant, $F(10, 70) = 4.18, p < 0.01$, but not particularly meaningful, and the main effects of Condition: and

Table 7

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at C3, eyes closed, for evening light (phase delay).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EC, C3	A (Condition)	0.36	1,7	0.57	0.57
	B (Hour)	4.18	10,70	0.000	0.001 **
	C (Frequency)	0.64	6,42	0.70	0.49
	A x B	2.40	10,70	0.02	0.07
	A x C	1.74	6,42	0.14	0.17
	B x C	1.43	60,420	0.03	0.04 *
	A x B x C	1.43	60,420	0.02	0.09

Note. EC = eye closed; C3 = electrode site

* $p < 0.05$, ** $p < 0.01$

TABLE 8

Mean values (standard deviations are in brackets below) for all normalized absolute spectral power for all bands across time at C3 eyes closed, for evening light (phase delay).

Time	Delta-1	Delta-2	Theta-1	Theta-2	Alpha-1	Alpha-2	Sigma
10:00	0.98 (0.29)	0.96 (0.28)	0.87 (0.26)	1.00 (0.60)	0.96 (0.28)	0.90 (0.42)	0.90 (0.23)
11:00	0.93 (0.17)	1.00 (0.24)	0.93 (0.23)	1.16 (0.57)	1.04 (0.26)	0.96 (0.30)	0.85 (0.18)
12:00	0.99 (0.27)	0.89 (0.21)	1.03 (0.42)	1.12 (0.45)	1.16 (0.51)	0.90 (0.30)	0.97 (0.13)
13:00	1.05 (0.24)	1.03 (0.27)	1.16 (0.38)	1.30 (0.89)	0.95 (0.37)	0.90 (0.40)	1.02 (0.18)
14:00	1.13 (0.33)	1.01 (0.17)	1.09 (0.45)	1.18 (0.64)	1.12 (0.46)	1.03 (0.41)	1.11 (0.17)
15:00	1.26 (0.31)	1.07 (0.26)	1.45 (0.57)	1.42 (0.61)	1.23 (0.46)	1.16 (0.51)	1.00 (0.15)
16:00	1.19 (0.32)	1.10 (0.24)	0.92 (0.35)	1.30 (1.06)	1.19 (0.51)	0.98 (0.30)	1.04 (0.15)
17:00	1.08 (0.21)	0.92 (0.42)	0.98 (0.41)	1.19 (0.58)	1.01 (0.39)	1.04 (0.30)	0.98 (0.17)
18:00	1.07 (0.21)	1.05 (0.27)	0.94 (0.23)	1.22 (0.82)	1.06 (0.32)	0.97 (0.26)	1.07 (0.14)
19:00	1.03 (0.33)	0.95 (0.28)	1.00 (0.60)	0.98 (0.48)	0.89 (0.28)	1.00 (0.26)	1.00 (0.17)
20:00	0.97 (0.25)	0.89 (0.15)	0.81 (0.21)	1.06 (0.55)	0.89 (0.19)	1.06 (0.30)	1.07 (0.14)

Note: All significant pairwise comparisons are in bold text.

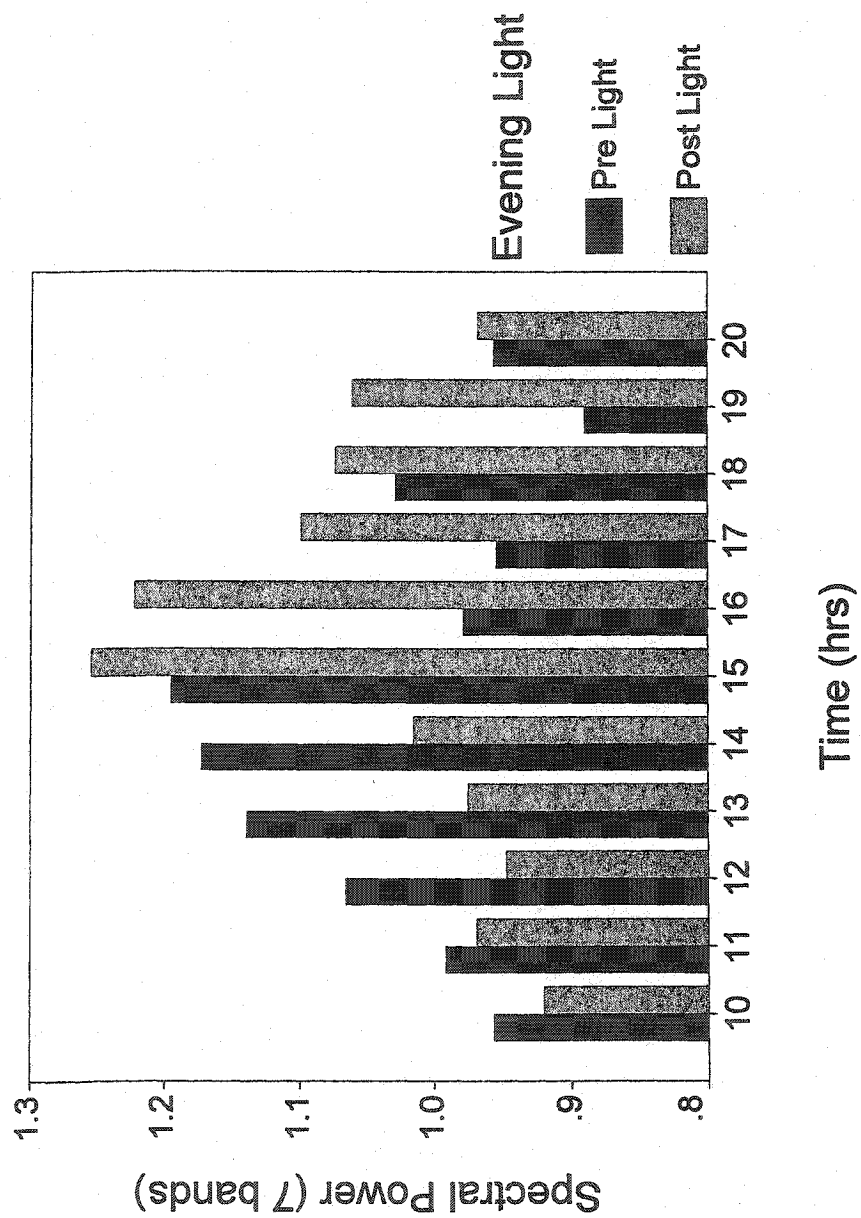


Figure 12. Group mean values for all bands with eyes closed at C3

Frequency were non-significant. All individual bands are again displayed in Appendix G.

The Condition by Hour by Frequency was non-significant in the evening light condition with eyes open at C3. The Condition by Hour was again highly significant, $F(10, 70) = 5.09$, $p < 0.001$ (see Table 9). The simple main effects tests associated with this interaction are shown in Table 10. Four tests were significant: Condition at 16:00h, $F(1,7) = 11.77$, $p < .05$; Condition at 17:00h, $F(1,7) = 18.29$, $p < .01$; Condition at 18:00h, $F(1,7) = 7.80$, $p < .05$; and Condition at 19:00h, $F(1,7) = 15.26$, $p < .01$. An increase in the mean spectral power can be seen following evening bright light exposure in the late-afternoon, (Table 10, Figure 13).

The Condition by Frequency and the Hour by Frequency interactions were non-significant. The main effects associated with these interactions were also non-significant. The group means for all bands are presented in Figure 13 and the mean values for each band are displayed in Appendix H.

Quantified EEG: Morning Light Stimulation

In the morning light condition, with eyes closed at 02, the Condition by Hour by Frequency was non-significant. Two tests were highly significant: the Condition by Hour, $F(10, 60) = 4.57$, $p < 0.000$; and the Hour by Frequency $F(10, 60) = 3.17$, $p < 0.000$ interactions (see Table 11). The simple main effect test associated with the Condition by Hour interaction are shown in Table 12. Significance was not found, as can be seen in Table 12.

Table 9

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at C3, eyes open, for evening light (phase delay).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EO, C3	A (Condition)	3.78	1,7	0.09	0.09
	B (Hour)	1.59	10,70	0.13	0.22
	C (Frequency)	1.67	6,42	0.15	0.21
	A x B	5.09	10,70	0.000	0.000 ***
	A x C	1.67	6,42	0.15	0.21
	B x C	1.53	60,420	0.01	0.18
	A x B x C	1.29	60,420	0.81	0.27

Note. EO = eye open; C3 = electrode site

*** $p < 0.001$

Table 10

Simple main effects of condition at each level of hour at C3 eyes open, for evening light (phase delay)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	1.00	(0.32)	1.00	(0.45)	0.00
11:00	0.94	(2.73)	0.98	(0.23)	-0.04
12:00	1.07	(0.37)	0.98	(0.25)	0.09
13:00	1.09	(0.39)	0.99	(0.33)	0.10
14:00	1.24	(0.64)	1.03	(0.36)	0.21
15:00	1.08	(3.38)	1.04	(0.27)	0.04
16:00	0.93	(2.17)	1.30	(0.67)	-0.37 *
17:00	0.87	(0.17)	1.11	(1.55)	-0.24 **
18:00	0.93	(0.18)	1.05	(1.55)	-0.12 *
19:00	0.91	(0.17)	1.03	(1.54)	-0.12 **
20:00	0.93	(0.22)	1.01	(1.54)	-0.08

Note. Peak increases in EEG spectral power are in bold text* $p < 0.05$, ** $p < 0.01$

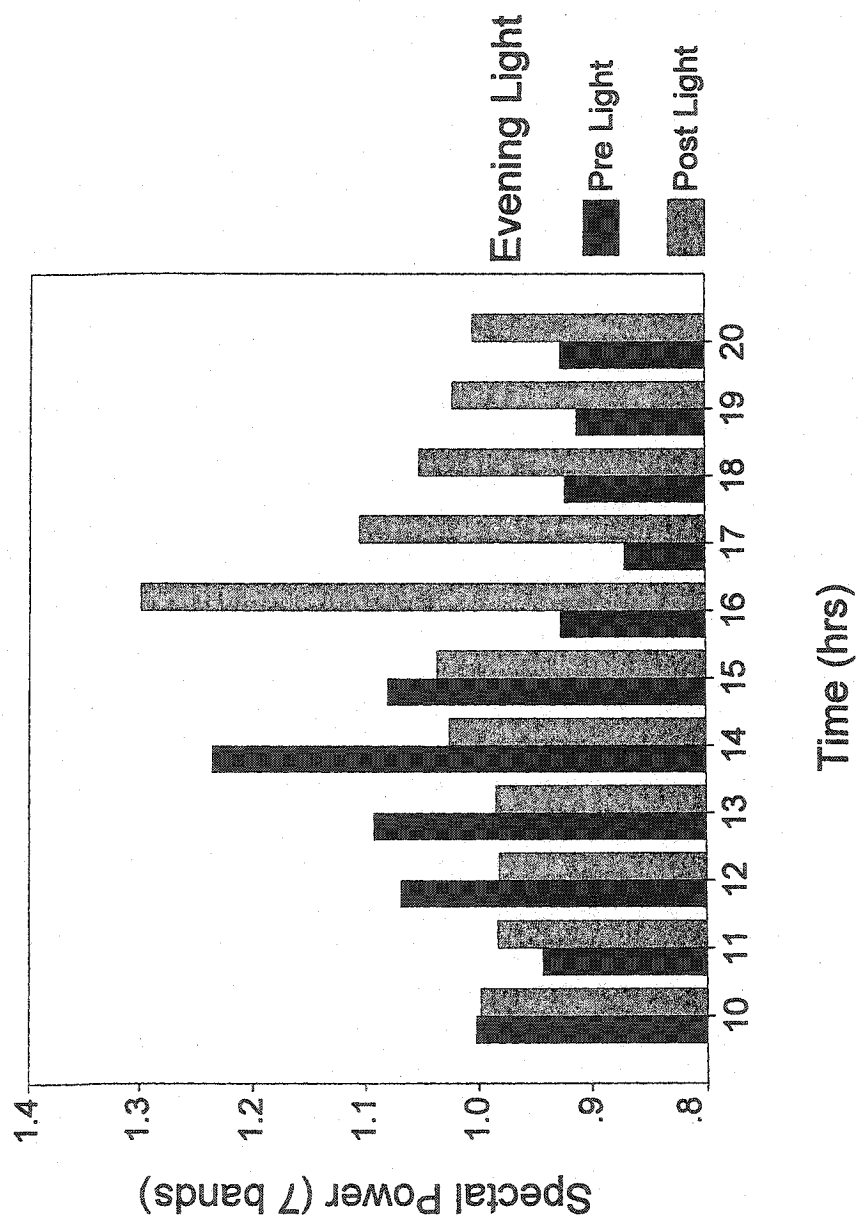


Figure 13. Group mean values for all bands with eyes open at C3

In order to interpret the results they were considered from the perspective of the simple main effects of hour in each condition. Significance was obtained for both Condition 1, $F(10, 60)=3.89$, $p < 0.001$ and Condition 2, $F(10, 60)=2.32$, $p < 0.05$. Finally pairwise comparisons were conducted. Among all possible pairwise comparisons in Condition 1, two tests were significant 12:00-13:00h, $F(1,6)=9.45$, $p < 0.05$ with an increase in power occurring at this hour and 15:00-16:00h, $F(1,6)=12.38$, $p < 0.05$ with a decrease in power occurring later in the afternoon. Only one test was significant for Condition 2, the 12:00-13:00h, $F(1,6)=8.42$, $p < 0.05$ which showed decrease in power occurring following bright light exposure.

The simple main effects of hour at each level of frequency was also analyzed; but once again in light of the main hypothesis the results are not particularly meaningful since power is collapsed over both conditions. Four tests, however, were significant: delta-1, $F(10,60)=3.00$, $p < 0.01$; theta-1, $F(10,60)=2.90$, $p < 0.01$; theta-2, $F(10,60)=2.56$, $p < 0.05$ and alpha-1, $F(10,60)=5.67$, $p < 0.0000$. Pairwise comparisons were conducted for all possible comparisons at each significant band. None of the possible pairwise comparisons were significant for delta-1, theta-1, theta-2 or alpha-2; therefore it might be due to some other weighted combination of the means. The mean

Table 11

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at 02, eyes closed, for morning light (phase advance).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EC, 02	A (Condition)	0.01	1,6	0.91	0.91
	B (Hour)	1.35	10,60	0.23	0.26
	C (Frequency)	1.17	6,36	0.35	0.35
	A x B	4.57	10,60	0.000	0.000 ***
	A x C	1.17	6,36	0.35	0.35
	B x C	3.17	60,360	0.000	0.000 ***
	A x B x C	1.12	60,360	0.27	0.32

Note. EC = eye closed; 02 = electrode site

*** $p < 0.001$

Table 12

Simple main effects of condition at each level of hour at 02 eyes closed, for morning light (phase advance)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	0.92	(0.21)	0.99	(0.41)	-0.07
11:00	0.89	(5.30)	1.08	(0.43)	-0.19
12:00	0.92	(0.26)	1.08	(0.32)	-0.16
13:00	1.13	(0.32)	0.94	(0.37)	0.19
14:00	1.15	(3.43)	0.95	(0.30)	0.20
15:00	1.10	(0.24)	0.94	(0.23)	0.16
16:00	0.99	(2.48)	0.91	(0.25)	0.08
17:00	1.03	(4.81)	0.96	(0.31)	0.07
18:00	0.95	(0.19)	0.94	(0.30)	0.01
19:00	0.97	(3.21)	1.03	(0.35)	-0.06
20:00	0.96	(0.23)	1.08	(0.44)	-0.12

Note. Peak increases in EEG spectral power are in bold text

Table 13

Mean values (standard deviations are in brackets below) for all normalized absolute spectral power for all bands across time at 02 eyes closed, for morning light (phase advance)

Time	Delta-1	Delta-2	Theta-1	Theta-2	Alpha-1	Alpha-2	Sigma
10:00	1.12 (0.51)	0.99 (0.19)	0.93 (0.26)	0.87 (0.31)	0.91 (0.36)	0.91 (0.28)	0.96 (0.29)
11:00	1.13 (6.59)	1.09 (4.44)	1.04 (6.48)	0.90 (0.35)	1.00 (0.47)	0.84 (0.37)	0.89 (0.16)
12:00	1.05 (0.22)	1.08 (0.33)	1.12 (0.32)	1.03 (0.21)	0.95 (0.32)	0.84 (0.37)	0.93 (0.25)
13:00	1.21 (0.41)	1.03 (0.26)	1.09 (0.32)	1.03 (0.36)	1.02 (0.49)	0.88 (0.41)	0.96 (0.20)
14:00	1.07 (0.23)	1.06 (0.25)	1.05 (0.35)	1.13 (0.36)	1.08 (0.38)	0.92 (0.33)	1.03 (6.61)
15:00	0.97 (0.18)	0.99 (0.21)	1.00 (0.19)	1.05 (0.28)	0.98 (0.32)	1.07 (0.29)	1.07 (0.24)
16:00	0.89 (0.13)	0.92 (0.21)	0.92 (4.24)	0.97 (0.21)	0.90 (0.25)	0.99 (0.24)	1.04 (3.38)
17:00	0.91 (0.13)	1.01 (5.66)	0.94 (0.31)	0.97 (4.48)	0.86 (0.26)	1.11 (0.20)	1.16 (5.79)
18:00	0.85 (0.13)	0.94 (0.29)	0.92 (0.18)	0.95 (0.21)	0.90 (0.27)	1.04 (0.34)	1.03 (0.23)
19:00	0.99 (0.27)	0.95 (0.16)	0.93 (0.19)	0.88 (0.25)	0.89 (0.30)	1.22 (0.31)	1.15 (6.17)
20:00	1.07 (0.31)	1.03 (0.48)	0.87 (0.21)	0.88 (0.33)	0.86 (0.35)	1.35 (0.27)	1.07 (0.26)

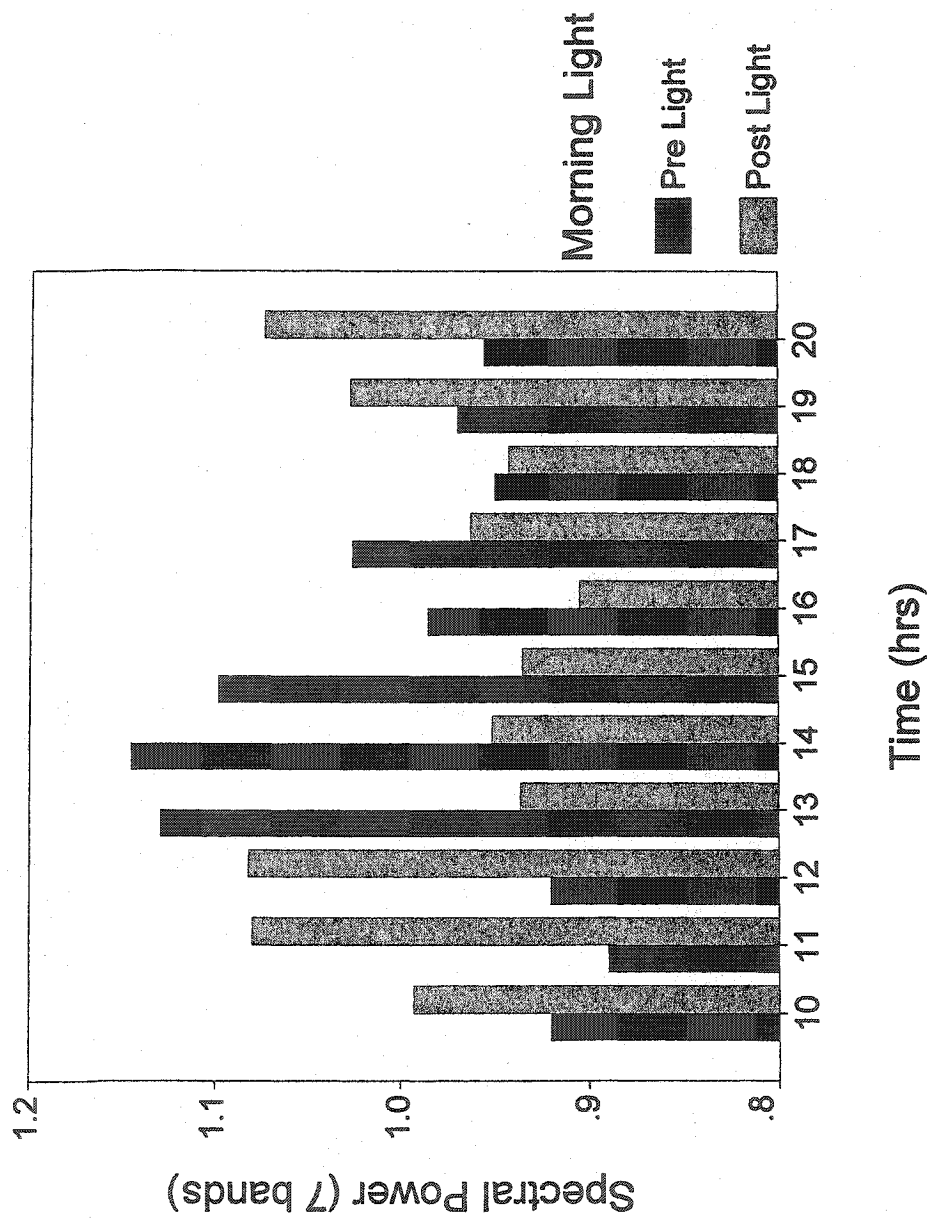


Figure 14. Group mean values for all bands with eyes closed at 02

values for all normalized absolute spectral power for each band across hours can be seen in Table 13.

The Condition by Frequency was non-significant, as was true also for the three main effects. Figure 14 shows the group means for all frequency bands before and after morning bright light exposure. As can be seen in Figure 14, the spectral power in all bands both showed a decrease and a phase advance of several hours. The 7 individual frequency bands are shown in Appendix I.

In the morning light condition, with eyes open at 02, the Condition by Hour by Frequency was non-significant. Two interactions were significant; the Condition by Hour, $F(10, 60) = 2.75, p < 0.05$, and the Hour by Frequency $F(10, 60) = 1.82, p < 0.05$ (see table 14). The results of the simple main effects analysis associated with the Condition by Hour interaction are shown in Table 15. Again significance was not found. In order to interpret the results, the simple main effects of hour in each condition were analyzed. Significance was obtained for both Condition 1, $(10, 60) = 2.93, p < 0.01$ and Condition 2, $F(10, 60) = 2.38, p < 0.05$. Finally pairwise comparisons were conducted. Among all possible comparisons in Condition 1, two tests were significant: 12:00-13:00h, $F(1, 6) = 9.45, p < 0.05$ with an increase in power occurring at this hour and 16:00 –17:00h, $F(1, 6) = 13.19, p < 0.05$ with a decrease in power occurring later in the afternoon. Only one test was significant in Condition 2, the 13:00-14:00h, $F(1, 6) = 15.95, p < 0.01$.

Table 14

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at 02, eyes open, for morning light (phase advance).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EO, 02	A (Condition)	0.56	1,6	0.48	0.48
	B (Hour)	2.49	10,60	0.01	0.04 *
	C (Frequency)	1.32	6,36	0.28	0.30
	A x B	2.75	10,60	0.01	0.02 *
	A x C	1.32	6,36	0.28	0.30
	B x C	1.82	60,360	0.001	0.01 *
	A x B x C	1.19	60,360	0.17	0.25

Note. EO = eye open; 02 = electrode site

* $p < 0.05$

Table 15

Simple main effects of condition at each level of hour at 02 eyes open, for morning light (phase advance)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	0.99	(0.21)	1.09	(0.48)	-0.10
11:00	0.97	(3.87)	1.16	(0.45)	-0.19
12:00	0.97	(2.34)	1.19	(0.39)	-0.22
13:00	1.11	(0.25)	1.07	(0.34)	0.04
14:00	1.08	(0.25)	1.01	(0.28)	0.07
15:00	1.07	(0.26)	1.00	(0.27)	0.07
16:00	0.97	(0.26)	1.00	(0.28)	-0.03
17:00	0.91	(4.71)	1.03	(0.27)	-0.12
18:00	0.93	(4.76)	1.02	(0.25)	-0.09
19:00	0.96	(0.14)	1.02	(0.28)	-0.06
20:00	1.03	(0.22)	1.04	(0.35)	-0.01

Note. Peak increases in EEG spectral power are in bold text

Table 16

Mean values (standard deviations are in brackets below) for all normalized absolute spectral power for all bands across time at 02 eyes open, for morning light (phase advance)

Time	Delta-1	Delta-2	Theta-1	Theta-2	Alpha-1	Alpha-2	Sigma
10:00	1.19 (0.33)	1.05 (0.27)	1.05 (0.27)	1.17 (0.38)	0.95 (0.48)	0.90 (0.28)	0.98 (0.35)
11:00	1.08 (0.34)	1.10 (3.87)	1.08 (0.31)	1.20 (6.35)	1.08 (0.40)	1.05 (0.46)	0.88 (0.27)
12:00	1.05 (0.27)	1.04 (0.17)	1.16 (0.33)	1.08 (0.22)	1.16 (0.32)	1.15 (0.51)	0.94 (4.17)
13:00	1.12 (0.16)	1.03 (0.18)	1.10 (0.23)	1.19 (0.32)	1.13 (0.40)	1.13 (0.38)	0.94 (0.32)
14:00	1.00 (0.22)	1.14 (0.20)	1.08 (0.29)	1.10 (0.30)	1.13 (0.28)	0.97 (0.26)	0.92 (0.26)
15:00	0.96 (0.13)	1.00 (0.19)	1.06 (0.23)	1.12 (0.22)	1.09 (0.29)	1.00 (0.41)	1.02 (0.31)
16:00	0.98 (6.48)	0.98 (0.16)	0.97 (0.23)	1.03 (0.19)	0.94 (0.16)	1.05 (0.31)	0.96 (0.30)
17:00	0.92 (4.70)	1.09 (5.80)	1.04 (0.20)	0.98 (0.21)	0.83 (0.21)	1.01 (0.26)	0.94 (5.12)
18:00	0.94 (0.17)	1.00 (5.62)	1.03 (3.36)	0.91 (6.38)	0.96 (0.24)	1.01 (0.34)	0.98 (0.29)
19:00	1.01 (0.12)	1.03 (0.17)	1.05 (0.18)	1.00 (0.22)	0.94 (0.27)	0.96 (0.28)	0.94 (0.29)
20:00	1.01 (0.14)	1.09 (0.32)	1.04 (0.21)	1.04 (0.30)	0.99 (0.34)	1.17 (0.41)	0.92 (0.27)

Note: All significant pairwise comparisons are in bold text.

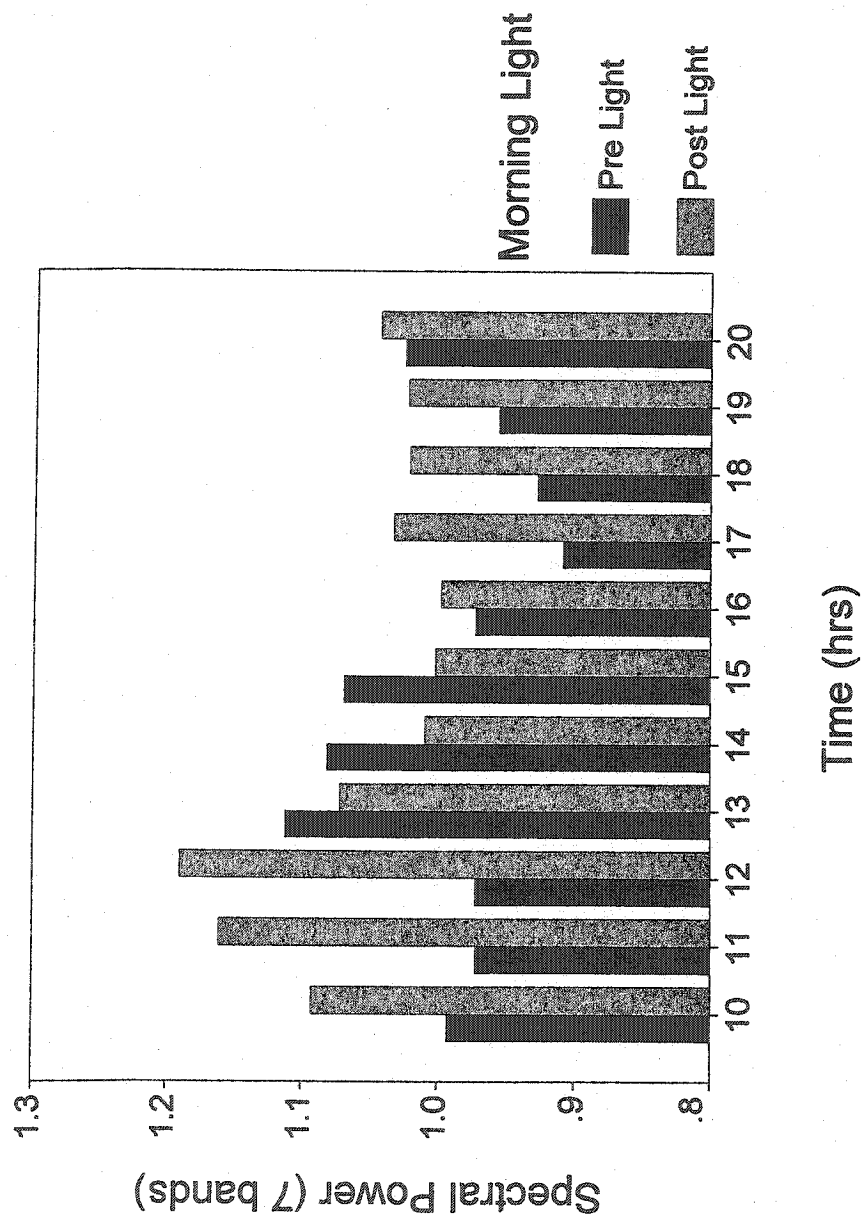


Figure 15. Group mean values for all bands with eyes open at 02

The simple main effect of hour at each level of frequency was also analyzed. Three tests were significant: delta-1, $F(10,60) = 3.24$, $p < 0.01$; theta-2, $F(10,60) = 3.31$, $p < 0.01$; and alpha-1, $F(10,60) = 2.83$, $p < 0.01$. Finally, pairwise comparisons were conducted for all possible comparisons. Among the pairwise comparisons for delta-1, one hour was significant: 13:00-14:00h, $F(1,7) = 7.06$, $p < 0.05$ and one hour for theta-2, 11:00-12:00h, $F(1,7) = 9.65$, $p < 0.05$ and one hour for alpha-1, 15:00-16:00h, $F(1,7) = 7.84$, $p < 0.05$. The mean values for all normalized absolute spectral power for all bands across hour can be seen in Table 16.

The Condition by Frequency was non-significant. The main effect of Hour was significant, $F(10,60) = 2.49$, $p < 0.05$, but not meaningful; and the main effects of Condition and Frequency were non-significant. As can be seen in Figure 15, the global spectral power phase advanced and increased following morning bright light exposure. The contribution of each individual frequency band to the overall spectral power can be seen in Appendix J.

Similar results were obtained for morning light exposure with eyes closed at C3, that is the Condition by Hour by Frequency was non-significant, and the Condition by Hour $F(10, 60) = 2.51$, $p < 0.05$ and the Hour by Frequency $F(10, 60) = 1.87$, $p < 0.05$ interactions were significant (see Table 17). The simple effects test associated with the Condition by Hour interaction are shown in Table 18. Three tests were significant: Condition at 16:00h, $F(1,6) = 16.06$, $p <$

Table 17

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at C3, eyes closed, for morning light (phase advance).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EC, C3	A (Condition)	1.87	1,6	0.22	0.22
	B (Hour)	2.06	10,60	0.04	0.06
	C (Frequency)	0.62	6,36	0.71	0.69
	A x B	2.51	10,60	0.01	0.04 *
	A x C	0.62	6,36	0.71	0.69
	B x C	1.87	60,360	0.000	0.01 *
	A x B x C	1.13	60,360	0.26	0.28

Note. EC = eye closed; C3 = electrode site

* $p < 0.05$

Table 18

Simple main effects of condition at each level of hour at C3 eyes closed, for morning light (phase advance)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	0.93	(3.52)	0.94	(0.21)	-0.01
11:00	0.94	(1.86)	0.95	(0.21)	-0.01
12:00	0.98	(3.50)	1.07	(2.55)	-0.09
13:00	1.08	(0.33)	1.00	(0.30)	0.08
14:00	1.08	(0.25)	0.94	(0.19)	0.14
15:00	1.03	(2.47)	0.91	(3.53)	0.13
16:00	1.03	(2.77)	0.90	(4.21)	0.12
17:00	1.04	(3.91)	0.95	(0.22)	0.09
18:00	0.96	(2.42)	0.86	(0.20)	0.10
19:00	0.98	(5.86)	0.97	(0.24)	0.01
20:00	0.96	(0.19)	0.95	(0.23)	0.01

Note. Peak increases in EEG spectral power are in bold text* $p < 0.05$, ** $p < 0.01$

Table 19

Mean values (standard deviation are in brackets below) for all normalized absolute spectral power for all bands across time at C3 eyes closed, for morning light (phase advance)

Time	Delta-1	Delta-2	Theta-1	Theta-2	Alpha-1	Alpha-2	Sigma
10:00	0.97 (0.17)	0.90 (0.76)	0.90 (0.18)	0.87 (0.19)	0.98 (0.23)	1.01 (0.24)	0.92 (0.15)
11:00	0.98 (0.29)	0.93 (3.55)	0.96 (0.11)	0.97 (0.20)	1.00 (0.24)	0.84 (0.18)	0.93 (0.14)
12:00	1.02 (0.30)	0.94 (0.15)	1.10 (0.29)	1.05 (0.18)	1.11 (0.29)	0.93 (0.29)	0.99 (8.30)
13:00	1.08 (0.27)	1.00 (0.15)	1.18 (0.45)	1.08 (0.25)	1.02 (0.48)	0.90 (0.30)	1.02 (0.14)
14:00	0.96 (0.20)	0.97 (0.12)	1.11 (0.32)	1.03 (0.26)	0.99 (0.34)	1.00 (0.15)	1.00 (0.14)
15:00	1.03 (0.24)	0.99 (0.15)	0.97 (0.18)	0.95 (0.18)	0.90 (0.21)	0.96 (0.19)	1.00 (8.27)
16:00	0.98 (0.22)	0.97 (7.38)	0.97 (0.16)	0.92 (0.17)	0.94 (0.20)	0.95 (4.56)	1.02 (4.33)
17:00	1.03 (0.17)	0.98 (4.91)	0.93 (0.15)	0.96 (0.19)	0.97 (0.26)	1.03 (0.23)	1.06 (5.69)
18:00	0.92 (0.17)	0.94 (0.19)	0.87 (0.19)	0.89 (0.18)	0.87 (0.21)	0.89 (0.23)	1.00 (4.65)
19:00	1.04 (0.21)	1.01 (0.15)	0.91 (6.67)	0.88 (0.20)	0.87 (6.61)	1.10 (0.21)	1.00 (6.22)
20:00	1.04 (0.25)	0.98 (0.15)	0.84 (0.18)	0.87 (0.17)	0.84 (0.15)	1.16 (0.19)	0.96 (0.19)

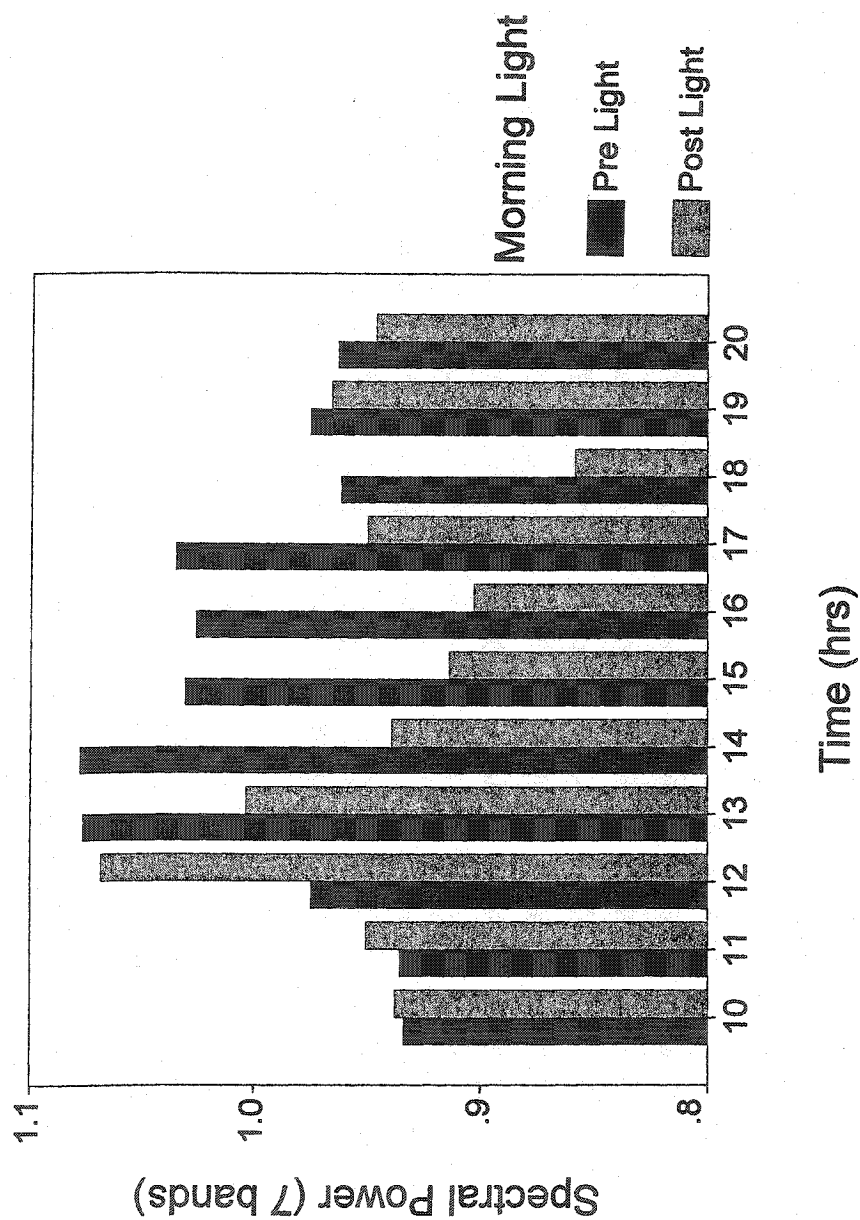


Figure 16. Group mean values for all bands with eyes closed at C3

.01; Condition at 17:00h, $F(1,6) = 7.58$, $p < .05$; and Condition at 18:00h, $F(1,6) = 6.44$, $p < .05$. A decrease in the mean spectral power can be seen following morning bright light exposure in the late afternoon.

The simple main effects of hour at each level of frequency were also analyzed. Two tests were significant: theta-1, $F(10,60) = 3.21$, $p < 0.01$; alpha-1, $F(10,60) = 2.08$, $p < 0.05$. Finally, pairwise comparisons were conducted. However, none of the possible 110 pairwise comparisons were significant for theta-1 or alpha-1; suggesting that the results might be due to some other weighted combination of the means. The mean values for all normalized absolute spectral power for each frequency band across hour can be seen in Table 19.

The condition by frequency was non-significant as were the three main effects. The group means values are presented in Figure 16 and the individual bands means are displayed in Appendix K. In Figure 16 a slight decrease in power can be observed.

The Condition by Hour by Frequency was non-significant in the morning light condition for eyes open at C3. The Condition by Hour interaction was significant, $F(10, 60) = 2.35$, $p < 0.05$ (see Table 20). In order to interpret the interaction the simple effects of Condition at each level of Hour was analyzed (see Table 21). However, all tests were non-significant. In order to interpret the results they were examined from the perspective of the simple main effects

Table 20

Results of analysis of variance of normalized absolute spectral power for all bands across time and condition at C3, eyes open, for morning light (phase advance).

7 Bands	Source of Variance	F	df	2-Tailed Probability	Huynh-Feldt Probability
EO, C3	A (Condition)	0.81	1,6	0.40	0.40
	B (Hour)	1.68	10,60	0.11	0.14
	C (Frequency)	0.67	6,36	0.67	0.63
	A x B	2.35	10,60	0.02	0.04 *
	A x C	0.56	6,36	0.76	0.63
	B x C	1.07	60,360	0.35	0.39
	A x B x C	1.33	60,360	0.06	0.15

Note. EO = eye open; C3 = electrode site

* $p < 0.05$

Table 21

Simple main effects of condition at each level of hour at C3 eyes open, for morning light (phase advance)

Time	Condition 1 pre light		Condition 2 post light		Mean Difference
	Mean	SD	Mean	SD	
10:00	0.96	(3.60)	1.11	(1.54)	-0.15
11:00	1.00	(3.26)	1.06	(1.55)	-0.06
12:00	1.02	(3.49)	1.13	(1.54)	-0.11
13:00	1.08	(2.38)	1.04	(1.54)	0.04
14:00	1.05	(1.54)	0.97	(1.55)	0.08
15:00	0.99	(4.59)	0.96	(3.75)	0.03
16:00	0.96	(5.42)	1.01	(1.54)	-0.05
17:00	0.93	(3.52)	1.04	(1.55)	-0.11
18:00	0.99	(1.54)	1.01	(1.56)	-0.02
19:00	0.96	(1.54)	1.06	(1.55)	-0.10
20:00	1.01	(2.36)	1.06	(1.56)	-0.05

Note. Peak increases in EEG spectral power are in bold text

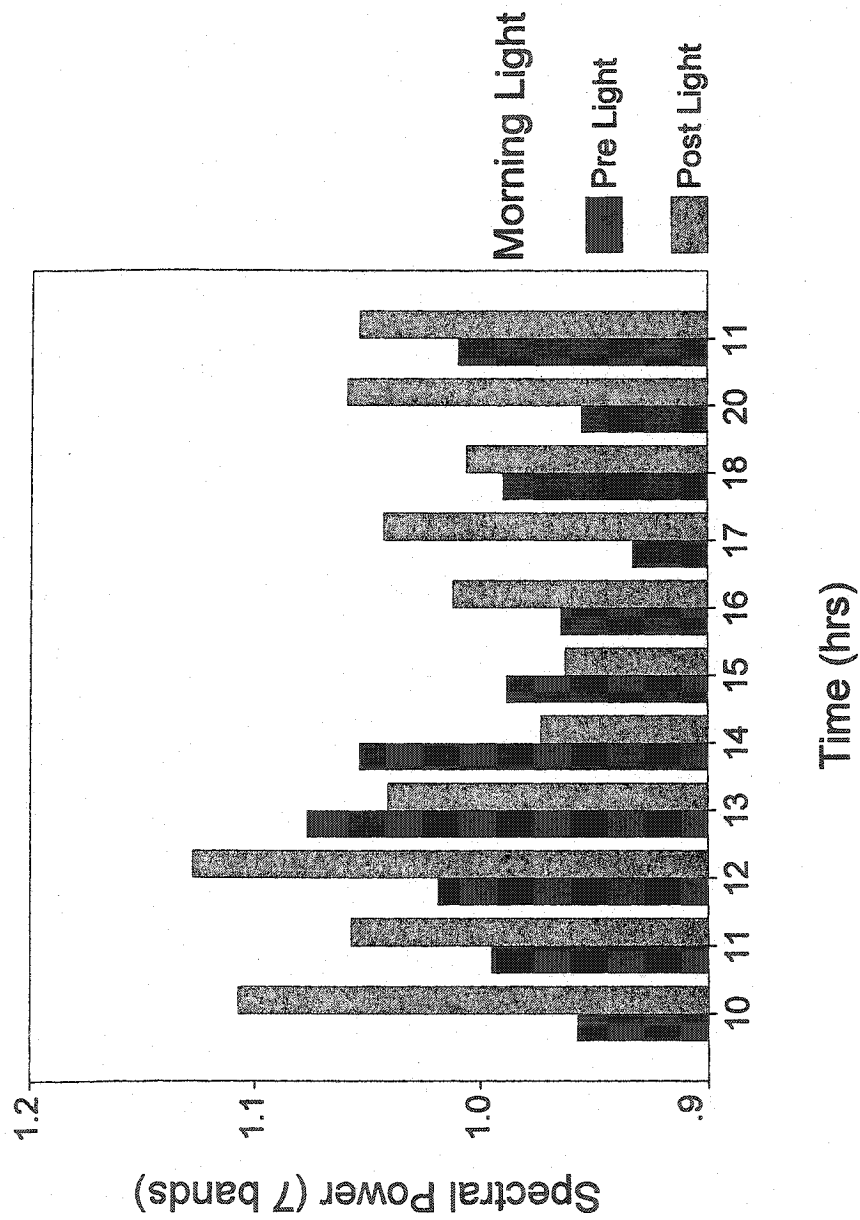


Figure 17. Group mean values for all bands with eyes open at C3

of Hour in each condition. Significance was obtained for Condition 2, $F(10, 60) = 3.04$, $p < 0.01$. Finally pairwise comparisons were conducted. Among all possible comparisons in Condition 2, only one test was significant. It was 11:00-12:00h, $F(1,6) = 7.22$, $p < 0.05$ with a decrease in spectral power occurring at this hour.

Both the Condition by Frequency and the Hour by Frequency interactions were non-significant. The main effects associated with these interactions were non-significant. As can be seen in Figure 17, the all band spectral power peak phase advanced by several hours. The individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma are displayed in Appendix L.

The individual frequency band figures indicate the directional shift with evening and morning bright light therapy for all bands other than sigma in the predicted direction. Sigma power appeared not to show any shift with bright light therapy.

CHAPTER IV

DISCUSSION

This discussion will first consider aspects of the data involved followed by the apparent relevance of the findings to our understanding of circadian aspects of sleep/wake regulation and ending with some suggestions for extending the research by future studies.

Curvefitting of Circadian Core Body Temperature

As recommended by Broughton et al., (1993) and by Lack and Wright, (1993), a polynomial least squared regression was used to fit the raw core body temperature data (using 1 minute samples). This was done separately for all eight subjects for both baseline and bright light exposure conditions.

The times of the curve fitted temperature minima for baseline and post stimulation evening light (phase delay) and morning light (phase advance) conditions were taken as the circadian temperature rhythm phase markers. The findings demonstrated that polynomial regression adequately explained the data and accounted for 94% of the variance in the evening light condition and 92% of the variance in the morning light condition. This close curve-fit was similar to the results reported by Broughton et al., (1993) and when combined with visual analysis of raw data indicated that this main marker of circadian phase (temperature minimum or "nadir") was well identified.

The main difficulty encountered when interpreting the temperature data is that it was recorded in ambulatory subjects and therefore one might expect some masking of the underlying temperature rhythm. The constant routine protocol which is frequently used to unmask the temperature rhythm was not employed because of the 9-day length of the protocol would lead to substantial sleep deprivation and would effect the day time performance and EEG results.

In order to minimize the environmental effects a strict regime was used throughout the study. Firstly, all subjects lived in an isolation chamber with no external time cues permitted, light was held constant and activity was restricted by lack of space and constant supervision. Secondly, meals were monitored and divided into small hourly snacks with intake controlled. Finally, all subjects maintained a fixed sleep/wake schedule for two weeks prior to entering the study and for two weeks following the initial condition before returning for the second one.

Evening Light Stimulation and Temperature

Our findings confirm the results widely reported in the literature that the phase of the human circadian core temperature rhythm can be reset by exposure to bright artificial light. It was predicted that following two nights of evening bright light exposure, the temperature minima would be phase delayed by one to two hours. Bright light exposure in the two hours before

bedtime delayed the core body temperature minimum by an average of 1: 46 hours (1 hr 46 min). Similar phase delays have been reported in other studies using evening bright light stimulation (Czeisler, Kronauer, Johnson, Allen, & Dumont, 1988; Drennan et al., 1989), although a somewhat greater delay was found in Czeisler, Kronauer, Allan, Duffy, Jewett, Brown, Ronda (1989). In the latter study it is notable that subjects were exposed to evening bright light over a greater number of days as compared with the current study (i.e., 3 days versus 2).

Morning Light Stimulation and Temperature

It was predicted that exposure to bright light on two consecutive mornings would phase advance the temperature minima by one to two hours. Morning bright light exposure for two hours successfully phase advanced the core body temperature minimum by an average of 53 minutes, a calculation, which includes one subject who was unresponsive. Others have also documented occasional normal subjects unresponsive to morning bright light therapy (Gallo & Eastman, 1993). Similar phase advances of approximately an hour were reported in papers by Dijk, Visscher, Bloem, Beersma, & Daan (1987) and by Dijk, Beersma, Daan, & Lewy (1989). On the other hand, the mean phase advance in this study was smaller in magnitude than those reported in some other studies. For example, following morning bright light Rosenthal et al., (1990) phase advanced the circadian core body temperature by 2 hours in patients. However, these patients had a delayed sleep phase

syndrome and subjects were exposed to two hours of bright light for two weeks before the shifts were determined. Czeisler, et al., (1988) demonstrated that 3 days of light exposure at about 10,000 lux for 4 to 5 hours resulted in a phase advance of 3 hours in a patient with delayed phase sleep syndrome.

Several plausible explanations may account for the greater phase advances found in the latter studies. Firstly, these studies involved patients with a circadian rhythm phase disorder, whereas in the current study the subjects were all healthy normal subjects. Secondly, the patients were exposed to bright light over a longer period of time (3-14 days), whereas in our study subjects were exposed for only two days. Finally, in the study by Czeisler et al., (1988) the patient received light for a much longer session (4 to 5 hours), whereas our subjects were exposed to bright light for two hours. Although all subjects in the current study were exposed to light of the same intensity, there was an inter-individual variation of effect. Such variation has been reported by others and might relate to differences in response to bright light in any or all of: the retina, the visual pathways leading to the SCN, the SCN, or the efferent temperature modulatory systems of the SCN.

The finding that the mean magnitude of the phase advance was less than for the phase delay may relate to the period of the natural endogenous circadian rhythm which in humans is somewhat longer than 24 hours so that the circadian system is always tending to phase delay rather than advance. It

was also noted by visual analysis that phase delay was associated with tendency to broaden the duration of the nadirs from the baseline shape, whereas phase advances narrowed them. This might be also expected for a periodicity that is longer than 24 hours.

Performance Baseline

It has been shown that, whether or not we have adequate prior night sleep, there is a transitory decrease in performance around the time of the afternoon nap zone (reviewed in Hockey & Colquhoun, 1972). It was predicted that during the baseline condition, poorest daytime performance would occur around the time of the nap zone. In the present study the daytime performance level sampled hourly varied as a function of time of day for both the mean and standard deviation of simple reaction time in a pattern similar to that expressing the afternoon nap zone using other techniques (Broughton & Mullington, 1992). Similar transitory afternoon decreases in performance have been reported in a number of studies (Bjerner et al., 1955; Blake, 1967; Browne, 1949; Hildebrandt, et al., 1974; Hockey & Colquhoun, 1972). This indicated that performance measures of this task were sensitive to waking alertness/drowsiness levels and were capable of showing the timing of the afternoon nap zone.

The relatively high variance of reaction time at all times of day is a well documented feature in studies involving repeated trials across the day

(Bonnet, 1985; Dinges, Orne, Whitehouse, Orne, 1987, Herscovitch & Broughton, 1981). This might relate to individual differences in RT capacity, boredom, lack of motivation or other factors. In this study, the focus was on the timing of poorest performance (slowest RT, greatest RT variability) across the daytime. Despite high variability at each hourly sample the hour of poorest performance was consistently present in one of the afternoon data points rather than in the morning or evening. The fact that this was so suggests that repeated performance sampling across the daytime period neither led to a progressive deterioration from fatigue nor a progressive improvement from increased motivation.

Light Stimulation and Performance

It was predicted that following evening light stimulation, the time of poorest daytime performance would be delayed by one to two hours. Following evening bright light exposure phase delays were in fact observed in all subjects and averaged approximately 2 hours (mean 1:54).

Conversely, it was predicted that following morning light stimulation poorest performance would be advanced by one to two hours. Following morning bright light exposure phase advances were observed in all but one subject. The mean advance was approximately 1 hour (mean 1:03).

As stated in the introduction, the simple reaction time test was chosen because of its sensitivity to decreased alertness induced by sleep deprivation

and its minimal learning effects. That this arousal sensitive measure shifted in both directions in parallel with the induced shift of the measure of the circadian clock supports the existence of a light sensitive circadian arousal process.

Circadian Core Body Temperature and Performance

The timing of lowest level in daytime performance was phase delayed and phase advanced in parallel with core body temperature shifts. The regression analysis between performance and temperature shifts for both phase delay and phase advance showed $r^2 = .82$, indicating that they are closely coupled. Two plausible explanations may account for the variability found between the two measures. Firstly, there was a large difference in sampling rate, as temperature was sampled every minute around the clock throughout the study, whereas performance was only sampled every hour during the daytime. Secondly, there was occasional difficulty in identifying the exact nadir in performance data. The finding never-the-less remains consistent with the proposed mechanism of the afternoon nap zone phenomenon.

As reported elsewhere, no significant learning effect was evident for the simple reaction time test (Herscovitch & Broughton 1981; Godbout & Montplaisir, 1986). Both mean reaction time and RT variability were equally affected. There was an insufficient number of gaps to analyze this measure in these rested normal subjects. It would appear that gaps may only be, or may mainly be, a sensitive measure of sleepiness/drowsiness in sleep deprived individuals and in-patients with excessive daytime sleepiness related to a

medical sleep disorder and in such individuals may often relate to "lapses" or actual micro-sleeps.

Quantified EEG Methods and Baseline Measures

Upon visual inspection of the Q-EEG data there seems to be some variability between the two means; however, by using a repeated measures design, significance was obtained. Since the data are paired (same person both pre and post) and the values in mean 1 and in mean 2 are related, the variance of the difference is actually much smaller than one would assume. This is because we are subtracting $2 \cdot R \cdot \text{stderr1} \cdot \text{stderr2}$ from the usual variance. This $2 \cdot R$ is the within subjects correction. As can be seen from the formula, the higher the correlation is between the values from mean1 and mean2, the smaller the variance of the difference and therefore the easier it is to find significance.

Quantified EEG as mentioned above also proved to be a sensitive measure of alertness and drowsiness across the day. It was predicted that during the baseline condition lowest daytime arousal indexed by increased spectral power in lower frequency bands will occur around the time of the nap zone. Consistent with this prediction a transitory period of increased spectral power for all frequencies combined (0.5-15.5 Hz) was consistently found in the mid-afternoon in the baseline conditions. This also suggests that this overall frequency band is a sensitive measure of waking alertness levels.

These findings are consistent with the results of Cacot, et al., (1995), Dumont, et. al., (1999) and of Sterman (1996, personal communication), all of whom described a transitory increase in spectral power for all frequency bands combined during the afternoon. The pattern of increased spectral power occurring across the daytime in individual frequency bands reported by others (Aeschbach, et al., 1999; Akerstedt & Gillberg 1990; Akerstedt, Kecklund & Knutson, 1991; Brunner, et al., 1993; Cajochen et al., 1995; Corsi-Cabrera et al., 1992; Dumont et al., 1999; Finelli, et al., 2000; Lafrance & Dumont 2000; Torsvall & Akerstedt 1987; Yan, Rivers, Boucher and Broughton. 1998) was not tested statistically in this study before and after bright light stimulation, but only when power was collapsed over both conditions.

Corsi-Cabrera et al. (1992) reported changes in the waking EEG as a consequence of sleep and sleep deprivation. They recorded 8 electrodes (C3, C4, T3, T4, P3, P4, O1 and O2) and found that the absolute spectral power for theta (3.66-7.32 Hz), alpha-2 (9.77-12.45 Hz) and beta (12.7-25.15 Hz) bands was significantly higher after one night of total sleep deprivation. Brunner and colleagues (1993) analyzed the C3 and C4 EEG signals and found that the power density of a high delta and low theta band (3.75-4.5 Hz) increased after four partial sleep deprivation nights (4 hours sleep/per night). Studies in our laboratory (Yan, Rivers, Boucher and Broughton 1998) found that sleep deprivation in normal subjects mainly increased absolute power in the theta range of the waking EEG and to a lesser extent in the high delta band. This

study had similar slow eye movement indices (a measure of drowsiness) in the baseline and sleep deprived conditions thereby controlling for possible greater sampling in periods of mild drowsiness after sleep deprivation.

Finelli et al., (2000) found the greatest increase occurred in the theta band during a 40-hour period prolonged wakefulness, changes also occurred in other frequency ranges but to a lesser extent. Several other studies examined changes in EEG over a 40-hour period of prolonged wakefulness using a constant routine protocol (Aeschbach, et al., 1999; Cajochen, et al., 1995; Dumont, et al., (1999). For example, Cajochen, et al., (1995) reported that the spectral power value for theta and alpha frequency bands increased during the 40-hour trial. Aeschbach, et al., (1999) also noted changes in the theta and alpha frequency bands. Using non traditional frequency bands Dumont et al., in a similar protocol of prolonged wakefulness reported changes in a number of frequency ranges. For instance, comparable time courses were noted for Cluster I (2.00-7.75 Hz), and Cluster III (11.00-14.75 Hz): both increased throughout the trial with a mid- afternoon peak and a dip in the middle of the night. Cluster II (8.00-10.75 Hz), also showed an increased in the mid-afternoon with a decrease in the middle of the night. Cluster V (18.00-24.75 Hz) showed a general increase across the day; and Cluster IV (15.00-17.75 Hz), showed no particular pattern. However, it must be recalled that in all these other studies subjects were sleep deprived, whereas in the present study subjects were all well rested.

In the above studies there was no consistent selective increase in spectral power in the low delta band range, as might be expected for the waking EEG, as well as for the sleep EEG, by the 2-process model of sleep/wake regulation (Borbély, 1982). In this model Borbély et al. (1982) hypothesized that delta power is related to an endogenous sleep enhancing factor which accumulates in the brain during the waking period, further increases during extended sleep deprivation (prolonged wakefulness), and is decreased or eliminated during sleep.

Several plausible explanations may account for the increased spectral power in an individual frequency band found in the latter studies. Firstly, in the literature specific frequency bands are often predicted to change and therefore are examined individually. In this study individual frequency bands were not analyzed statistically, because the large number of repeated tests would greatly increase the risk of Type 1 error. Secondly, the relatively small sample size may have contributed to the general lack of statistical significance found when the simple main effects tests were conducted examining the individual frequencies. Finally, at the time the study was performed there was no compelling reason to predict changes in any single frequency band. Nevertheless, post-hoc visual inspection of each individual frequency band showed a consistent increase in spectral power in the mid- afternoon for all frequency bands delta-1, delta-2, theta-1, theta-2, alpha-1 and alpha-2, but not for sigma. In respect to the lowest frequency range (delta-1), there is always concern that

ocular artifacts may contaminate the data. However, it must be recalled that in the eyes open condition the subjects maintained visual fixation. Moreover, the same pattern was found in other frequency ranges. The changes reported for delta -1 were therefore most probably not due to ocular contamination but rather represented a real EEG change with fluctuating diurnal waking arousal level.

The cause of the deviant pattern seen in the sigma frequency band is uncertain (see Appendices E7, F7, G7, H7, I7, J7, K7, L7). It seems unlikely that it can be explained by muscle artifact, as the latter is usually much higher in frequency (around 40-60Hz). A more likely explanation is that the EEG frequencies sensitive to variations in alertness/drowsiness are slower than the sigma frequency range. In other studies, sigma was not considered a sensitive indicator of alertness/ drowsiness (Brunner, et al., 1993; Cajochen et al., 1995; Corsi-Cabrera et al., 1992; Yan et al., 1998). Furthermore, Finelli, et al., (2000) showed a strong negative correlation between subjective alertness and theta $r^2=0.82$, and a weak correlation between subjective alertness and sigma $r^2= 0.20$. It should again be mentioned that in all the above studies subjects were sleep deprived, whereas in our study the subjects were well rested and the results might be expected to reflect varying arousal levels within wakefulness rather than actual state change into physiological drowsiness. Finally, the 2- process model of sleep/ wake regulation (Borbély, 1982) predicts Q-EEG changes in the sleep EEG and not in the waking EEG;

specifically it predicts increases in delta activity during sleep after sleep deprivation (Borbély, 1981).

Sigma power, as mentioned, was not a sensitive measure. As, sigma activity is generally the frequency band of lowest amplitude and least spectral power its apparent lack of sensitivity to waking arousal levels compared to the visually robust changes in other frequency bands may well explain the sensitivity of spectral power in the overall 0.5-15.5 Hz band in this study.

Evening Light Stimulation and Q-EEG

It was predicted that evening bright light stimulation would phase delay the time of lowest daytime arousal, indexed as an increase in overall EEG spectral power, by one or two hours. Evening bright light stimulation induced a phase delay in the timing of lowest arousal as indexed by EEG spectral power. This was significant for all frequencies combined at both electrode sites and for both the eyes open and eyes closed conditions. The only exception was for the evening light (phase delay) condition, with eyes closed, at C3. The latter approached significance ($p = 0.07$) so that, with an increase in sample size, it would most probably also have reached significance. Visual analysis of individual frequency bands other than the insensitive sigma band showed that, of 24 band combinations (6 bands, two electrodes, eyes open and eyes closed), all but two bands showed a shift in the predicted direction.

This shift in global EEG spectral power is consistent with the proposed mechanism of the afternoon nap zone.

Furthermore, with eyes closed at C3 a significant change in the individual bands was noted for delta-2 and theta-1. For delta-2 an increase in spectral power was noted from 12:00-13:00h, with a decrease in spectral power at 16:00-17:00h and again an increase at 17:00-18:00h. Similarly for theta-1 an increase in spectral power occurred at 14:00 - 15:00h followed by a decrease in spectral power at 15:00-16:00h. In respect to the main hypothesis these results are not meaningful since the data were collapsed across the pre and post light exposure conditions.

The proposed mechanism of the nap zone also predicts that evening light (phase delay) should lead to a greater increase in spectral power during the nap zone resulting from the delay in the circadian arousal process and its later intercept with process-S. The results also support this second prediction. A significant increase in all band spectral power occurred between 16:00-18:00h for all bands at O2 with eyes open and eyes closed and at C3 with eyes open. The only exception was for the evening light condition, with eyes closed, at C3, as discussed above.

Morning Light Stimulation and Q-EEG

It was predicted that morning light stimulation would phase advance by one to two hours the time of lowest daytime arousal index by increased

spectral EEG power. Morning bright light stimulation induced a phase advance in the timing of lowest arousal as indexed by the maximum overall spectral power in the waking EEG. This was significant for all frequencies combined, at both the electrode sites, and for both eyes open and eyes closed. This shift in global EEG spectral power is consistent with the proposed mechanism of the afternoon nap zone.

Visual analysis of individual frequency bands excluding sigma showed that, of 24 band combinations (6 bands, two electrodes, eyes open and eyes closed), all bands showed a shift in the predicted direction.

Concerning the individual frequency bands a shift in timing of peak power was noted during eyes open at O2 for delta-1, theta-2, and alpha-1. For delta-1 a decrease in power was noted at 13:00 - 14:00h, for theta-2 from 11:00 - 12:00h, and for alpha-1 from 15:00 - 16:00h. In addition a significant shift in individual frequency bands was noted during eyes closed at both O2 and C3. With eyes closed at O2, delta-1, theta-1, theta-2 and alpha-1, and with eyes closed, C3 theta-1 and alpha-1 were significant. In an attempt to interpret the results the effect was further examined using post hoc comparisons. However the results were not significant.

The results of the hour X frequency interaction analyses are difficult to interpret for a number of reasons. Firstly, as mentioned earlier, the current hypothesis is based upon pre versus post light stimulation comparisons, whereas the interaction is seen in data in which the baseline and treatment

conditions have been collapsed. Secondly, interpreting the change in spectral power in the context of the previous literature is also difficult, because spectral power measures were collapsed over both conditions. Thirdly, there did not seem to be any consistency between bands and the times of decreased power in the morning light condition. Finally, although significant, at two of the electrodes with eyes closed the effect is not very large since significance was not obtained when the results were examined from another perspective (post hoc comparisons).

The proposed mechanism of the nap zone also predicts that morning light (phase advance) should lead to a decrease in spectral power due to an earlier intercept with process-S. The results also support this second prediction of the hypothesis. In the morning light condition a significant decreased spectral power was observed following bright light exposure for eyes closed and with eyes open, at both electrode sites.

The finding that the timing of both arousal-sensitive measures (i.e., both performance and Q-EEG) of the nap zone are phase delayed by evening light and phase advanced by morning light, and that these shifts are highly correlated, is strong supporting evidence for the existence of a SCN-dependent circadian arousal system in humans similar to that described by Edgar et al. (1993) in sub-human primates.

This appears to be the first study to test a hypothesis of the mechanism of the afternoon nap zone. However, in a more recent paper reviewing

adolescent sleepiness (Carskadon and Acebo, 2002) predict the effects of moving the circadian phase on the afternoon nap zone. Better understanding the mechanism of this phenomenon is important in the context of its deleterious effects on performance, the increase in vehicular accidents attributed to drowsiness at this time, its role in the siesta still followed by many especially in the non-industrialized world, and the increased risk of sleep episodes and involuntary sleep "attack" in sleep disordered patients around the time of the mid-day. It is also important in relation to better understanding the 24-hour regulation of wake/sleep and alert wakefulness/sleepiness and to modeling the same in particular to predict periods at risk of inappropriate sleep and of difficulty obtaining sleep.

In summary, both performance and quantified EEG variables showed the presence of a transitory afternoon nap zone. This was statistically significant for both the mean and standard deviation of simple reaction time and for spectral EEG power of all frequency bands combined, and in visual analysis of data, for all individual bands other than sigma. Treatment with evening bright light phase delayed the timing of poorest performance and of greatest drowsiness as indexed by quantified EEG. Conversely, morning bright light phase advanced these measures of the afternoon nap zone. These findings are compatible with the hypothesis that in humans the timing of the afternoon nap zone is controlled by a combination of process –S and an

SCN-dependent circadian arousal system whose phase can be shifted by bright light exposure.

Concerning future related research, it would be of interest to conduct a similar study with a larger subject sample to see if increasing the overall power would increase the overall significance in the individual frequency bands. In addition, a subjective alertness measure could be added to further clarify times during the day when subjects felt more or less alert. This could then be correlated with the EEG bands and performance variables. Also of interest to assess is the issue of individual variability and its possible predictors and whether the same response characteristics hold true for patients with sleep disorders characterized by daytime sleep episodes such as narcolepsy-cataplexy syndrome, various hypersomnias and obstructive sleep apnea.

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Appendix A
Subject Information Sheet



HÔPITAL GÉNÉRAL D'OTTAWA OTTAWA GENERAL HOSPITAL

Response of daytime brainwaves to bright light stimulation.

The objective of this research project is to determine whether alertness across the daytime period as measured by computer analysis of brainwaves responds to morning or evening bright light stimulation the prior day.

Prior to the study itself, you will fill in a sleep questionnaire, have a diagnostic overnight sleep study (to exclude certain sleep disorders) and have a period of home regularization of the timing of your night sleep monitored by a wrist movement recorder.

Studies will be done using portable battery driven recorders. Night sleep during the study will be maintained between 11 p.m.- 7 a.m. During the daytime every half hour you will sit quietly for about 5 min in a comfortable chair, looking quietly (to avoid artefacts in the recording) at a dot in front of you for 2 min and then with eyes closed for 2 min, after which you will resume your normal activities. For the next two days you will be exposed to bright light for 2 hours in the morning. Again during the wake portion of the day, other than during bright light stimulation, you will return to chair for quiet 5 min periods. After a break from the laboratory you will return and follow the same procedure except that the light exposure will be in the evening.

No hospitalization is required. You will be remunerated for your participation. No drugs or placebos are involved. There are no known discomforts. The only personal benefit is learning something about the timing and nature of sleepiness in your case.

There are no known risks to this protocol. Comparable ones have been used in several other laboratories but with different objectives. Participation is voluntary and you are free to withdraw at any time for any reason without any penalty. Although there are no particular personal benefits, the findings will greatly help our understanding of the mechanisms controlling the nature and the timing of sleep and of a number of sleep disorders.

If you do agree to participate in this study, your chart will be reviewed by the investigators and laboratory technicians involved with the trial. The investigators and laboratory technicians have a policy of strict confidentiality and only they have access to the records. Also, you will not be identified in any publication or presentation arising from this study. You will be able to obtain information about the study at any time. You will receive a copy of the consent form and will be able to discuss the study with Dr. Broughton or your contact person in the laboratory (Mike Houlihan at

Appendix B
Consent Form



CONSENTEMENT DU PATIENT/
PROCURATION À DES RECHERCHES MÉDICALES

PATIENT/PROXY CONSENT FOR MEDICAL RESEARCH

Nom de l'étude

Name of research project

Je confirme que j'ai expliqué la nature ainsi que les complications connues de ce projet de recherche/procuration du patient.

I confirm that I have explained the nature of and known complications of the research project to the patient/proxy.

(chercheur)

(researcher)

Je consens à la participation de :

I consent to the participation of :

Nom du patient

N° de projet

Patient's name

Research no.

à l'étude précitée et j'autorise par la présente le(s) médecin(s) et le(s) chercheurs(s) à procéder aux examens et/ou à dispenser les traitements suivants :

in the above study and I hereby authorize the physician(s) and investigator(s) to proceed with the following questionnaire, examinations and/or to administer these treatments:

J'ai lu la feuille d'explication détaillée approuvée par le Conseil d'éthique en recherches et je suis au courant des effets secondaires et des risques connus ayant trait aux examens et aux traitements.

I have read the detailed information sheet approved by the Research Ethics Board and am aware of the known side effects and risks related to the examinations and treatments.

J'ai également reçu une description de tous les avantages à attendre de ces examens et de ces traitements. On m'a fait connaître d'autres formes d'examen et de traitement.

I have also received a description of any benefits that may be expected from these examinations and treatments. As well, other forms of treatment and exams have been disclosed to me.

J'ai eu l'occasion de poser des questions au sujet de ces examens et de ces traitements et on y a bien répondu.

I have been given an opportunity to ask questions concerning the examinations and treatments involved and the questions which I have asked have been adequately answered.

On m'a dit que je pouvais retirer le consentement et suspendre la participation à l'étude à n'importe quel moment et pour quelque motif que ce soit et que cette action n'affectera pas la qualité des soins en cours et futurs.

I have been told that I can withdraw consent and stop participation in the study at any time and for any reason, and that such action will not affect the quality of ongoing and future care.

Je reconnais qu'en agissant, comme procurateur, ce sera dans le meilleur intérêt du patient.

I acknowledge that if I am acting as a proxy that I am acting in the best interest of the patient.

En toute connaissance de cause, je consens volontairement à ce que _____ participe à cette étude.

With full knowledge of this, I voluntarily consent to the participation of _____ in the study.

Ce protocole a été approuvé par le Conseil d'éthique en recherches de l'Hôpital général d'Ottawa. Ce conseil étudie les aspects éthiques de tous les projets de recherche sur les humains. Si je le désire, je peux contacter le président de ce comité.

This protocol has been approved by the Research Ethics Board of the Ottawa General Hospital. This Board considers the ethical aspects of all hospital research projects using human subjects. If I wish, I may contact the Chairperson of the Board with questions.

Nom (lettres moulées) - Name (print)

Signature

Lien de parenté - Relationship

PATIENT OU PERSONNE LÉGALEMENT RESPONSABLE (PROCURATION) - PATIENT OR PERSON LEGALLY RESPONSIBLE (PROXY)

Nom du témoin (lettres moulées) - Name of witness (print)

Signature

Date (j/d-m/m-a/y)

Appendix C
Sleep Questionnaire

Sleep History

A. PERSONAL DATA:

Name:					
Address:					
Phone #:		Age:		Sex:	Male Female
Preferred hand:	Right Left	Occupation:		Shifts:	

B: SLEEP HABITS:

1. What time do you usually go to bed on weekdays?			hh:mm
2. What time do you usually go to bed on weekends?			hh:mm
3. On average how long does it take you to fall asleep after you turn out the lights?			min
4. On average, how long do you actually sleep at night?			hr
5. Do you awaken during the night?			YES NO
	If YES	How long are these arousals?	min
		How often do these occur?	/night
6. Are you refreshed when you awaken in the morning?			YES NO
7. Do you nap during the daytime?			YES NO
	If YES	How often are the naps?	/week
		How long are the naps?	min
8. Do you find yourself falling asleep when you don't mean to?			YES NO
	If YES	Do you dream during such an episode?	YES NO
9. Are you bothered by sleepiness during the day?			YES NO
10. Have you ever experienced doing something without being aware at the time of the action?			YES NO
11. Have you ever experienced sudden body paralysis or severe weakness triggered by emotional stimuli such as humor or fear?			YES NO

12. Have you ever experienced weakness or paralysis upon going to sleep or awakening from sleep?		YES NO
13. Have you ever hallucinated as you are falling asleep or as you are waking up?		YES NO
14. Do you snore loudly or have difficulty breathing at night?		YES NO
15. Have you experienced any of the following either prior to sleep onset or immediately upon awakening from sleep?		
	a: a restlessness of the legs	YES NO
	b: "nervous legs"	YES NO
	c: a creeping sensation in your legs	YES NO
	d: twitching	YES NO
16. Has anyone ever told you that your arms or legs jerk or twitch while you are apparently asleep?		YES NO
17. Are you aware or has anyone ever told you that you:		
	a: talk while you are apparently asleep	YES NO
	b: walk while you are apparently asleep	YES NO
	c: grit your teeth while you are apparently asleep	YES NO
	d: wet the bed during sleep	YES NO
	e: were a bed wetter between the ages of 8 and 14	YES NO
	f: have disturbing dreams	YES NO
18. Are you satisfied with the quality of your sleep in general?		YES NO
If NO please list complaints or make comments.		
19. Are you taking medication?		YES NO
If YES	For what purpose?	
	What type?	
	Frequency of use?	

C: FAMILY HISTORY:

20. Has anyone in your family been known to have any sleep problems?		YES	NO
If YES	What type of problem?		
	What relation is this person to you?		

D: PHYSICAL HEALTH STATUS:

21. Do you have a medical condition (e.g., diabetes, epilepsy, kidney/liver disfunction, menopause, pregnancy, etc.)?		YES	NO
If YES	Please specify:		
22. On average, how many cups of coffee and/or tea do you drink each day?		/day	
23. On average, how many cigarettes, cigars or pipefuls of tobacco do you smoke daily?		/day	
24. On average, how many alcoholic beverages do you drink on weekdays?		/day	
25. On average, how many alcoholic beverages do you drink on weekends?		/day	
26. Do you smoke marijuana or use illegal drugs?		YES	NO
If YES	What drugs?		
	Approximate weekly use?		

Thank You!

Appendix D
Morning/Eveningness Questionnaire

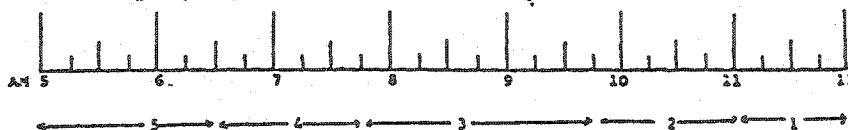
The final questionnaire

Instructions:

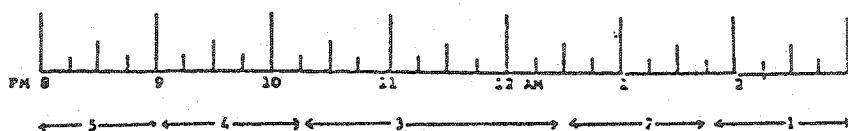
1. Please read each question very carefully before answering.
2. Answer ALL questions.
3. Answer questions in numerical order.
4. Each question should be answered independently of others. Do NOT go back and check your answers.
5. All questions have a selection of answers. For each question place a cross alongside ONE answer only. Some questions have a scale instead of a selection of answers. Place a cross at the appropriate point along the scale.
6. Please answer each question as honestly as possible. Both your answers and the results will be kept, in strict confidence.
7. Please feel free to make any comments in the section provided below each question.

The Questionnaire, with scores for each choice

1. Considering only your own "feeling best" rhythm, at what time would you get up if you were entirely free to plan your day?



2. Considering only your own "feeling best" rhythm, at what time would you go to bed if you were entirely free to plan your evening?



3. If there is a specific time at which you have to get up in the morning, to what extent are you dependent on being woken up by an alarm clock?

Not at all dependent.....	☐	4
Slightly dependent.....	☐	3
Fairly dependent.....	☐	2
Very dependent.....	☐	1

4. Assuming adequate environmental conditions, how easy do you find getting up in the mornings?

Not at all easy.....	☐	1
Not very easy.....	☐	2
Fairly easy.....	☐	3
Very easy.....	☐	4

5. How alert do you feel during the first half hour after having woken in the mornings?

Not at all alert.....	☐	1
Slightly alert.....	☐	2
Fairly alert.....	☐	3
Very alert.....	☐	4

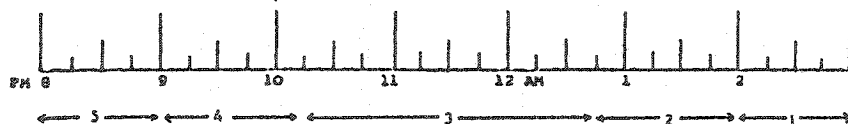
6. How is your appetite during the first half-hour after having woken in the mornings?

Very poor.....	☐	1
Fairly poor.....	☐	2
Fairly good.....	☐	3
Very good.....	☐	4

A MORNINGNESS-EVENINGNESS QUESTIONNAIRE

7. During the first half-hour after having woken in the morning, how tired do you feel ?
- | | | |
|-----------------------|--------------------------|---|
| Very tired..... | ☐ | 1 |
| Fairly tired..... | ☐ | 2 |
| Fairly refreshed..... | ☐ | 3 |
| Very refreshed..... | ☐ | 4 |
8. When you have no commitments the next day, at what time do you go to bed compared to your usual bedtime ?
- | | | |
|---------------------------|--------------------------|---|
| Seldom or never later.... | ☐ | 4 |
| Less than one hour later. | ☐ | 3 |
| 1 - 2 hours later..... | ☐ | 2 |
| More than two hours later | ☐ | 1 |
9. You have decided to engage in some physical exercise. A friend suggests that you do this one hour twice a week and the best time for him is between 7.0 - 8.0 AM. Bearing in mind nothing else but your own "feeling best" rhythm How do you think you would perform ?
- | | | |
|---------------------------------|--------------------------|---|
| Would be on good form.... | ☐ | 4 |
| Would be on reasonable form | ☐ | 3 |
| Would find it difficult.. | ☐ | 2 |
| Would find it very .. difficult | ☐ | 1 |

10. At what time in the evening do you feel tired and as a result in need of sleep ?



11. You wish to be at your peak performance for a test which you know is going to be mentally exhausting and lasting for two hours. You are entirely free to plan your day and considering only your own "feeling best" rhythm which ONE of the four testing times would you choose ?
- | | | |
|-------------------------|--------------------------|---|
| 8.00 - 10.00 AM..... | ☐ | 6 |
| 11.00 AM - 1.00 PM..... | ☐ | 4 |
| 3.00 - 5.00 PM..... | ☐ | 2 |
| 7.00 - 9.00 PM..... | ☐ | 0 |

12. If you went to bed at 11.0 PM
at what level of tiredness
would you be ?

Not at all tired..... ☐ 0
A little tired..... ☐ 2
Fairly tired..... ☐ 3
Very tired..... ☐ 5

13. For some reason you have gone
to bed several hours later than
usual, but there is no need to
get up at any particular time the
next morning. Which ONE of the
following events are you most
likely to experience ?

Will wake up at usual time
and will NOT fall asleep ☐ 4
Will wake up at usual time
and will doze thereafter ☐ 3
Will wake up at usual time
but will fall asleep again ☐ 2
Will NOT wake up until
later than usual ☐ 1

14. One night you have to remain awake
between 4.00 - 6.00 AM in order to
carry out a night watch. You have
no commitments the next day. Which
ONE of the following alternatives
will suit you best ?

Would NOT go to bed until
watch was over ☐ 1
Would take a nap before
and sleep after ☐ 2
Would take a good sleep
before and nap after ☐ 3
Would take ALL sleep
before watch ☐ 4

15. You have to do two hours of hard
physical work. You are entirely
free to plan your day and
considering only your own "feeling
best" rhythm which ONE of the
following times would you choose ?

8.00 - 10.00 AM..... ☐ 4
11.00 - 1.00 AM..... ☐ 3
3.00 - 5.00 PM..... ☐ 2
7.00 - 9.00 PM..... ☐ 1

16. You have decided to engage in
hard physical exercise. A friend
suggests that you do this for one
hour twice a week and the best
time for him is between 10.00 -
11.00 PM. Bearing in mind
nothing else but your own "feeling
best" rhythm how well do you think
you would perform ?

Would be on good form... ☐ 1
Would be on reasonable form ☐ 2
Would find it difficult. ☐ 3
Would find it very .. ☐ 4
difficult

Diagram illustrating the 24 hours of a day, divided into 12 hours (1 to 12) and then 12 hours (1 to 12) again, representing the cycle of the day. Below the clock face, arrows indicate the duration of each season: 1 for Winter, 5 for Spring, 4 for Summer, 3 for Autumn, 2 for Winter, 1 for Spring, and 1 for Summer.

Definitely an "evening" type

Appendix E

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at 02, eyes closed, for baseline and for evening bright light (phase delay).

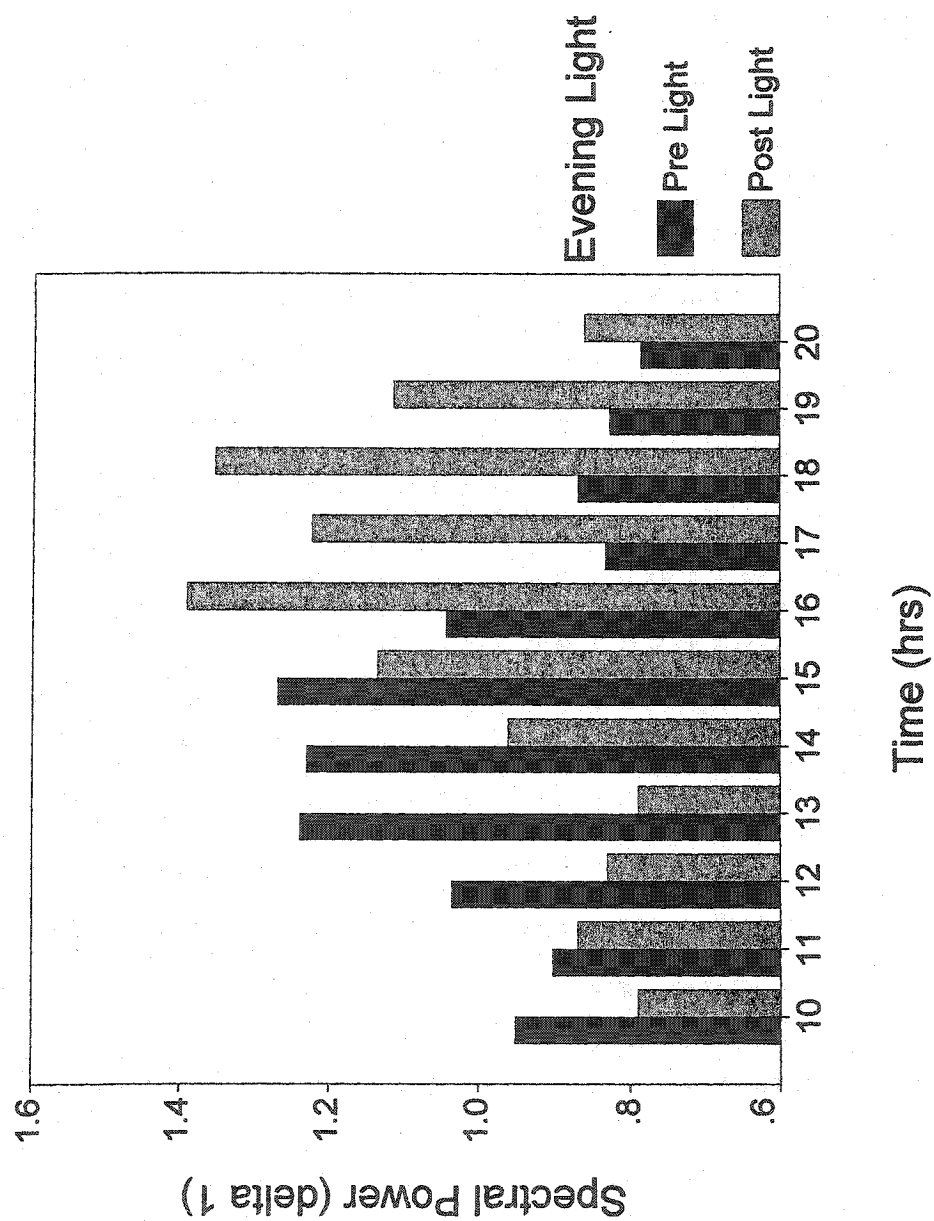


Figure E1. Mean values for delta 1 with eyes closed at 02

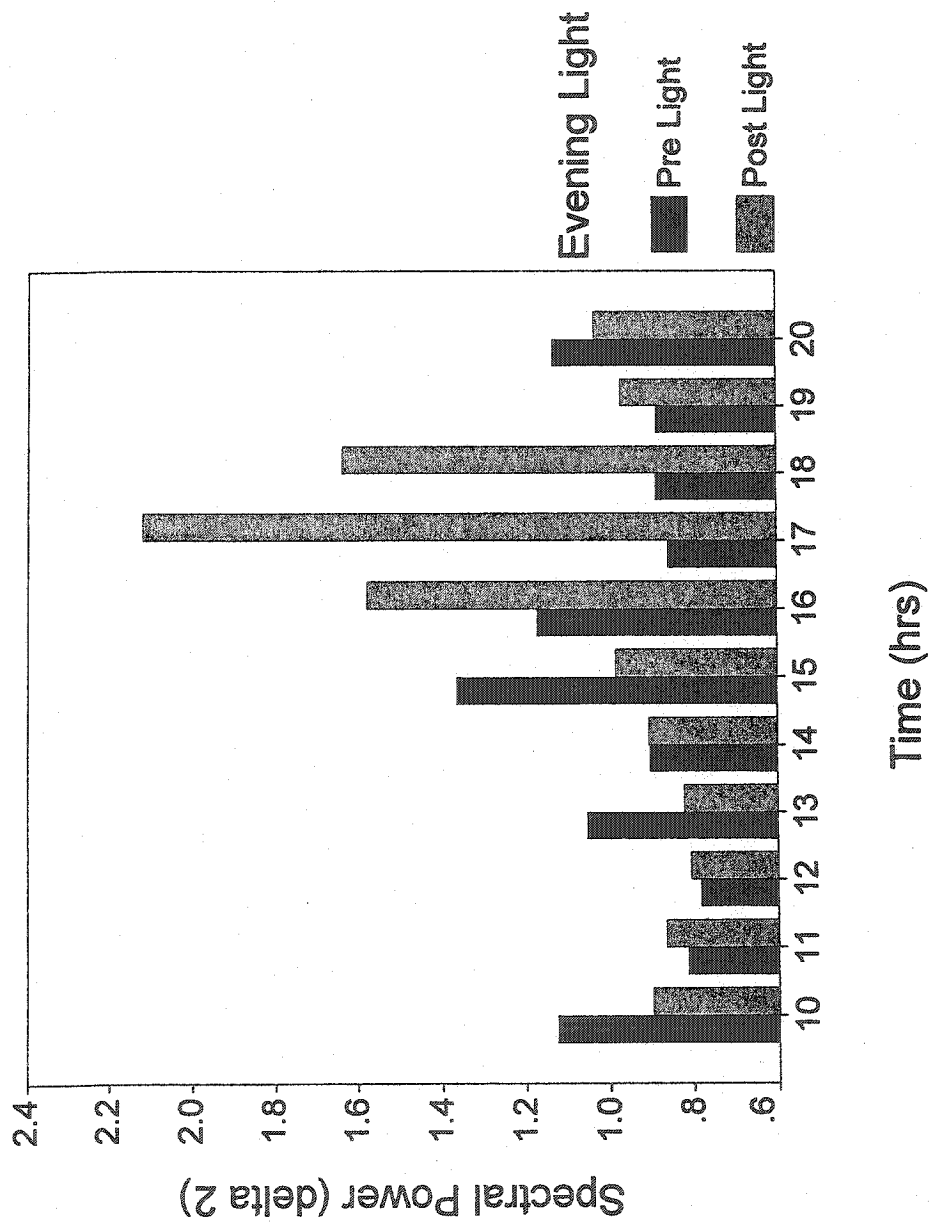


Figure E2. Mean values for delta 2 with eyes closed at 02

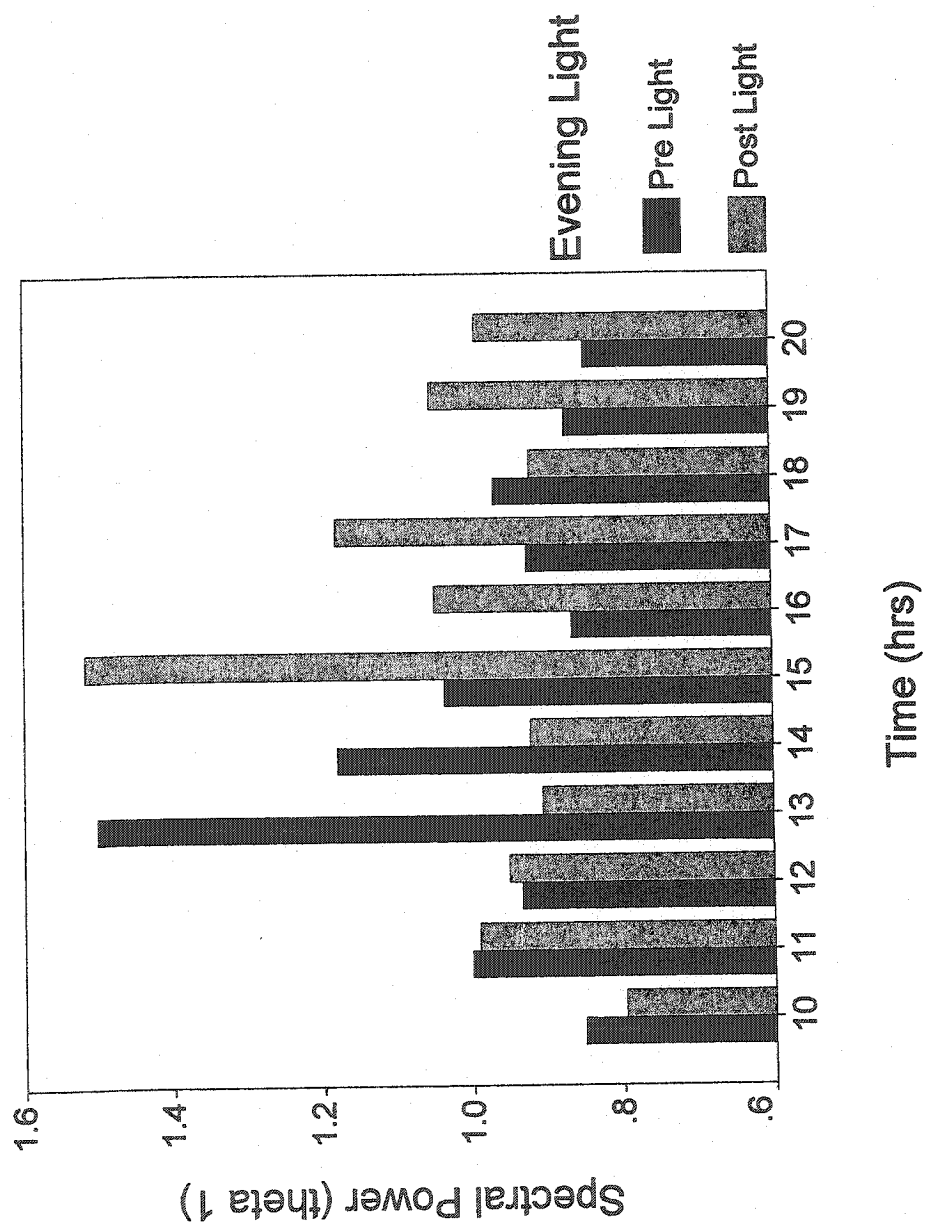


Figure E3. Mean values for theta 1 with eyes closed at 02

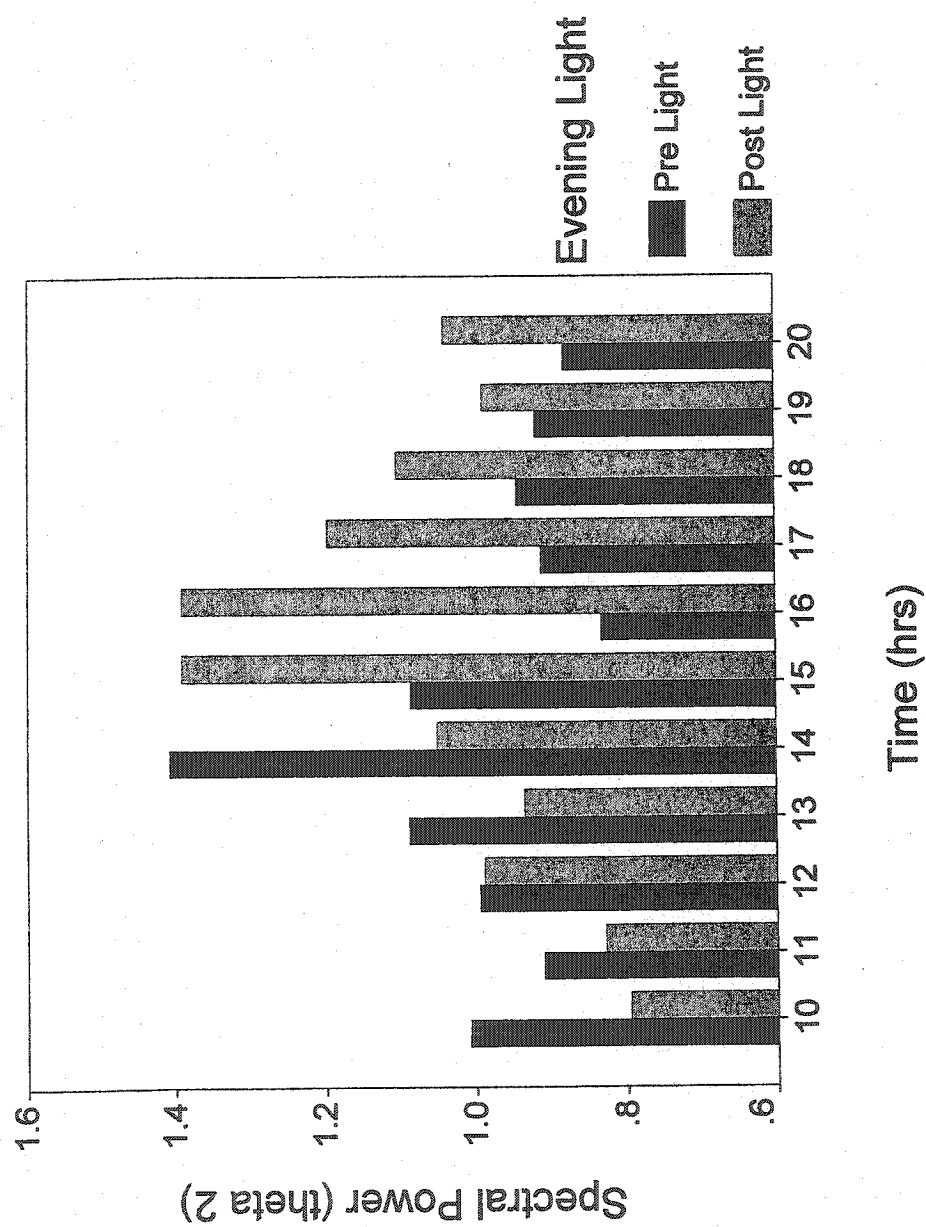


Figure E4. Mean values for theta 2 with eyes closed at 02

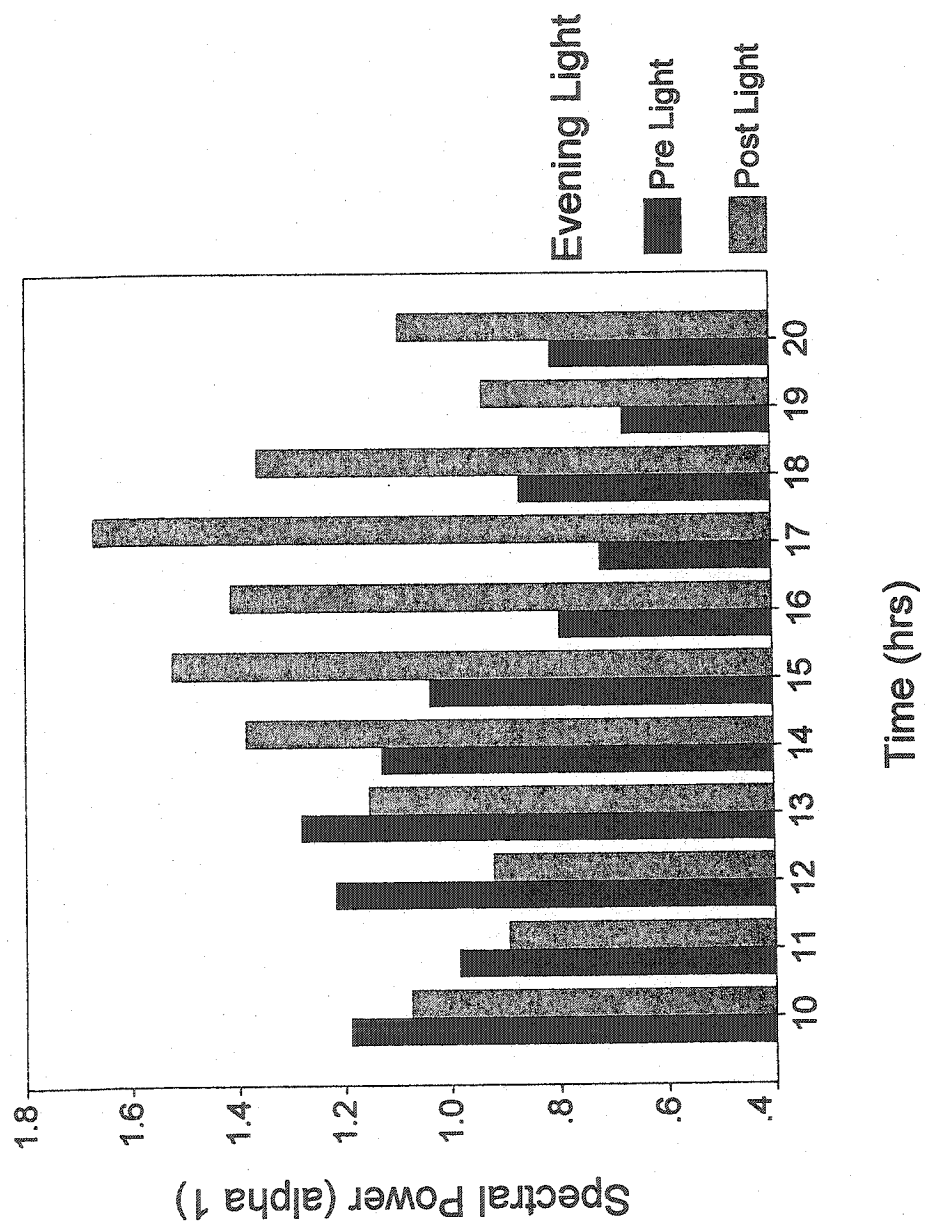


Figure E5. Mean values for alpha 1 with eyes closed at 02

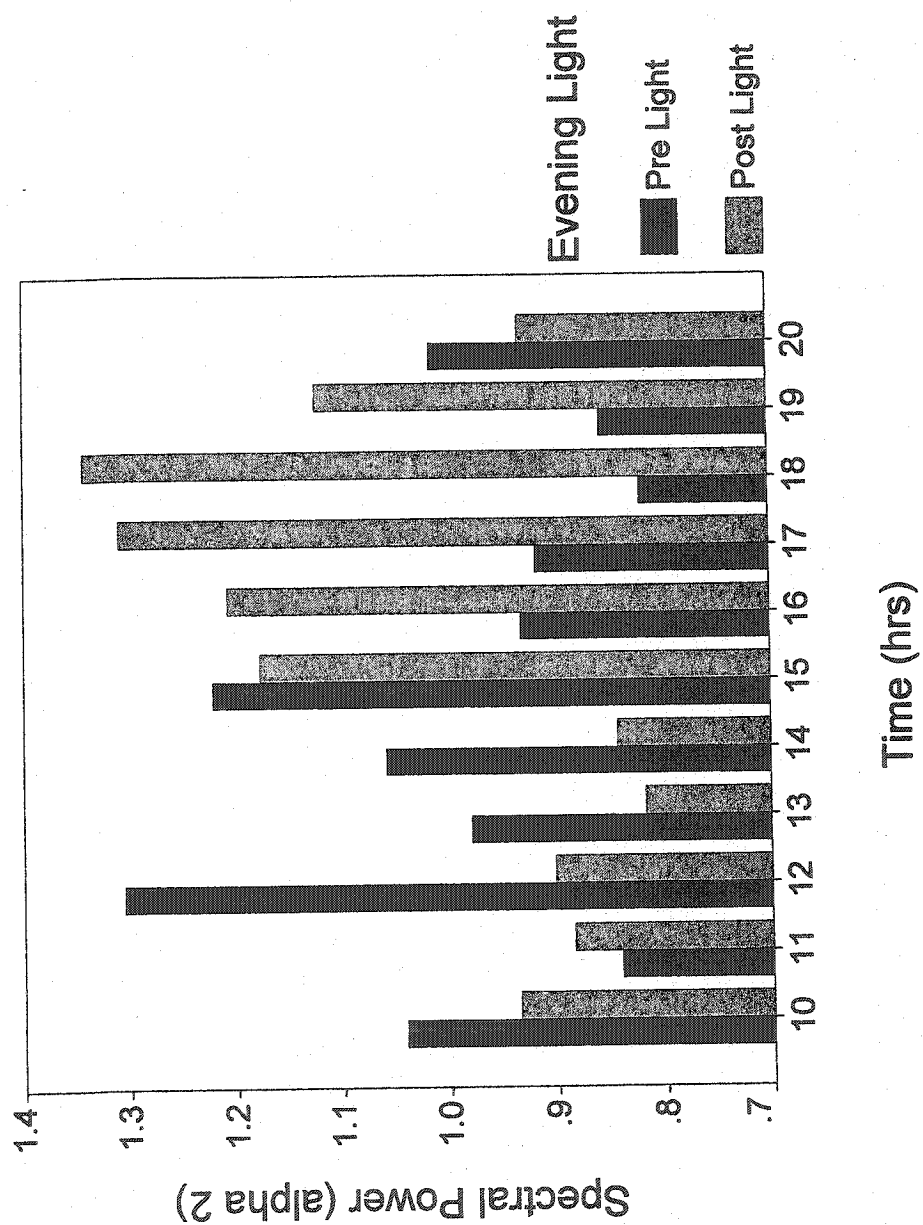


Figure E6. Mean values for alpha 2 with eyes closed at 02

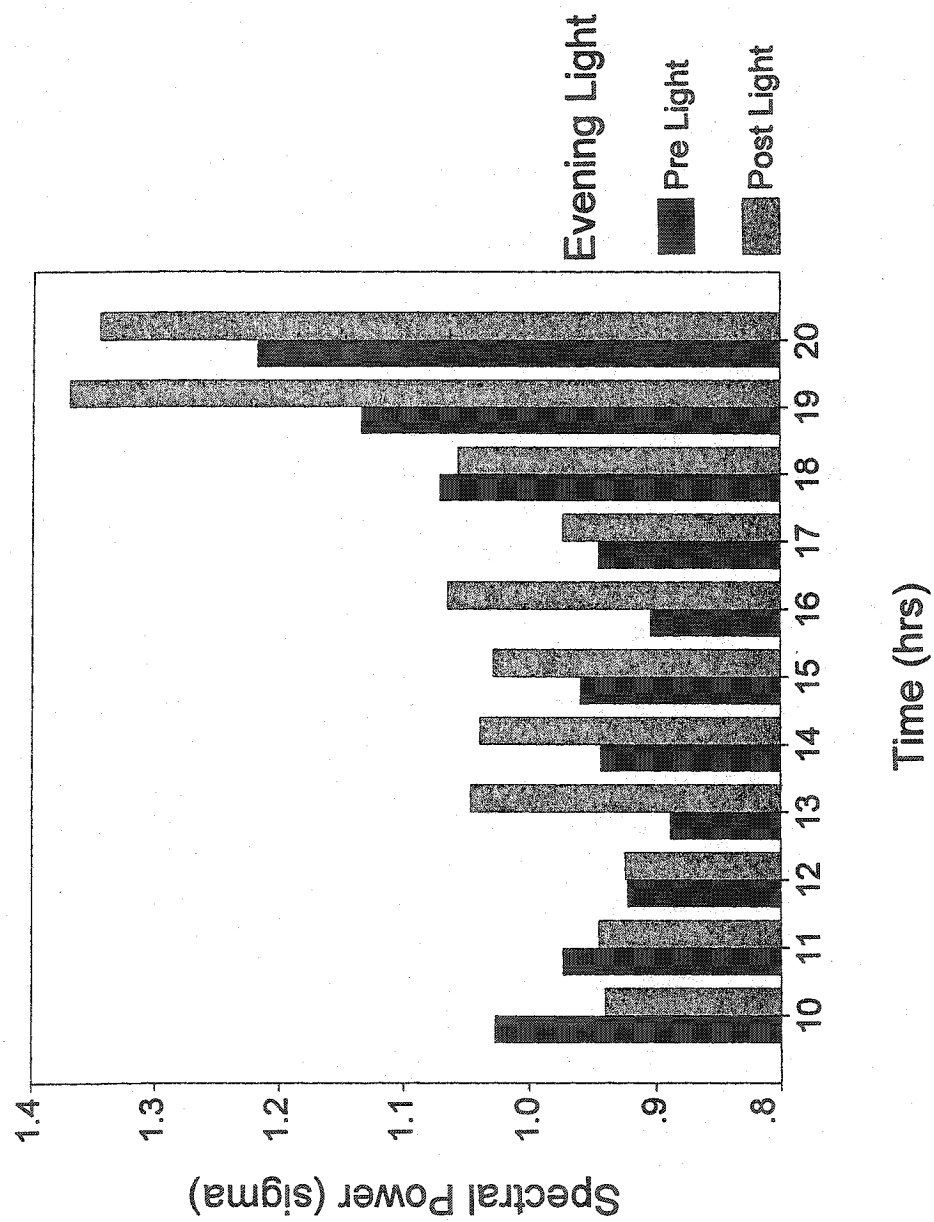


Figure E7. Mean values for sigma with eyes closed at 02

Appendix F

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at 02, eyes open, for baseline and for evening bright light (phase delay).

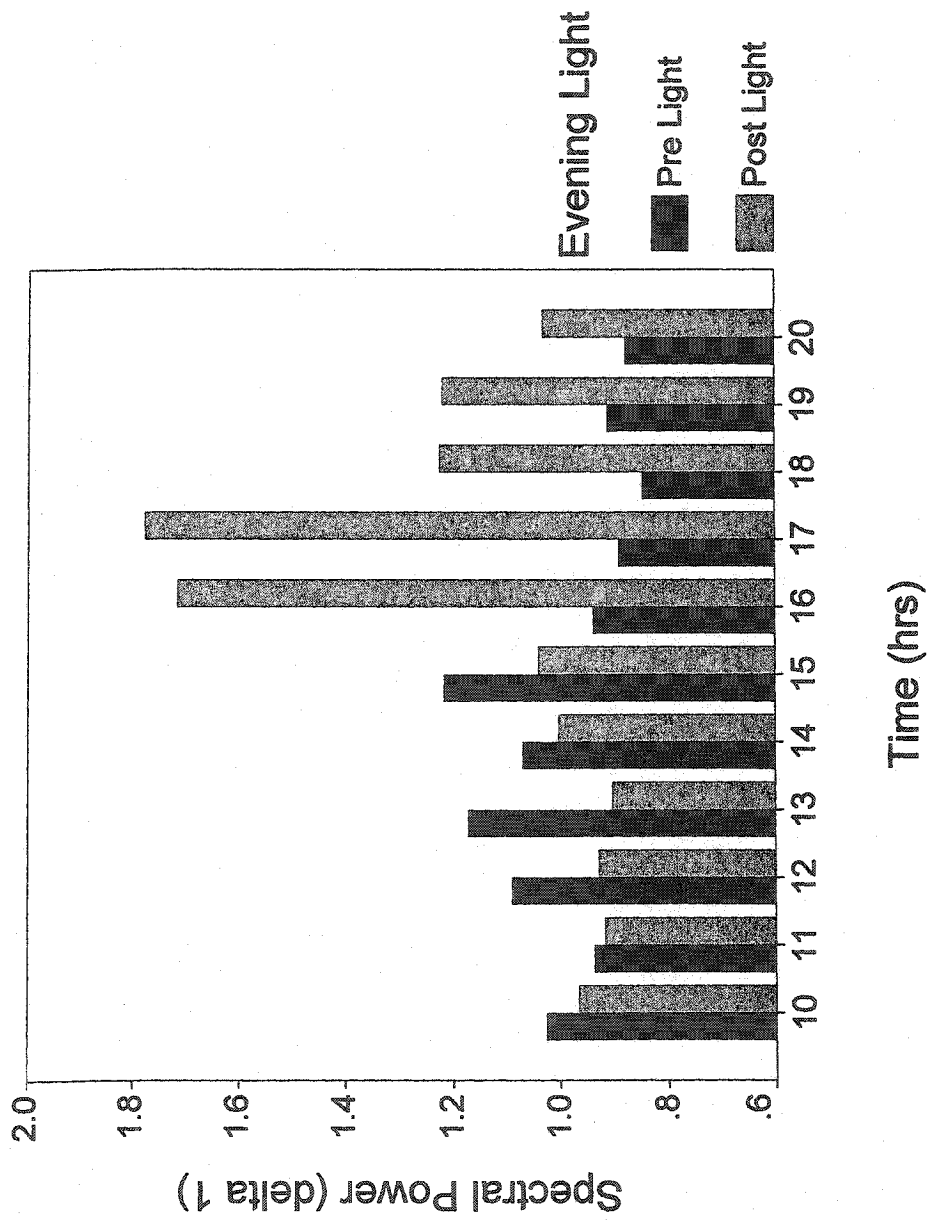


Figure F1. Mean values for delta 1 with eyes open at 02

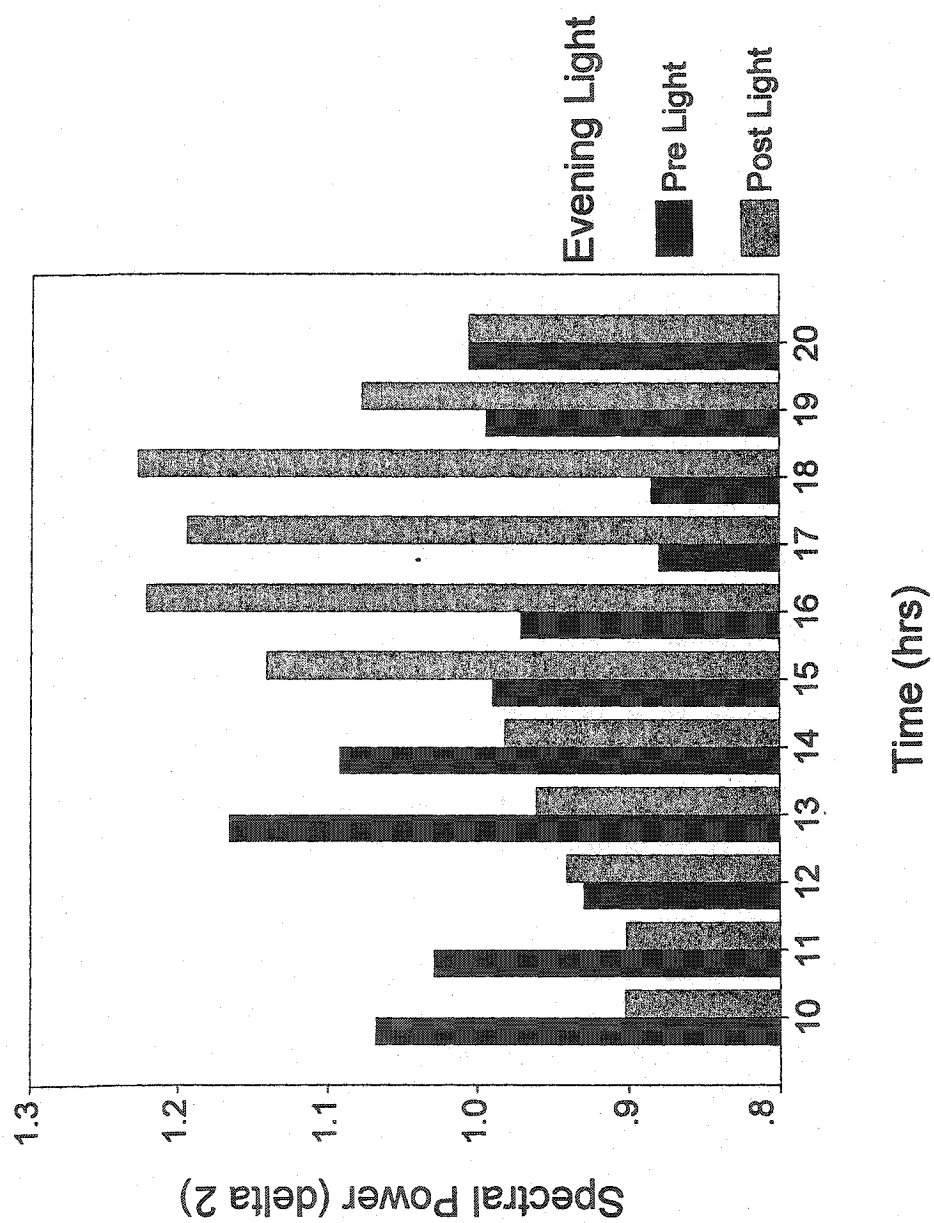


Figure F2. Mean values for delta 2 with eyes open at 02

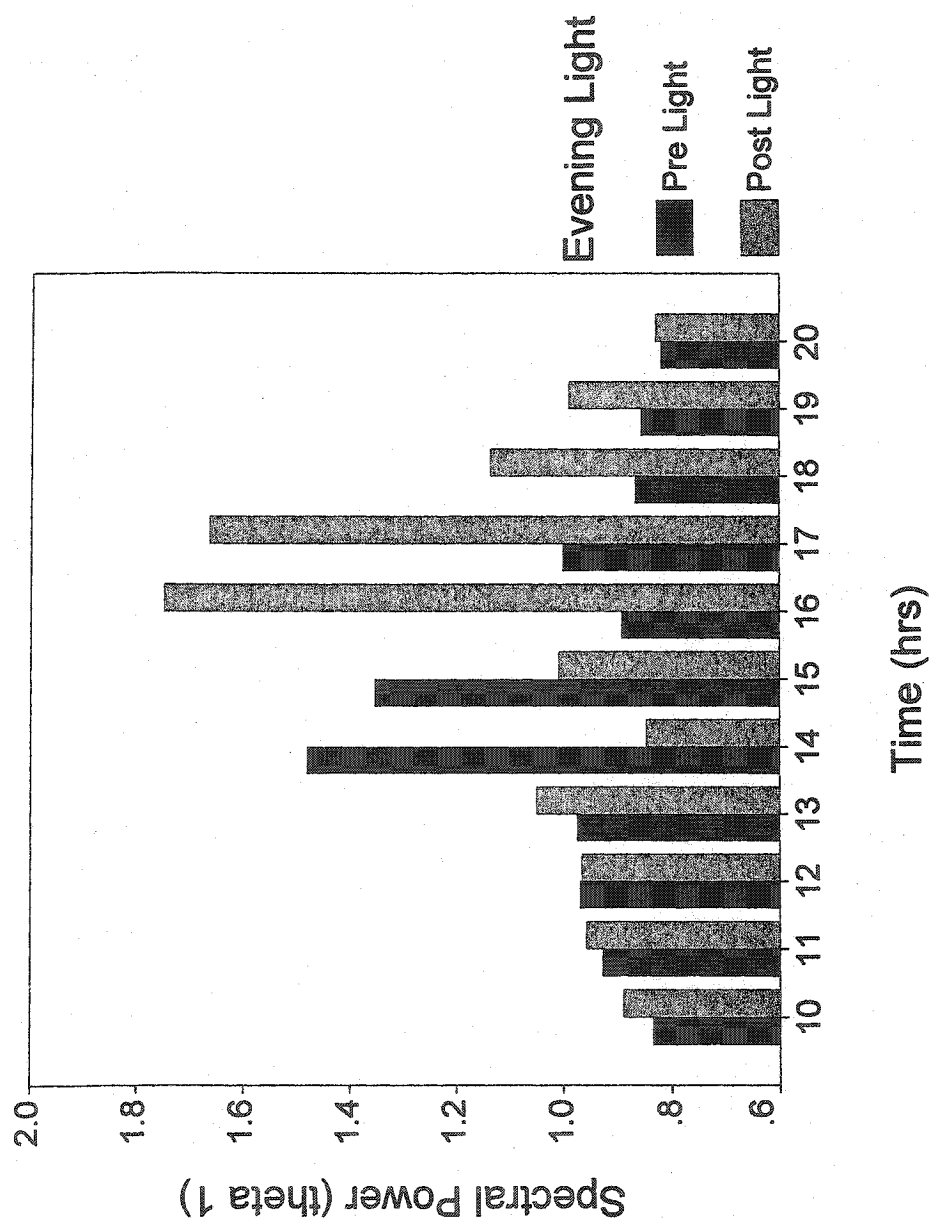


Figure F3. Mean values for theta 1 with eyes open at 02

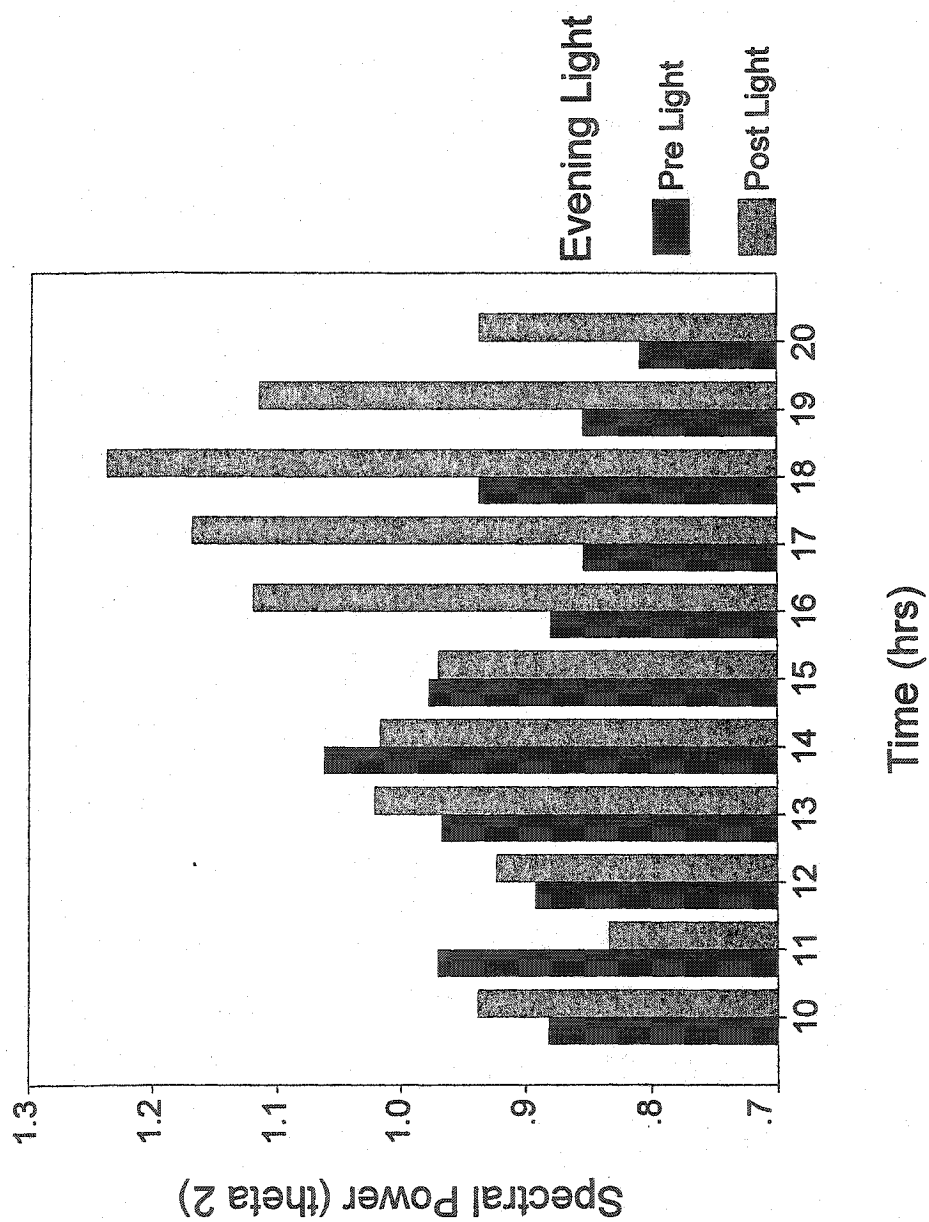


Figure F4. Mean values for theta 2 with eyes open at 02

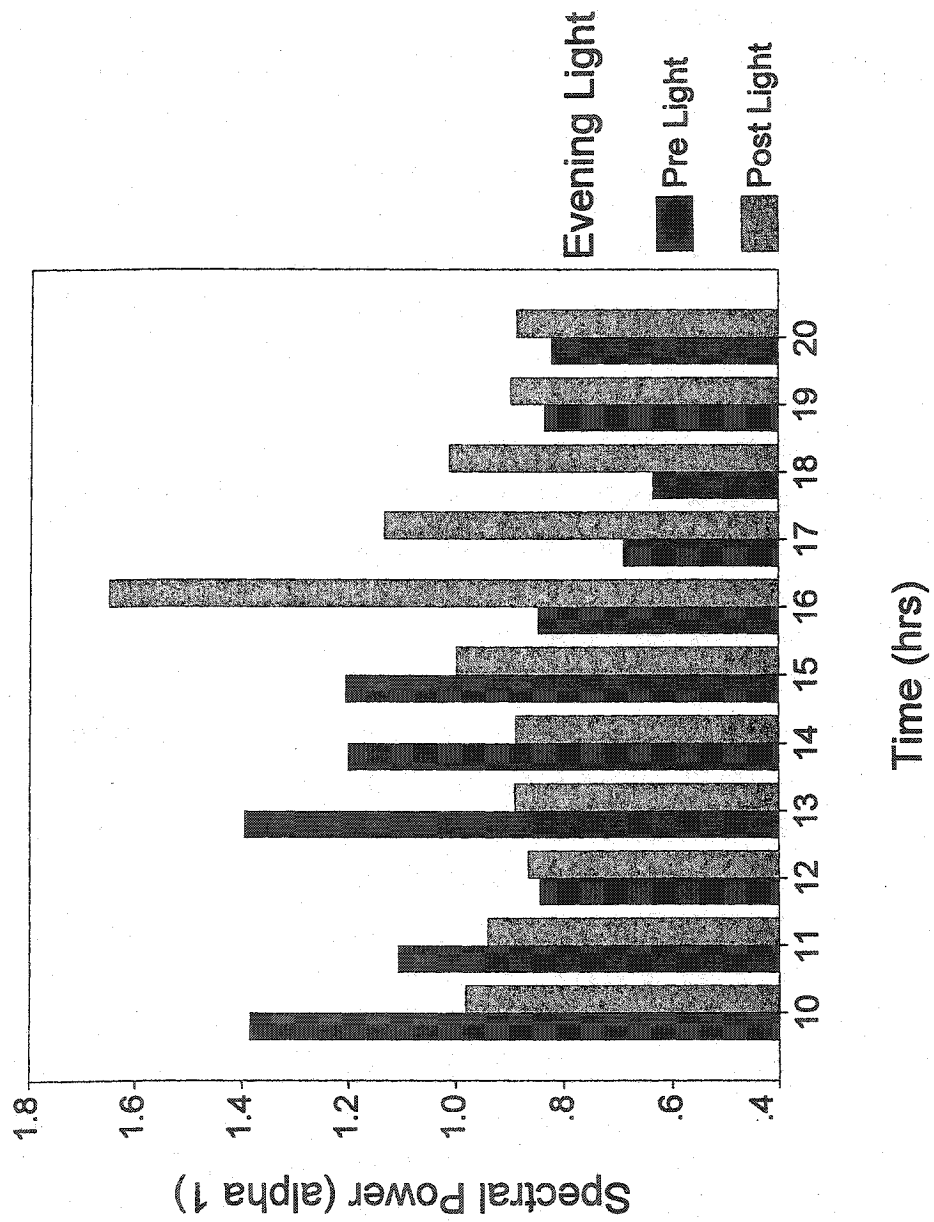


Figure F5. Mean values for alpha 1 with eyes open at 02

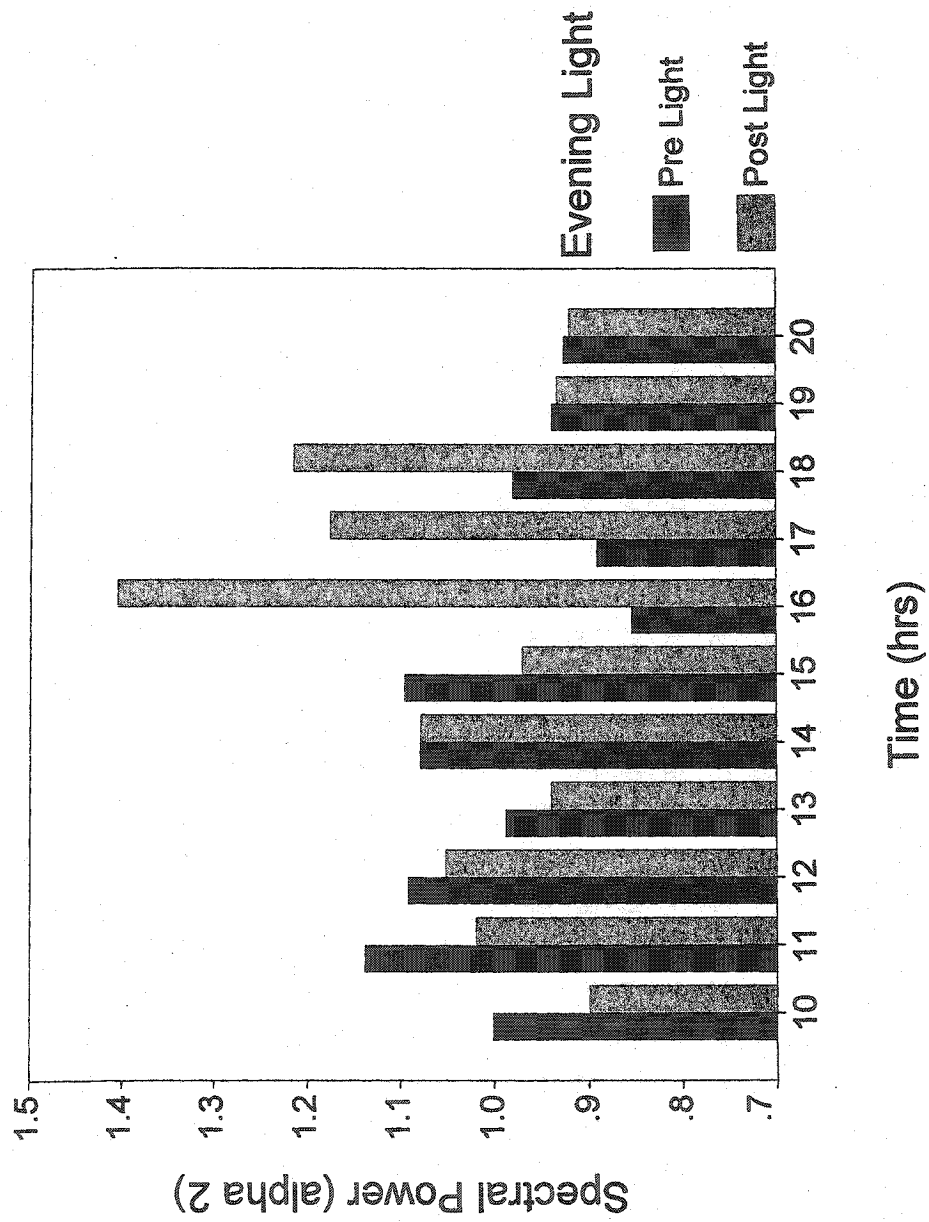


Figure F6. Mean values for alpha 2 with eyes open at 02

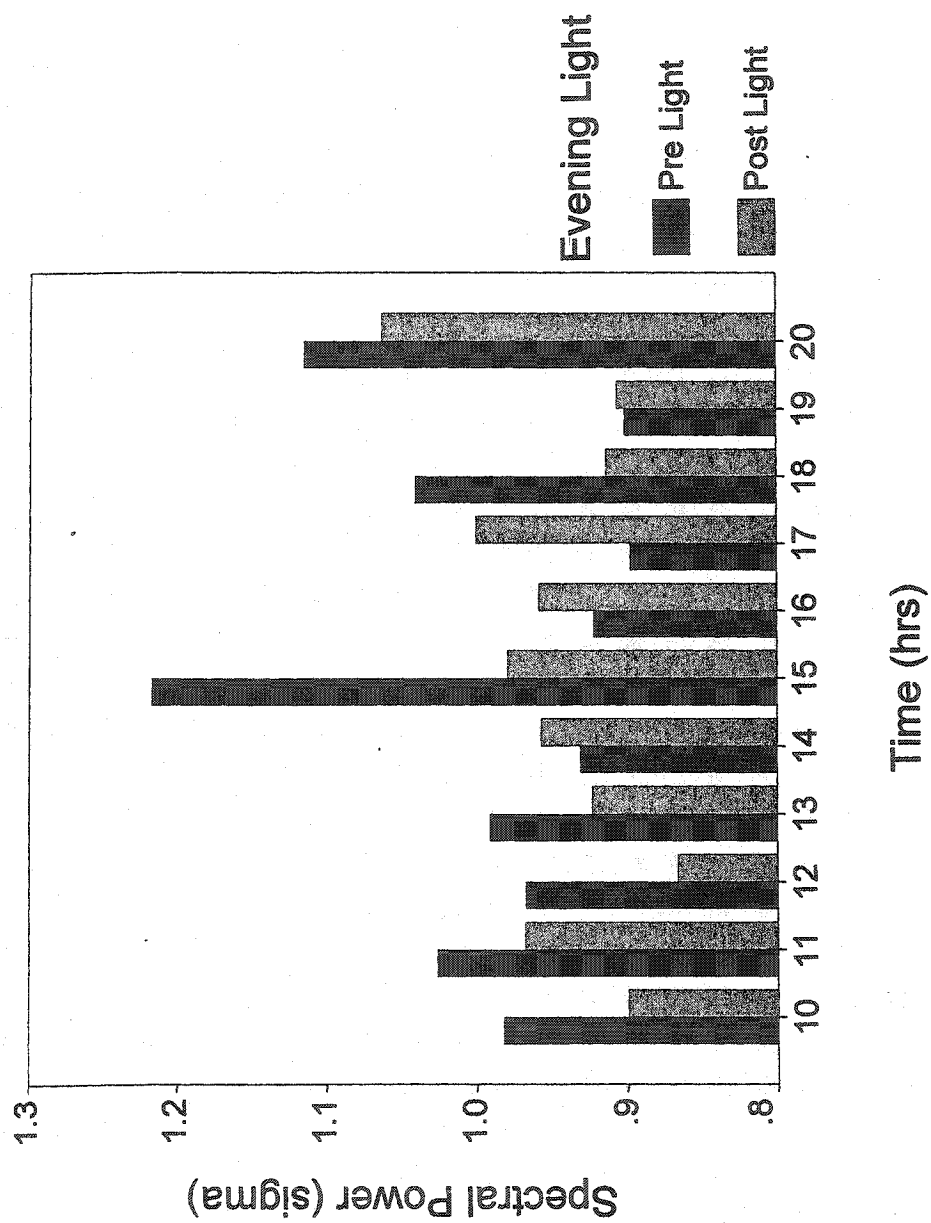


Figure F7. Mean values for sigma with eyes open at 02

Appendix G

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at C3, eyes closed, for baseline and for evening bright light (phase delay).

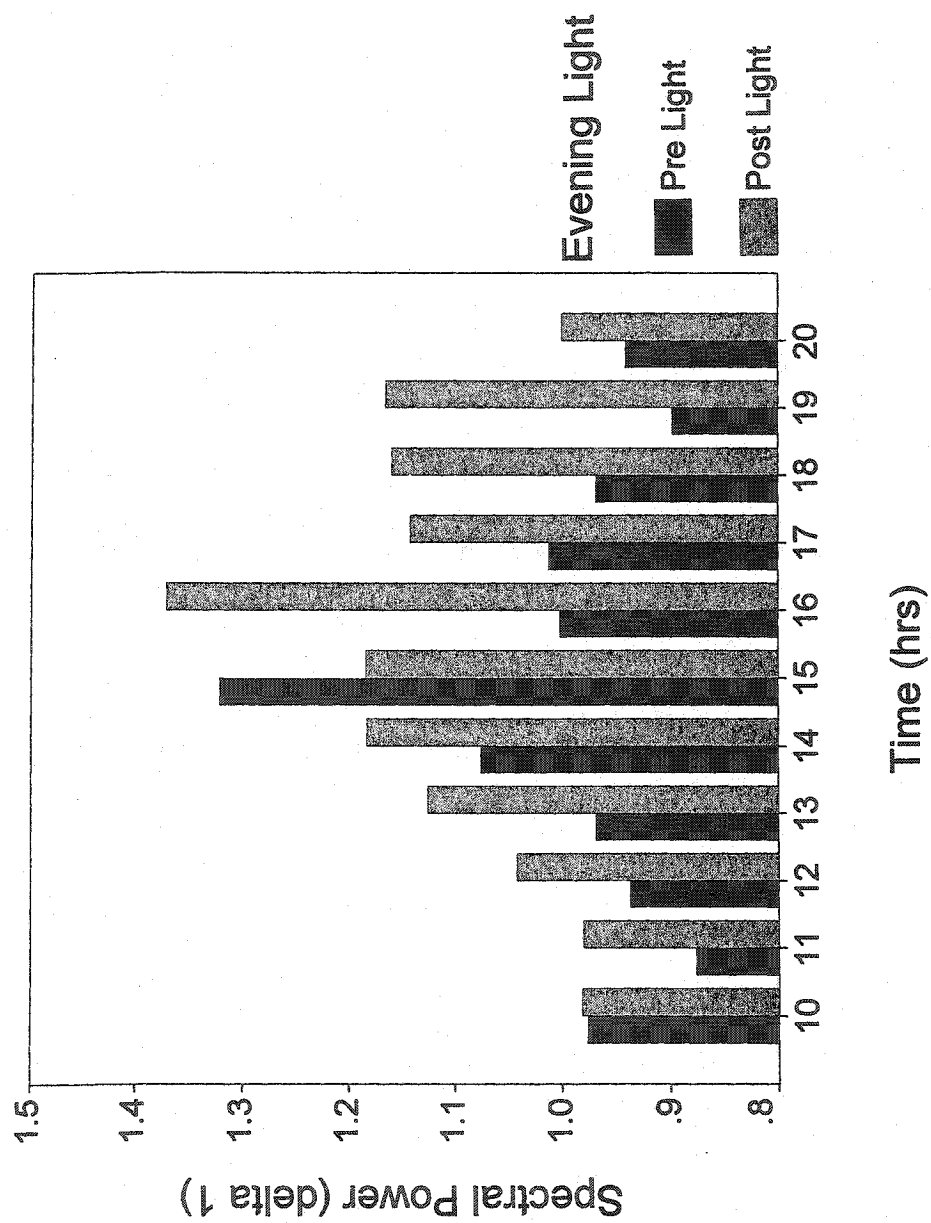


Figure G1. Mean values for delta 1 with eyes closed at C3

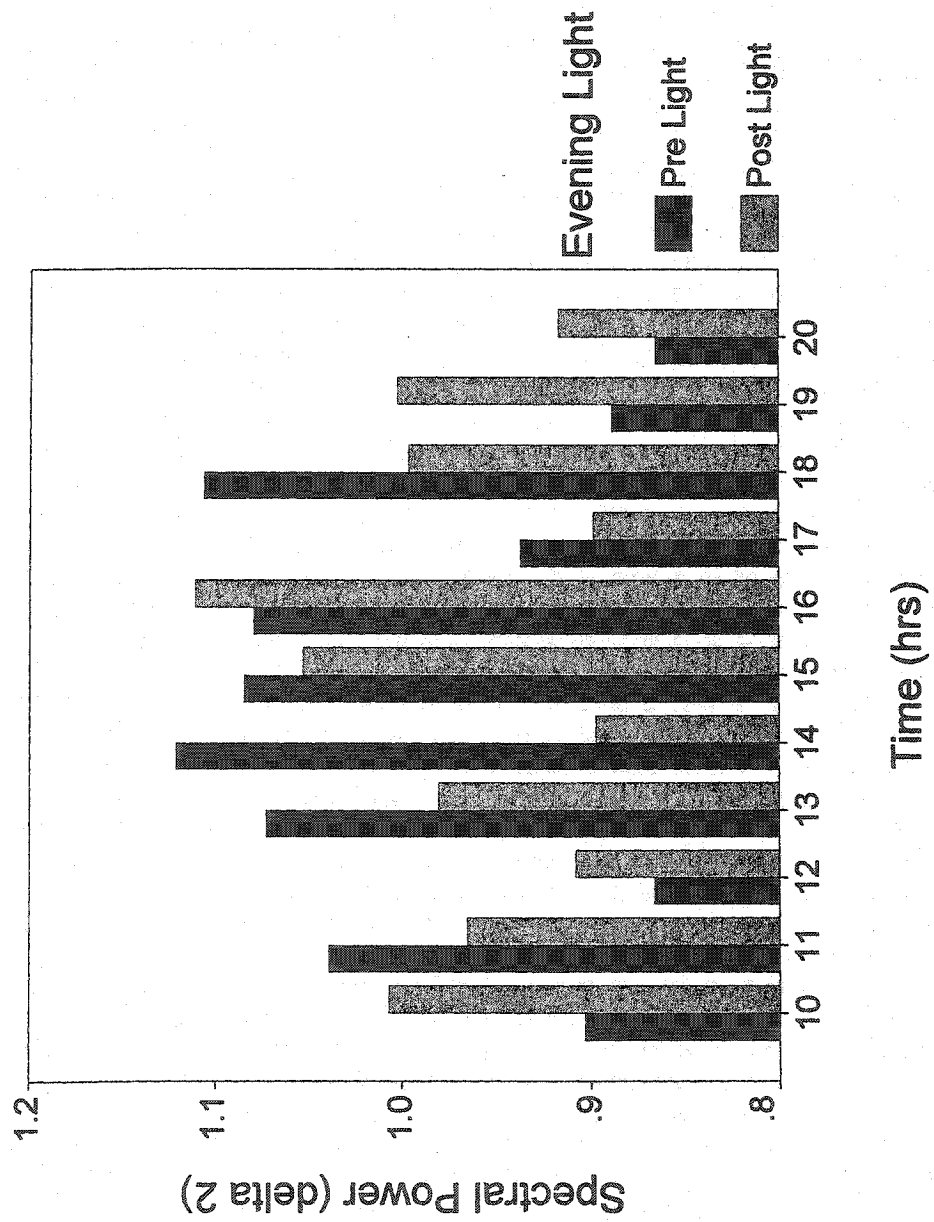


Figure G2. Mean values for delta 2 with eyes closed at C3

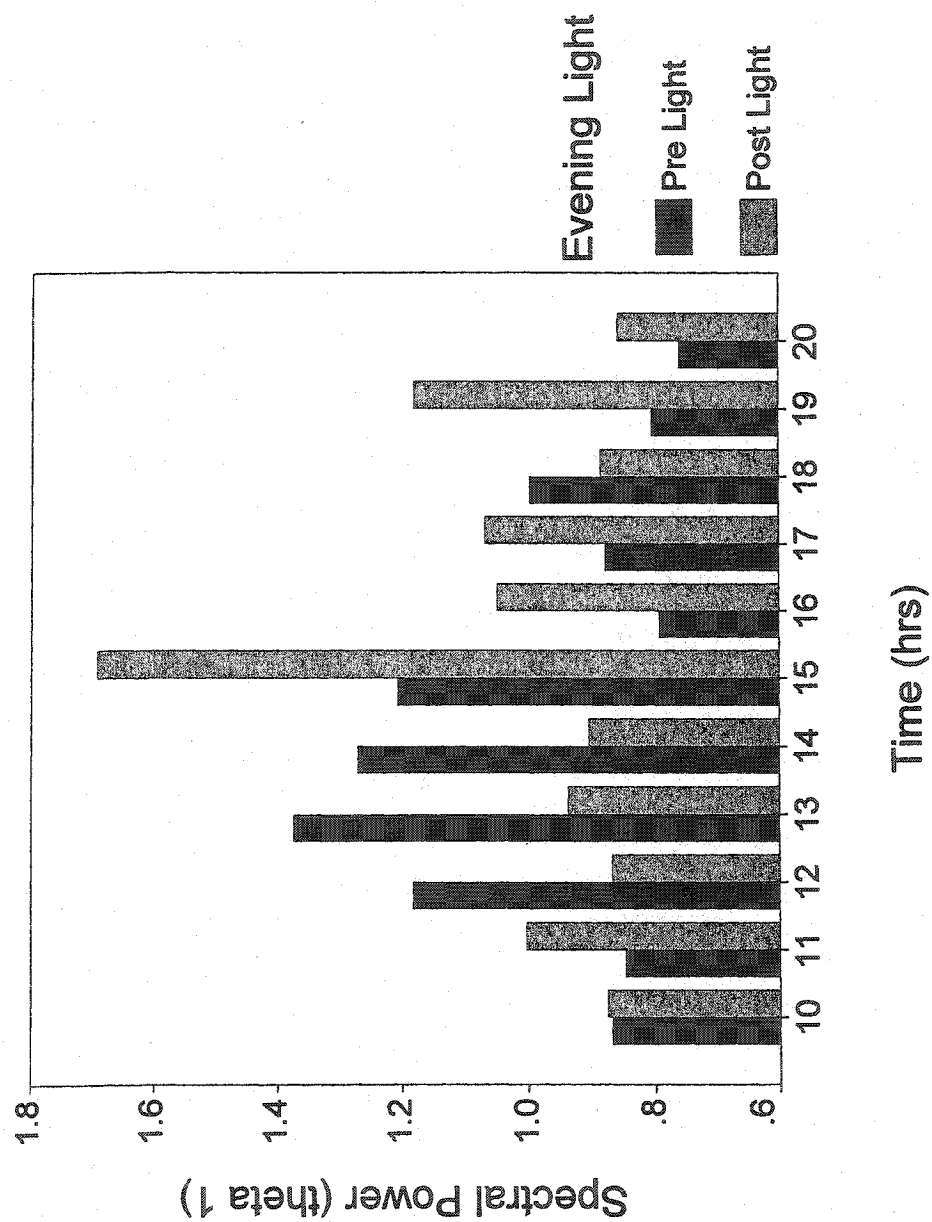


Figure G3. Mean values for theta 1 with eyes closed at C3

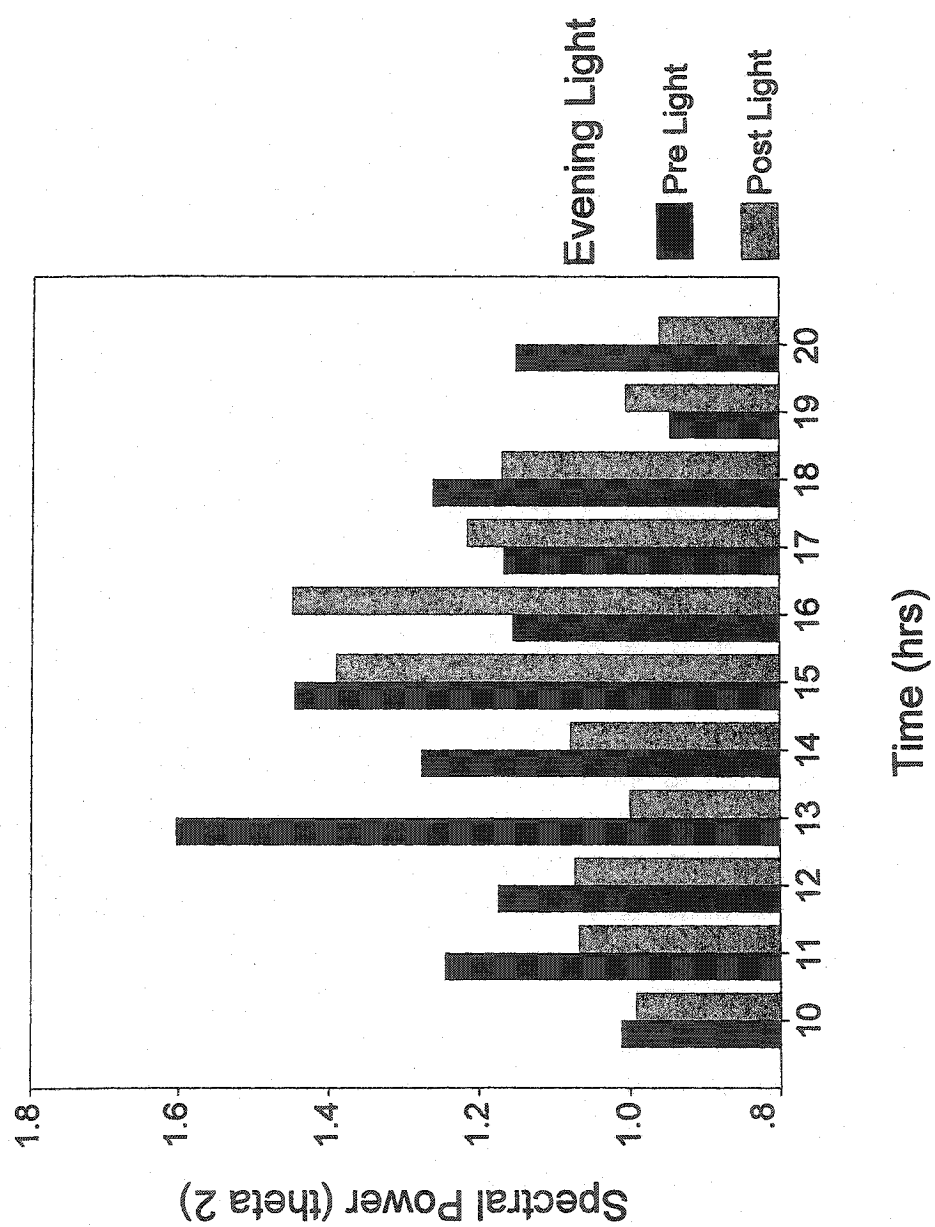


Figure G4. Mean values for theta 2 with eyes closed at C3

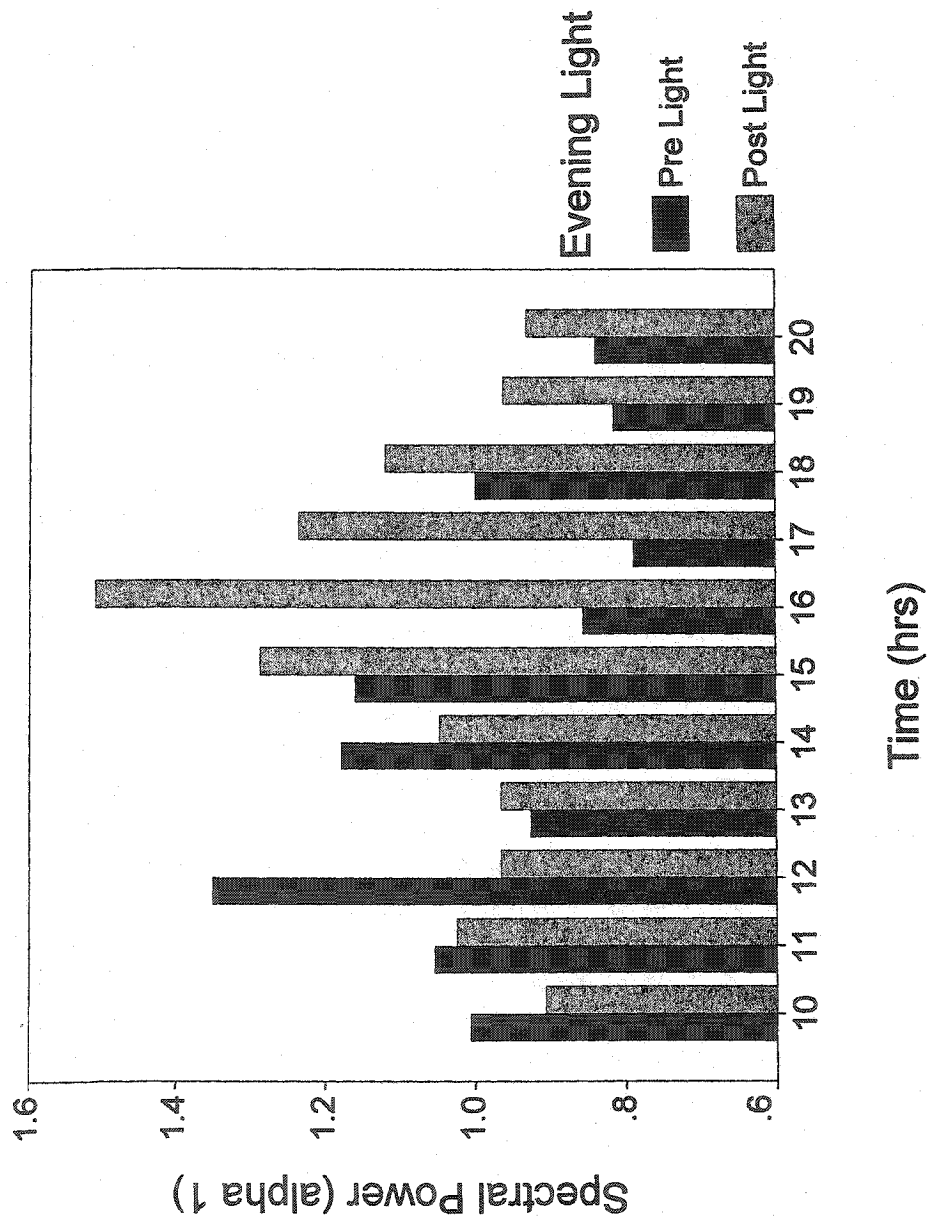


Figure G5. Mean values for alpha 1 with eyes closed at C3

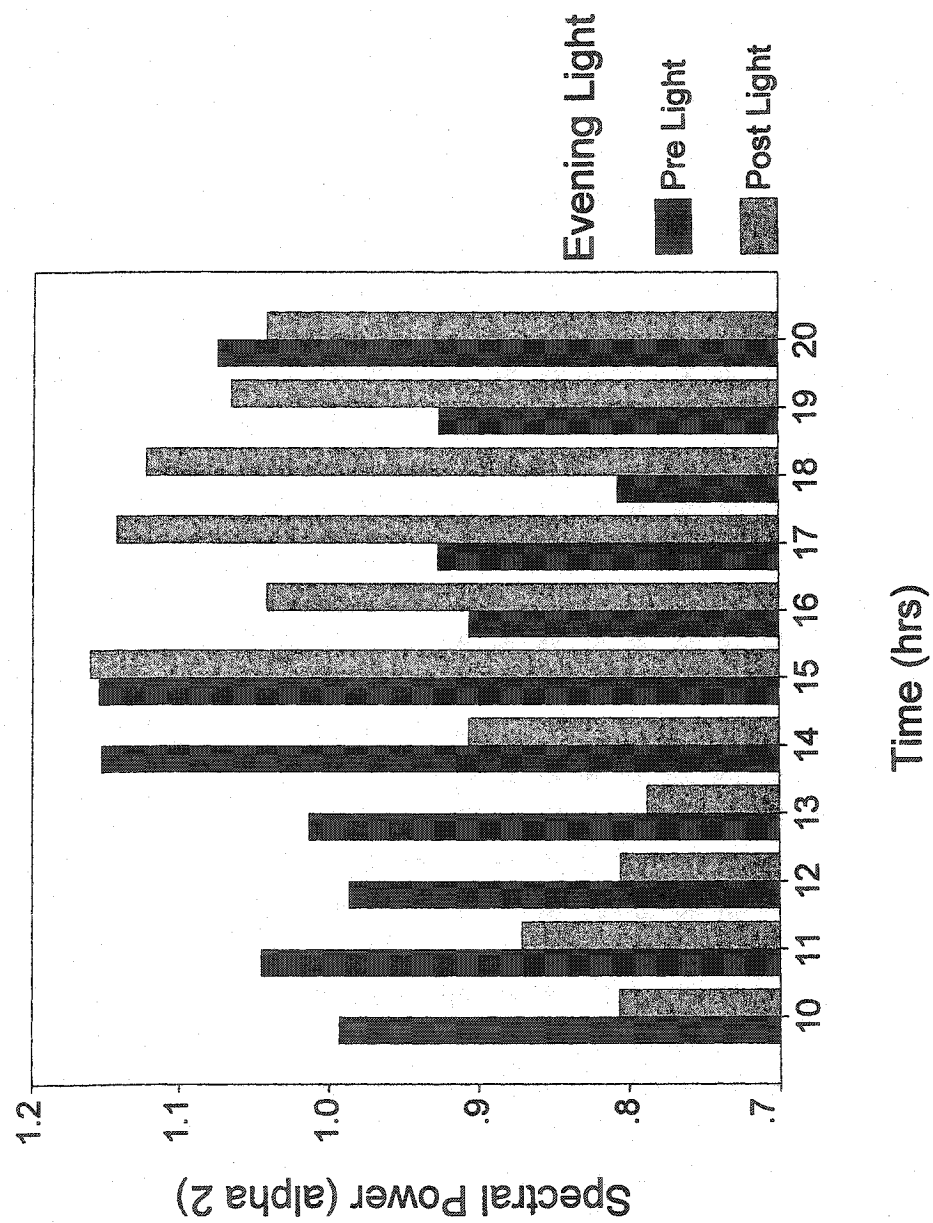


Figure G6. Mean values for alpha 2 with eyes closed at C3

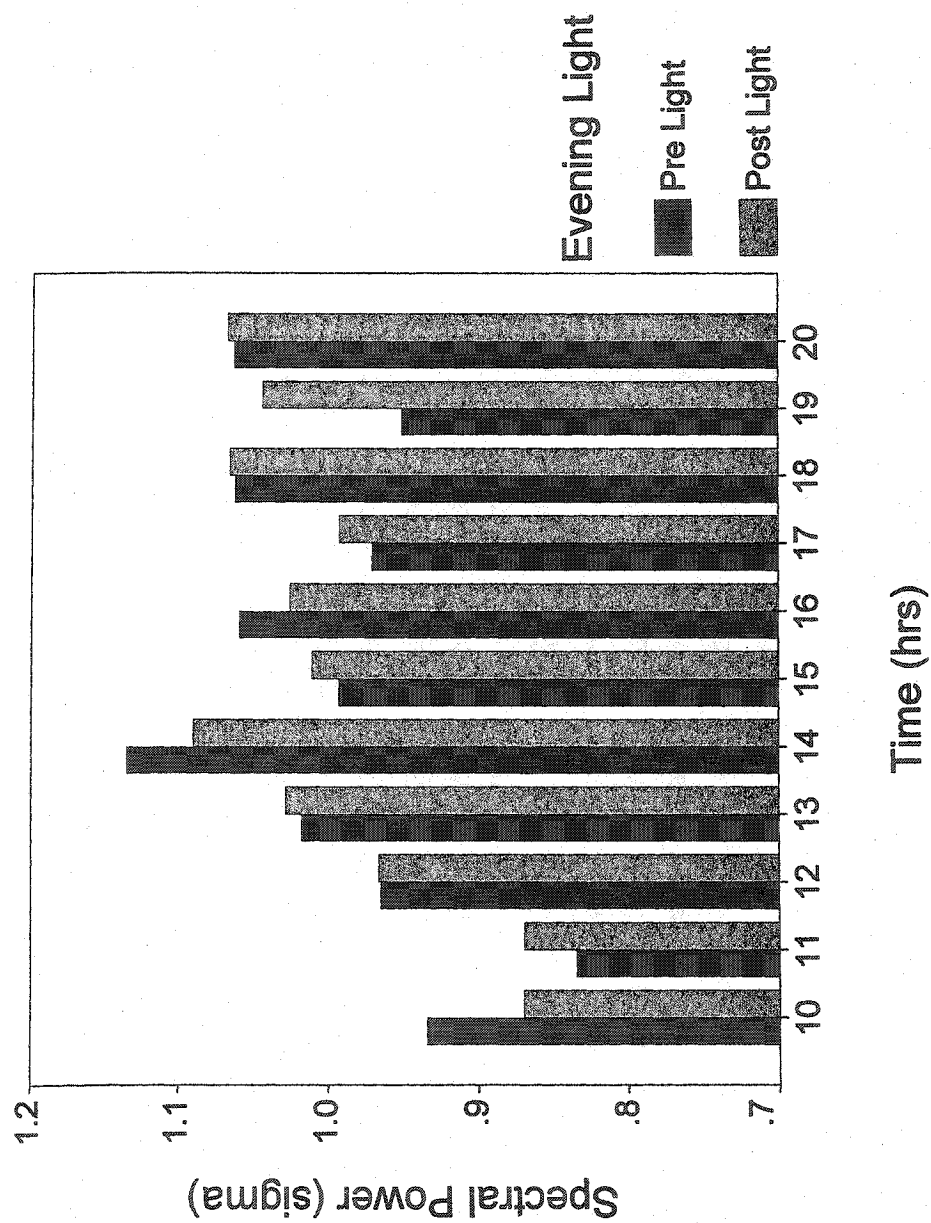


Figure G7. Mean values for sigma with eyes closed at C3

Appendix H

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at C3, eyes open, for baseline and for evening bright light (phase delay).

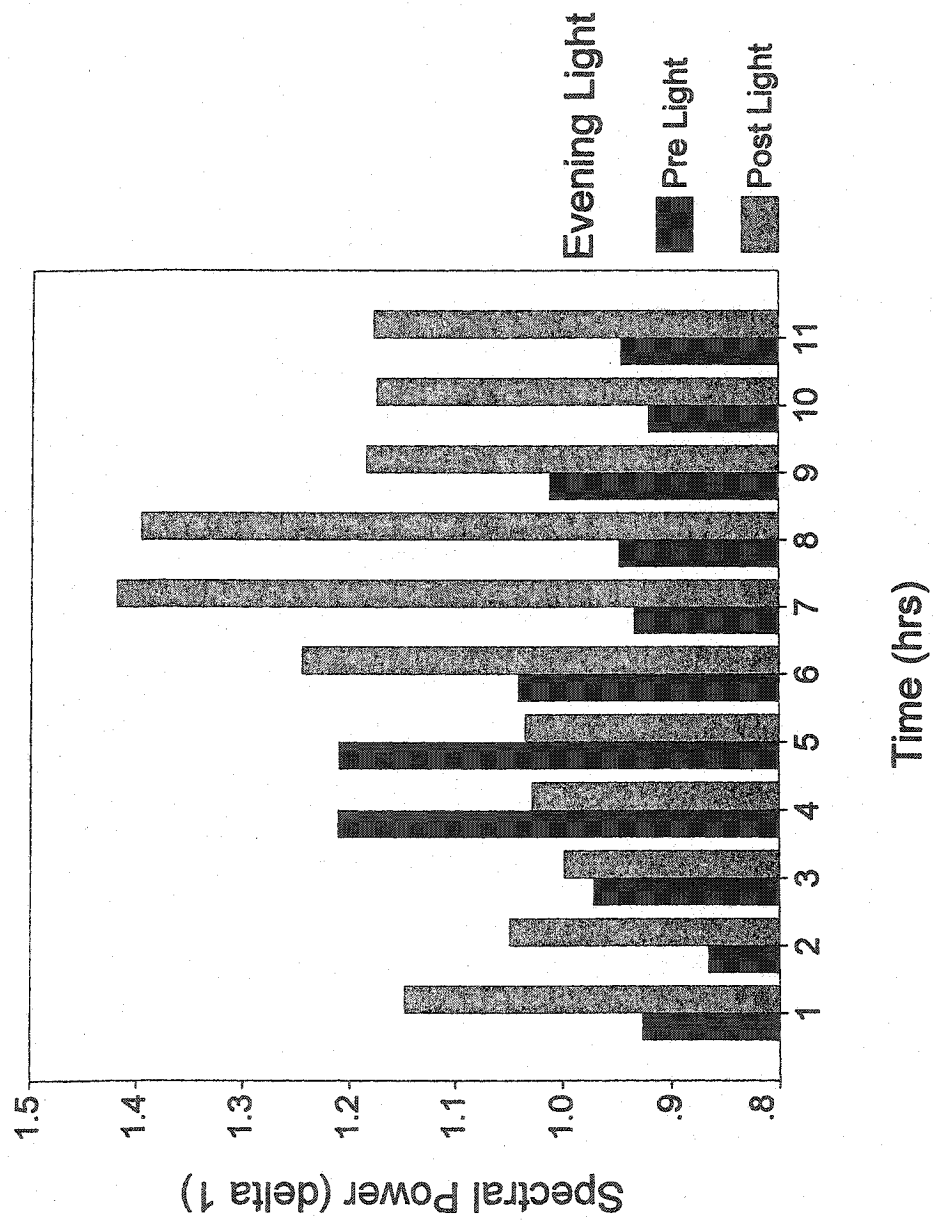


Figure H1. Mean values for delta 1 with eyes open at C3

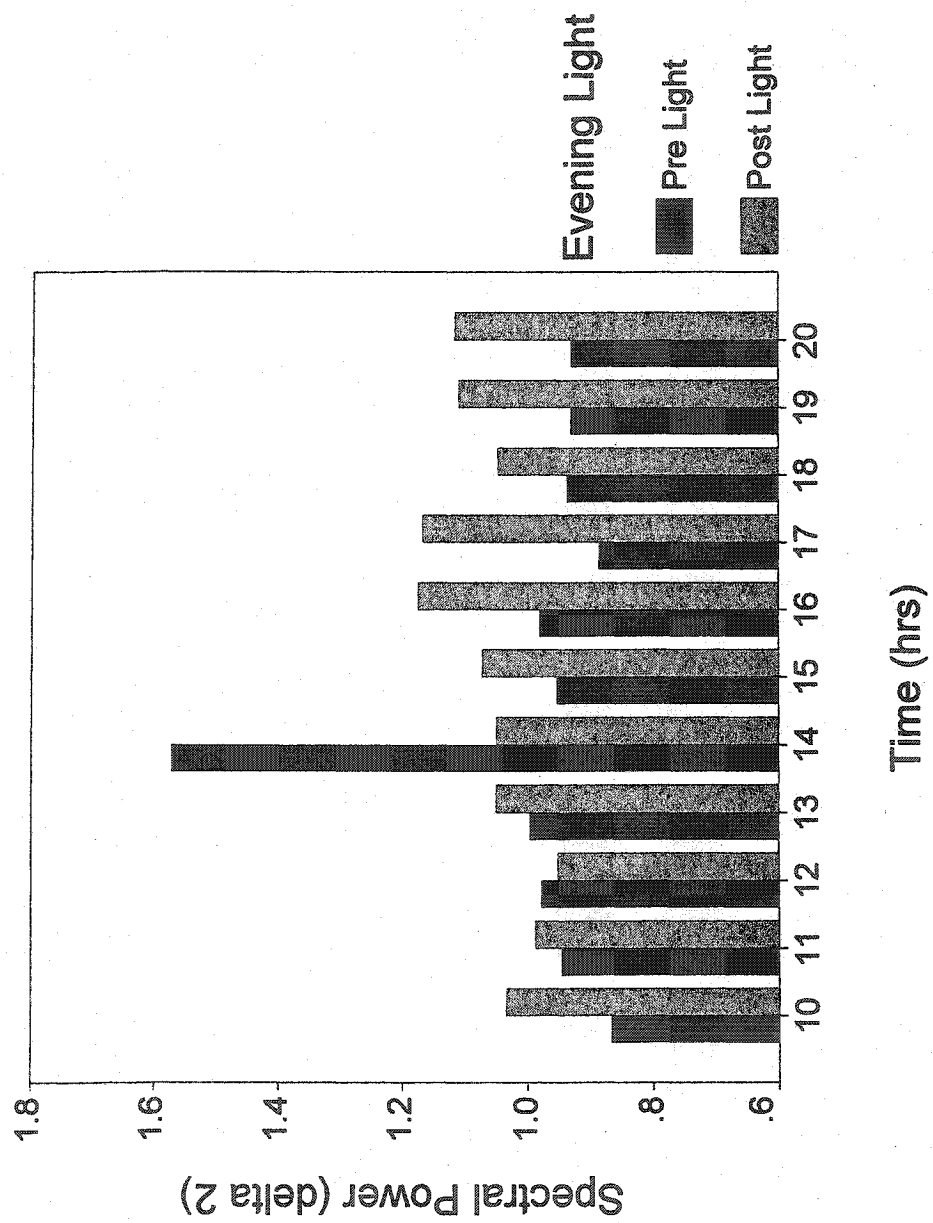


Figure H2. Mean values for delta 2 with eyes open at C3

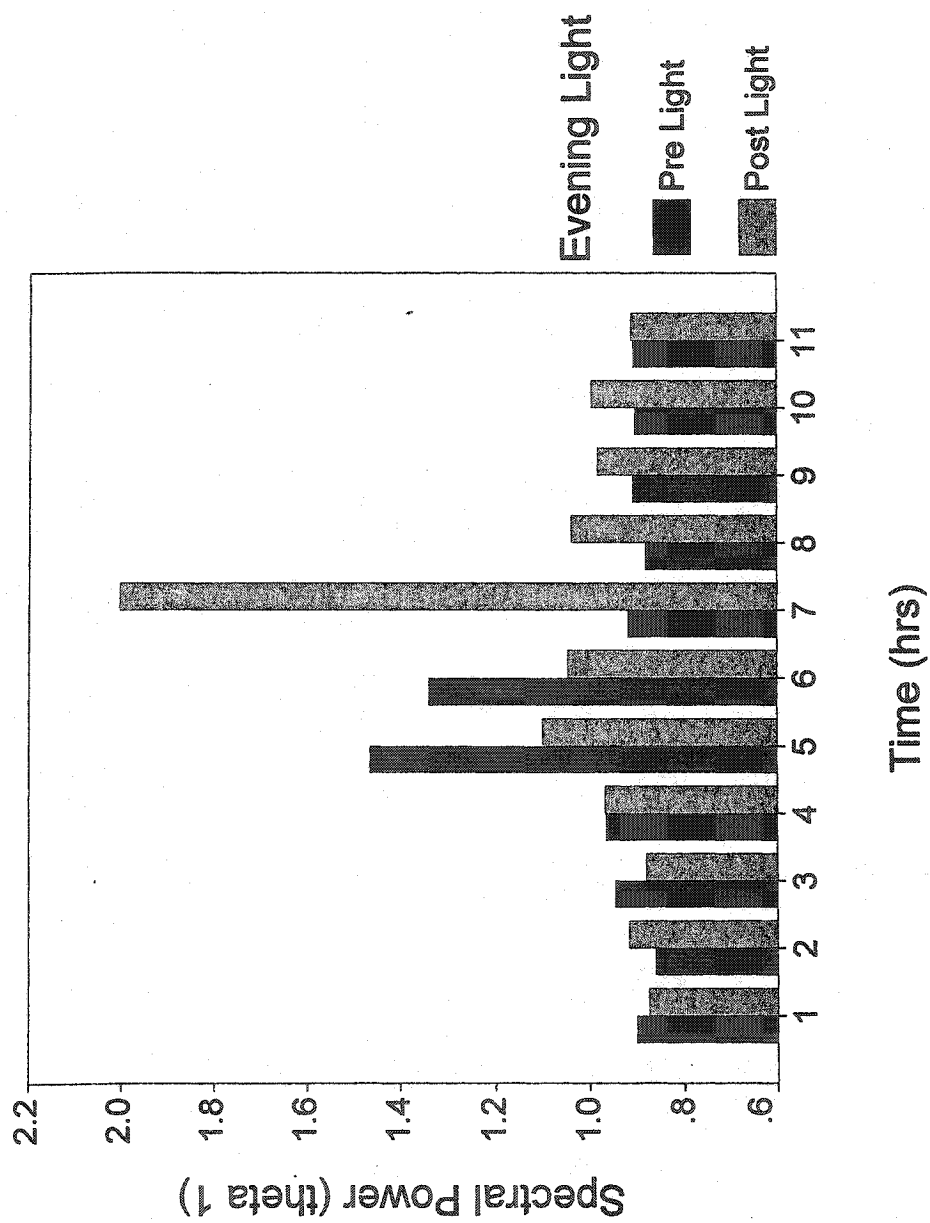


Figure H3. Mean values for theta 1 with eyes open at C3

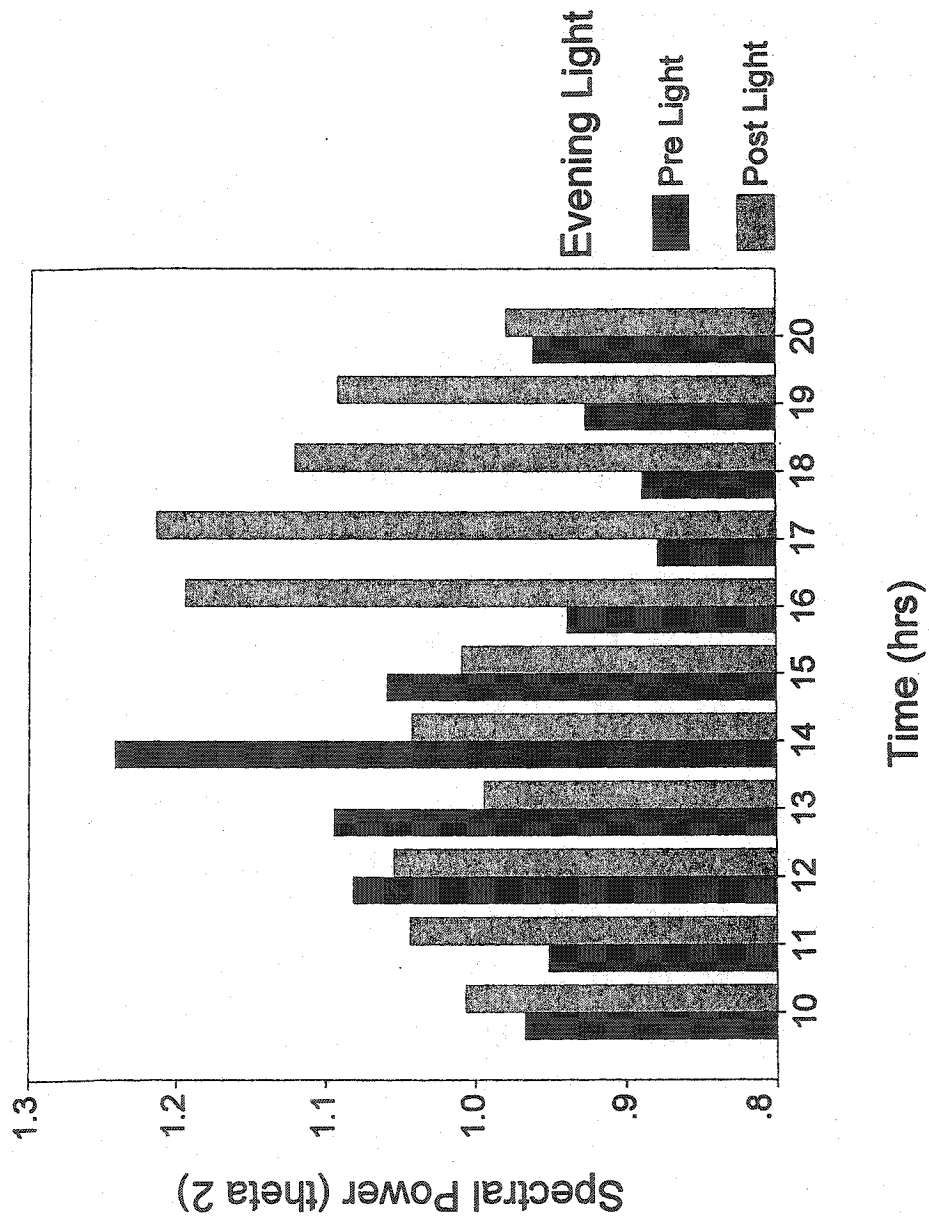


Figure H4. Mean values for theta 2 with eyes open at C3

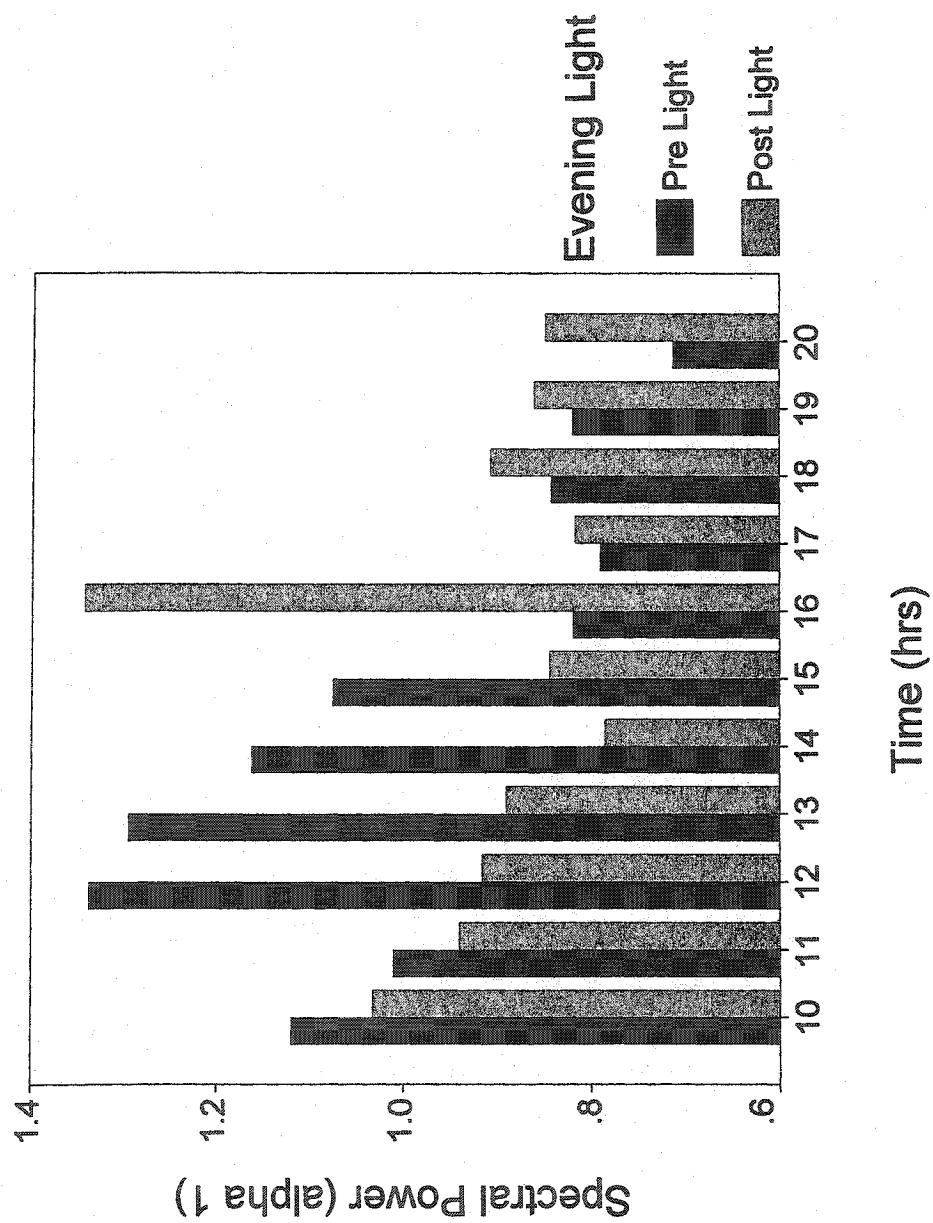


Figure H5. Mean values for alpha 1 with eyes open at C3

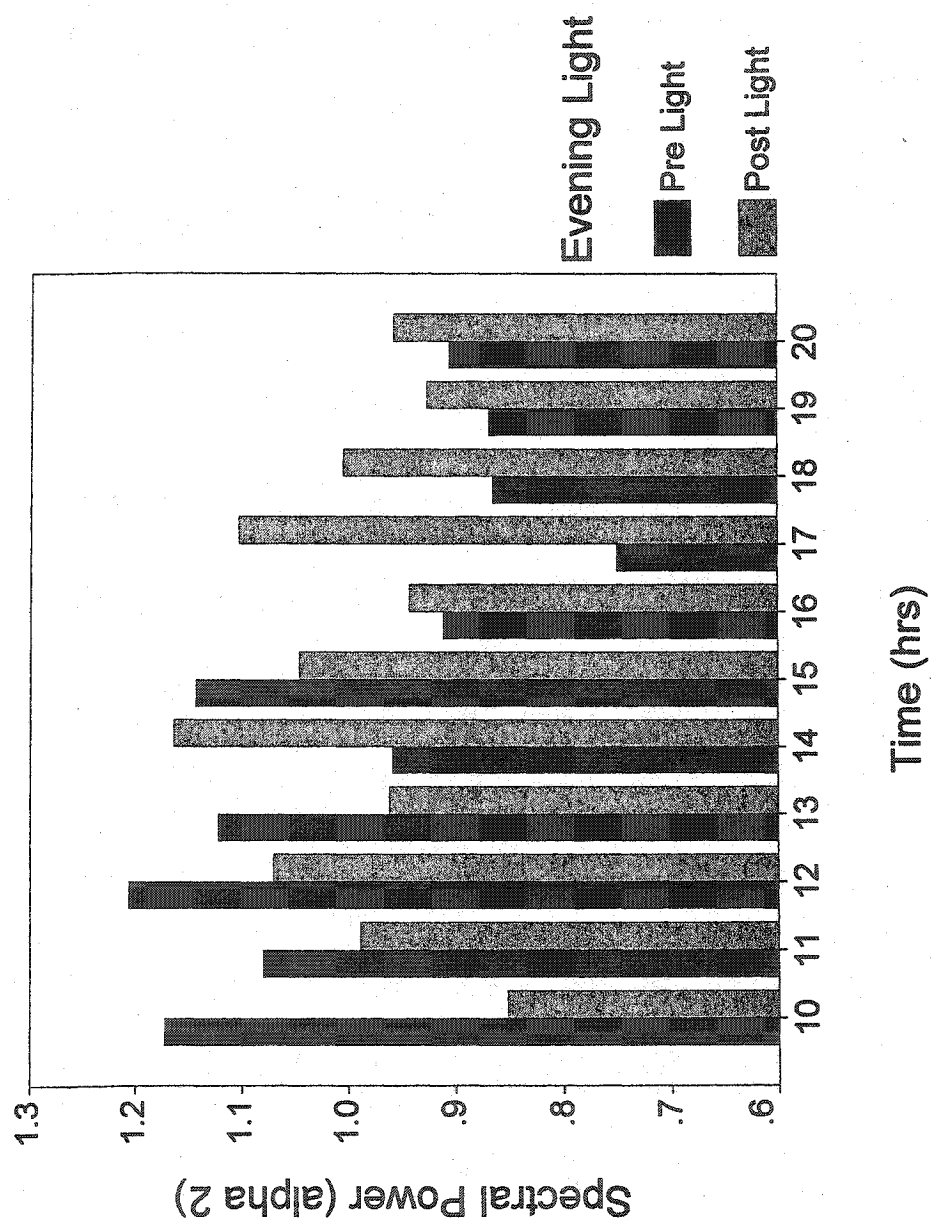


Figure H6. Mean values for alpha 2 with eyes open at C3

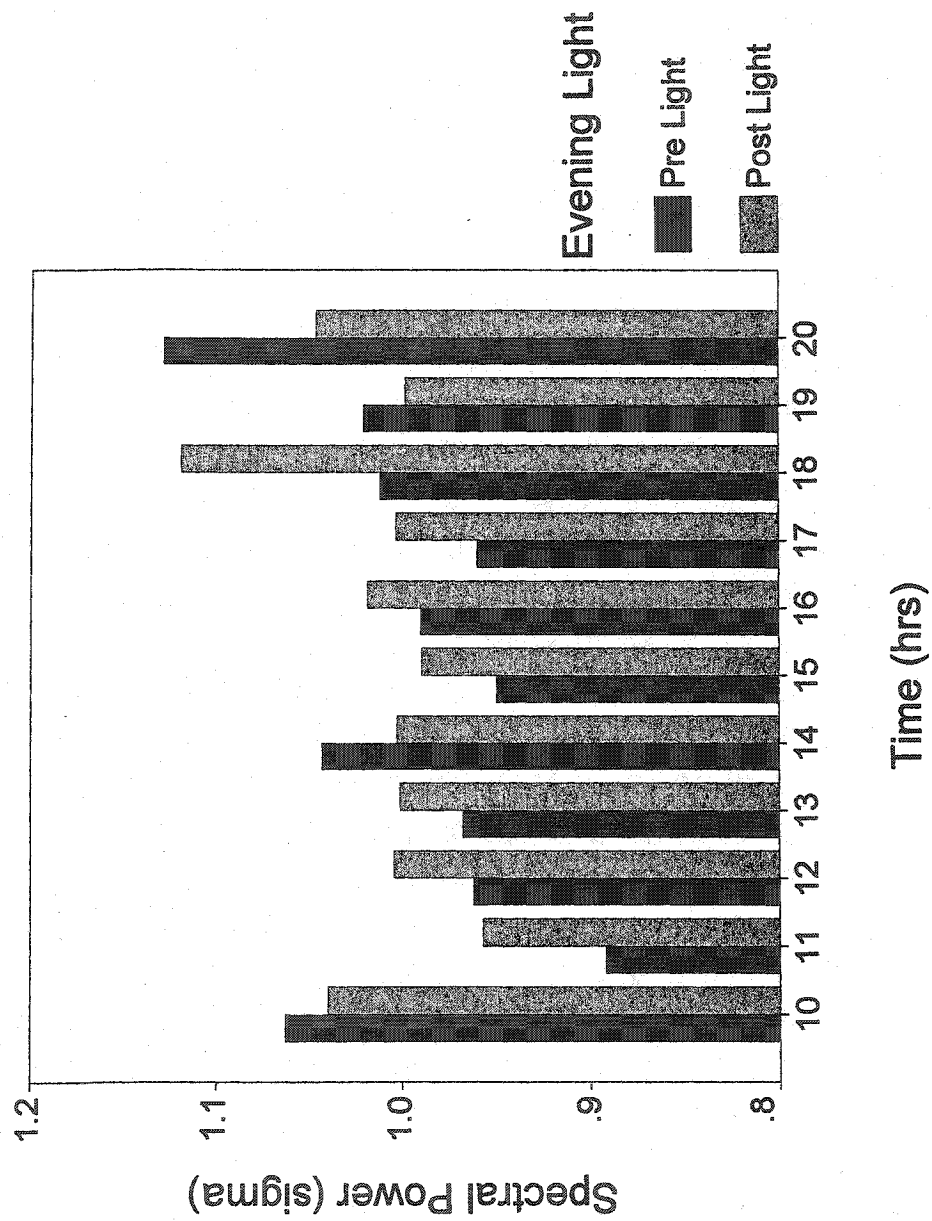


Figure H7. Mean values for sigma with eyes open at C3

Appendix I

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at 02, eyes closed, for baseline and for morning bright light (phase advance).

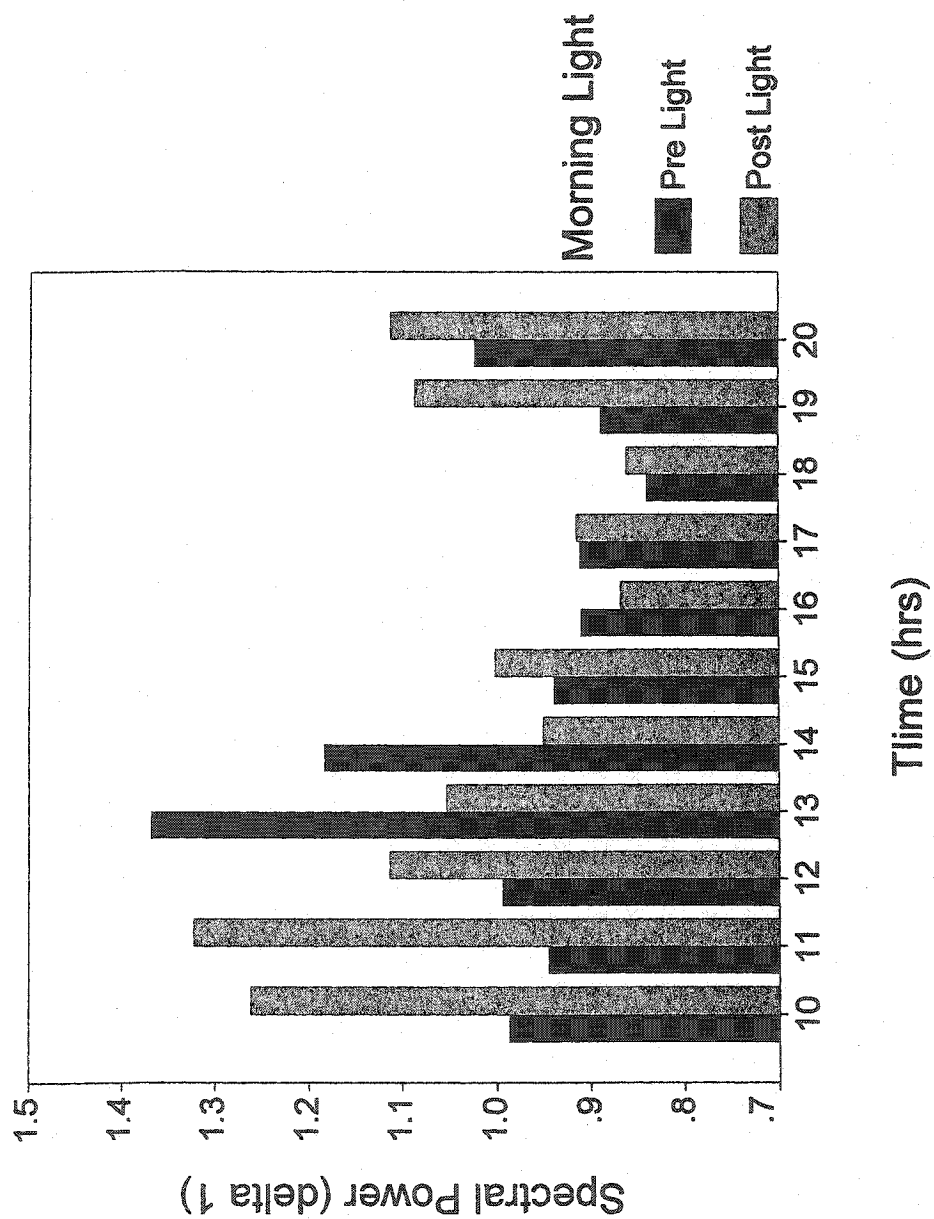


Figure I1. Mean values for delta 1 with eyes closed at 02

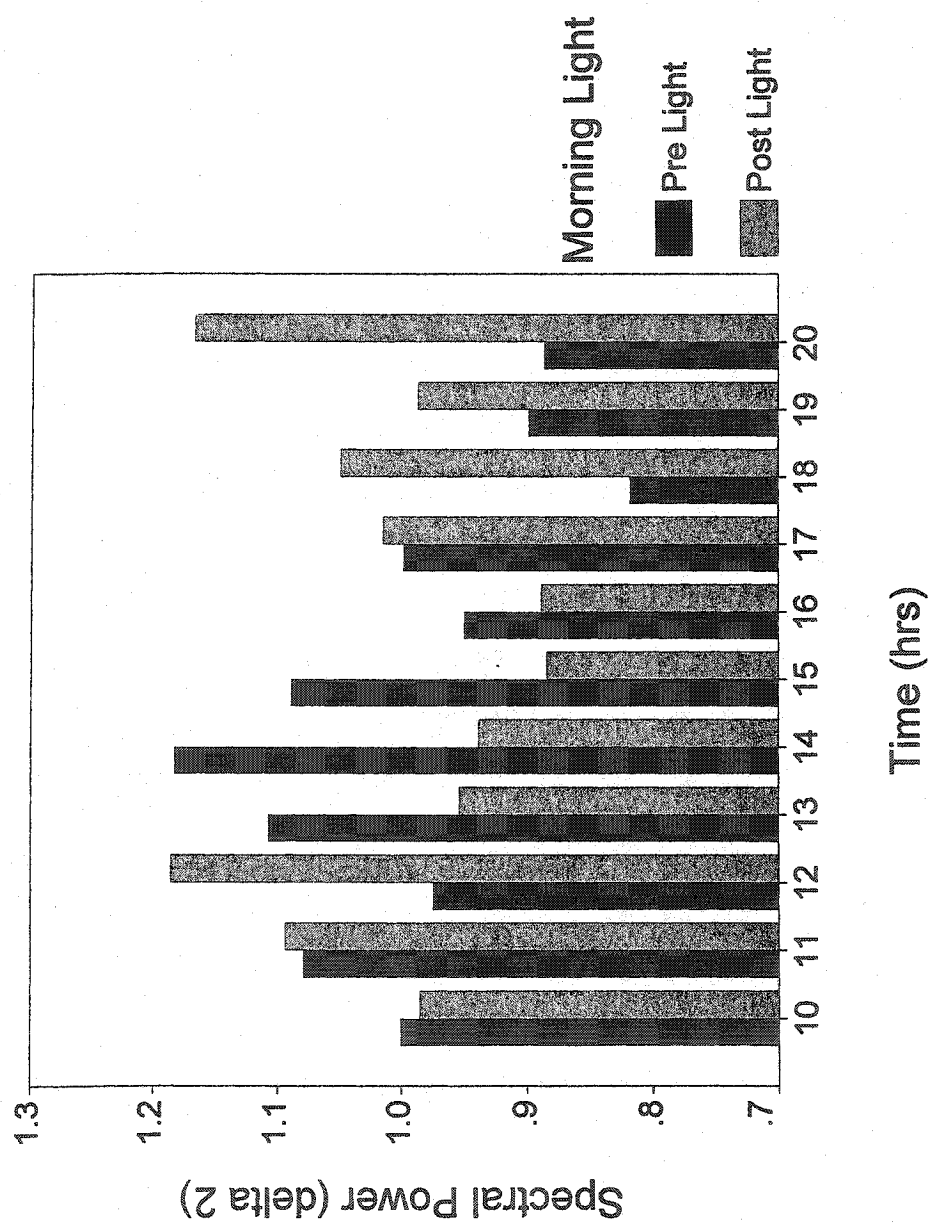


Figure I2. Mean values for delta 2 with eyes closed at 02

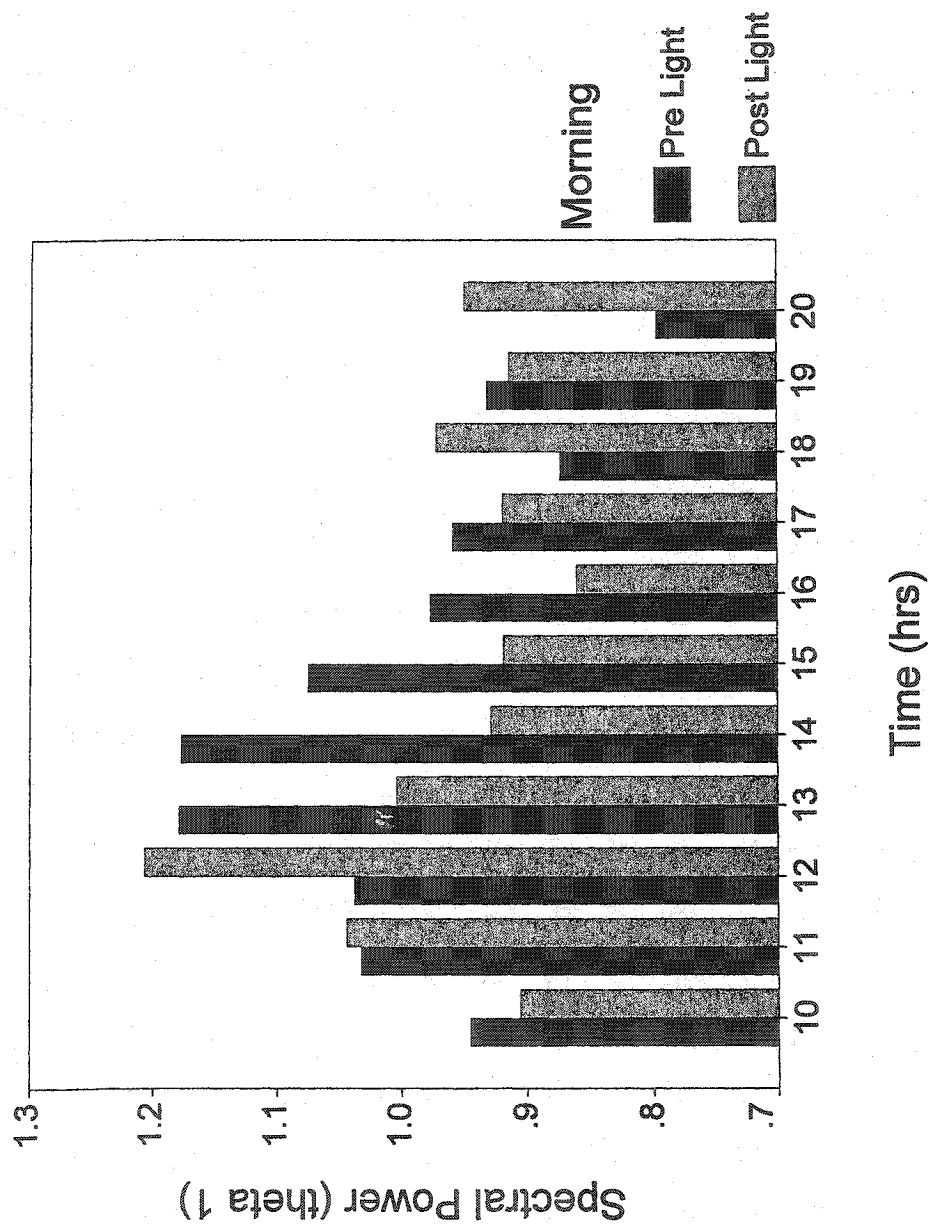


Figure I3. Mean values for theta 1 with eyes closed at 02

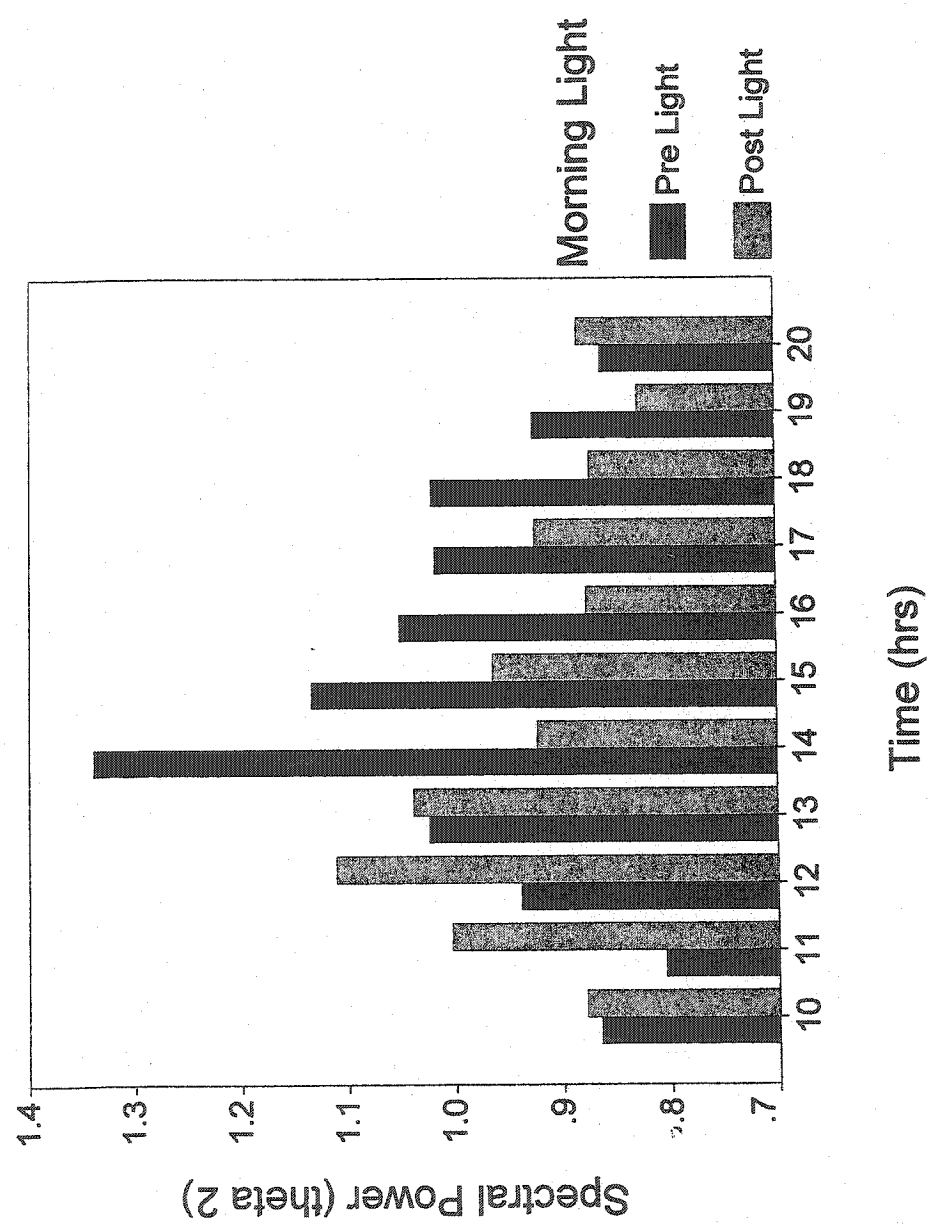


Figure 14. Mean values for theta 2 with eyes closed at 02

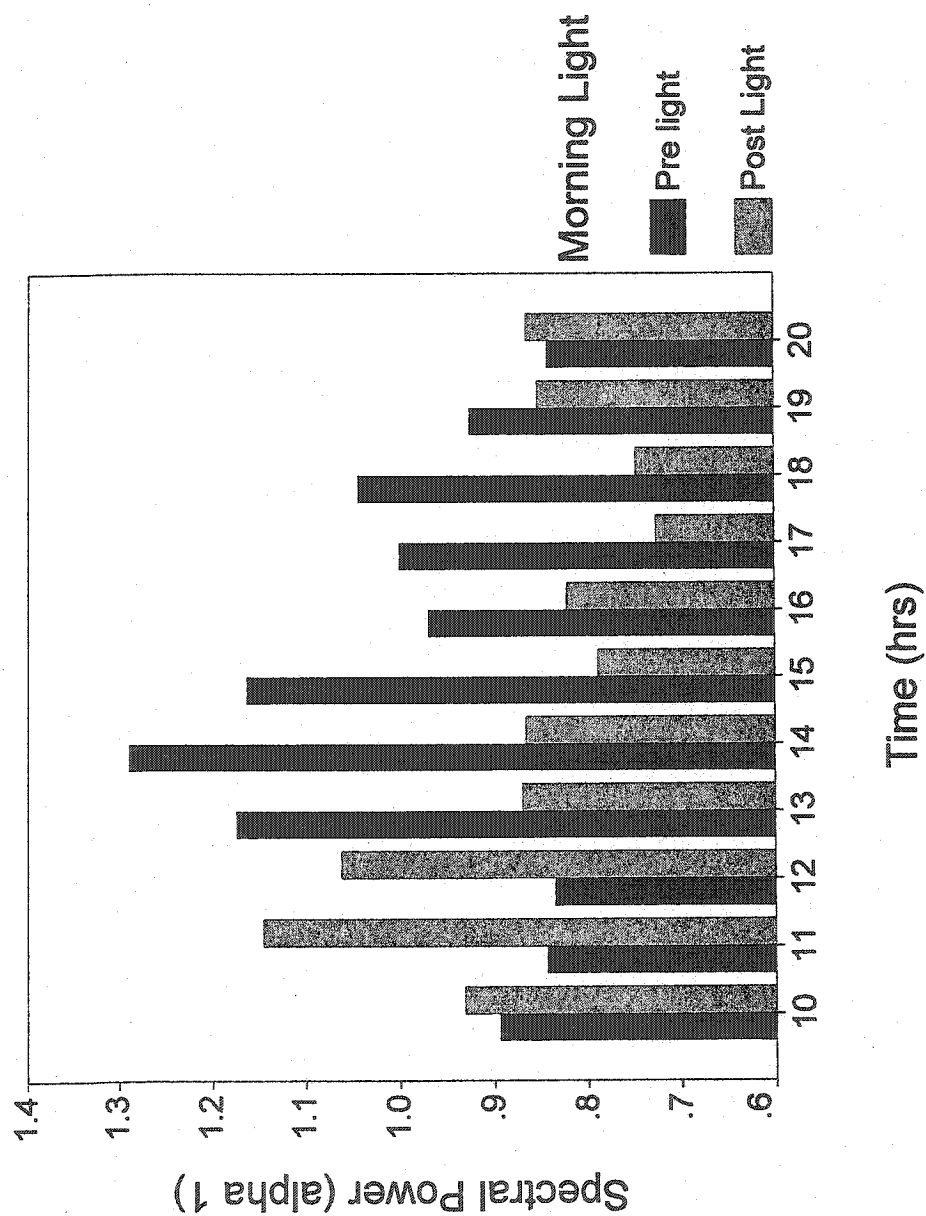


Figure I5. Mean values for alpha 1 with eyes closed at 02

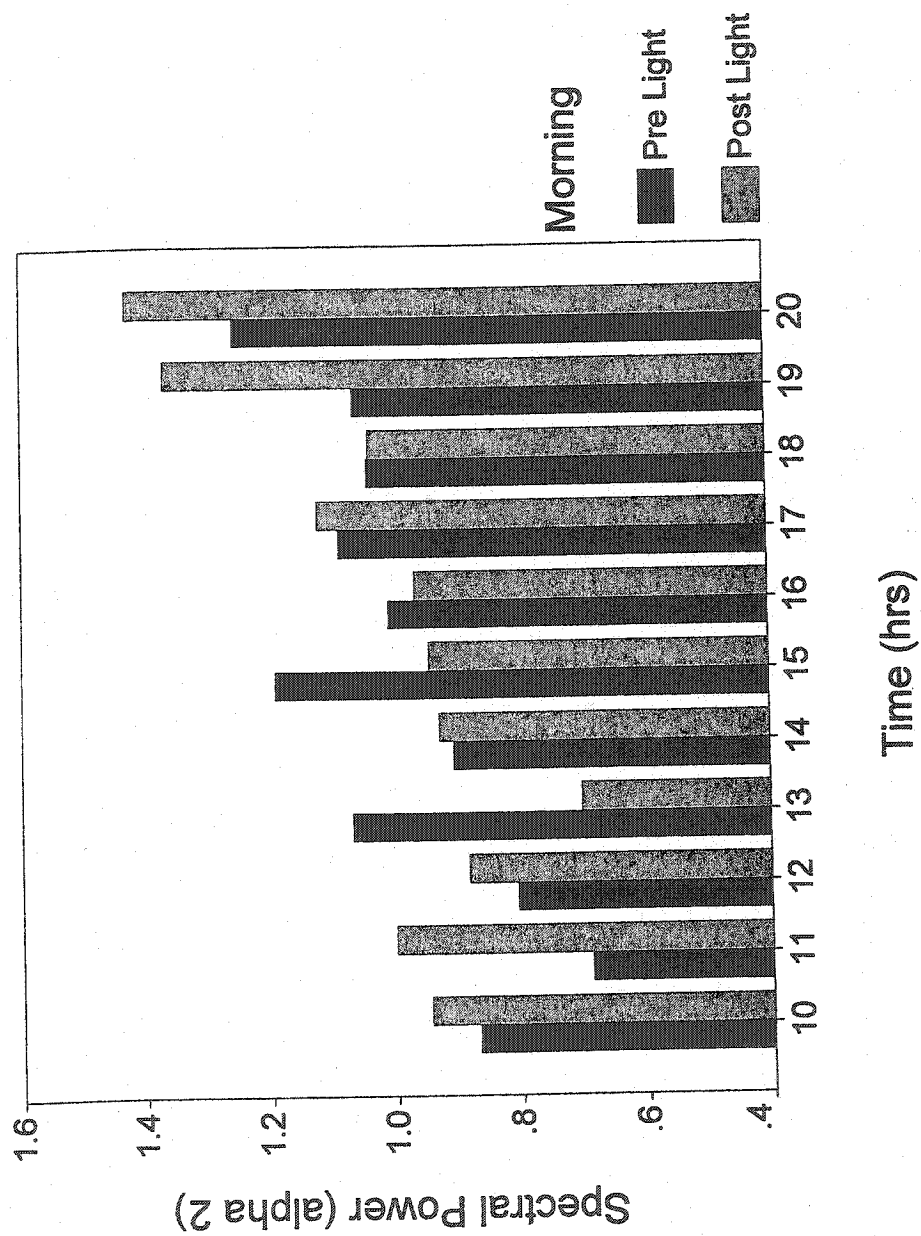


Figure 16. Mean values for alpha 2 with eyes closed at 02

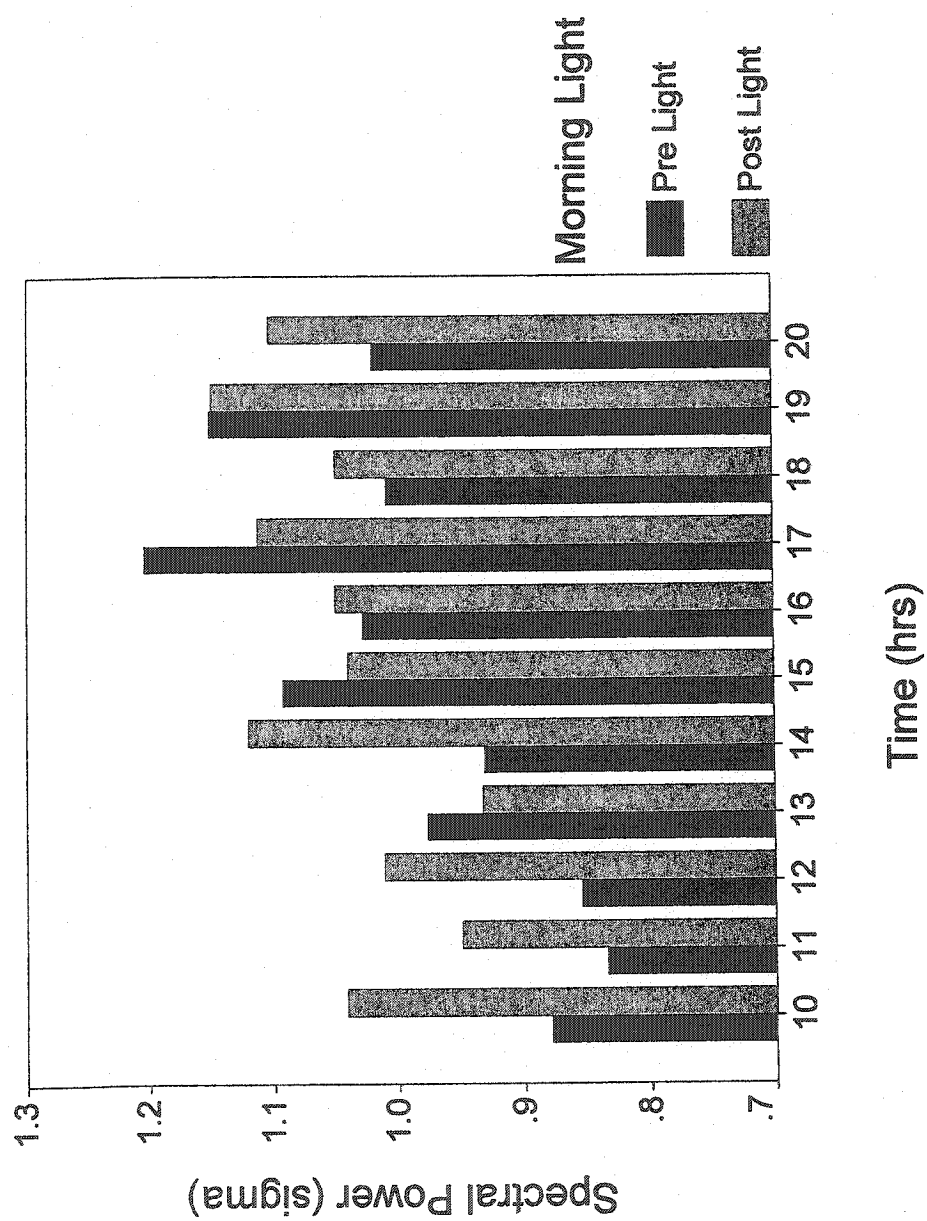


Figure 17. Mean values for sigma with eyes closed at 02

Appendix J

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at 02, eyes open, for baseline and for morning bright light (phase advance).

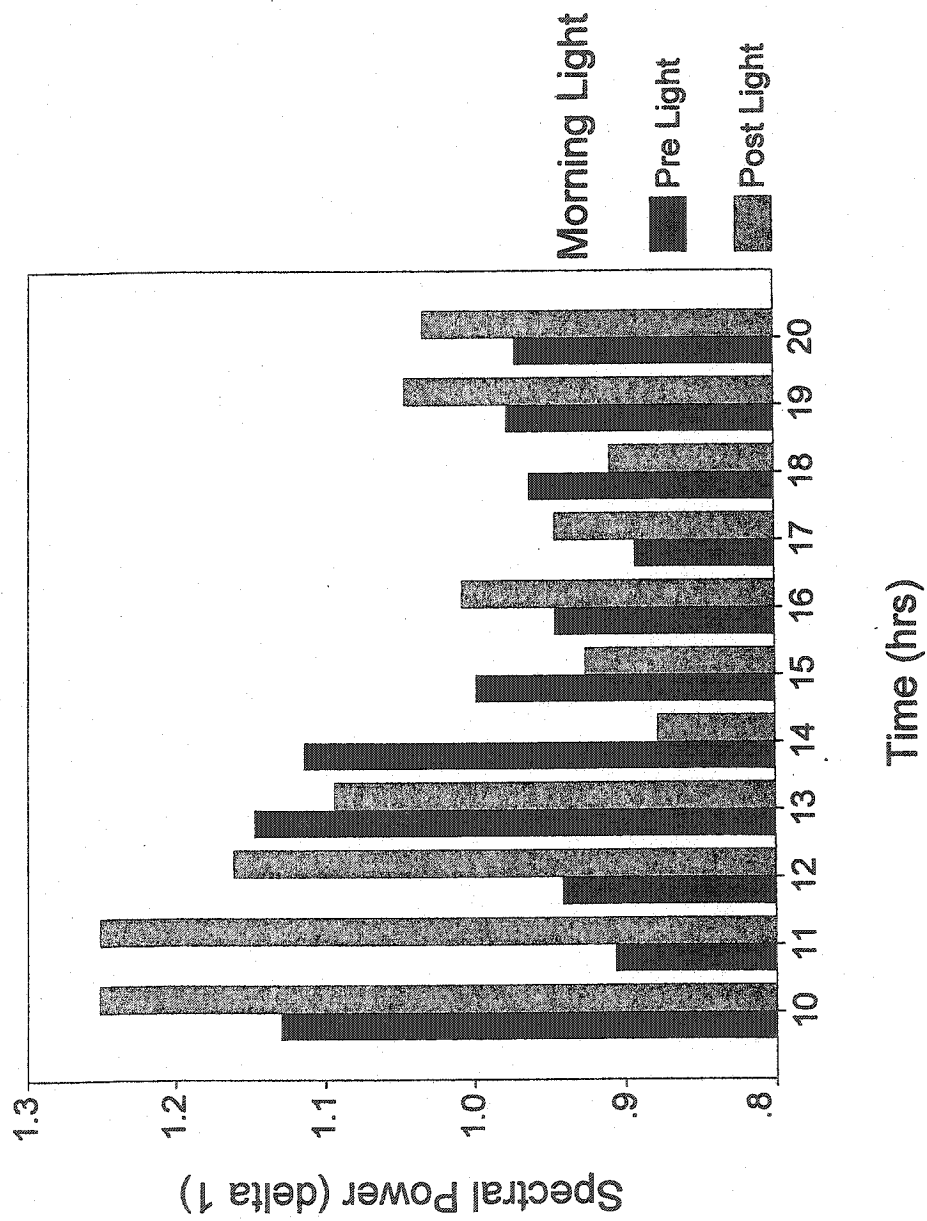


Figure J1. Mean values for delta 1 with eyes open at 02

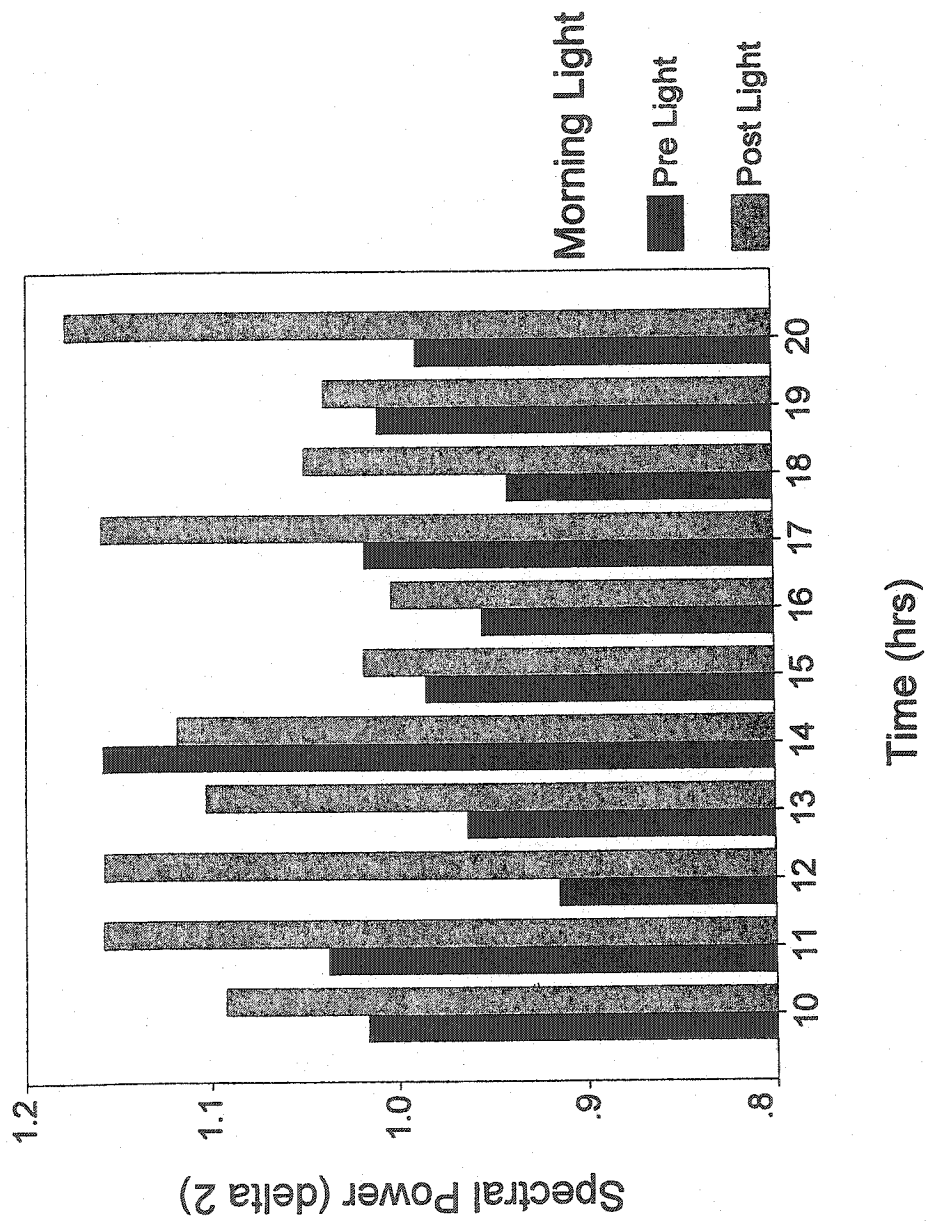


Figure J2. Mean values for delta 2 with eyes open at 02

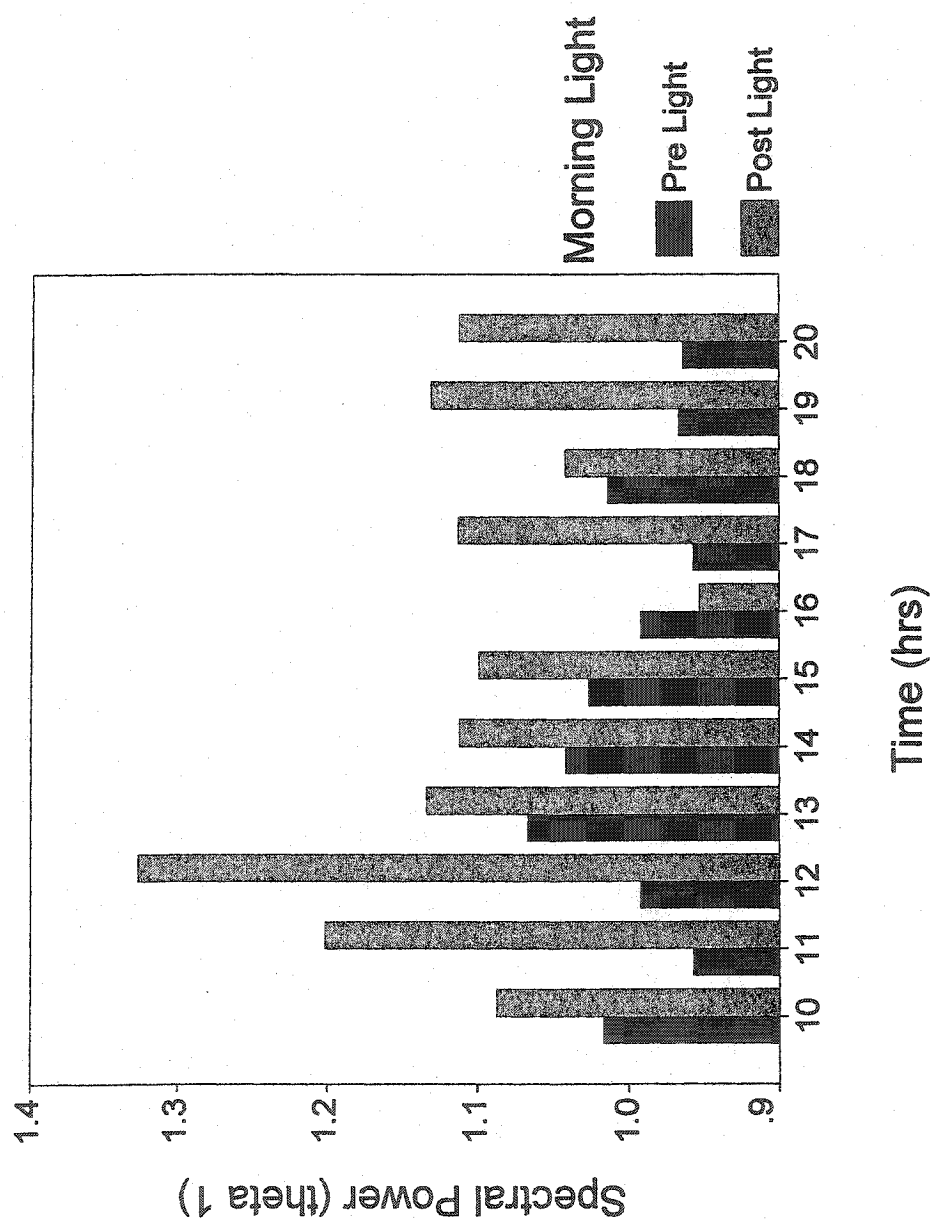


Figure J3. Mean values for theta 1 with eyes open at 02

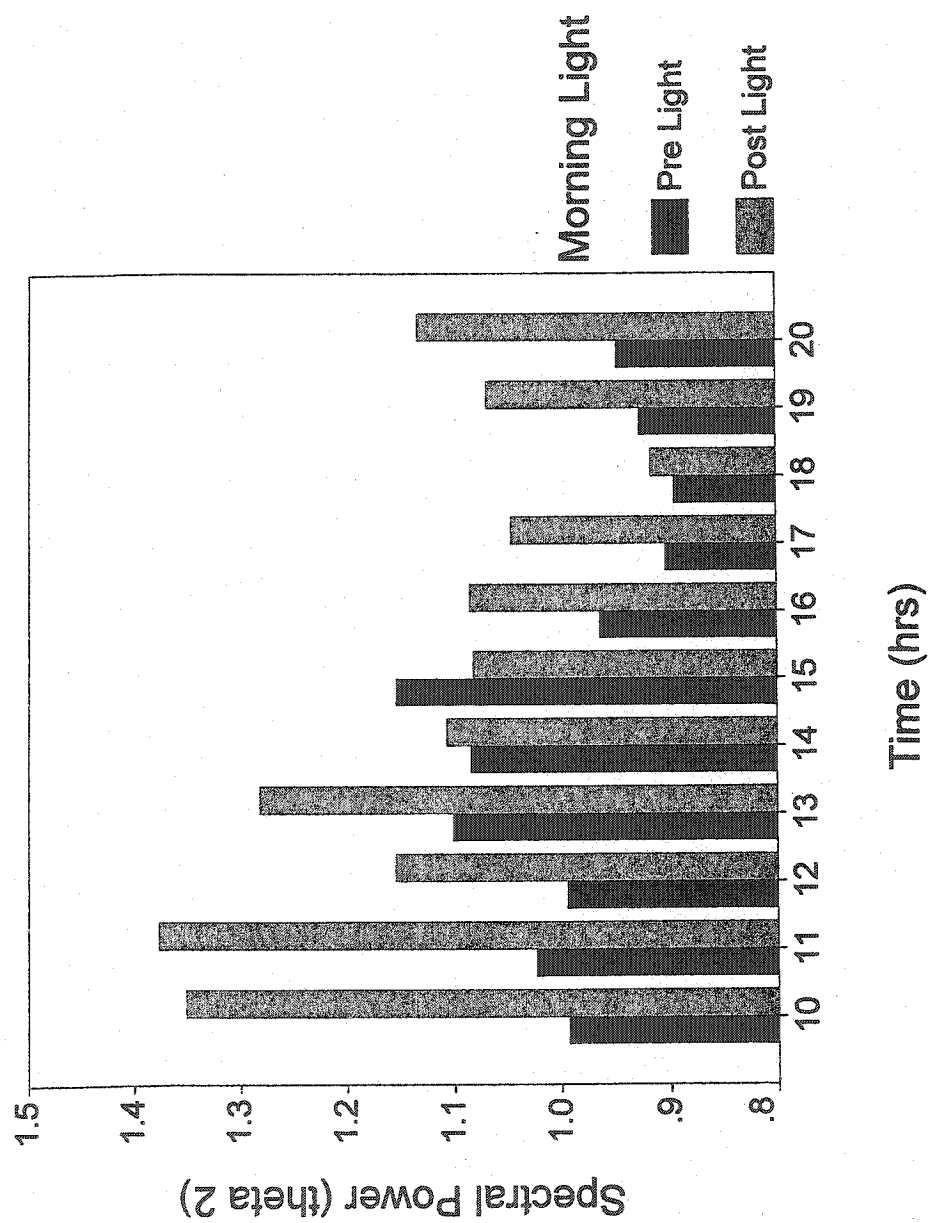


Figure J4. Mean values for theta 2 with eyes open at 02

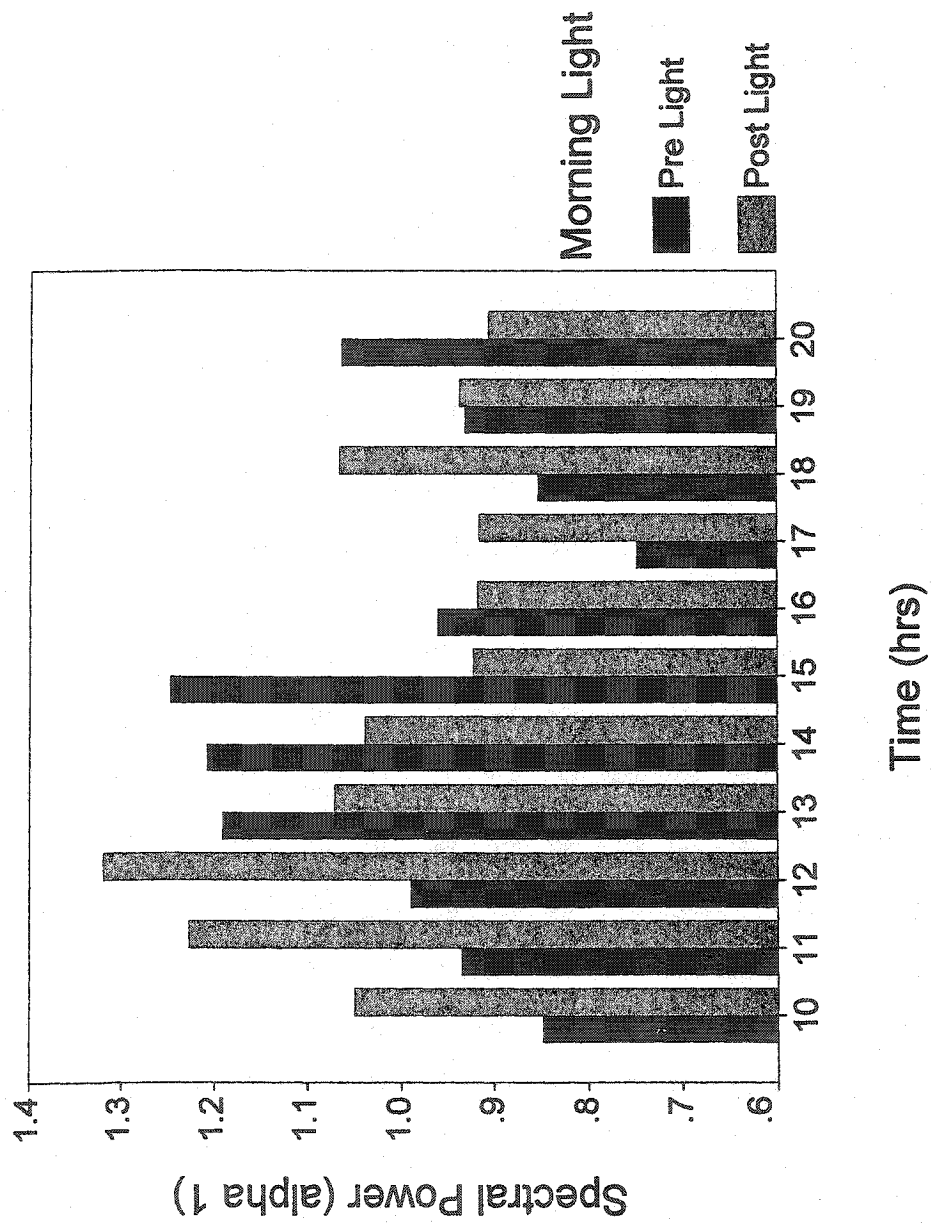


Figure J5. Mean values for alpha 1 with eyes open at 02

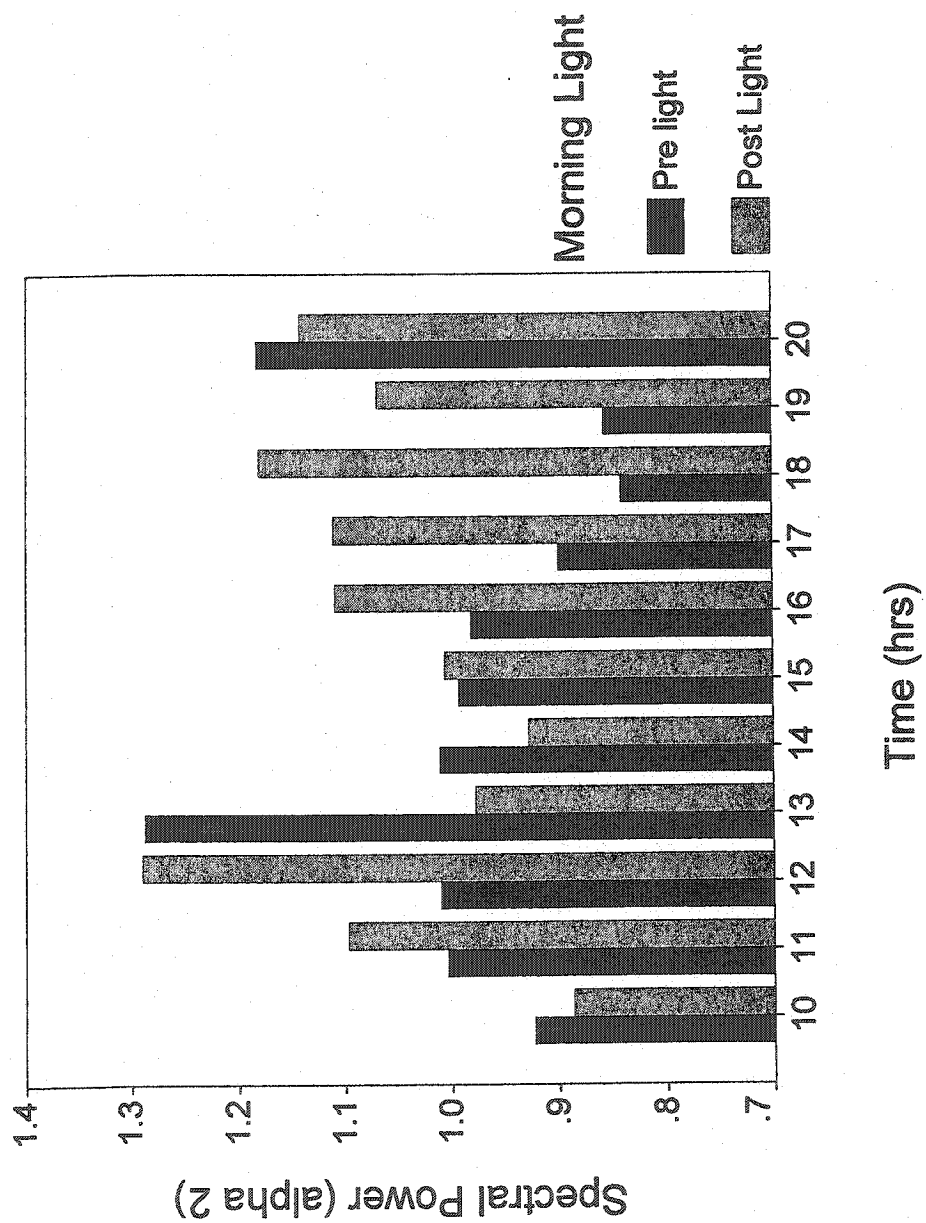


Figure J6. Mean values for alpha 2 with eyes open at 02

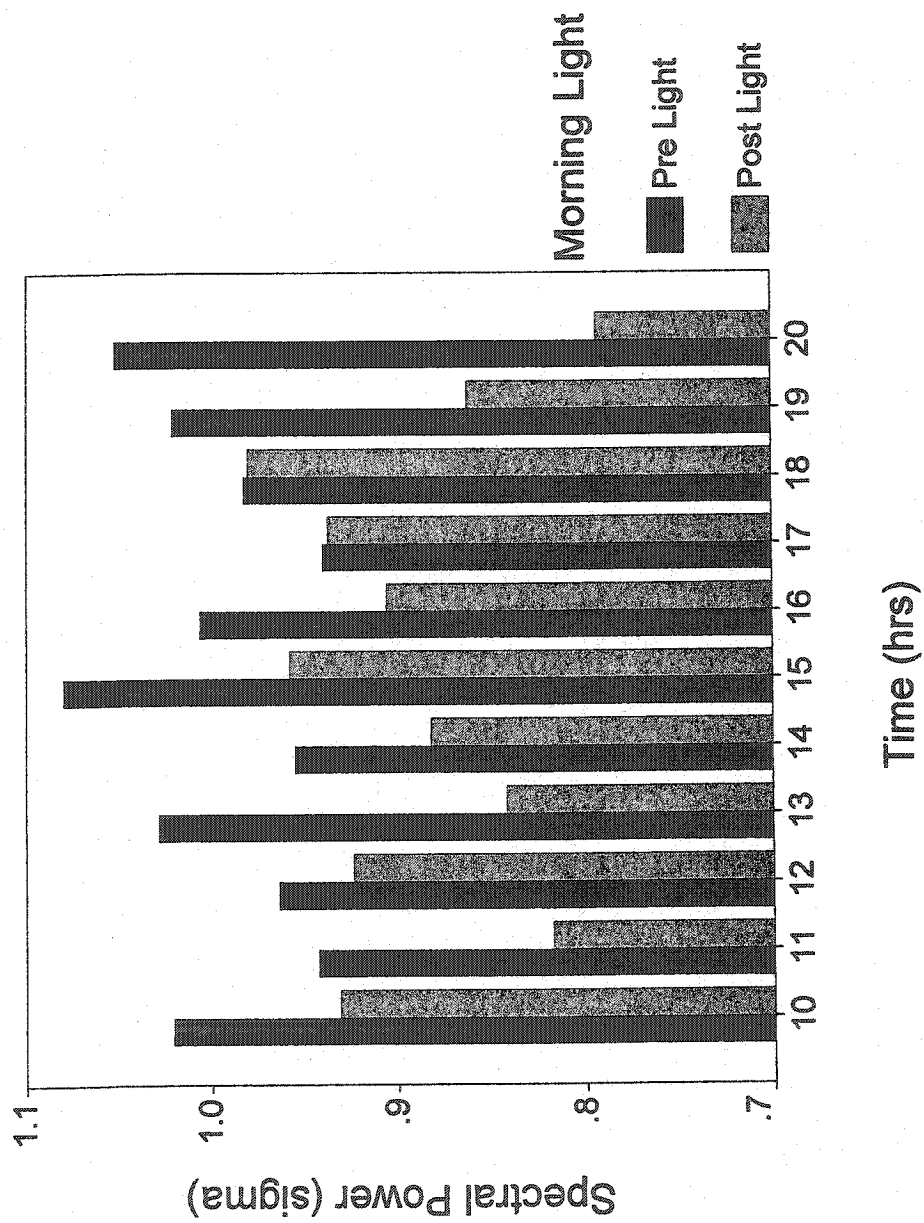


Figure J7. Mean values for sigma with eyes open at 02

Appendix K

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at C3, eyes closed, for baseline and for morning bright light (phase advance).

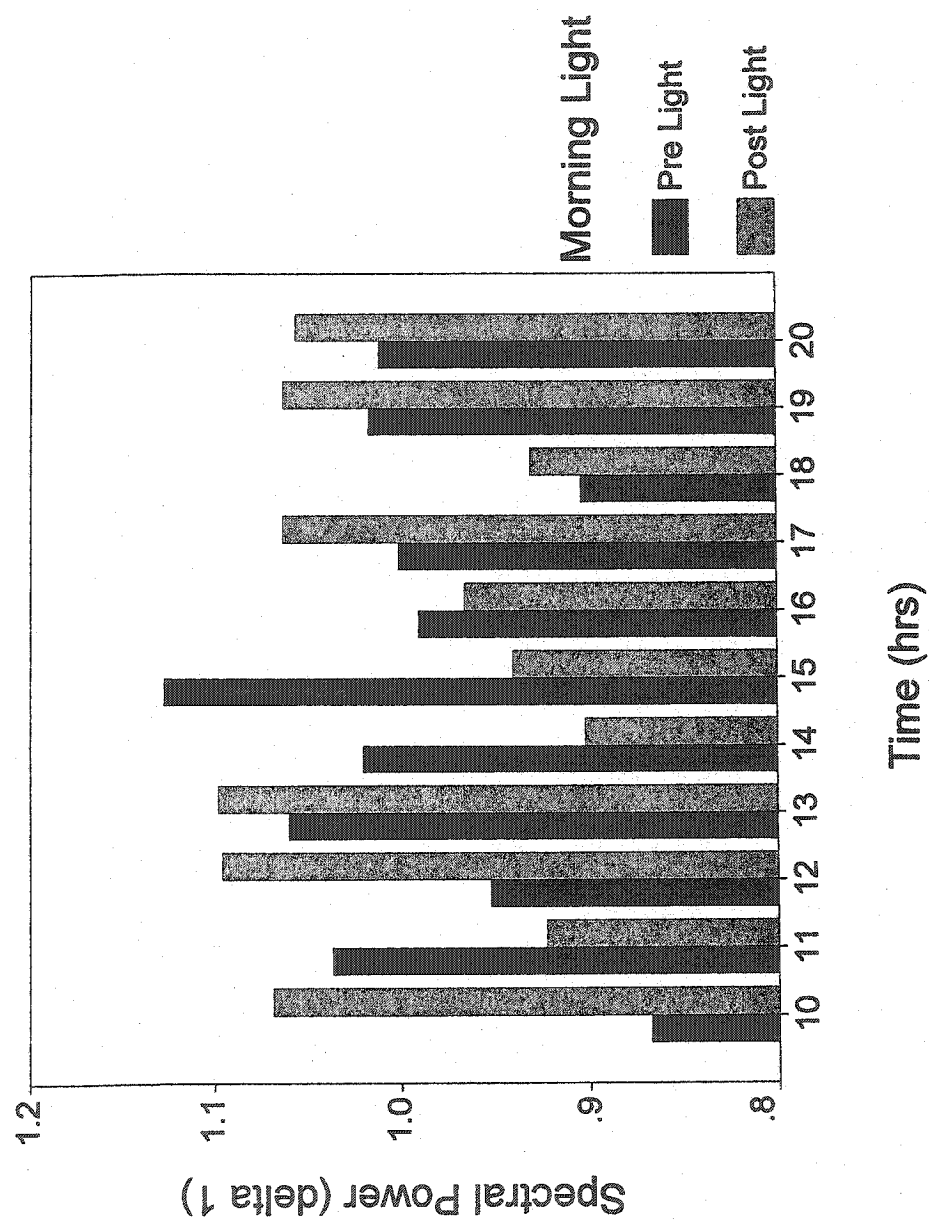


Figure K1. Mean values for delta 1 with eyes closed at C3

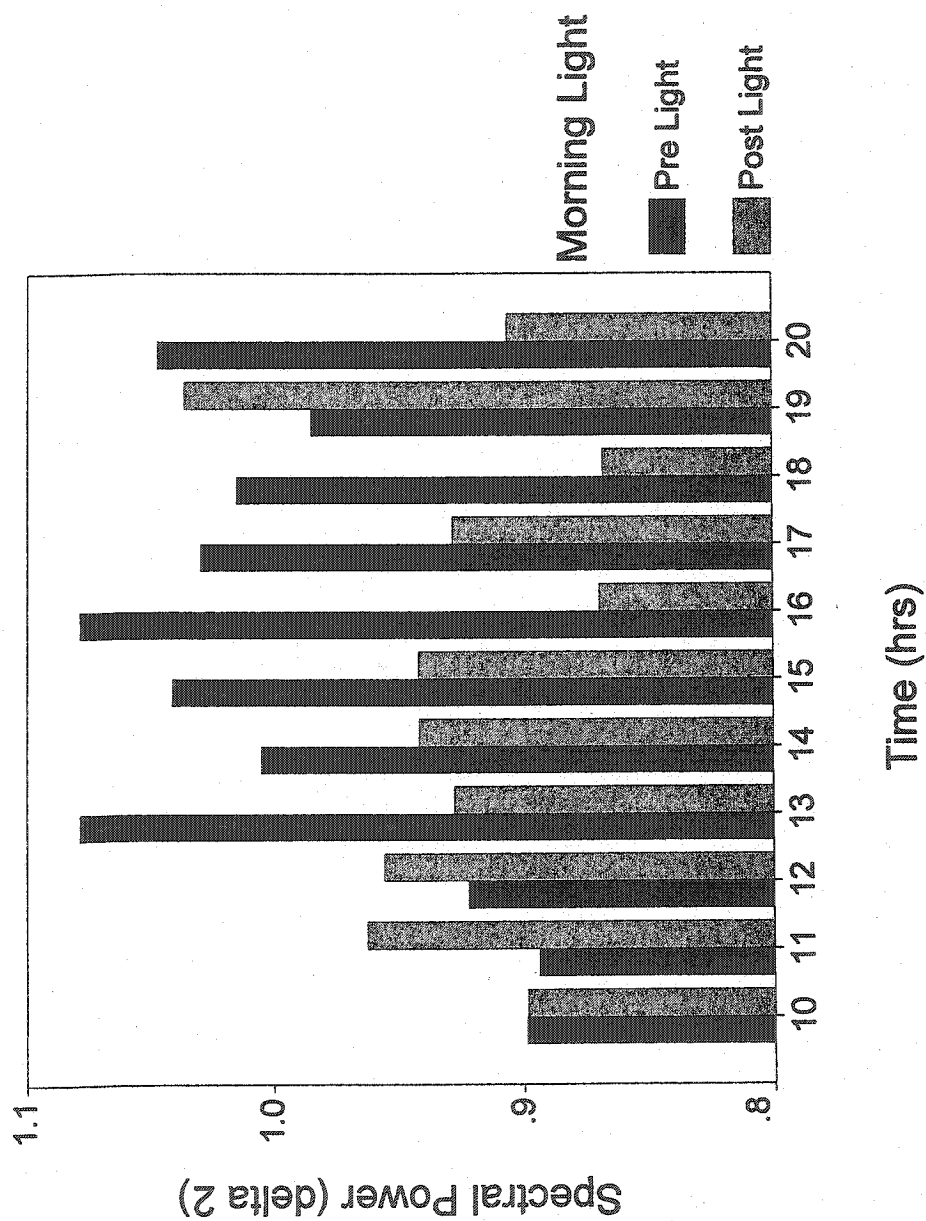


Figure K2. Mean values for delta 2 with eyes closed at C3

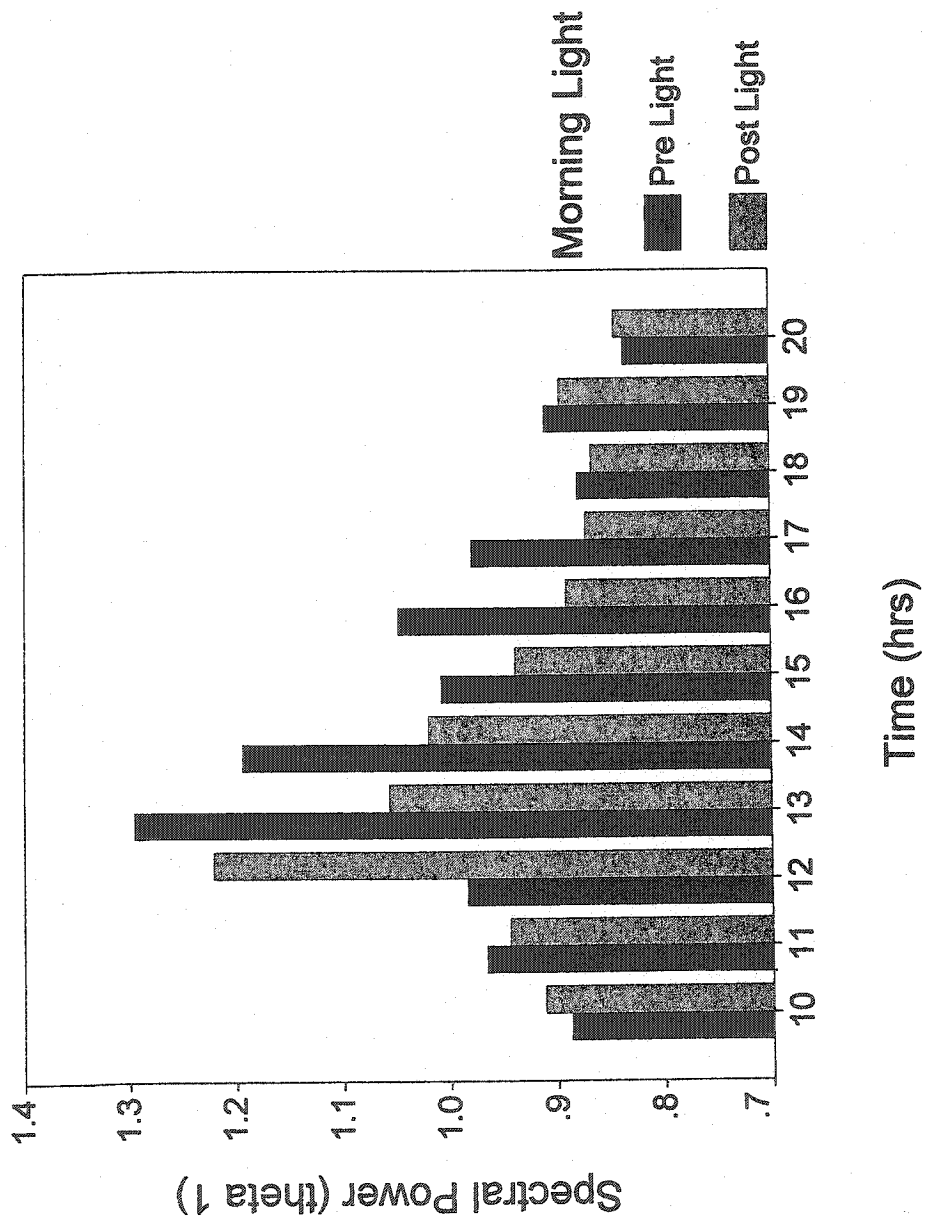


Figure K3. Mean values for theta 1 with eyes closed at C3

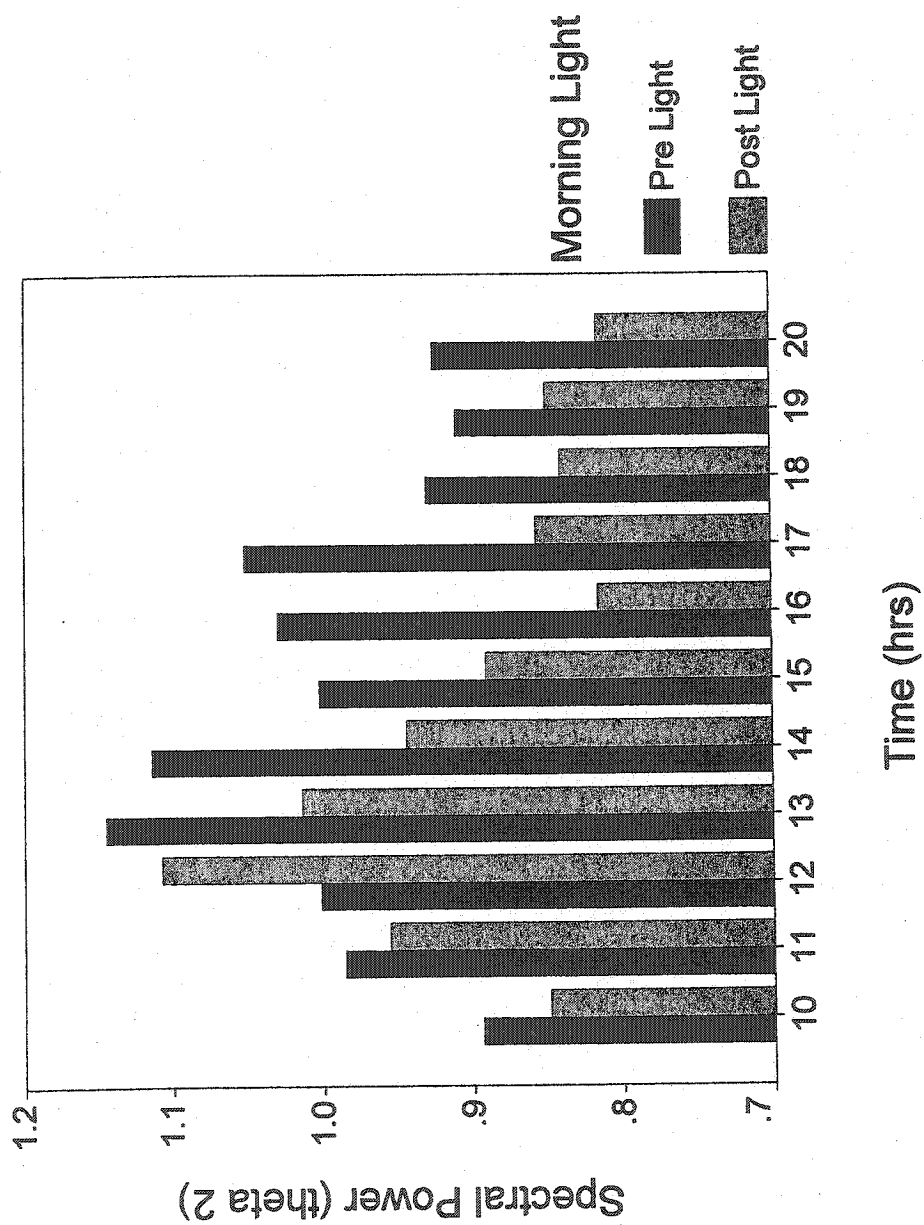


Figure K4. Mean values for theta 2 with eyes closed at C3

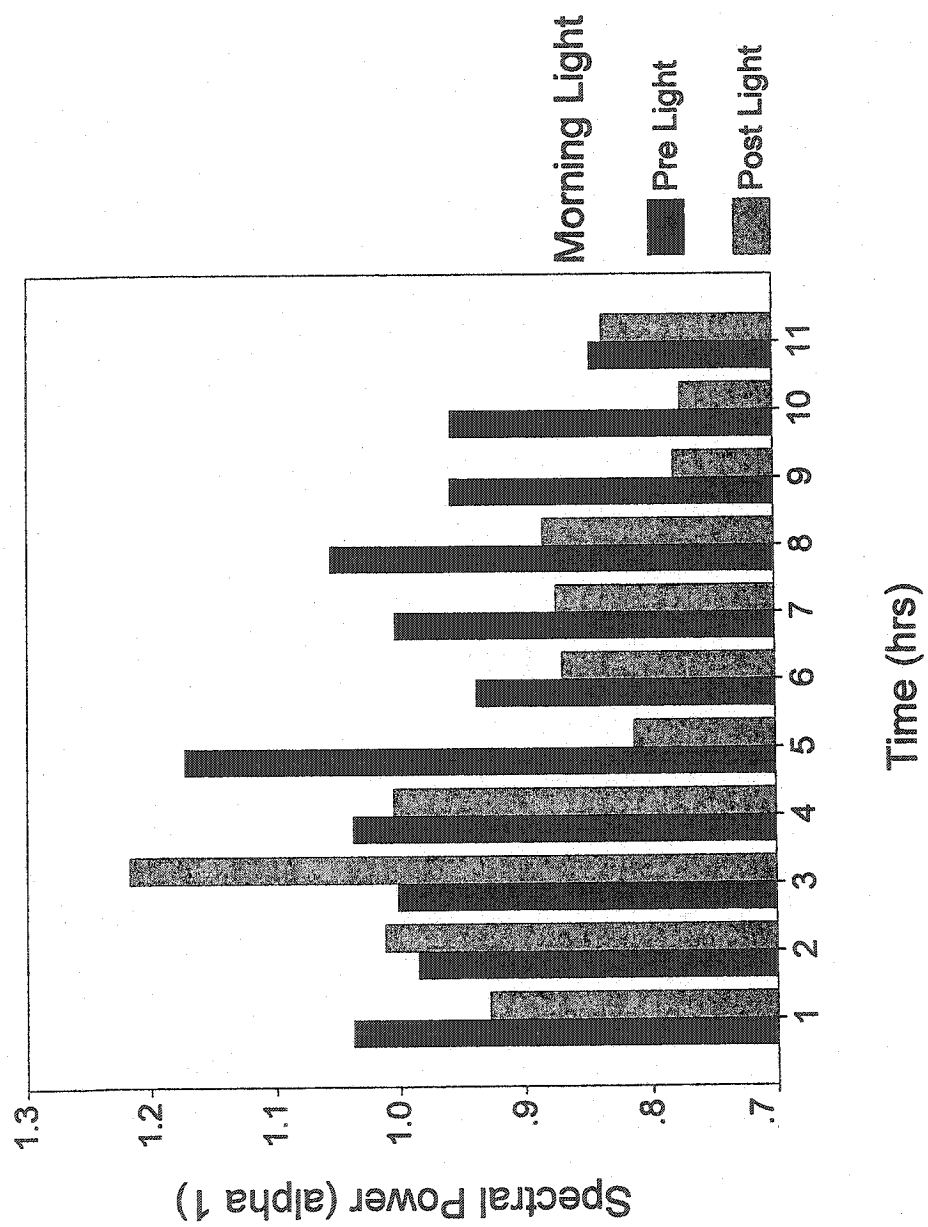


Figure K5. Mean values for alpha 1 with eyes closed at C3

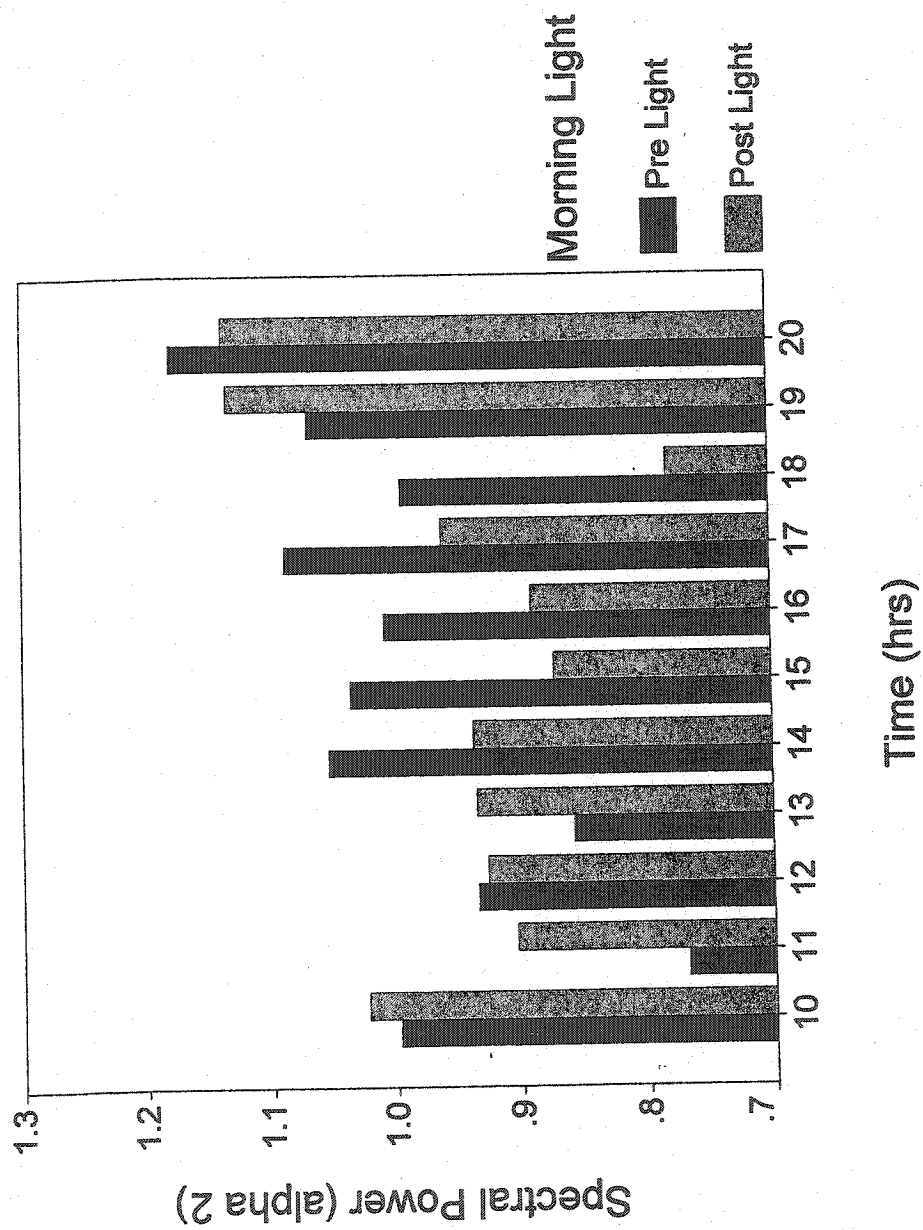


Figure K6. Mean values for alpha 2 with eyes closed at C3

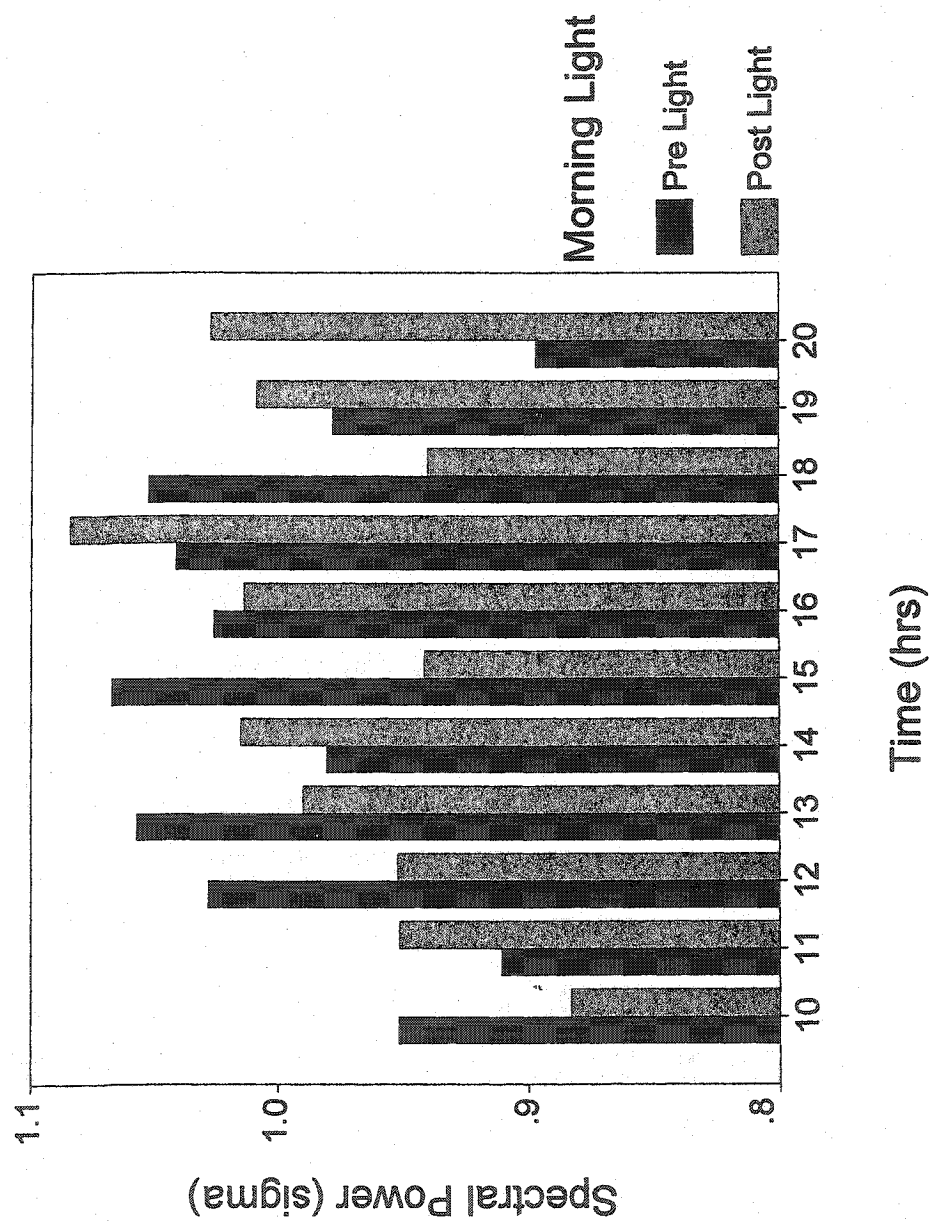


Figure K7. Mean values for sigma with eyes closed at C3

Appendix L

Figures of individual mean values for delta-1, delta-2, theta-1, theta-2, alpha-1, alpha-2, and sigma at C3, eyes open, for baseline and morning bright light (phase advance).

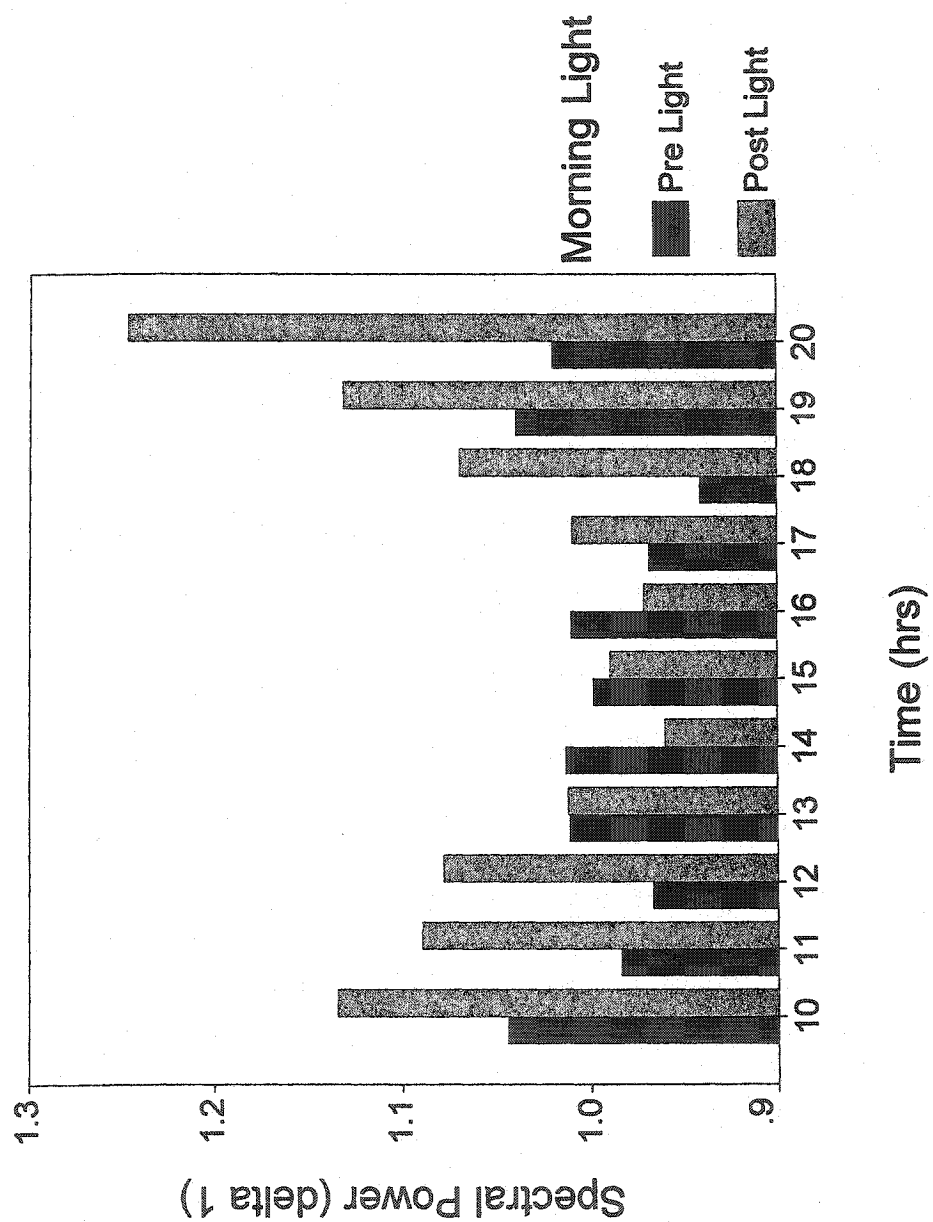


Figure L1. Mean values for delta 1 with eyes open at C3

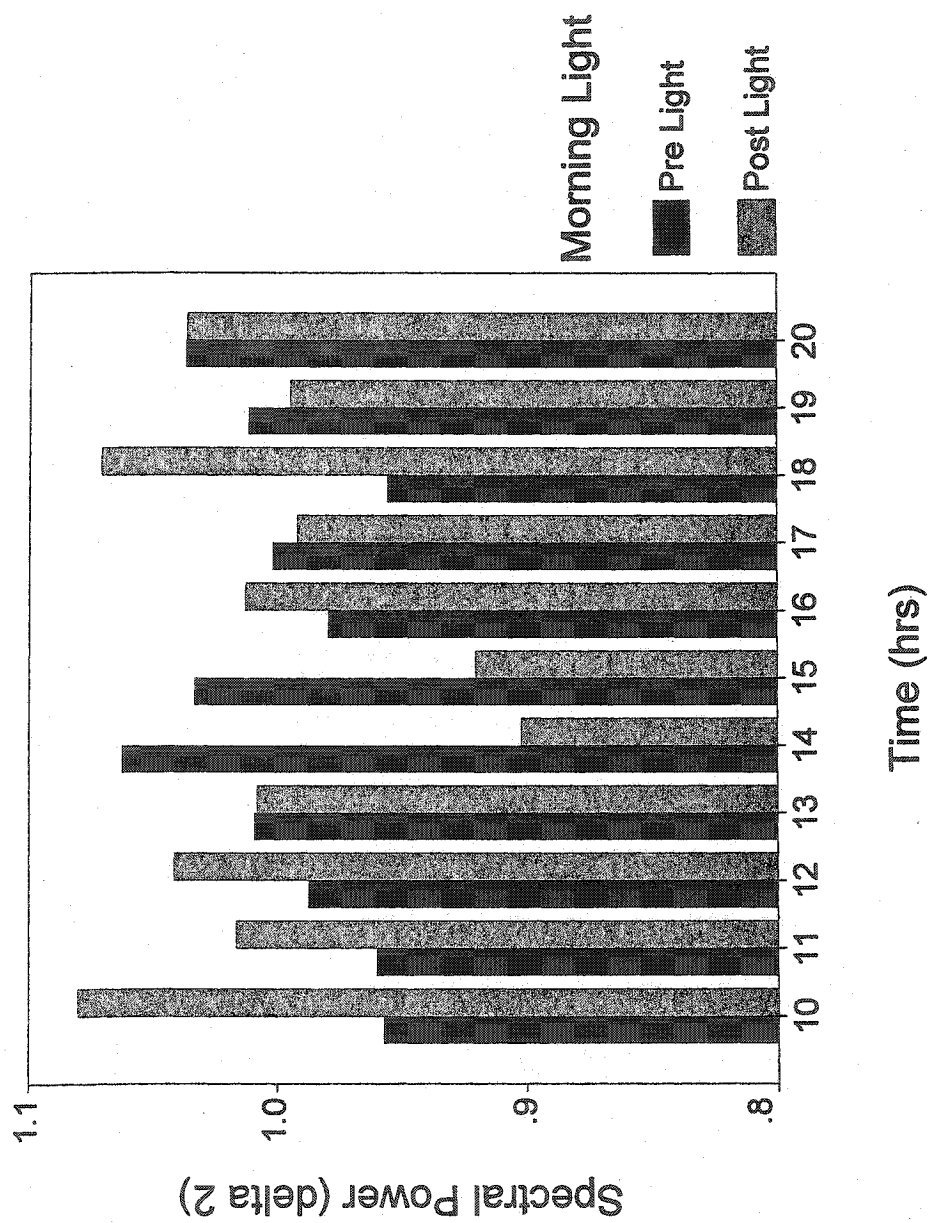


Figure L2. Mean values for delta 2 with eyes open at C3

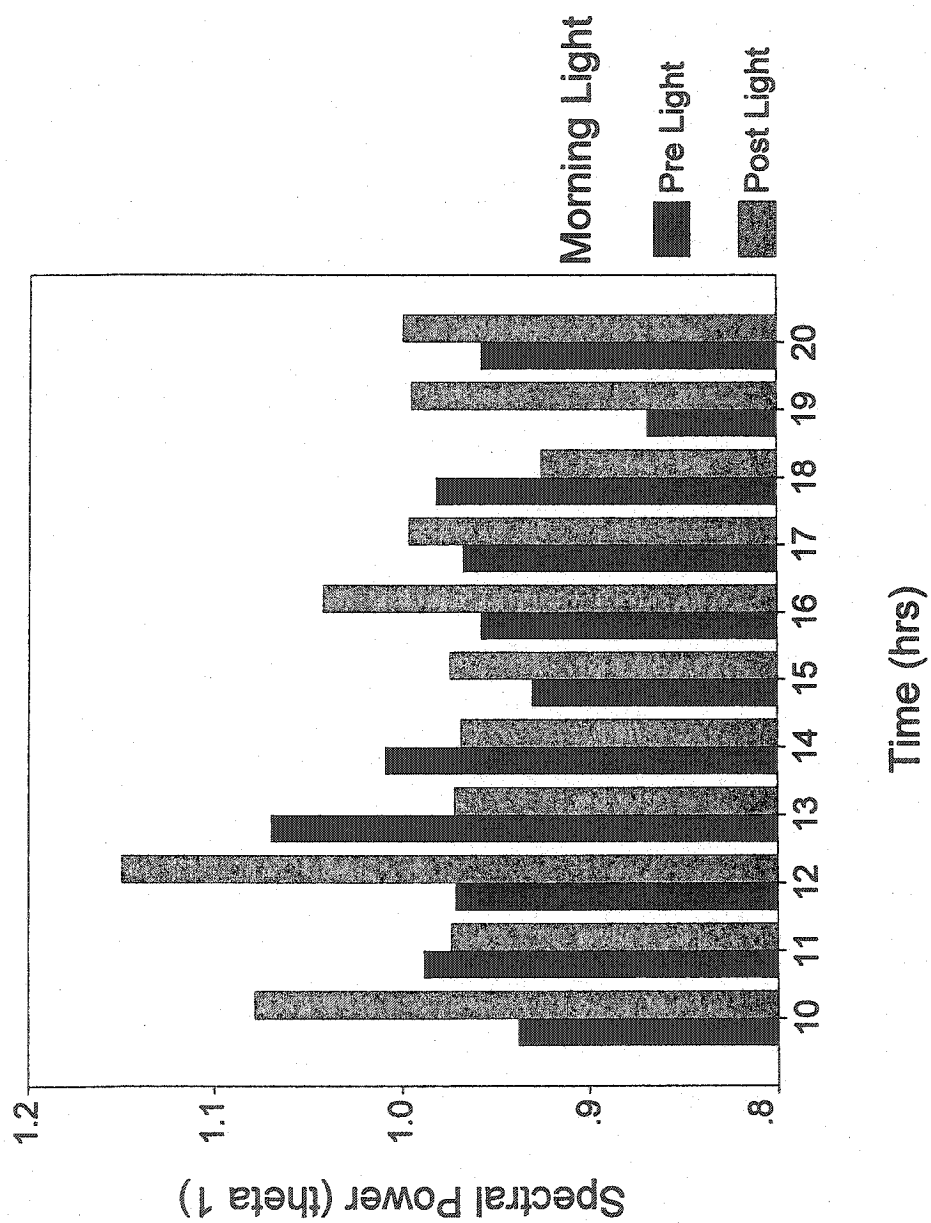


Figure L3. Mean values for theta 1 with eyes open at C3

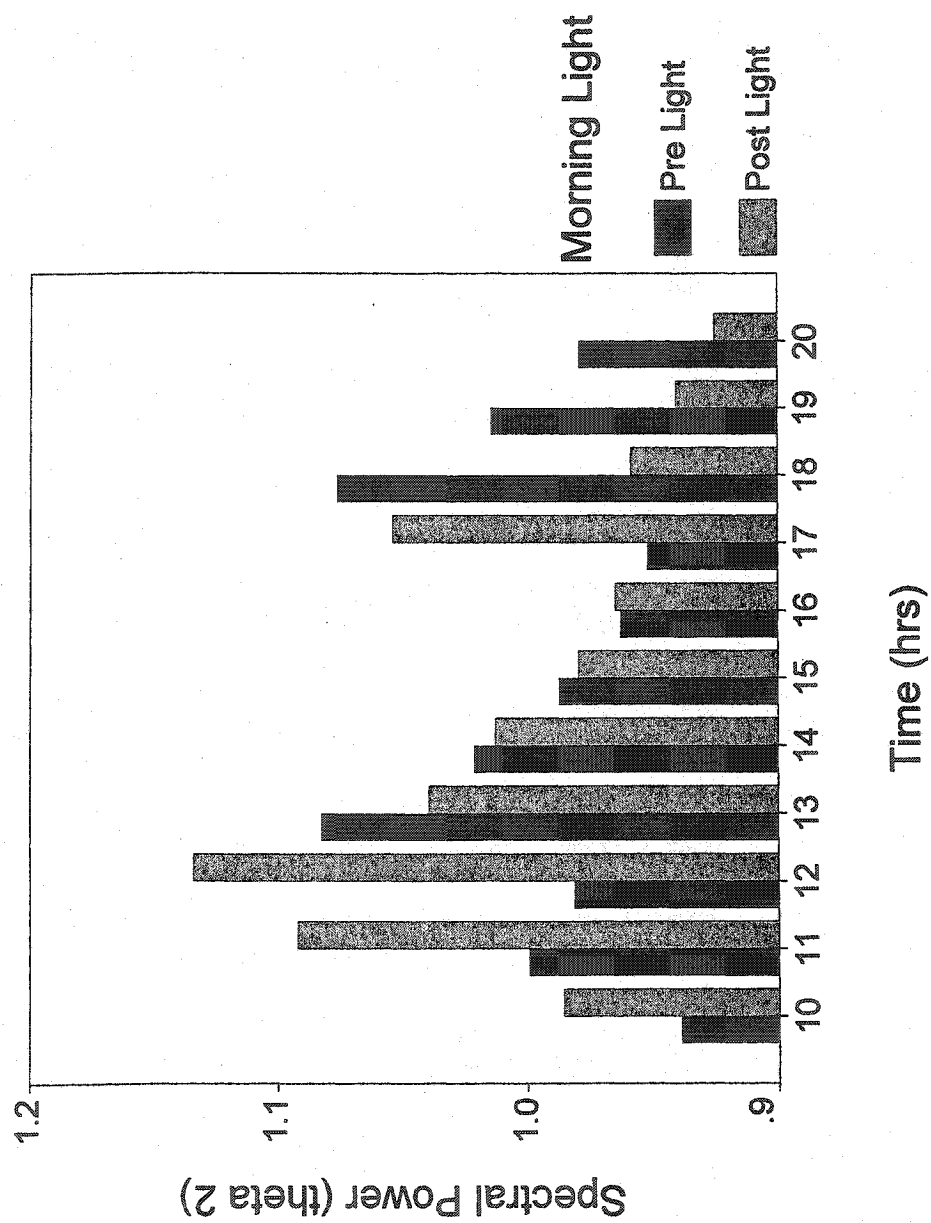


Figure L4. Mean values for theta 2 with eyes open at C3

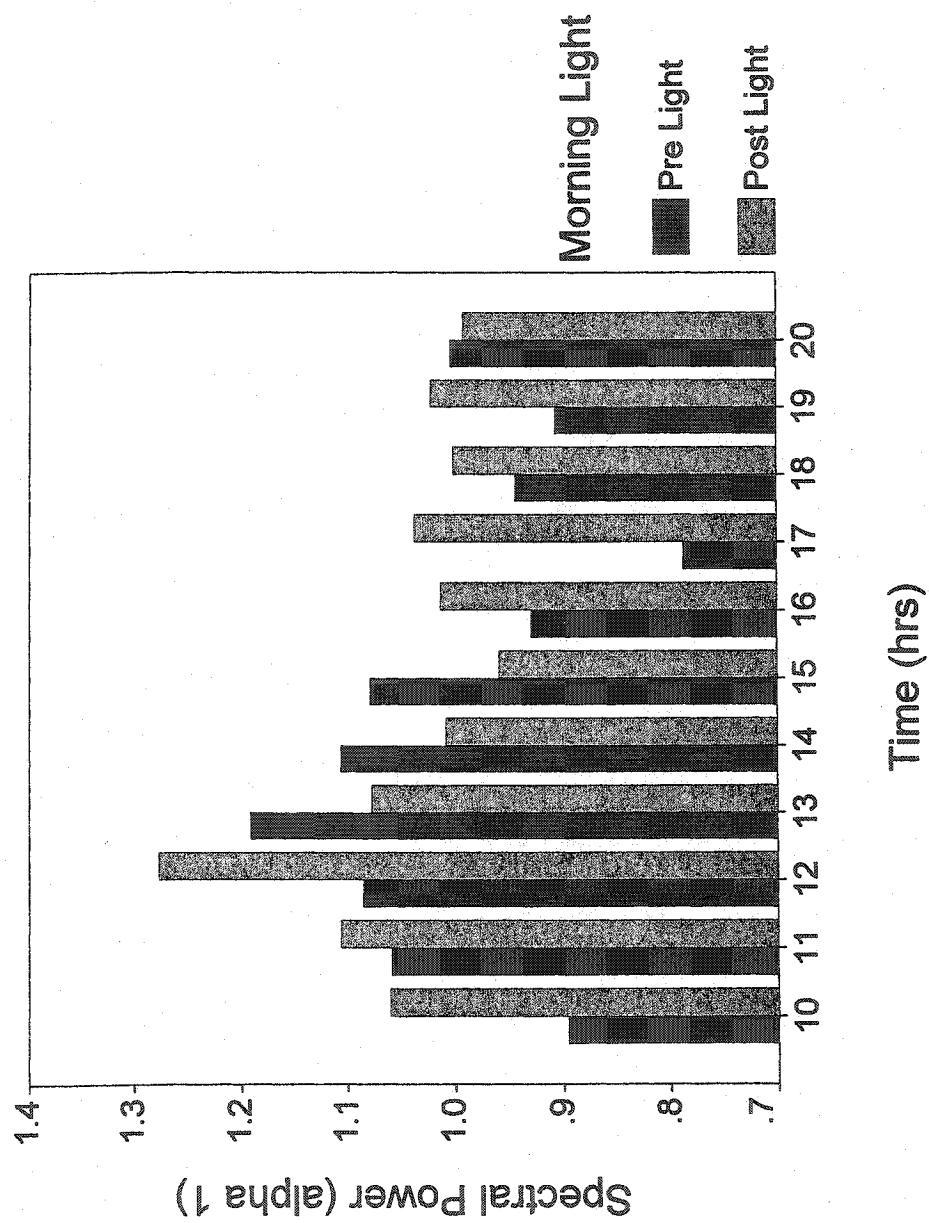


Figure L5. Mean values for alpha 1 with eyes open at C3

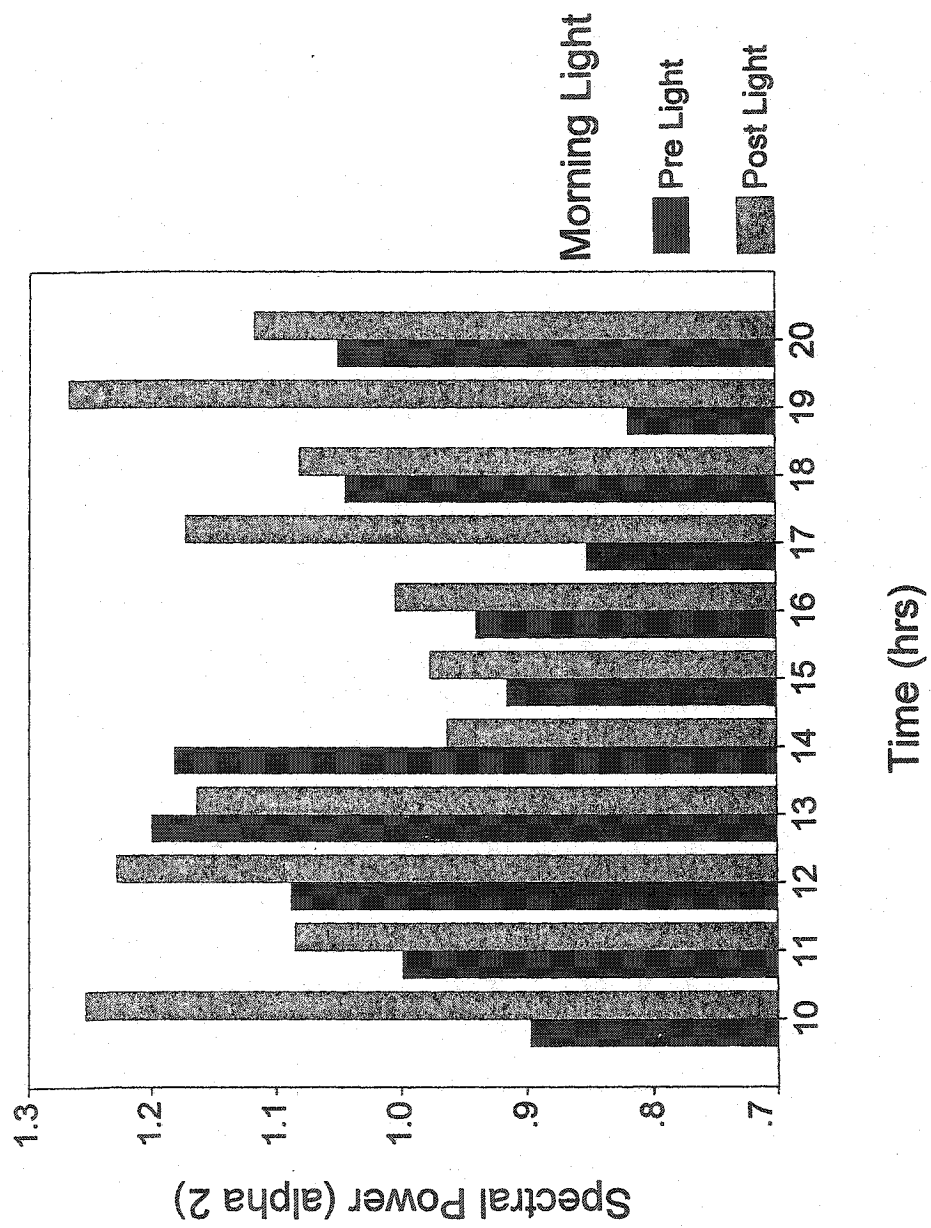


Figure L6. Mean values for alpha 2 with eyes open at C3

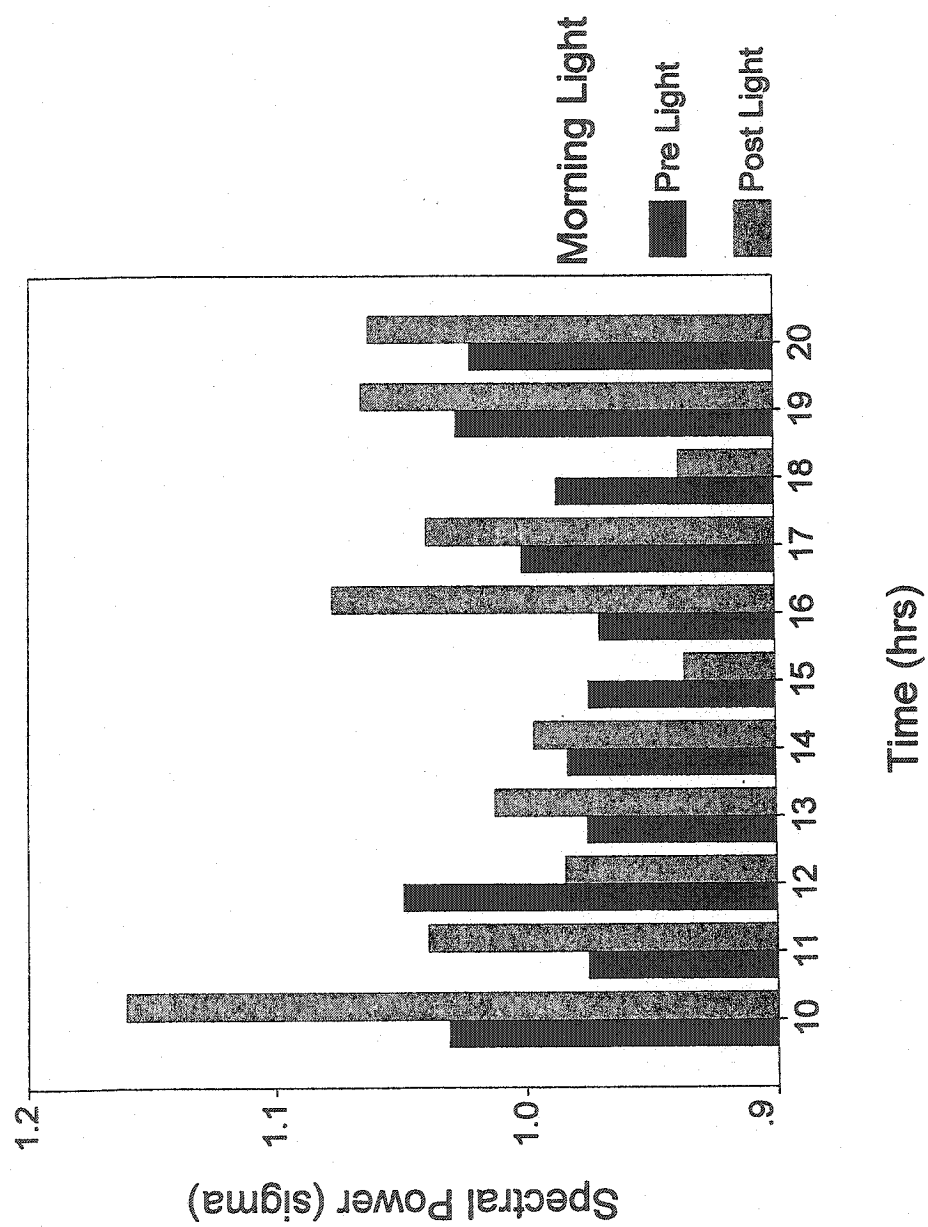


Figure L7. Mean values for sigma with eyes open at C3