Prevention of Physiologic Maladaptation to Night-Shift Work by Phototherapy

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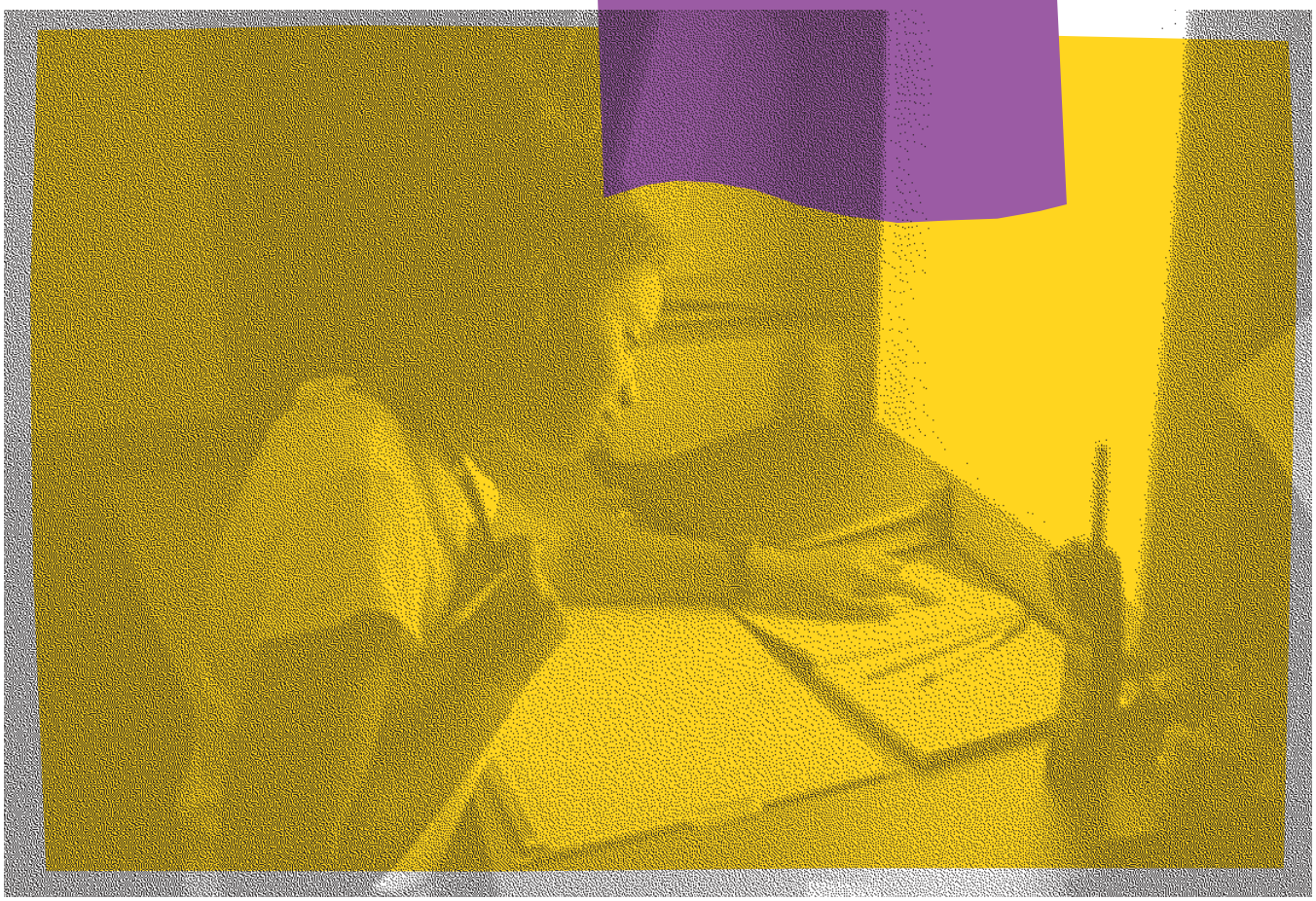
REPORT



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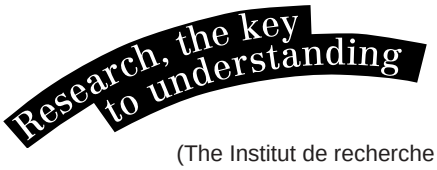

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ÉTUDES ET RECHERCHES

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REPORT

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GENERAL SUMMARY

It is estimated that one third of jobs held in Quebec are performed outside of conventional working hours. This is particularly predominant in sectors requiring (e.g. health care, public protection) or choosing (e.g. manufacturing) 24-hour operations. It is well established that shift work and night work in particular are associated with significant sleep deprivation, decreases in alertness and performance levels, and an increased risk of serious accidents in the workplace. Moreover, the problems of adaptation to irregular work hours become more severe with age, while modern society does not necessarily insulate the older worker from the harmful consequences of shift work. It is therefore of utmost importance to develop strategies to counter the harmful effects of night work, and to improve the health, safety, satisfaction and productivity of the worker population.

A popular misconception regarding work at irregular hours suggests that individuals working in intensely active environments could willfully surmount the natural tendency to sleep. Indeed, a number of studies have demonstrated that the opposite is true. The delicate harmonious relationship of the body's physiological and psychological functions with the environment is persistently disrupted in the night shift worker, even after a significant period on the inverted schedule. It is suggested that this is a direct result of the misalignment of the body's internal hour with the night worker's schedule. As an example, one may consider one hospital worker who works a night shift in Montreal, and another who works simultaneously in Moscow, Hong Kong, or Tokyo. Only the first worker will suffer the consequences of maladaptation to the work schedule, since the latter, despite working at the same geophysical hour, lives on a day-oriented schedule and is in harmony with both the dictates of the internal clock and societal norms.

A number of laboratory and field studies have demonstrated that the human circadian pacemaker is extremely sensitive to light. Thus, a variation in the temporal organization of light exposure throughout the day can shift the pacemaker to new internal 'time zones'. This study sought to exploit the dynamic nature of the human biological clock, and apply principles of circadian physiology to workers in the health care sectors in Quebec. The aim of this study is to accelerate the adaptation of the worker to the night schedule and concomitantly improve daytime sleep quality, and levels of alertness and performance on-shift. This line of investigation will provide information on the prevention long-term medical consequences associated with night shift work by first correcting the fundamental temporal misalignment that persists between the circadian pacemaker and the work schedule of the night shift worker. Specifically, this study aims to quantify the efficacy of a practical intervention administered in the workplace. The basis of this intervention is the judicious control of exposure to light and darkness.

To our knowledge, this study is among the first to integrate a field and laboratory approach to the sophisticated study of human circadian rhythms in full-time night shift workers. Laboratory investigations were planned to evaluate the phase of the circadian pacemaker both before and after 3 weeks of full-time night shift work. With this approach, we were able to obtain an unbiased estimate of the effectiveness of the intervention regimen provided in the workplace. Fifteen (15) nurses and auxiliaries (6 men, 9 women, aged 25 to 50 years) working full time night shifts in hospitals from the greater Montreal area were recruited for this study. The workers were assigned to one of two experimental conditions. Workers undergoing the

treatment condition were intermittently exposed the light of phototherapy lamps during the first 6 hours of each night shift. These subjects also wore goggles with tinted lenses during the morning commute home. Control group subjects remained in their habitual lighting environments in the workplace, and wore clear goggles during the morning commute. Both groups of subjects maintained regular sleep/wake times, and were indicated to remain in the dark for an 8-hour period on days following a night shift. Naps during work breaks were prohibited. Workers lived on a free schedule on days off.

All workers participating in this investigation began the study after a vacation period (lasting at least 2 weeks) during which they returned to a regular day-oriented schedule. They were then admitted to the laboratory for a 50-hour investigation during which their sleep was recorded via a standard method, and the oscillation of the biological clock was ascertained using a method known as the constant routine. Following the laboratory investigation, workers returned to their regular schedule of night shifts. During night shifts, research assistants on site with each worker, administered the phototherapy regimen and regularly sampled the workers' subjective vigilance. Daytime sleep episodes following night shifts were recorded. Following the 3-week period of night shifts, workers re-entered the laboratory for an evaluation of sleep quality and of the phase of the circadian pacemaker. With this approach, it was therefore possible to follow the progression of the circadian pacemaker, and to quantify its immediate effect on sleep quality and subjective vigilance. By this method, an unequivocal measure of the efficacy of the intervention regimen was determined.

Subjects receiving the intervention regimen displayed a significant adjustment of the circadian pacemaker to the night-oriented schedule. In these subjects, circadian rhythms of core body temperature and salivary melatonin concentration regained an appropriate alignment with the shifted sleep-wake schedule of the night shift worker. A certain amount of adaptation was also observed in control group subjects. However, this adaptation was incomplete and inconsistent across subjects within the group. It was also observed that phototherapy administered during a succession of night shifts produces a significant improvement in sleep quality.

The present study has demonstrated the efficacy and the applicability of a workplace intervention based on principles of circadian physiology. Specifically, this intervention judiciously controlled exposure to light and darkness throughout the day, and proved effective despite the subject workload. On the basis of these results, simple and practical recommendations have been devised and are suggested to improve the health of shift workers. Despite the limited length of the study, a reduction in the reporting of symptoms frequently associated with shift work was observed in the treatment group. These preliminary findings are subject to confirmation with more refined measures. Nevertheless, these results carry important ramifications for the prevention of the long-term consequences of shift work and underline the importance of further study of workers on irregular schedules.

INTRODUCTION

Work at irregular hours is not a phenomenon unique to the modern age. In the time of the Roman Empire, for example, conductors of horse-drawn transporters were prohibited from further congesting busy Roman city streets in the day (Scherrer, 1980), and were restricted to working after sundown. Thomas Edison's invention of the incandescent light at the turn of the 19th century directly led to the lengthening of the workday. The simple light bulb made 24-hour operations a viable possibility during the industrial revolution, and resulted in the prevalence of work at irregular hours (Scherrer, 1980). Throughout antiquity, work at unconventional hours has persisted, as it does today.

In Québec, it is estimated that one-third of those employed in permanent positions work during hours outside of conventional daytime hours (Statistics Canada Labour and Household Surveys Analysis, 1998). Particularly, a predominance of those who work full time at night do so in the sectors requiring (e.g. hospital environments, public protection) or choosing (e.g. manufacturing) 24-hour operations. These numbers are reflected in other industrialised nations (Bureau of Labour Statistics, 1997), while it is estimated that number of shift workers in developing nations is higher (Kogi, 1985). However, as recognised by the International Labour Organisation (Kogi, 1998), working a regular schedule of unusual hours is not without its consequences. The human circadian pacemaker, refined through the halls of evolution to adjust to its geophysical environment, does not naturally favour a life oriented towards periods of darkness. Therefore, a deliberate and substantial change in the orientation of sleep and wake times, as demonstrated in the night shift worker, promotes a desynchrony of the rest/activity cycle with the body's internal clock called the 'endogenous circadian pacemaker'. This endogenous circadian pacemaker drives most of the body's rhythms, including sleep structure, physiological function, hormone production and alertness. Living at abnormal circadian phases may be deleterious to one's sleep, vigilance, performance, mood, and overall health. Providentially, the endogenous circadian pacemaker is not static. It has indeed been demonstrated that the application of principles of circadian physiology may be useful in promoting the adjustment of the body to work on an irregular schedule (Czeisler et al., 1982), and to night work in particular (Eastman et al., 1995a).

Circadian physiology

One of the earliest recorded observations that the living organism contained an endogenous rhythm was an 18th century botanical commentary made by one Jean-Jacques d'Ourtous de Mairan (Moore-Ede, Sulzman, Fuller, 1982). Since that time, the ubiquitous presence of a principal endogenous clock has been observed across most living organisms (Miller et al., 1996; Weaver, 1998; Moore-Ede et al., 1982). An endogenous rhythm, in its strictest sense, is one that is generated by the circadian pacemaker in a persistent manner. It is well established that the overt rhythms of a variety of physiological and behavioral variables, including the endogenous component of core body temperature (Benedict, 1904; Mosso, 1887), neuroendocrine secretion (Weitzman et al., 1978), sleep organization and propensity (Dijk & Czeisler, 1995), subjective alertness and mood, cognitive performance, and short-term memory (Folkard & Åkerstedt, 1989; Dijk et al., 1992; Boivin et al., 1997; Johnson et al., 1992; Czeisler et al., 1994; Åkerstedt & Folkard, 1995) are comprised of an endogenous circadian component that continues to oscillate even in the absence of periodic environmental fluctuations.

Postmortem studies in humans have revealed the existence of neuroanatomic sites, analogous to those observed in other mammals, that are essential to the temporal organization of the circadian system and to its entrainment by light (Lydic et al., 1980; Sadun et al., 1986; Klein et al., 1991). In mammals, initial evidence based on lesions (Moore & Eichler, 1972; Stephan & Zucker, 1972), transplantation (Ralph et al., 1990; Sawaki et al., 1984; Lehman et al., 1987; Davis & Viswanathan, 1993), metabolic (Schwartz & Gainer, 1977), electrophysiologic (Inouye & Kawamura, 1979; Rusak & Groos, 1982; Green & Gillette, 1982) and genetic studies (Ralph et al., 1990; Ralph et al., 1988), revealed that the suprachiasmatic nucleus, a bilateral cluster of neurons in the anterior hypothalamus, is the essential component of the circadian timing system (Klein et al., 1991; Meijer & Rietveld, 1989). A second series of evidence, based on autoradiographic tracing methods (Hendrickson et al., 1972), transection (Rusak, 1977) and electrophysiologic studies (Groos & Meijer, 1985; Meijer et al., 1986), demonstrated that light exerts a direct biological effect on the endogenous circadian pacemaker via a distinct neuronal monosynaptic pathway, the retinohypothalamic tract (Klein et al., 1991; Moore & Eichler, 1972; Moore & Lenn, 1972; Rusak, 1979). This direct pathway explains the direct biological effect of light on circadian rhythms. Although an intrinsic oscillation may be detected in a number of peripheral tissues (Cermakian et al., 2000; Miller et al., 1996), the SCN functions to co-ordinate the expression of physiological rhythms.

The action of the endogenous circadian pacemaker within overall physiology is multidimensional. The neurons of the SCN, capable of an intrinsic oscillation, act in a series of feed-forward and feedback loops to generate an observable rhythmicity in the body's physiology. For example, they contribute to the rhythms of hormone production (Lewy et al., 1999; Wever, 1999; Van Cauter & Spiegel 1999) and thermoregulation (Colin et al., 1968; Weitzman et al., 1978). Among the many observable endogenous rhythms, those of core body temperature and melatonin secretion are amongst the most widely studied. The variation of the endogenous temperature rhythm is quasi-sinusoidal, with a progressive elevation of core body temperature in the morning, a maximum at the end of the day, and a progressive descent in the early night to reach its minimum about 1-2 hours before the habitual time of waking (Czeisler et al., 1992; Dawson et al., 1992). Melatonin, a reliable circadian marker, is almost undetectable in the day, but its secretion begins in the evening hours and peaks during the night. By mechanisms not yet completely understood, the SCN drives rhythms related to sleep and alertness (Dijk & Czeisler, 1994; Dijk & Czeisler, 1995; Czeisler et al., 1980; Daan et al., 1984). The quality of sleep is driven by what is accepted as a two-process model (Daan et al., 1984; Dijk & Czeisler, 1994; Dijk & Czeisler, 1995; Borbély, 1998; Borbély & Achermann, 1992). This paradigm describes sleep as the result of a complex interaction between two variables. The first component, *Process S* is defined as the homeostatic sleep variable that increases as the time awake grows longer, and decreases as the sleep episode is initiated. The second process of sleep, *process C*, is independent of the sleep and wake cycle, driven endogenously, and defines the best times for sleep initiation and termination. These processes differentially affect the various stages of sleep. Process S influences mainly the occurrence of slow wave sleep and slow wave activity in the brain. Process C influences mainly the occurrence of REM sleep (rapid eye movement sleep).

The quality of sleep and waking are significantly influenced by circadian phase (Czeisler et al., 1994; Johnson et al., 1992; Jewett et al., 1999; Dijk et al., 1992). For instance, sleep duration will be improved if sleep is initiated in the descending limb of the core body temperature cycle (Dijk et al., 1999; Dijk & Czeisler, 1995; Strogatz et al., 1986; Dijk &

Czeisler, 1994) as occurs in day-active individuals. In contrast, the sleep episode will be abbreviated if sleep is initiated on the ascending limb of the core body temperature cycle. This situation occurs frequently in night shift workers especially following the first night shift. Vigilance and performance are also dependent on a complex interaction of homeostatic and circadian processes (Åkerstedt & Folkard, 1997). Namely, these variables will progressively deteriorate with the length of the waking period. Their circadian variation is such that both variables will reach their peak and lowest scores very close to the crest and nadir of the core body temperature cycle (Åkerstedt & Folkard, 1997; Czeisler et al., 1994; Johnson et al., 1992; Jewett et al., 1999; Dijk et al., 1992).

Entrainment by light of the human circadian pacemaker

A second dimension to circadian physiology involves the period of the endogenous oscillation. Humans living in isolation will function on a day slightly longer than the geophysical day (about 24.2 h) (Moore-Ede et al., 1982; Czeisler et al., 1999). However, under normal circumstances, human subjects adjust to their environment by a mechanism called circadian entrainment. This phenomenon implies that synchronisers from the environment are forcing the organism to adjust its oscillations to those of its geophysical world. It was once held that social interaction and the sleep-wake cycle were the primary means of entrainment to a 24-hour day (Wever, 1970; Aschoff et al., 1971; Campbell et al., 1995b). It was subsequently shown, however, that humans were sensitive to the biological action of bright light that could suppress the expression of nocturnal melatonin secretion, a reliable circadian marker (Lewy et al., 1980). It was later demonstrated that the endogenous pacemaker of humans responded to light in a way that was akin to what was observed in other organisms (Czeisler et al., 1989; Boivin et al., 1996; Jewett et al., 1991; Lewy et al., 1980; ; Czeisler, 1995; Boivin et al., 1994).

In practical terms, it was found that a cycle of light applied just before the minimum of the core body temperature cycle (around 06:00) could shift the circadian oscillation towards a later time (phase delay). In comparison, light exposure just after the temperature minimum could shift the circadian oscillation towards an earlier time (phase advance). Light applied during the middle of the subjective day would exert minimal phase shifts (Jewett et al., 1997). A dose-response relationship between the intensity of the light stimulus and its resetting effect on the circadian pacemaker was also determined (Boivin et al., 1994; Boivin et al., 1996; Kronauer, 1990; Boivin & Czeisler, 1998; Horne & Östberg., 1976). While it was initially held that the circadian pacemaker would only respond to bright light ($\geq$ 2,500 lux), it was subsequently found that the biological pacemaker was keenly sensitive to light and that resetting could occur with simple indoor room light exposure (Boivin et al., 1996; Waterhouse et al., 1998; Zeitzer et al., 2000; Trinder et al., 1996; Bojkowski et al., 1987).

The capacity to reset the oscillation of the circadian pacemaker may not be limited to the biological activity of light. Numerous studies have suggested a resetting effect for behavioural stimuli (Mrosovsky & Salmon, 1987; Klerman et al., 1998), exercise (Van Cauter et al., 1993; Van Reeth & Turek, 1989; Eastman et al., 1995b), melatonin administration (Arendt & Deacon, 1997), and dark pulses (Ellis et al., 1982). However, the effect of these factors on resetting is still, in large part, being established and light exposure was not carefully controlled in several early studies. Yet, the influence of non-photic synchronisers cannot be dismissed. Despite this,

light remains the most powerful synchroniser of the endogenous circadian pacemaker (Boivin et al., 1996).

Shift work

The repercussions of shift work

Shift work entails a number of consequences for the worker. Perhaps the most evident effect of an irregular schedule is the toll exacerbated on worker's family and social interactions (Costa, 1996; Barton et al., 1998). A particular strain is exerted on the night worker who is a contributing member of a day-functional family.

Certain health consequences have been described for the shift worker, as well. For some time, an association has been made between shift work and an increased risk for cardiovascular pathology (Knutsson et al., 1999; Nakamura et al., 1997; Harrington, 1994). Further, it has been suggested that the worker is particularly prone to disease because of the effect of the rapid shift from a day to a night-oriented schedule on the endocrine system. Altered hormonal responses, in turn, may be responsible for the pathogenesis of non-insulin dependant diabetes, coronary heart diseases and gastrointestinal illnesses (Ribeiro et al., 1998; Romon & Bertin-Lebrette, 1998; Hampton et al., 1996; Bosworth & Dawkins, 1980). In the female shift worker, some associations between a full-time schedule of night work and breast cancer, reduced fertility, spontaneous abortion, and pre-term births have been detected (Nurminen, 1998; Hansen, 2001; Xu et al., 1994). Studies on the risks associated with shift work may often produce ambiguous results once the numerous confounding factors (e.g. Socio-economic class) are considered in the analysis models (McNamee et al., 1996; Pisarski et al., 1998; Nurminen, 1998). Factors such as marital status and the number of children in the household may have a profound effect on the quality of life of the shift worker. Women continue to bear most of the house and familial responsibilities, and their total daily hours of sleep following shifts may be severely diminished as a result (Kurumatani et al., 1994; Knutsson et al., 1997; Gadbois, 1980). Nevertheless, shift workers who work full-time at night report particularly high numbers of events for which they were hospitalised (Koller, 1983) and tend to require more medical consultations (Koller et al., 1978). Overall, a significant number of workers perceive that their health problems are related to their work (Koller et al., 1978), although the mechanisms that lead to the observed difficulties remain yet unclear.

Another important consequence associated to night shift work is the problem of obtaining sleep of recuperative value. Indeed, the night shift worker is often faced with the demands of home life during times that should be reserved for sleep. In addition, a number of shift workers may also have on-call duties, which will further reduce the opportunity for restorative sleep (Pilcher & Coplen, 2000). While the abbreviation of the day sleep episode may easily be accorded to daytime noise and social and familial responsibility, the role of the circadian pacemaker in the sleep process will also predict the abbreviation of diurnal sleep (Daan et al., 1984; Dijk & Czeisler, 1995; Dijk et al., 1990). Over a series of shifts between which daytime sleep is not restful, an acute and chronic sleep debt may occur (Ahsberg et al., 2000). In addition, it is not uncommon for shift workers to avoid sleep for the entire 24-hour period preceding the first night shift worked. The resultant decreases in vigilance and performance,

together with the misalignment of the endogenous pacemaker may place the night shift worker at particular risk for sharp drops in performance and vigilance levels during the shift (Hanecke et al., 1998; Spencer, 1987; Fathallah & Brogmus, 1999; Hamelin, 1987; Åkerstedt, 1988).

Promoting the adjustment of the worker to the schedule

Evidence has been presented that some shift workers may spontaneously adapt, or show various states of partial adaptation, following night work (Sack et al., 1992; Hennig et al., 1998). A few factors that may predict adaptability to night shift work have been suggested. Characteristics of the circadian phase such as the amplitude of the temperature cycle (Folkard et al., 1979) and chrononotype have been suggested as predictors of an ability to adapt to shift work. Morningness-eveningness is a chrononotype characteristic often used to describe a subject's natural patterns of sleep and wake times (Horne & Östberg, 1976). These natural patterns have, in turn, been related to slight differences in the endogenous phase of the circadian pacemaker. Morning-types will rise earlier, and have a circadian phase occurring slightly earlier as well. Evening types, contrarily, will have a slightly later phase of core body temperature, and will tend to rise later (Hall et al., 1997; Lack & Bailey, 1994). The suggestion has been made that evening types, with late bedtimes, will more easily adapt to a bedtime delayed into the morning hours and display larger phase-delaying shifts of the circadian pacemaker in response to synchronisers (Steele et al., 1997; Mitchell et al., 1997)

It has been observed that morning type subjects on a night-oriented schedule will have daytime sleep of poorer quality (Breithaupt et al., 1978). This concept is not easily applied to the general population since most persons do not fall in the extremes of chrononotype (Horne & Östberg, 1976). The number of shift workers who reveal shifting in the absence of an intervention are in the minority, where it has also been shown that even in subjects demonstrating a significant level of work satisfaction, circadian adjustment is incomplete (Weibel & Brandenberger, 1998; Roden et al., 1993). Moreover, subsequent studies have revealed that these adaptations may in some part be explained by patterns of light exposure (Dumont et al., 2001).

A plethora of countermeasures to the difficulties incurred in shift work have been suggested. A popular approach is one involving the strategic planning of naps (Åkerstedt, 1998; Dinges, 1995). Short sleep episodes, outside of the main sleep episode may have an immediate effect on improving alertness (Colquhoun, 1985) and performance (Åkerstedt et al., 1993; Bonnet & Arand, 1994), and often occur to compensate for an abbreviated main sleep episode. However, it has also been demonstrated that naps may negatively influence the quality of the subsequent sleep episode. Moreover, it has been suggested that the compensatory effect of napping on performance may be negligible (Rosa, 1993; Åkerstedt et al., 1998). Other suggested countermeasures to the difficulties encountered in adjusting to night shift work include alerting devices (Verwey & Zaidel, 1999), exogenous melatonin for the promotion of sleep or shifting of circadian phase, (Dawson & Armstrong, 1996; Deacon & Arendt, 1996; Samel et al., 1991; Dawson et al., 1995; Jorgensen & Witting, 1998), caffeine (Bonnet & Arand 1994; Walsh et al., 1995; Reyner & Horne, 1997; Rosenthal et al., 1991), and bright light for its alerting effects (Foret et al., 1998).

While these countermeasures may not be without merit, a circadian adaptation to night work seems beneficial to the night shift worker, especially when on a regular night schedule. From the standpoint of sleep quality, circadian adjustment may promote an increase in sleep propensity and length during the day. Indeed, it has been shown that greater sleep quality is associated with adapted circadian rhythms (Benhaberou-Brun et al., 1999). From the described model for the regulation of alertness (Åkerstedt & Folkard, 1997), circadian readaptation to an inverted schedule may also promote vigilance at an appropriate time (Czeisler et al., 1994). The capacity of light to rapidly reset the oscillation of the circadian pacemaker makes the possibility of entrainment of the night shift worker a viable one.

Much of our practical understanding of the effectiveness of bright light in circadian adaptation to a night-oriented schedule comes from laboratory simulations. Initial laboratory studies performed demonstrated that an appropriately timed bright light stimulus (5000-12000 lux) could induce a phase shift of the circadian pacemaker to the schedule of typical night worker (Czeisler et al., 1990; Eastman, 1992). The timing of sleep and darkness has also been found to be of importance in order to promote adaptive phase shifts to night oriented schedules with bright light (Mitchell et al., 1997). Moreover, a number of studies have stressed the importance of protection from morning light on the commute home (Eastman et al., 1994; Mitchell et al., 1997) since bright light exposure at that time could enforce the maintenance of a day-oriented circadian adaptation. Field studies on the night shift worker population have been of fundamental importance in reinforcing the efficacy of bright light in the workplace and the importance of the pattern of light exposure for adaptation to the work schedule (Bjørvatn et al., 1999; Hakola et al., 1996; Dumont et al., 2001).

STUDY AIMS

The object of this study is to determine the efficacy of an intervention regimen aimed at shift workers in the field. Of primary importance is that the intervention is based on principles seeking circadian adaptation to the inverted sleep-wake schedule. The treatment proposed in this study was designed to strategically influence the pattern of light exposure throughout the day. Appropriately timed bright light, the tempering of morning light with tinted goggles and regular sleep/darkness times all work in concert to create an overall pattern of light exposure that may be beneficial to the readaptation process of the night shift worker.

Full-time night shift workers from hospitals in the greater Montreal area were approached for their participation in this study. The efficacy of the intervention regimen was evaluated in the laboratory via the constant routine procedure (a specialized technique design to unmask endogenous circadian oscillation), and in the field with ambulatory alertness and sleep measures.

Specifically, the present study aimed to test the following hypotheses:

1. an intervention consisting of 6 hours of intermittent bright light (~ 2000-7000 lux) exposure in the workplace, the wearing of shaded goggles during the morning commute home, and the maintenance of a regular schedule of sleep/darkness can accelerate the adaptation of the human circadian pacemaker to night work. This adaptation will manifest itself as a harmonious phase relationship between endogenous circadian rhythms of core body temperature and salivary melatonin and the shifted sleep-wake cycle. Thus, in subjects receiving the treatment, the phase alignment between the endogenous circadian pacemaker and the sleep-wake cycle will resemble that observed in day-oriented subjects and will be comparable to the initial condition observed. In the absence of this intervention, a temporal misalignment between the circadian pacemaker and the inverted sleep-wake schedule will persist.

2. the judicious exposure to light can improve alertness levels and the quality of daytime sleep as reported by night workers. These results, as obtained from constant routine procedures performed in the laboratory, may be interpreted as reflective of an appropriate synchronization of the circadian pacemaker and the inverted sleep/wake schedule.

3. this intervention regimen can reduce the occurrence of somatic and psychological symptoms frequently associated with night work, although the limited period of observation in the present study may preclude the quantification of this effect.

METHODS

Inclusion and exclusion criteria

Six male and nine female full-time night shift workers aged between 25 and 50 years (mean ± S.D.: men: 40.6±7.6 years; women: 42.5±8.2 years) were recruited from hospitals in the metropolitan Montreal area to participate in this study spanning over 3 years. Participants all worked a full-time schedule of night shift work, defined as minimum of 8 night shifts per 15 days. The number of shifts and nights off, though comparable between all subjects, varied in its temporal distribution amongst the sponsoring hospitals (**Table 1**).

The recruitment procedure involved a full physical and psychological evaluation with each candidate, following an initial contact at their place of work. Subjects revealing the presence of serious sleep, physical or psychological pathology were excluded. One subject, S08, had a history of neurological tumors in the frontal region, but was sequelae-free as of 12 years prior to the study start**,** and was admitted to the study. Of the 9 women participating in the study, 2 were menopausal. The remaining 7 women had regular menstrual cycles. The menstrual phase at which the study was initiated was not expressly controlled, however menstrual phase at the start of the study was comparable between groups (control group: 2 follicular, 3 luteal.; treatment group: 2 follicular, 2 luteal). Subject chronotype was also ascertained in each subject using a translated version of the Morningness-Eveningness questionnaire described by Horne and Östberg (1976). The distribution of years of full-time night work, chronotype and season of study was comparable between the control and treatment groups. Due to the limited sample size, it was not possible to perform reliable multifactorial analyses on the impact of each of these factors on circadian adaptation to night shift work.

All candidates were asked to limit their intake of caffeine (≤ 5 cups/day) and cigarettes (≤ 10/day) during the investigation. These indications were generally observed and average (± S.D.) coffee (control: 1.7 $\pm$ 1.0 ; treatment: 1.4 $\pm$ 1.1) and cigarette consumption (control: 9.3 $\pm$ 7.7 ; treatment: 8.3 $\pm$ 5.2) was comparable between groups. For four workers (2 control, 2 treatment) limiting nicotine intake proved impossible, and these smoked ≤ 20 cigarettes/ day. Alcohol consumption was also prohibited on work days and minimal on days off (mean consumption (± S.D.): 2.7 ± 3.9 drinks per week). None of the participating workers had a history of chronic use of neuroleptics or sleep-agents. The use of these substances, as well that of herbal or natural supplements, was prohibited throughout the study period.

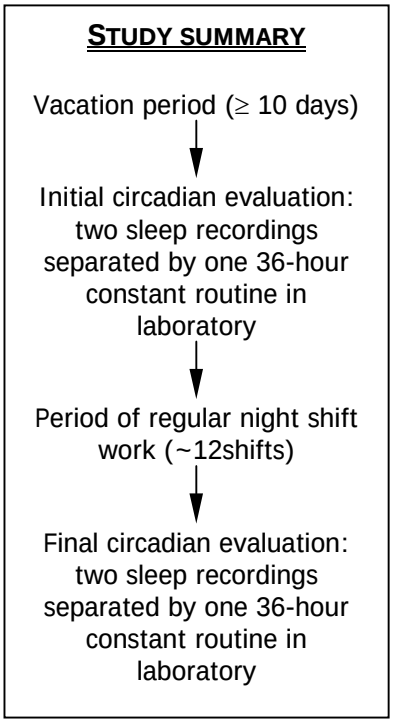
Informed consent was obtained prior to the experiment start in accordance with the procedures of the Douglas Hospital Research Ethics board, and the hospital sponsoring the participation of the subject, where applicable.

The 15 subjects participating in this study were observed under one of two conditions, for a total of 19 different experiments. This study was originally planned with a paired design, where each worker would participate in both a control and treatment phase of the study. However, a major reorganization of the Québec healthcare system limited our capacity to recruit subjects, and the study was revised to an unpaired design. Subjects s02, s03, s06, and s07 each

participated in both phases of the study separated by a mean (± S.D.) 0.7 ± 0.2 year period between both phases of study.

Study design

In order to gain a complete assessment of circadian adaptation to full time night shift work, this study was divided into 3 segments (**Figures 1A, 1B**). All participants were first observed in the laboratory following at least 10 days of vacation where they returned to a day-oriented schedule. Subjects were given the instruction to restrict their sleep patterns to a single nocturnal sleep episode during the vacation period. Naps were discouraged. Subjects recorded sleep and wake times, food intake, and physical activity in appropriate logs. Bed and wake times were confirmed by wrist actigraphy (Actiwatch-64, or Actiwatch-L, Mini-Mitter, Bend, OR, U.S.A.) and daily telephone calls to the laboratory the week prior to admission to the laboratory.



Baseline measurement

Following the vacation period, subjects were admitted to the temporal isolation suites of the Center for Study and Treatment of Circadian Rhythms for a 36-hour circadian evaluation preceded and followed by sleep episodes. The laboratory, equipped to with ceiling-mounted banks of cool-white fluorescent fixtures (4100 ^{0}K, TL80 F32T8/TL841 from, Philips, U.S.A., or Octron 800, F032/841 from Sylvania, U.S.A.) covered with lenses emitting less than 1% radiant energy up to 400 nanometers (K-S-H Uvalite Plus, K-S-H Inc., U.S.A.) is designed to permit the study of circadian rhythms under controlled lighting conditions.

Following a short period for acclimatization to their new environment, subjects slept in complete darkness (~0.03 lux). The timing of the initial sleep episode was calculated based on the mean sleep and wake times in sleep-wake logs and actigraphy data, scaled to an 8-hour duration from the middle of the mean sleep time. Upon awakening, subjects underwent an evaluation of the oscillation of the endogenous circadian pacemaker via the constant routine procedure (described below). Following the circadian evaluation, subjects were permitted to sleep *ad libitum.*

Sleep

In order to screen for intrinsic sleep pathologies in night shift workers, the initial sleep episode of each night shift worker was recorded via a 9-channel polysomnographic montage including the EEG (electroencephalogram) , EMG (electromyogram) , LOC (left outer canthus), ROC (right outer canthus), EKG (electrocardiogram) with screening for periodic leg movements in sleep and sleep apnea. EEG was derived from C3-A2, C4-A1, O1-A2, and O2-A1. EMG for

detection of periodic leg movements were derived from right and left tibialis muscles, while respiration was monitored via a bucco-nasal thermistance. All subsequent sleep episodes were recorded using a standard 5-channel polysomnographic montage (central end occipital EEG, EMG, LOC, ROC). Polysomnographic recordings were performed via either a differential amplifier with modifiable filter (Grass Instrument Co., Quincy, MA, U.S.A.) or a combined differential and referential amplifier with fixed filters (Lamont Medical Inc., Madison, WI, U.S.A.). Polysomnographic signals were digitized at a sampling rate of 128 Hz or 250 Hz and stored to workstations equipped with Eclipse (version 3.0, Stellate Systems, Montreal, Qc.) or Harmonie (version 4.0 Stellate Systems, Montreal, Qc) sleep recording interface software. Sleep stages were scored using 20-second epochs according to standard criteria (Rechtschaffen & Kales, 1968).

Intervention regimen

Subsequent to the laboratory observation, subjects returned to their regular schedule of full time night shift work. In this ambulatory segment of the study, subjects were studied under one of two experimental conditions.

Participants observed under the 'treatment' condition were exposed to a bright light (~2000-7000 lux) stimulus emitted from portable lighting units (Sunbox, Sunsquare, and SunRayII, Sunbox Company, Gaithersburg, MD, U.S.A) in the first 6 hours of each 8-hour night shift. The timing of this stimulus was based on a mathematical model for the effect of light on the circadian pacemaker (Kronauer & Czeisler, 1993).

A research assistant, on site with the subject, implemented and monitored the progression of the light therapy. Portable light units were arranged in the participant's workspace such that the intensity of light in the workspace reached the desired levels. Subjects, in turn, were given the instruction to remain under the lights as much as possible, and to look into the lights as much as possible. Research assistants logged the time spent by each subject under the lights, as well as the times spent in different lighting environments in the work area. At all times during the study, subjects wore a combined light and activity monitor (Actiwatch-L, Mini-Mitter, Bend, OR, U.S.A.). Measures from this device served to confirm the timing of light exposure. A research assistant, on site with the subject, monitored the light intensity of the work environment throughout the course of the night. Combined light and activity measures taken at the level of the wrist served to confirm recorded light values. In addition, light measures during shifts were taken with a research photometer (Kleton K7020, Projean Instruments, Montreal, Qc, or IL1400A, International Light, MA, U.S.A.). In the final hours of the night shift, the portable lights were shut off, and the subjects remained in their habitual light environments.

Subjects were instructed to avoid naps during their shifts, and on days following night shifts when they slept at home. Similarly, they were given the instruction to maintain regular sleep habits in the days following night shifts, where they were to remain in absolute darkness and attempt to sleep for an 8 hour-period beginning 2 hours after the end of the shift. Research assistants aided in the preparation of the sleeping quarters before the start of the experiment, and ensured that light levels were sufficiently dim. Windows were covered over with aluminum foil such that no light could enter the room. Subjects recorded their sleep and wake times in logs.

These values were confirmed by daily telephone calls to the laboratory and by wrist actigraphy. On nights off, subjects were permitted to sleep freely, although naps were discouraged. Sleep and wake times were recorded.

Due to the importance attributed to light exposure in the morning commute, each subject in the treatment group was given a pair of goggles with tinted lenses (Astrospec 3000, and Flashback with SCT-gray lens tint, 15% visual light transmission, Uvex, Smithfield RI, U.S.A) and was instructed to wear them when outdoors in the two hour period between the end of the night shift and the beginning of the sleep episode.

The course of study was identical for 'control' group subjects with the exceptions that they worked in their habitual lighting environments during the night shifts and were given clear goggles to wear during the commute home. Light levels in their sleeping quarters were not adjusted for the study.

For all subjects, the period of ambulatory study was scheduled to last a minimum of 12 shifts, spread out according to the subject's normal work pattern with days off interspersed.

Diurnal sleep

The quality of daytime sleep following night shifts was quantified using two methods of sleep recording either by the Nightcap (Respironics, Marietta, GA, U.S.A.) device or by a portable polysomnograph. For the majority of day sleep episodes, subjects wore the Nightcap which is a portable sleep monitoring device consisting of an eye movement sensor worn over the eyelid, and a body movement sensor worn at the crown of the head. The device recorded the nature of the sleep episode based on eye and body movements and provided scored information on the quality of the sleep episode including the duration of sleep, sleep efficiency and the number of REM (Rapid Eye Movement) periods (Nightcap version 1.1 beta software, Respironics, Marietta, GA, U.S.A.). Results derived from the Nightcap were automatically scored according to a predefined algorithm. Each minute of the sleep episode was designated as a body movement or an eye movement minute or neither. Sleep states (awake, NREM, or REM) were assigned to each minute of the sleep period according to the concentration of body movement versus eye movement minutes. At least 3 times per ambulatory period, daytime sleep episodes in subject homes were recorded via a portable polysomnographic montage technique as installed by a qualified technician. The sleep episode was digitized to an ambulatory polysomnograph (HandyStore, Glonner Electronic GMBH, Germany) at a rate of 250 Hz. Information was then transferred, reformatted to a bipolar method and scored by a standardized technique (Rechtschaffen & Kales, 1968).

Vigilance

Subjective vigilance was ascertained in the workplace using 100 mm visual analogue scales, identical to those administered in the laboratory. As before, subjects were asked to indicate their level of alertness on a scale. The sampling of subjective vigilance was chiefly dependant on the availability of the subject to perform the self-assessments. Tests were planned for 3 times per hour in the workplace. Attempts were made to ensure that at least one assessment per hour was performed.

Medical symptoms

At the end of each night shift, subjects completed 20-item and 6-item questionnaires describing the intensity and subjective duration of medical symptoms frequently associated with shift work (Appendix). In one questionnaire, they were asked to rate the degree to which they experienced any of a number of symptoms commonly associated with night shift work. They also completed a symptom questionnaire on which they ranked the relative amount of time during the shift that they experienced symptoms of fatigue in the workplace, from "no symptoms during shift" to "symptoms throughout shift".

Post Intervention evaluation

The morning following the final night shift during which subjects were observed, shift workers were admitted to the laboratory, where they slept for 8 hours according to the daytime sleep schedule they were instructed to keep during the ambulatory period. Upon awakening, subjects underwent a second 36-hour constant routine for the evaluation of the oscillation of the circadian pacemaker. Upon completion of the constant routine, subjects were again permitted to sleep *ad libitum*.

Constant Routine

The effects of normal activity, food ingestion and exogenous influences easily obscure the manifestations of the endogenous clock in core body temperature and hormone production. The constant routine procedure, initially described by Mills *et al* (1978) and modified by Czeisler et al. (1986), is one designed to unmask the endogenous oscillation of the circadian pacemaker. The subject undergoes a regimen of extended wakefulness in a semi-recumbent position, in a dimly lit environment (<7 lux). Caloric requirements, determined by a qualified nutritionist and reduced by 30% for limited activity, are met via small hourly snacks. Throughout the procedure, the subject is in contact with the laboratory staff, trained to avoid the revelation of time cues, who assist the subject in staying awake.

Throughout the constant routine procedures, physiological and behavioral measures are collected. Core body temperature data was sampled once per minute and stored via a portable device (Mini-Logger, Mini-Mitter, Bend OR, U.S.A.) connected to a temperature sensor (Steri-probe, Cincinnati Sub-Zero Products, Inc., Cincinnati, OH, USA).

Saliva samples, destined for the assay of melatonin concentration, were collected at 60-minute intervals. In order to stimulate saliva production, subjects chewed slips of paraffin wax**,** or smelled or sipped small amounts (<0.5 ml) of lemon juice. Samples were then frozen and stored at -20^0C until the time of assay.

Salivary melatonin concentration was determined *in duplicata* via direct radioimmunoassay (Buhlmann Direct Saliva Melatonin radioimmunoassay, Alpco Diagnostics, N.H., U.S.A.). The intra- and interassay coefficients of variation were 4.8% and 8.3% for mean nighttime concentrations of 124.4 pg/ml and 25.4 pg/ml, respectively, with a sensitivity of 0.2 pg/ml. Cross reactivity of the kit was less than 0.001% for serotonin and 0.027% for N-acetyl serotonin.

Subjective vigilance during constant routines was determined with 100 mm, bipolar, linear, non-numeric visual analog scales (VAS) administered at 20-minute intervals (Dijk et al., 1992). Subjects were instructed to rate their current state of alertness on the 10-cm line, with 0 being the most sleepy and 10 being the most alert they've ever felt.

Statistical analysis

Circadian markers

The circadian phase of core body temperature is defined as the time of the fitted minimum of the endogenous oscillation of core body temperature. The calculation of this phase, determined with data from each constant routine, is done with a dual-harmonic regression model (Brown & Czeisler, 1992), without the serial correlated noise parameter. In order to compensate for the masking effects of the preceding sleep episode and the increased activity at the onset of the constant routine, the first five hours of temperature data sets were not included in the analyses.

The phase of the secretion of melatonin is expressed here as the midpoint between the time at which the plasma melatonin concentration rose past the 24-hour average and the time at which the concentration fell below the 24 hour average (Zeitzer et al., 1999). The expression of the melatonin rhythm was also described as the time of the upward and downward crossing of the 24-hour average concentration. These times represent the times when the concentration of salivary melatonin rose past the 24-hour average in the ascending limb of the secretion and when it dropped below the 24-hour average concentration on the descending limb of the expression. The time elapsed between the upward and downward crossing of the 24-hour average of melatonin concentration is also calculated.

Phase shifts, calculated in decimal hours for both of these physiological markers, are the difference between the time of occurrence of the phase in the two constant routines, thus: $phase_{initial} - phase_{final}$. Consequently, and by convention, phase advances (final phase occurring earlier in the day) result in positive value phase shifts, and phase delays (final phase occurring later in the day) result in negative value phase shifts.

The adjustment of the endogenous rhythms of core body temperature and melatonin secretion to a daytime or night-time schedule was also assessed from a phase angle calculated as the difference between the time of awakening and the time of the fitted minimum, thus: $Time_{awakening} - Time_{phase}$.

Data were statistically analysed using a group by repeated measures of time (laboratory visit) model for Analysis of Variance (ANOVA). Data was first verified as conform to a normal distribution with the Kolmogorov-Smirnov statistic. Significant interactions detected in the ANOVA were investigated with simple main effects analyses.

Vigilance

In order to perform comparisons, test times were aligned on hours from awakening (the start of the constant routine), and scores were averaged per subject over 2 hour bins, then across subjects. Alertness test times from the second constant routine were aligned to each subject's target times of awakening during day sleep episodes of the ambulatory observation period. Comparisons of mean levels of alertness between groups were quantified for each constant routine using a group x bin model for ANOVA. Due to missing data in some subjects at the start and end of the constant routine, subjective alertness data were analysed for the 3-35th hours of awakening, or for the 3-31st hours of awakening for the initial and final constant routines, respectively. Post–hoc analyses were performed with the Tukey's HSD. One subject in the treatment group, s09, became unable to complete tests of subjective alertness during the constant routine. This subject's data was excluded from these analyses. Using this model, constant routine data was compared between groups for each constant routine as well as between the initial and final conditions for each group.

In 5 of 38 cases, subjects had difficulty in completing the constant routine procedure, and it was cut short from the planned 36-hour length. However, in all of these cases, sufficient data was accumulated for the accurate determination of circadian phase from the physiological markers of core body temperature and salivary melatonin concentration.

Sleep in the laboratory

In order to compare the objective quality of sleep between groups, the total number of epochs scored to each sleep stage per subject was first calculated into 1-hour bins. The number of epochs scored for each sleep stage per hour was then averaged across subject groups. Thus, minutes of stages 1, 2, 3, 4, and REM sleep were reported hourly for each group. Sleep efficiency, calculated as the minutes of sleep per hour of sleep opportunity (standardised to 8 hours), is expressed as a percentage. Only sleep episodes preceding constant routines, with a standardised length of eight hours, were analysed. Between group differences were analysed using a group x time model for ANOVA on the 8 hours of sleep. Significant point differences were further analysed using the Tukey's HSD. Results from treatment group subject s07 were unusable, and were excluded from these analyses.

Ambulatory measures

Sleep schedules during the vacation and ambulatory periods were analyzed from logs kept by the subjects and confirmed with activity data. Reported times were converted to decimal hours and compared with two-tailed t-tests for groups of unequal variances.

During the ambulatory observation, one subject, s02, did not respect the indications for sleep and wake times. On average, the subject slept a shortened main sleep episode in the morning (mean length 4.3 hours), and took 1-2 naps in the afternoon (mean length 3.5- 4.1 hours). This sleep pattern was persistent in the both phases of study. Thus, this subject's data was excluded from the analyses discussed below because it was substantially different from the group.

The temporal distribution of night shifts and days off throughout the ambulatory period differed for each subject. To ensure the between-subject comparability of the data collected, a threefold approach to the analysis of data collected during the period of night work was devised. Measures of sleep quality, subjective vigilance, and medical symptoms, as described below, were analysed as a function of time in each of three manners. In the first approach, values were averaged per bin based on the number of the shift within the ambulatory period, where the first night shift worked after the initial constant routine was assigned the shift number 1. Scores were averaged per subject into 3-shift bins, and then averaged over subjects into the respective experimental groups. In the second approach, values were averaged for bins based on the number of calendar days from the start of the experiment. The first analysis bin represents the first series of 9 calendar days. A time bin of 9 calendar days was selected in order to ensure that each subject would have at least one measurement contributing to the group mean per 9-day period. Values were averaged per subject into the time bin, and subsequently averaged into subject groups. In the third approach, values were averaged into 1-day bins based on the number of consecutive night shifts worked before the daytime sleep episode. Each subject's measurements per 'consecutive shift' bin were averaged, and group means where derived from these scores. To ensure a reasonable sample size, the analyses were limited to consecutive shifts 1, 2 and 3 only, although a subgroup subjects may have worked a longer series of night shifts. Evaluation for group differences were performed using a model of ANOVA for repeated measures. Planned comparisons were performed, using the Tukey's HSD.

As with analyses previously described, the results obtained during the ambulatory period of the control and treatment conditions of subject s02, were excluded as a result of that subject's non-compliance to the experimental directives.

Sleep

To evaluate the comparability of the two methods of measuring ambulatory sleep, 41 simultaneous recordings of the Nightcap and the ambulatory polysomnograph were compared. Ambulatory sleep episodes were therefore quantified according to the above methods on the three most reliable measures from the two recording devices: total sleep time ($r=0.623$, $p<0.01$), number of REM periods ($r=0.328$, $p=0.04$) and sleep efficiency ($r=0.681$, $p<0.01$). All other measures were not significantly correlated. In instances of simultaneous sleep recordings, only data from the standard polysomnography was used in analyses.

Vigilance

Self-ratings of sleepiness (scale 0-10) during the night shift were analysed as a function of cumulative shift worked, calendar days from the start of the experiment, and consecutive shifts worked, as described above. Due to missing data points, the results obtained for the treatment condition of subject s06 were excluded from all analyses of subjective vigilance.

Medical symptoms

In order to ascertain a global index of the severity of a range of complaints associated with night shift work, subjective scores for the severity of symptoms were tabulated as a sum of

all symptom scores reported by each subject per night. The results from 6 questions (referring to the previous sleep episode) were omitted from these analyses since they did not necessarily relate to the night shift, or a daytime sleep episode. They were therefore excluded to avoid the effect of an uncontrolled confounding element. Each symptom could have a severity score from 1 (very mild) to 10 (very pronounced). Scores for the remaining 14 symptoms were summed per subject per shift (total minimum score=14, total maximum score =140). A score was also attributed for the duration of symptoms as subjectively assessed by the subject. Each symptom could have a subjective duration of 0 ('no symptoms during the shift) to 6 (almost the entire shift). The total scores for the 6 items were tabulated per subject per shift (total minimum score=0, total maximum score =36) Analyses on measures of symptom severity and subjective duration were performed according to the approach previously described for ambulatory measures. Due to missing data points, results from treatment group subjects and s06 and s16 were excluded from all analyses of symptom severity and duration. Similarly, data from control group subject s13 were excluded from analyses of subjective symptom duration as a function of experimental day.

Light exposure

Light exposure levels were quantified based on a model previously described (Hébert et al., 1998). Minutes of exposure to given light levels, obtained from actimetry recordings on shift days were quantified into a 4x5 'light exposure' by 'time of day" grid. The light exposure component of the grid consisted of 4 bins of light intensities: 0-10 lux, 10-100 lux, 100-1000 lux, and >1000 lux. Time of day was quantified as 5 periods in the day calculated based on hours from the shift start: 'first 6 hours of shift', 'last two hours of shift', 'commute', 'day sleep period', and 'evening'. These periods, significant in the frame of the this study, corresponded to the 6-hour period during which treatment subjects would have received bright light, the end of the shift, the 2-hour window allotted to the commute home during which subjects would have worn goggles, the 8-hour period designated for sleep/darkness, and the 6-hour period between wake-up and the start of the next night shift. Analyses were performed on data corrected for goggles usage. Minutes of light exposure were thus compared between groups using two-tailed t-tests for unequal variances, with an appropriate correction (Bonferroni to 0.0025) for repeated tests. Actimetry data for control subjects s05 and s06, and treatment subject s04, was unusable, and not included in these analyses.

Light levels determined with the use of calibrated research photometers were also analysed. To determine the mean level of light exposure at the level of the eye, light intensity readings were first averaged for each hour of the shift per subject, and then across groups. Mean intensity levels were then compared between groups using a model for ANOVA for group x repeated measures. A similar analysis was performed on light intensity data with the time course of the night shift divided into two parts corresponding to the first six hours of the shift and the last two hours of the shift.

All results are expressed as mean ±S.E.M, unless otherwise specified.

RESULTS

Vacation period

Mean chronotype scores for the control and treatment groups were (±S.E.M.) 48.4±4.9 and 37.3±5.7, respectively. Both groups showed a similar loading for evening-type behaviour, and were comparable (p=0.4).

Sleep schedule

Following a period of at least 10 days on a day-oriented schedule, subjects were admitted to the laboratory for an initial evaluation of the endogenous oscillation of the circadian pacemaker via the constant routine procedure. This evaluation was preceded by a sleep episode, the timing of which was determined based on the average sleep times during the vacation period. Mean sleep times (±S.E.M.) for the control and treatment groups were 8:50±0:17 and 8:21±0:10 in length respectively, with mean bedtimes of 23:32 ±0:10 and 23:57±0:12, and wake times of 8:22±0:20 and 8:17±0:13, respectively. A two-tailed t-test for groups of unequal variances revealed that bedtimes, wake times and sleep period lengths were comparable between the two groups (p=0.1, p=0.9, and p=0.1, respectively).

The time of the first sleep episode in the laboratory was based on the mean sleep times for the subjects in the seven days preceding the study start, and adjusted to an 8-hour length. Following adjustment, mean bed and wake times for the control and treatment groups were 00:13±0:29 and 00:19±0:24 and 8:13±0:29 and 8:19±0:24, respectively.

Circadian evaluation at day baseline

Core body temperature

The time of the fitted minimum of the endogenous circadian variation of core body temperature was determined in all subjects as described above. At the start of the study, all subjects displayed normal circadian rhythms of core body temperature (Czeisler et al., 1992; Dawson et al., 1992),well-adjusted to a daytime schedule. Mean initial phases of core body temperature in the control and treatment groups were 4.87±0.65 and 6.20 ± 1.23 hours, respectively. A simple main effects analysis on the times of fitted minimum within the ANOVA model revealed that both groups were comparable at the initial phase ($F_{(1,30)}$=0.47, p=0.5). Similarly, the amplitude of the oscillation of temperature was comparable between the two groups ($F_{(1,15)}$=1.84, p=0.2). The phase angle between the time of awakening and the phase of the core body temperature cycle was calculated as +3.36 ±0.46 and +2.12 ± 1.13 hours for the control and treatment groups, respectively. These phase angles were also comparable between both groups ($F_{(1,30)}$=0.44, p=0.5).

Melatonin

At the start of the study, all subjects also displayed a normal, day-oriented rhythm of melatonin secretion (Shanahan & Czeisler, 1991; Copinschi et al., 1999). The midpoint of salivary melatonin concentration was determined for the control and treatment groups at 3.92±0.49 and 3.79 ±0.47 hours, respectively. A simple main effect analysis on the midpoint of melatonin secretion within the ANOVA model revealed that these times were comparable between groups ($F_{(1,30)}$=0.01, p=0.94). The between-groups comparability of the patterns of salivary melatonin secretion was also ascertained. The 24-hour average concentration of salivary melatonin was comparable between the two groups ($F_{(1,15)}$=0.01, p=0.9), and was calculated as 3.26±0.55 and 3.33 ±1.06 pg/ml for the control and treatment groups, respectively. The time of upward crossing of the 24-hour average concentration was found to be 23.03±0.51 and 22.85±0.47 hours for the control and treatment groups, respectively. The time of downward crossing was 8.82±0.48 and 8.72±0.50 hours for the control and treatment groups, respectively. ANOVA detected no significant effect of group for the times of upward or downward crossing of the 24-hour average melatonin concentration ($F_{(1,15)}$=0.72, p=0.4, and $F_{(1,15)}$=1.50, p=0.3). Finally, the time between the upward and downward crossing of the 24-hour average concentration was also comparable between the groups ($F_{(1,15)}$=1.88, p=0.2), with values of 9.79 ± 0.19 and 9.86 ±0.21 hours for the control and treatment groups, respectively. The phase angle between the midpoint of melatonin secretion and the time of awakening was determined to be +4.30±0.28 and +4.53±0.30 hours for the control and treatment groups. These phase angles, were also statistically comparable ($F_{(1,30)}$=0.02, p=0.9) following simple main effects analysis.

Vigilance

The variations of subjective alertness also displayed an appropriate alignment to a day-oriented schedule in both groups, with lowest alertness scores occurring at the end of the projected sleep episode (**Figure 6**, upper panel). Highest scores were reached during the subjective day. All time points were comparable between the control and treatment groups ($F_{(1,14)}$=0.09, p=0.8).

Sleep

The sleep episode preceding the initial constant routine was comparable between groups for the amount of waking ($F_{(1,7)}$=0.06, p=0.8), stage 1 sleep ($F_{(1,7)}$=0.07, p=0.8), stage 2 sleep ($F_{(1,7)}$=0.03, p=0.9), stage 3 sleep ($F_{(1,7)}$=0.60, p=0.4), stage 4 sleep ($F_{(1,7)}$=0.03, p=0.9), REM sleep ($F_{(1,7)}$=0.23, p=0.6), and sleep efficiency ($F_{(1,7)}$=0.05, p=0.8). Planned comparisons revealed a significantly greater number of minutes of stage 1 sleep in the control group at the 5th hour of the sleep episode (p=0.03). An increased number of minutes of stage 3 sleep was observed in the control group at hour two of the sleep episode (p=0.05), with a concomitant trend towards a significantly greater number of minutes of REM sleep (p=0.06).

Ambulatory observation

Duration of ambulatory period

Control and treatment group subjects were observed over an average of 12.2 ±0.2 and 11.9 ± 0.1 shifts, respectively. This period length was comparable between groups (p=0.2). The number of shifts worked by each subject prior to their re-admission to the laboratory was also compared between groups. A two-tailed, Student's t-tests for groups of unequal variance confirmed that the mean number of shifts worked by the control and treatment groups, just prior to the second constant routine, 4±0.5 and 4.2± 0.8, were comparable (p=0.8). On average, the number of days between laboratory visits was 19.75±0.5 for the control group and 19.1±0.4 for the treatment group (p=0.3).

Sleep schedule

(**Table 2**)

On shift days, mean bedtimes were 9:42 ± 0:12 and 9:45 ± 0:08, mean wake times were 17:07 ±0:14 and 17:27 ±0:15 for the control and treatment groups, respectively. Bedtimes and times out of bed did not differ significantly between groups, (p=0.9 and p=0.4, respectively). Mean times in bed was 7:25 ± 0:11 hours and 7:42 ± 0:12 hours for control and treatment subjects, and was comparable between groups (p=0.2).

On days off, subjects returned to a day-oriented schedule. Mean bedtime of the main sleep episode was 52 minutes earlier in the control group where bedtimes were at 23:56 ± 0:26 and 00:48 ± 0:44, for the control and treatment groups respectively. However, this difference did not reach statistical significance (p=0.3). Mean time out of bed for the control and treatment groups were 8:58 ±0:30 and 9:02 ± 0:43, respectively, and were also comparable (p=0.9). The mean sleep episode lengths were of 49 minutes longer for the control group compared to the treatment group. However, this difference did not reach statistical significance either (p=0.1), where mean sleep lengths were 9:02 ± 0:26 and 8:13 ± 0:12 for the control and treatment groups, respectively. Finally, in both the control and the treatment groups, the mean reported bedtimes and time out of bed on days off were comparable to those just prior to the initial constant routine, (control group, p=0.6, and p=0.3, respectively; treatment group, p=0.6, and p=0.4, respectively.).

Five subjects reported having taken evening naps prior to returning to work after nights off. Subjects s03, and s11, s13 of the control group reported naps lasting from average times of 18:40 ± 1:44 to 20:25 ± 1:46, for an average length of 1:44 ±0:14. Two subjects (s03 and s06) in the treatment group reported naps, for average naps times of 14:33 ± 3:57 to 18:12 ± 3:23 for average lengths of 3:39 ±0:34 hours. These nap times were comparable between the groups (p=0.5 for bedtimes, p=0.6 for wake times , and p=0.14 for nap length). Only subject s02 napped on shift days. This subject's data was therefore excluded from these analyses as described above.

Daytime sleep

(**Figure 8**)

Two-factor analysis (factors: group; time as cumulative shifts) of the total minutes of daytime sleep evaluated as a function of the cumulative number of shifts worked in the ambulatory period revealed significant main effects for group ($F_{(1,15)}$=5.63, p=0.03) and for shift number ($F_{(1,15)}$=3.98, p=0.01). Post-hoc comparisons revealed significantly longer sleep times for the treatment group at bins corresponding to the first series (p=0.04), and the last series (p=0.008) of 3 cumulative shifts. No significant differences were detected in the number of REM periods in control versus treatment group subjects ($F_{(1,15)}$=0.03, p=0.8). Similar analyses on sleep efficiency over cumulative shift number revealed no statistically significant effects, however, a trend towards the a significant increase in sleep efficiency of treatment group subjects was borne between the first two bins observed (p=0.07).

Analyses on total sleep time, number of REM periods and sleep efficiency, performed as a function of bins of 9 calendar days, revealed no statistically significant differences in means. However means of total sleep time and sleep efficiency were consistently greater in the treatment group.

The analyses of sleep parameters over the number of consecutive shifts worked revealed a significant effect for experimental group ($F_{(1,15)}$=4.73, p=0.05), but not for time. Planned comparisons performed within the ANOVA revealed a trend towards a greater number of minutes asleep for the treatment group by the second consecutive night (p=0.07), which reached statistical significance by the third consecutive work period (p=0.05). No between-group differences were detected in the number of REM periods in day sleep episodes, although a trend towards a main effect of time was detected (p=0.06). The treatment group displayed a trend of higher sleep efficiencies, which approached statistical significance by the second consecutive shift (p=0.06).

Vigilance

(**Figure 9**)

Levels of subjective alertness analysed as a function of the cumulative number of shifts worked revealed alertness levels in the treatment group which were higher than those of the control group in the first series of 3 cumulative shifts (p=0.05). Neither analyses of self-rated vigilance scores as a function of calendar days nor the number of consecutive shifts worked revealed a significant effect of group or time. In general, however, alertness scores within the treatment were higher.

Medical symptoms

(**Figure 10**)

Analysis of variance performed on reported symptom severity as a function of series of cumulative shifts revealed only a main effect for shift number ($F_{(1,13)}$=7.12, p=0.0006). Similar

analyses performed on scores of subjective symptom duration revealed a significant group x time interaction ($F_{(1,13)}$=2.94, p=0.04). Simple main effects analyses detected a significant effect for time at the bin corresponding to the first series of 3 cumulative shifts (p=0.05), with longer subjective duration of symptoms in the control group.

The analysis of symptom severity as a function of bins of 9 calendar days, revealed only a significant main effect for time ($F_{(1,12)}$=4.76, p=0.02). Similar analyses on subjective symptom duration revealed a significant main effect of calendar days ($F_{(1,13)}$=2.72, p=0.02), with more reported symptoms in the control group at scores that approached statistical significance (p=0.08).

Light exposure

Mean levels of light exposure on shift days, are represented in **Figure 2**. On shift days, the treatment group received an average of 51±11 minutes of light > 1000 lux in intensity during the first 6 hours of the shift. This value was significantly greater than the mean 0.07 ± 0.07 minutes of light of this intensity received by the control group at this time, (p =0.002). Contrarily, the control group received an average of 194 ±30 minutes of light in the 10-100 lux range during the first 6 hours of the shift. This value was significantly greater than the mean 86±11 minutes of exposure to light of this intensity for the treatment group, (p=0.01). (**Figure 3**).

Light exposure also differed significantly at the time of the commute, with the correction for goggle use. The control group received significantly more light in the > 1000 lux range with 32±4 minutes compared to 4±1 minutes for the treatment group, (p=0.0007). The control group also received a significantly greater mean number of minutes of 100-1000 lux light, with 28±2 versus 18±2 minutes for the treatment group, (p=0.002). The treatment group received a mean 64±6 minutes of <10 lux light, where the control group received a significantly lower 28±6 minutes, (p=0.0009).

Analysis of variance performed on measured light intensity per hour in the workplace revealed a significant group x time interaction ($F_{(1,7)}$=4.75, p=0.0001). Simple main effects analyses revealed significant differences in light intensity for the first 6 hours of the shift (p=0.04; p= 0.0002; p=, 0.0028; p=0.0002; p=0.0019, p=0.0003) corresponding to the time of phototherapy,. A parallel analysis on measured light intensity in the workplace during the night shift also revealed a significant group x time interaction ($F_{(1,16)}$=13.67, p=0.002) where simple main effects analysis revealed a significant difference in mean light intensities in the first 6 hours of the shift. (p<0.0001).

Circadian evaluation following period of night shift work

(**Table 3**)

Core body temperature

(**Figure 4**, upper panels)

Final phase of the core body temperature cycle in the control and treatment groups was 8.96±2.20 and 15.53 ± 1.00 hours, respectively. ANOVA for repeated measures revealed a significant group time interaction ($F_{(1,15)}$=5.99, p=0.03). Simple main effects analyses revealed that the mean final phases of core body temperature varied significantly between the control and treatment group, ($F_{(1,30)}$=11.50, p=0.002). The final phase of core body temperature was significantly different from the initial phase in both the control and treatment groups, ($F_{(1,15)}$=7.30, p=0.02 and $F_{(1,15)}$=37.99, p<0.0001, respectively). The mean shift in the nadir of core body temperature for the control and treatment groups were –4.09±1.94 and –9.32±1.06 hours, respectively. A two-tailed t-test for groups of unequal variances revealed that the shifts of the nadir of core body temperature were significantly different (p=0.04). The amplitude of the oscillation of temperature remained comparable between the two groups ($F_{(1,15)}$=1.84, p=0.2). The phase angle between the mean time out of bed during the ambulatory period, and the phase of the core body temperature cycle was calculated for each subject. Mean phase angles were +8.16 ±2.23 and +1.92 ± 0.88 hours for the control and treatment groups, respectively. ANOVA on these values revealed a significant group-time interaction, ($F_{(1,15)}$=4.78, p=0.04). Simple main effects analyses confirmed that the phase angles prior to and following the intervention regimen were comparable in the treatment group, ($F_{(1,15)}$=0.02, p=0.9), but not in the control group, ($F_{(1,15)}$=8.81, p=0.01).

Melatonin

(**Figure 4**, lower panels)

The midpoint of salivary melatonin secretion following the ambulatory period was determined for the control and treatment groups at 9.00±2.48 hours and 15.10 ±0.97 hours, respectively. A significant group-time interaction was detected ($F_{(1,15)}$=6.28, p=0.02). Simple main effects analysis revealed that these times differed significantly between groups following the intervention regimen, ($F_{(1,30)}$=10.69, p=0.003). The final phases of melatonin secretion differed significantly from the initial phases in both the control ($F_{(1,15)}$=8.36, p=0.01) and treatment groups ($F_{(1,15)}$=41.42, p<0.0001). The mean shifts in the midpoint of melatonin secretion were –5.08±2.32 and –11.31±1.13 hours, respectively, and differed significantly between groups (p=0.02). The patterns of salivary melatonin secretion were also ascertained. The 24-hour average concentration of salivary melatonin remained comparable between the two groups following the intervention regimen ($F_{(1,15)}$=0.01, p=0.9). The time of upward crossing of the 24-hour average concentration was found to be 9.85±0.90 and 13.28±2.43 hours for the control and treatment groups, respectively. The between-groups differences were statistically significant ($F_{(1,15)}$=44.93, p<0.0001). Post-hoc analyses revealed that these time points were significantly different from those of the initial condition in both the control ($F_{(1,15)}$=15.59, p=0.001) and treatment groups, ($F_{(1,15)}$=31.17, p<0.0001). The time of downward crossing of the 24-hour average concentration was found to be 10.73±2.42 and 20.34±1.07 hours for the control and treatment groups, respectively. A significant effect of time was observed here as well

($F_{(1,15)}$=42.70, p<0.0001). Post-hoc comparisons detected that these group mean times did not differ significantly from each other ($F_{(1,30)}$=3.04, p=0.09). However, a significant difference in these times was detected for both the control and treatment groups when they were compared with their initial conditions ($F_{(1,15)}$=13.23, p=0.002, and $F_{(1,15)}$=32.13, p<0.0001 for the control and treatment groups) The length of time that the concentration remained greater than the 24-hour average concentration remained comparable between the groups ($F_{(1,15)}$=1.88, p=0.2), with values of 9.45 ± 0.61 and 10.49 ±0.39 hours for the control and treatment groups, respectively. ANOVA detected no difference between these values and those of the initial condition ($F_{(1,15)}$=0.17, p=0.7). The phase angle between the midpoint of melatonin secretion and the time out of bed was determined to be +8.12±2.54 and +2.34±0.88 hours for the control and treatment groups (**Table 3**). ANOVA performed on these phase angles, revealed a significant group-time interaction ($F_{(1,15)}$=5.20, p=0.04). Simple main effects analyses revealed that these phase angles differed significantly between groups following the intervention regimen ($F_{(1,30)}$=9.88, p=0.004). Calculated phase angles in the treatment group following the intervention were comparable to those in the initial condition ($F_{(1,15)}$=1.38, p=0.2, respectively). However, in the control group, this phase angle was 3.82 hours larger than the initial condition and showed a strong trend towards significance ($F_{(1,15)}$=4.21,p=0.06) (**Figure 4**, lower panels).

Vigilance

The variations of subjective alertness in the final condition (**Figure 6**, lower panel) reveal higher levels of alertness during the time of the subjective night in the control group of subjects compared to the treatment group. At the 23rd hour of awakening, this difference was significant, (p=0.054). During the subsequent period of awakening, levels of alertness in the control group, initially higher than those in the treatment group, decline. However, these did not reach statistically significant levels.

The initial and final conditions for each experimental group were also compared (**Figure 7**). The relationship between the sleep-wake cycle and the diurnal rhythm of subjective vigilance for the control group at the final constant routine differed significantly from that observed in the initial condition. This resulted in significant differences at hours 19 (p=0.02), 21 (p=0.01), 23 (p=0.005), and 25 (p=0.02) of the constant routines, which correspond to the projected sleep episode The relationship between the sleep-wake cycle and the diurnal rhythm of subjective vigilance for the treatment group in the final condition was comparable to that observed in the initial conditions ($F_{(1,14)}$=0.39, p=0.5).

Sleep

Analyses performed on sleep in the laboratory immediately following the intervention period revealed no significant between-groups differences minutes of waking ($F_{(1.7)}$=0.32, p=0.6), stage 1 sleep ($F_{(1,7)}$=0.03, p=0.9), stage 2 sleep ($F_{(1,7)}$=0.56, p=0.5)stage 3 sleep ($F_{(1,7)}$=0.12, p=0.7), stage 4 sleep ($F_{(1,7)}$=0.00, p=0.9), REM ($F_{(1,7)}$=2.24, p=0.2), or sleep efficiency ($F_{(1,7)}$=0.33, p=0.6) throughout the night. However, when nocturnal and diurnal sleep episodes were compared within the control group, significantly more time awake (p=0.02) and lower sleep efficiency (p=0.02) were detected in the 8th hour of the diurnal sleep episode

following the ambulatory period. Moreover, analysis of REM sleep within the control group revealed a significant group x sleep hour interaction ($F_{(1,7)}$=2.91, p=0.0082). Simple main effects analyses of the diurnal sleep episode revealed significantly more minutes of REM in the 6th hour (p=0.02) and less minutes of REM the 8th hour (p=0.0007) when compared with the initial nocturnal sleep episode. Similar analyses performed on treatment group subjects revealed an unchanged distribution of REM sleep. In this group, significantly fewer minutes of stage 1 sleep (p=0.04), and more minutes of stage 3 sleep (p=0.05) were also observed in the first hour of the sleep period when compared with the initial nocturnal sleep.

DISCUSSION

The misalignment of the endogenous circadian pacemaker to a night-oriented schedule is important in the genesis of the malaise often associated with working full-time night shifts. This study sought to promote circadian entrainment to the work schedule with an intervention of both bright light and regular sleep/darkness. It also aimed to describe both the nature and quality of the entrainment via constant routines.

This experimental series was most demanding by virtue of its combined field and laboratory design. To the authors' knowledge, it is the first study to quantify under constant routine conditions the effect of a bright light-regular sleep/darkness intervention on the circadian adaptation of night shift workers to their inverted schedule. This experimental approach therefore allows the precise evaluation of circadian adaptation to night shift work. Circadian phase markers obtained under ambulatory conditions are generally masked by the effects of activity, meal intake, and environmental disturbances. Mathematical models for the unmasking of such data have been proposed (Waterhouse et al., 1999). However, these models are not consistently reliable (Klerman et al., 1999) and the error incurred in the estimation of circadian phase in the night shift worker may be particularly high.

For all workers, the initial circadian evaluation performed in this study followed a day-oriented period, and provided a baseline upon which the effect of the intervention regimen could be judged. The baseline recording also provided an element of homogeneity in this naturally heterogeneous study group. At the start, workers revealed robust circadian rhythms, well adapted to a day-oriented life. Physiological markers were comparable in their temporal alignment. Moreover, the entrainment of both groups to a daytime schedule was complete, where mean phase of core body temperature occurred about 2 hours before the regular time of awakening (Czeisler et al., 1992; Dawson et al., 1992), melatonin secretion reached a maximum approximately 4 hours before awakening (Shanahan & Czeisler, 1991; Copinschi et al., 1999), and the trough of subjective vigilance at the end of the habitual sleep episode (Johnson et al., 1992; Van Dongen et al., 1997; Dijk et al., 1992). One worker displayed an unusual initial phase of core body temperature where the minimum was observed much later that the habitual time of awakening. No element of this worker's sleep-wake habits previous to or during the vacation period predicted that he would exhibit such a late circadian phase. Moreover, the circadian variation of melatonin concentration in this worker was properly aligned to his sleep-wake schedule. In human studies, we infer the oscillation of the pacemaker from the expression of its efferents. Thus, while the temperature and melatonin rhythms are believed to be equally reliable markers of the oscillation of a single circadian pacemaker (Shanahan & Czeisler, 1991), it is suspected that the phase of this worker's salivary melatonin concentration more closely expressed the actual phase of the pacemaker. This points to the importance of measuring multiple variables in the study of human circadian rhythms.All of this worker's results were included in these analyses.

With the exception of the imposed experimental conditions, the ambulatory period of the two subject groups were spent in similar fashions. Subjects in both groups worked a comparable number of shifts (~12), and the period between laboratory visits was also comparable (~19 days). Sleep schedules following night shifts and on days off were similar (**Table 2**). Compliance to the

imposed sleep schedule was good, except for subject s02 who was excluded from the analyses. Across both workers groups, a general return to a diurnal schedule was observed as of the first night off. This was as true for workers who had a single night off as it was for those with a series of nights off. Five workers also reported naps exclusively on the last rest day preceding a return to work. This phenomenon is one that is borne out in the literature (Rosa, 1993; Åkerstedt et al., 1989; Knauth & Rutenfranz, 1980). In particular, Rosa et al. observed in a population of shift workers that a predominance of naps were taken just prior to the initiation of a series of shifts. While naps on shift days were prohibited in our worker group, subsequent analyses of on-shift alertness and performance scores may determine if the naps prior to night shifts had the same alerting effect as noted by others (Bonnet, 1991; Bonnet & Arand, 1994; Rogers et al., 1989; Rosekind et al., 1995; Gillberg et al., 1996).

During the intervention period, the groups differed only in their levels of exposure to light. According to the phase response curve of the endogenous circadian pacemaker to bright light (Czeisler et al., 1989; Minors et al., 1991; Honma & Honma, 1988), the pattern of exposure to light during shift and commute times played a most important role in the disparity observed in the entrainment of these two groups. For workers in the treatment group, exposure to light was controlled with respect to its capacity to effectively promote the anticipated phase delay shifts of the endogenous circadian oscillator. By comparison, the control group was exposed to light of lesser intensities later in the phase delay portion of the endogenous circadian pacemaker's phase response curve to light. To accentuate this tendency, this group was exposed to bright sunlight in the early morning, a situation which could have promoted a phase advance (from the phase as it was expressed at the baseline measurement). As demonstrated in **Figure 2**, the levels of light exposure in the sleeping quarters did not vary significantly between groups. It was noted anecdotally at the initiation of the study, that the majority of workers in the control group slept in rooms darkened much like those of the treatment group.

Following the period of night shift work, circadian rhythms were robustly expressed. The final circadian phase in the treatment group adjusted to follow the 9-hour phase delay in the sleep-wake schedule most closely. For workers having undergone the intervention, the magnitude of shift of the sleep-wake cycle and of the oscillation of the circadian pacemaker were indistinguishable ($F_{(1,30)}=0.02$, $p=0.9$). Moreover, the entrainment of this group of workers to a night schedule was complete and comparable to the entrainment of this group to the baseline condition. Results of the analyses of vigilance levels and sleep during the ambulatory period also support this interpretation. In the non-adjusted control group, the comparison of the inital and final conditions observed reveal significant differences. For example, the temporal distribution of REM sleep in the final diurnal sleep episode was significantly different from that of the initial nocturnal sleep. Specifically, diurnal sleep displayed a significant increase and a significant decrease in the minutes of REM sleep in the 6^{th} and 8^{th} hours of the sleep episode, respectively. This would suggest that final circadian phase was advanced in relation to the sleep-wake schedule. Contrarily, the organization of the night and day sleep in the treatment group were more comparable, which supports a complete circadian adaptation in this group. An increase in the amount of stage 3 sleep was observed in the final conditions, which suggests the presence of some sleep deprivation. More sophisticated spectral analyses of the EEG will investigate this question further.

Circadian variation of vigilance levels in the final condition of the treatment group was comparable to that of the initial condition (**Figure 7**). Control group workers, however, inappropriately displayed high levels of vigilance in the times that would have been asleep. These elevated levels of vigilance at the times when they should have been the lowest constitute the greater part of the between-group differences during the final constant routine. A successful intervention, and a consequent alignment of the circadian pacemaker with the inverted sleep-wake schedule, should have resulted in lower alertness scores during the projected time of the sleep period and higher scores during the period of awakening (Johnson et al., 1992; Dijk et al., 1992; Monk & Carrier, 1998). This interpretation is consistent with ambulatory measurements demonstrating reduced vigilance during the projected daytime sleep episode for night workers of the treatment group. However to clarify this interpretation, it would have been preferable to have a longer constant routine in the laboratory and more sophisticated objective measures of vigilance and performance.

Most full-time night shift workers have difficulty maintaining day sleep, mostly due to an inefficient temporal relationship between the sleep-wake cycle and the endogenous circadian pacemaker that results in an abbreviated day sleep period (Borbély & Achermann, 1992; Daan et al., 1984). We would therefore expect sleep of greater quality in the night shift worker adjusted to the inverted sleep-wake schedule. Ambulatory recordings of diurnal sleep following night shifts revealed that treatment group subjects slept significantly longer (up to 82 minutes) than did control group subjects (**Figure 8**), although both groups spent a comparable length of time in bed (**Table 2**). It is well known that day sleep in the average, maladjusted, shift worker may be truncated by 1-2 hours (Åkerstedt, 1995). Because of the comparability of diurnal times in bed between groups, we do not attribute any differences in time asleep to social factors (e.g. household responsibilities). However, no significant difference was detected in the number of REM periods during ambulatory sleep recordings. It must be stressed, however, that this measure is the least reliable of those derived from the Nightcap device, and that any observed effect may have been occluded in this measurement. Shortened diurnal sleep is most likely related to the fact that circadian phase, as observed in the control group, is adverse to the promotion of day sleep.

Together, these results suggest that an intervention regulating both the exposure to light and the timing of the sleep/darkness period may promote a complete circadian adaptation to full time night shift work. The specific contributions of the control of the sleep/wake cycle and, by extension, non-photic synchronisers are difficult to quantify. However, the comparability of sleep schedules across groups taken together with the differences in the experimental conditions suggests that the adaptive phase shifts in the treatment group are indeed the result of an improved pattern of exposure to light and darkness.

Bright light applied at different circadian phases is known to elicit different phase shifts in the core body temperature (Wever et al., 1983; Czeisler et al., 1986; Drennan et al., 1989) and melatonin rhythms (Lewy et al., 1987; Broadway et al., 1987; Drennan et al., 1989). In the context of shift work, bright light has been mandated for its direct activating effect on the reversal of sleepiness and the improvement of performance scores and short term memory (Dawson et al., 1995; Foret et al., 1998; Campbell et al., 1995a; Lowden et al., 2000). It has also been effectively used in the home setting following night shifts to promote an appropriately-timed sleepiness (Bjørvatn et al., 1999) and a shift in hormonal rhythms back to a diurnal pattern

(Midwinter & Arendt, 1992). Particularly relevant to this study is the part of the literature dealing with the nuances of the pattern of light exposure required for shifting the endogenous circadian pacemaker itself.

A study by Mitchell et al. (1997) underlines the applicability of a well-timed exposure to light and darkness in producing adaptive phase shifts to night work. In this study, the interplay between the timing of sleep darkness and bright light exposure was examined. All workers slept in darkened bedrooms and wore goggles when outdoors in the early day. Mitchell et al. demonstrated that steadily delaying (occurring progressively later) bright light during a simulated night shift, together with a morning sleep/darkness period was most effective in producing an adaptive phase delay. They also demonstrated that steadily advancing (occurring progressively earlier) bright light and an evening sleep/darkness period could also promote the phase shift the demasked temperature minimum into the sleep period.

Most recently, Dumont et al. (2001) reported the pattern of light exposure in a group of full time night shift workers. The nurses in this study entered the laboratory for observation after a number of consecutive shifts. The levels of light exposure were then correlated to the phase shifts observed in the rhythms of urinary 6-sulfatoxymelatonin (aMT6s) in the nurses. It was noted that nurses who displayed delays in their rhythms of (aMT6s) were less exposed to the bright morning light. Further still, it was noted that this cluster may have slept in darker rooms and at earlier times, again reinforcing the tendency of the endogenous circadian pacemaker to delay.

The patterns of exposure to light described by both Mitchell and Dumont are further substantiated by observations made by Koller et al. (1994). Koller noted that hormonal phases of salivary melatonin and cortisol were more reflective of a day-oriented schedule when morning light exposure was high. Koller further notes that morning light levels were dim for workers who phase delayed.

These studies reflect, in both laboratory and field situations, what was observed in the present study. As in the Mitchell et al. study (1997), the present studies' intervention of delaying bright light exposure and morning sleep episodes promoted an appropriate delay of the endogenous circadian pacemaker. Moreover, Mitchell, Dumont and Koller all point to the significant effect that shielding from morning light may have had on the entrainment of this studies' treatment group.

Indeed, the overall pattern of exposure to light is a variable of great importance when adaptation to shift work is desired. Bjørvatn et al. (1998) allude to this in their study of oil platform workers who reveal lower on-duty sleepiness scores within a few shifts; a similar observation is made by Ross et al. (1995). They suspect, as we do and as supported by others (Czeisler et al., 1990; Barnes et al., 1998; Eastman et al., 1994) that the workers who displayed a (verified or inferred) adaptation were shielded from bright morning light.

The pattern of exposure to light during the 6-hour bright light treatment window, is also of interest. In laboratory studies, it is possible to give the instruction that the worker look directly into a bank of bright lights. In this study's group of hospital workers, required to make regular rounds to patient rooms darkened at nights, this was not only impractical, but it was unfeasible.

It has recently been demonstrated, however, that the intermittent light to which the shift workers were exposed may have had a significant biological effect, even though they were occasionally out of the light for prolonged intervals. Rimmer et al. (2000) report a resetting effect in subjects exposed to intermittent light where, for example, 44 minutes of each 90-minute cycle were spent in darkness. Further still, a significant resetting effect was observed when exposure to bright light was for as little time as 5.3 minutes per 25-minute period. As hospital setting varied in this study (summarised in **Table 1**), so did the workload of our workers. While certain workers were afforded longer intervals at the lamps, those with more patient-interactive positions may have spent shorter and more irregular intervals at the lamp. All workers were required, at some point, to leave the station to perform their duties. As described by Rimmer et al. (2000), bright light can induced a significant phase shift even when administered in short, repeated intervals, interrupted by darkness. Lowden et al. (2000) also report that intermittent light exposure given to a group of night shift workers had some effect in decreasing on-shift sleepiness over time. The potency of an intermittent pattern of light exposure has also been substantiated in a simulated shift work study by Baehr et al. (1999). In their study, they noted that exposure to rather long (40 minutes) intervals of bright light could induce phase resetting. It must be noted that both of these studies employed light that was considerably brighter (~9500 lux and ~5000 lux, respectively) than what was used in the present study. Moreover, the 'dim' intermittent periods reported by Baehr et al. were much brighter than the typical illumination on hospital wards and in patient rooms at night.

The intensity of the bright light stimulus given was also important. The mean levels of light received by our treatment group, workers were comparable to the medium intensity (~1230 lux) that Martin and Eastman (1998) found to be effective for phase shifting in a night shift worker simulation. Moreover, Martin and Eastman observed a resetting effect of light of <250 lux. The dose response of the human circadian pacemaker to light (Boivin et al., 1996; Kronauer, 1990; Boivin & Czeisler, 1998) predicts the effect observed by Martin and Eastman, and again validates the efficacy of the bright light treatment given the present study's treatment group. By virtue of the non-linear relationship between the intensity of the light stimulus and its resetting response, intensely bright light may not be necessary for adaptation in the workplace.

The rest/activity cycle during days off was also comparable between both groups of workers. In the present study, one of the inclusion criteria was that the participants work a minimum of 8 shifts per 15 days. However, no predetermination as to the temporal arrangement of work shifts (summarised in **Table 1**) was made. Bougrine et al. have investigated the effect of days off in a simulation study (Bougrine et al., 1998). In this study, they initiated a bright light treatment during a series of 12 simulated work nights with days off interspersed. They observed full adjustment of the curve of urinary aMT6s in nurses working a longer series of shifts with bright light and a partial adjustment in nurses working shorter series of shifts with bright light. Particularly relevant to this study, is that the adjustment, even in the group displaying partial adaptation, was not reversed after nights off. In the present study, nurses re-entered the laboratory after a short series of ~4 shifts, comparable between both groups. It is therefore possible that the full and partial entrainment observed in the treatment and control groups after ~19 days may reflect a quasi-stable phase relationship between the endogenous circadian pacemaker and the sleep-wake cycle.

The results obtained in this investigation support the observations made by other groups in previous shift work studies. Eastman et al. have previously described the use of goggles in a

simulated shift work study. In a 2x2 experimental paradigm, they examined the effect of a bright light treatment, goggles use, and combinations of the two on circadian adaptation to a 12-hour shift in the sleep-wake schedule. Certain dissimilarities exist between what was recreated in the Eastman simulation and what was observed in the present study. First, subjects not receiving bright light in the Eastman study were to remain in light of <500 lux (mean levels were not documented). In the field, it was rare that subjects not receiving bright light were exposed to light as high as 500 lux at eye level. Further, Eastman's control of morning light exposure with goggles of 1% visual light transmission may have been offset by the effect of naps taken by the subjects outside the prescribed sleep episode. Finally, following the simulated shifts, Eastman observed both phase advances and delays. In the present study, almost all subjects, including those without bright light and shaded goggles, revealed phase delays. However, since continuous measurements of circadian phase under field conditions are not as reliable as those under controlled conditions (Klerman et al., 1999), we can only assume that the changes we observed were indeed phase delays. Nevertheless, the results reported here are in line with those of Eastman, as phase shifts observed with the combined bright light and appropriate darkness were of the greatest magnitude. It is of particular interest that Eastman et al. noted that phase shifts observed in the goggles-alone condition and the bright light-alone condition were approximately equal. From these results it may be possible to infer in the context of this study, that bright light treatment and regular sleep/dark periods may have had distinct roles in the process of resetting and stabilising shifts of the pacemaker throughout the ambulatory period.

Czeisler et al. (1990) have also previously described the complete readaptaion of a group of simulated night shift workers to their inverted schedule. Certain elements of our investigation reflect what was performed in the Czeisler study. In both studies the treatment group was given a regimen of bright light timed to phase delay, and a regular 8-hour period of darkness in the morning. However, in the Czeisler study, the treatment group wore no protection from morning light, and the control group was given no instruction as to the sleep/dark schedule. Nevertheless, a robust phase delay was observed in the treatment group following only 4 cycles of the regimen, with one week separating the initial and the final constant routines. The mean phase delay observed in the temperature and melatonin rhythms of our treatment group were comparable to those observed in this study, while the shifts observed in the present study's control group were larger.

Preliminary results from a study by Horowitz et al. (2000) describe the effects of regular sleep/dark scheduling and a bright light intervention, and the interactions of the two. Four groups of subjects were set on simulated work schedules under either bright light (~2500 lux) or room light (~150 lux), and on a fixed or free sleep/darkness schedule. It was noted that both the fixed sleep/darkness schedule group and the bright light group displayed significant shifts and that the effects of both interventions together were additive. While the shift workers in the present study's control group remained in their habitual work environments, they too underwent an intervention. They, like subjects in the treatment group and those of the Horowitz fixed schedule group, were instructed to maintain a regular, morning, 8-hour sleep/darkness period, and to abstain from taking naps. The initial results from the Horowitz laboratory study directly predict what is observed in the present study, where the group of subjects given only a fixed schedule displayed significant phase shifts in the physiological markers of the endogenous circadian pacemaker.

The phase shifts we observed in the control group may be explained by the schedule of exposure to light. By inciting sleep episodes in the morning, a significant portion of the phase advance section of the phase response curve is not exposed to light. Also, a majority of control group subjects described here were studied in the summer. Therefore, where the pattern of light exposure at this latitude has been described (Hébert et al., 1998), control group subjects may have been exposed to a significant amount of evening light. In the context of the biological effect of light of limited intensities (Boivin et al., 1996), it is possible that a phase delay signal may have been given to the pacemaker of control group subjects by evening light. In support of this possibility, it has been demonstrated that the human circadian pacemaker exhibits no dead-zones in its light-induced resetting capacity, and is therefore sensitive to light throughout the day (Jewett et al., 1997). Moreover, the relatively dim levels of light exposure typical with the control group subjects' days, as a background to an evening light exposure, may have also influenced the shifts in observed rhythms (Czeisler et al., 1989; Jewett et al., 1997). Thus, it may be proposed that intervention given in this study acts by improving control of the pattern of light exposure. In the treatment group, the control of the overall pattern of light exposure, (including an artificial bright light exposure during the work shift) may have rapidly induced the phase delay in a period comparable to that of the studies mentioned above (Czeisler et al., 1990; Van Cauter et al., 1994; Horowitz et al., 2000). Indeed, Eastman, in a night shift work simulation (Eastman, 1992), found that a timed bright light exposure could shift the oscillation of the endogenous circadian pacemaker to a 12-hour shift in the sleep-wake schedule at a rate of about ~2 hours/day. It would be expected, therefore, that if this intervention was evaluated sooner in the course of the ambulatory period, we would observe a more marked difference between the phase shifts of the two groups. For the control group, the regulation of the pattern of exposure to light may have promoted phase adaptive phase delays by virtue of the endogenous pacemaker's sensitivity to light even of dim intensities. In fact, a number of control group subjects suggested that the maintenance of a regular sleep schedule improved their quality of life.

It is a possibility that the control group results are the artefacts of a healthy worker's effect in this population (Koller et al., 1978). Sack et al. (1992) have previously observed that certain shift workers do spontaneously adapt to the night schedule. Further still, several groups have suggested that age may play a significant role in this process of 'natural adaptability'. Quera-Salva et al. (1996) have described a population of workers natually displaying a circadian adaptation in which younger workers predominate. This observation is supported by Campbell (1995), who suggests that middle-aged subjects may have a more difficult time adapting to night shifts. While our groups were evenly distributed in age, they were, on average, slightly younger than the reported "middle age". However, the limited sample size in the present study prevents us from analysing the effect of age or gender in circadian adaptation to night shift work.

The exclusion of subject s02, from the analyses described herein, was strictly on the basis of non-adherence to the required schedule of a single daytime sleep/dark episode. It is of note, however, that this subject's schedule of a truncated, main sleep episode along with daytime naps not only closely represents the status of the typical shift worker, but is in fact a sleep schedule that has been recommended to night shift workers (Åkerstedt, 1998). Since this subject received the treatment and did not adhere to the sleep/darkness indication, the results obtained may provide insight into the effectiveness of the components of this intervention regimen. The impact of the regularity of the sleep schedule, and, of the exposure to light in between daytime naps will have to be further qualified in future studies.

The return to a diurnal schedule as of the first night off (Table 2), as observed in our study group, is commonly observed in night shift workers (Bjørvatn et al., 1998; Quera-Salva et al., 1996; Bjørvatn et al., 1999).Our data seems to speak against the suggestion that shifting the shift worker to the work schedule may be deleterious to the workers ability to function on days off (Budnick et al., 1995; Dawson et al., 1995; Monk, 2000). In our groups, mean sleep times on days off (set by the individual), were longer and seemed to reflect a response to sleep deprivation accrued during night work. Proper phase alignment of the circadian pacemaker to the sleep-wake cycle positively influences the quality of sleep, physiological responses and performance in the night shift worker. Moreover, the intervention provided in this investigation seems to offset the appearance of medical symptoms frequently associated with night work. Further investigations are required to distinguish this effect from a possible placebo. This study clearly shows the efficacy of an intervention consisting of bright light and a regular schedule of sleep/darkness in the field. It supports, in a practical context, the proven importance of the pattern of exposure to light to the oscillation of the endogenous circadian pacemaker. While it would have been worthwhile to include a measure of the workers' subjective rating of the efficacy of the intervention, it seems unlikely that a placebo effect could justify phase shifts of physiological variables as observed in the treatment group. Even pharmacological approaches to overcoming shift work such as melatonin (Deacon & Arendt, 1996; Playe, 1999; Dawson et al., 1995) could exert their most important effect by inhibiting exposure to light at key times. Although the present study included only shift workers in the hospital environment, we may safely presume that the physiology of circadian adaptation would be similar in workers in other settings (i.e. industrial). We may therefore make practical, directed recommendations with respect to light exposure and the control of the sleep-wake cycle, which may promote circadian adaptation night work in the average shift worker.

CONCLUSION

The primary aim of the present study was to test the efficacy of an intervention regimen based on principles of circadian physiology in the adaptation of workers to a full-time schedule of night work. The proposed intervention sought to control the exposure to light and darkness throughout the day in order to promote a shift of the circadian pacemaker to a new internal hour. Thus, the pacemaker would adopt a more harmonious alignment with the shifted sleep-wake cycle of the night shift worker and would more closely approximate the phase relationship of a permanent day worker. It is expected that a long-term result of this approach would be to reduce the numerous somatic symptoms and medical complications frequently associated with work at night, while simultaneously increasing worker productivity and job satisfaction. Indeed, previous studies have demonstrated that a judicious exposure to bright light and to darkness may be effectively used to treat adaptation difficulties of circadian etiology including circadian maladaptation to night shift work. By extension, this approach may be used to in the promotion of worker adaptation to a non-conventional work schedule. To our knowledge, the present study is among the first to combine a field study investigation with a sophisticated approach to the study of human circadian rhythms in the laboratory.

Thus, in confirmation of the specific study hypotheses delineated at the onset of this investigation, we may affirm that:

1. an intervention including a 6-hour intermittent exposure to bright light (~2000-7000 lux) in the workplace, the wearing of tinted goggles during the morning commute , and the maintenance of a regular schedule of sleep/darkness can accelerate the adaptation of the human circadian pacemaker to a schedule of night work. This adaptation manifests itself as a harmonious phase relationship between circadian rhythms of core body temperature and salivary melatonin concentration and the shifted sleep/wake schedule. Thus, the phase relationship between the endogenous circadian pacemaker and the sleep/wake cycle is comparable to that observed in this population during the circadian evaluation following a period of day-oriented life. In the absence of this intervention, a misalignment between the circadian pacemaker and the sleep/wake cycle persists.

2. the intervention regimen tested herein can improve the quality of daytime sleep of night shift workers. Indeed, in the treatment group longer sleep period lengths were observed in the home following a succession of night shifts. Furthermore, the temporal distribution of REM in diurnal sleep was comparable to that observed in the initial nocturnal sleep episode. This suggests that an alignment between circadian phase and the sleep-wake cycle is re-established. While reports of subjective vigilance obtained during ambulatory and laboratory observations are more difficult to interpret, they consistently indicate a more appropriate alignment of the circadian pacemaker with the sleep/wake schedule in the treatment group. This finding warrants further investigation with the use of more sophisticated objective measures of vigilance and performance.

3. The intervention regimen tested herein can effectively reduce certain symptoms frequently associated with night work. This observation is surprising considering this

study's limited observation period. It would be of utmost importance to distinguish this observation from any placebo effect in longer and more detailed studies.

Further conclusions may also be drawn on the basis of the results reported here:

4. The maintenance of a regular schedule of sleep/darkness may account for the partial circadian adaptation observed in the control group. This observation is easily translatable to the workplace, and its concept is readily applicable as a counter-fatigue measure for night shift worker. We suggest that the use of phototherapy in the workplace accelerates circadian adaptation by reducing the time required for the reentrainment of the circadian pacemaker to an inverted sleep/wake schedule. The sampling of circadian markers to chart the progression of circadian adaptation throughout the ambulatory period would have been necessary to test the validity of this hypothesis. Subsequent investigations will more closely address this question.

5. An important aspect of the intervention regimen was the careful exposure to light and darkness throughout the day. This was achieved via a comprehensive approach including bright light exposure in the workplace, the shielding from morning light with the use of tinted goggles, and the maintenance of a regular schedule of 8 hours of sleep/darkness. We suggest that this comprehensive approach is most effective since, as the results described herein will confirm, an approach using only one of the three aspects of this intervention will result in an incomplete circadian adaptation. The recommendations derived from this observation may have serious economic implications. Thus, an impetus is in place for subsequent studies that will serve to elucidate the specific contribution of bright light versus dark goggles in circadian adaptation to night work.

6. This study has also served to confirm the practicality of the treatment and the applicability of the results to the work environment. Indeed, phototherapy may be effectively used in the workplace even when exposure to bright light is intermittent.

7. The proposed intervention regimen retains its beneficial aspects even as the night worker returns to a day-oriented schedule on days off

Finally, the results of this study allow the formulation of practical recommendations for full-time night shift workers.

1. Avoid naps during night shifts. While napping may have an immediate alerting effect, it may significantly hinder the consolidation of a daytime sleep/darkness episode, thereby undermining the capacity for circadian adaptation to the night schedule.

2. Keep sleep quarters as dark as possible during the main daytime sleep episode.

3. Wear tinted lenses during the morning commute home in order to minimize the effect of cues to the circadian pacemaker that promote synchronization to day-oriented life.

4. During night shifts, keep the workplace as bright as possible. When possible, make use of phototherapy lamps, even if exposure is intermittent.

It must be emphasized that these recommendations are directed to those working full-time night shifts. The plight of workers on rotating schedules is more complex, and a set of recommendations would have to be specifically devised and tested for this population.

The efficacy of any fatigue-management program lies primarily in its sensitization of the night workers' environment to the inverted work schedule. While this aspect was not directly addressed in the scope of this investigation, all of the workers described in this study were in situations supportive of their maintenance of a regular sleep-wake schedule. One subject (s02) did not conform to the study directives and showed no adaptation in the control or the treatment condition.

APPLICABILITY OF THE FINDINGS

The circadian physiology of the shift worker is an integral part of factors affecting work-related activities. It is conceivable that future investigations on the circadian rhythms of the shift worker will form an important part of the IRSST established scientific mandate (Bourdouxhe et al., 1997). This investigation is already in line with the organization's specific goals and integrates 20 years of advances in the study of circadian physiology. This study takes as one of its primary aims to promote the transfer of scientific information from the academic milieu to those principally implicated with night shift work. Moreover, the nature of this investigation has permitted the testing of academically based hypotheses in the practical milieu, thereby ascertaining a concept of its general applicability. Thus, despite heavy workplace demands, hospital workers from the greater Montreal area have gained substantial benefits from appropriately-timed phototherapy treatments in the workplace. It has been established that bright light has an immediate effect on the human circadian pacemaker of the night shift worker, and that this effect is sustained, even the worker is away from the light source. (Rimmer et al., 2000)

The present study has demonstrated that an intervention regimen based on principles of circadian physiology is both practical and effective in its application to night shift workers. Those working full-time night shifts can avoid naps during the night shift, and consequently consolidate the main sleep episode into a single period after the end of the night shift. We suspect that this simple practice can account for the partial circadian adaptation observed in control group subjects. Effectively, the observed adaptation in the control group was better than initially anticipated. We reason that the bright light treatment in the workplace and dark goggles during the morning commute accelerate the process of circadian adaptation to the inverted sleep-wake schedule. This interpretation justifies for the increased sleep and waking quality observed after a period of consecutive night shifts. The more appropriate alignment of circadian rhythms of core body temperature, salivary melatonin and subjective vigilance to a night-oriented schedule in the treatment group also confirm this conclusion. The findings of this investigation clearly support the use of bright light therapy in the workplace in the promotion of circadian adaptation to full-time night shift work. The use of intermittent light introduces the possibility that phototherapy may be used to some benefit in a number of work environments.. Further study will elucidate the practical limitations of such an approach in the workplace. The maintenance of regularly-timed sleep episodes in darkened quarters as well as the wearing of dark goggles during the morning commute must be evaluated as inexpensive and potentially effective components promoting circadian adaptation to night work. The latter approaches may be especially applicable in work environments when a phototherapy regimen is impractical (e.g. truck drivers, or police officers).

IMPLICATIONS OF THE FINDINGS

The results of the current study serve to confirm the efficacy of an intervention regimen including bright light in the workplace in circadian adaptation to night shift work. The results of this study have already been presented at the '**Comité Scientifique'** and the '**Comité d'exploitation des résultats de la recherche'** of the IRSST January 24th, and March 13th , 2001, respectively. The findings of this investigation have been presented in a number of regional and provincial scientific meetings (see list). The results have also been accepted fore presentation at the next annual meeting of the **Associated Professional Sleep Societies (APSS)** to be held in Chicago, June 2001. Further, these results were the basis for the development of a symposium entitled ***"Circadian adjustment to shiftwork: How much should bright light interest us?"***, conceived by the principal investigator of this study, and to be held at the aforementioned meeting. This investigation was also the subject if a Master's thesis submitted to the department of Psychiatry of McGill University. The author of the memoir, Ms. Francine O. James, was the graduate student in charge of this project. It is expected that these results will form the basis of three scientific publications to be submitted this year on circadian adaptation to night shift work, the improvement of daytime sleep quality with phototherapy, and the improvement on workplace vigilance levels with bright light treatment in the workplace. Among the peer-reviewed journals to be considered in the publication of this data are **Annals of Internal Medicine**, **Ergonomics**, **Sleep**, and **Work and Stress**. It is also expected that a number of non-academic articles will be written in order to disseminate the findings of this investigation to night shift workers and their employers. Among the vehicles sought to achieve this goal will be the journal of the '**ASTASS'**, and the journal of the *'Association Sectoriale des Affaires Sociales* , **'Objectif Prévention'**. Other media to be targeted will include the on-line journal **'Piste',** and the bulletin of the **F.I.I.Q.** (*Fédération des Infirmières et Infirmiers du Québec*). Physicians in the province will also be alerted to the significance of the findings via journals such as **'Le Clinicien'** or **'Le Médecin du Québec',** journals in which the principal investigator publishes regularly. The results of this investigation will additionally be given forum at the meeting of the **'ADHSST'** in Mont Saint-Sauveur, to be held in 2002, and at the first public forum of the **Association of Workers' Compensation Boards of Canada** to be geld in Toronto in November 2001. The later conference, entitled ***'Research Solutions: putting research to work to reduce work-related injury and disease'*** involves the participation of work accident commissioners from across the country and seeks to accelerate the transfer of research-derived knowledge to those primarily affected in the workplace environment.

The results of the current investigations support the use of appropriately timed phototherapy in the workplace in the promotion of circadian adaptation to night shift work. We have also demonstrated that the maintenance of a regular schedule of sleep/darkness in darkened quarters, and the wearing of tinted lenses during the morning commute following a night shift, may be effective, inexpensive, and practical measures to promote circadian adaptation to night shift work. The validation of the potency of these approaches will stem from subsequent investigations. An information session designed to disclose the results of this study is envisaged. Night shift workers, Nursing Directors, Human Resources Managers, and Health and Safety Representatives of the sponsoring hospitals will be invited to participate. We expect that the findings of this study are convincing enough to support important changes in current concepts on the hygiene of work, sleep and circadian rhythms in the shift worker. The integration of the principles discussed herein in fatigue management programs for night shift workers is practical

and feasible. The principal investigator in this study is presently initiating a similar program for fatigue management in Canadian truck drivers with the collaboration of the '***S.A.A.Q.***' and **Transport Canada**. This investigation will form the basis for the inception of a new study proposal on the development of practical interventions for the promotion of worker adaptation to rotating and complex work schedules. The pursuit of this line of investigation towards the development of effective interventions is indeed of primary consequence to the health and safety of Quebec's workforce.

SCIENTIFIC PUBLICATIONS

1. James FO and Boivin DB. Adaptation to night shift work via a regular schedule of sleep/darkness. Presented at the **Department of Psychiatry Student Research Day**, McGill University, June 2000, Montreal, Qc, Canada.

2. James FO and Boivin DB. 'Impact the la régularité de l'horaire de sommeil sur l'adaptation au travail de nuit'. Presented at the '**Journée Scientifique du Réseau de Recherche en Santé Mentale du Québec du FRSQ'** June 2000, Montreal, Qc, Canada.

3. James FO and Boivin DB. Circadian adaptation to full-time night shift work with bright light treatment in the workplace. Presented at the **McGill Psychiatry Research Day**, November 2000, Montreal, Qc, Canada.

4. James FO. Circadian adaptation to full-time night shift work with bright light intervention regimen. Masters thesis submitted to the **Faculty of Graduate Studies and Research, Department of Psychiatry**. Mc Gill University. March, 2001. *Supervised by D. B. Boivin.*

5. James FO and Boivin DB. Circadian adjustment to night shift work with a bright light intervention regimen in the workplace. Accepted for oral presentation at the **15th Annual Meeting of the Associated Professional Sleep Societies,** June 2001, Chicago, IL, U.S.A.

6. James FO. 'Adjustment circadian au travail de nuit avec intervention de lumière vive.' Presented at the '**Séminaires-étudiants du Centre de Recherche en Sciences Neurologiques**,' University of Montreal, Montreal, Qc. Canada.

7. Boivin DB (Chairman). Circadian adjustment to shiftwork: how much should bright light interest us? **15th Annual Meeting of the Associated Professional Sleep Societies,** June 2001, Chicago, IL, U.S.A.

8. James FO and Boivin DB. Judicious control of the pattern of light exposure in circadian readaptation to night shift work. Presented at the **First Scientific Meeting of the Canadian Sleep Society**, May 2001, Ottawa, On, Canada.

RESEARCH TEAM

The nature of this experimental series, both in its design and in its duration, demanded the talents of a significant number of persons. Night shift workers were first approached in their place of work for their participation in this study. This was possible through the willing intervention of Occupational Health and Safety managers, Human Resources Directors and Directors of Nursing. In-laboratory studies were performed within the specially designed temporal isolation suites of the **Center for Study and Treatment of Circadian Rhythms** within the **Douglas Hospital Research Centre** as affiliated with the **Department of Psychiatry of McGill University**. Finally, all ambulatory observations were performed within the department of the participating workers, under the auspices of the hospital of employ. The recruitment of night shift workers, the sophisticated study of circadian physiology in the laboratory, and the testing of the intervention in the workplace, performed over a 4-year period required a significant team effort.

This study was conceived and directed by **Diane B. Boivin** (Ph.D. Neuroscience; M.D.; Assistant Professor, Department of Psychiatry, McGill University; Director, Center for Study and Treatment of Circadian Rhythms, Douglas Hospital Research Centre), who designed the experimental protocol, initiated contact with health care centres in the greater Montreal area and directed information sessions for interested night shift workers, and their employers. Dr. Boivin is the scientific investigator, supervisor, and the principal author of this report.

The results of this investigation were the basis of a Master's thesis presented to the Department of Psychiatry of McGill University by **Francine O. James** (M.Sc. Psychiatry, B.Sc. Immunology). Ms. James was responsible for the daily denouement of the experimental series and was implicated in the co-ordination of night shift worker participation and the harmonisation of their work schedules and experimental participation. She was also responsible for data collection during ambulatory study, and the treatments of data analyses presented herein.

Data collection within the cadre of this study took place on several fronts. Within the setting of the Center for Study and Treatment of Circadian Rhythms, **Anthony Hosein** (B.A., Psychology, Chief Technician) co-ordinated experimental staffing and the collection of physiological samples, and was implicated in the treatment of the data discussed within the cadre of this report. Several research assistants and medical students were also implicated in the collection of data and preliminary analyses. A substantial aspect of this study comprised of the evaluation of sleep via polysomnography. Ms. **Élyse Chevrier** (technician in medical electrophysiology) was responsible for the quality of sleep recordings performed both in the laboratory and during the ambulatory period. She supervised, and subsequently scored all polysomnographic recordings.

This study was represented a significant learning opportunities for a number of students in McGill University's Faculty of Medicine, including **Harris Constantatos, Alain Bestawros,** and **Seetha Radhakrishnan,** who where involved in the collection and the analyses of data. **The staff of the Center for Study and Treatment of Circadian Rhythms**, including a number of research assistants and technicians too numerous to be mentioned within this space, provided a concerted effort towards the completion of this project and the creation of this document.

The author wishes to thank Ms. **Nicole Dubuc** of the Douglas Hospital Reach Centre for her invaluable editorial assistance in the preparation of this report.

ACKNOWLEDGEMENTS

This study was hinged upon the willing participation of a group of dedicated shift workers and their employers. The investigator wishes to recognise the sponsoring hospitals and their Human Resources Directors, Nursing Directors, and Health and Safety Officers who first, deemed the issue a priority, and second, designated the appropriate funds and time required for workers' recruitment and participation. Indeed, a number of hospitals approached were receptive to the study concept, and planned outreach and information sessions for their night workers. The investigator is grateful for the commitment shown by these institutions. The investigator particularly wishes to acknowledge the health centres sponsoring night shift workers' participation, namely **Douglas Hospital**, the ***Institut de Réadaptation de Montréal***, ***Hôpital Notre-Dame-de-la-Merci***, ***Hôpital Jean-Talon,*** the ***Centre Hospitalier de l'Université de Montreal – Pavillon Hôtel-Dieu***, ***Hôpital Charles-LeMoyne, Hôpital Maisonneuve-Rosemont***, and ***Hôpital Ste.-Justine***. These institutions, the departments and colleagues of the participating workers and the departmental co-ordinators welcomed and enabled the essential presence of the research team within the hospital milieu. Indeed, they were among the agents for the success of this investigation.

The shift workers participating in this investigation deserve a particular vote of thanks. Those who participated in this study showed genuine interest in the study matter, and gave freely of their time, as supported by their families, friends and colleagues. The investigator particularly values their contribution. Indeed this document is partly the fruit of their labour.

This investigation was sponsored by the IRSST, who value the merit of research and its application to the workplace. The investigator is particularly indebted to **Manon Truchon** (Ph.D., Scientific Advisor) who provided invaluable counsel on the direction of this study.

FIGURES AND TABLES

TABLE 1.
SUMMARY OF NIGHT SHIFT WORKERS PARTICIPATING IN THIS STUDY.
Subject data including the subject posting at the tifme of the study, years of experience of full time night shift work, and season of study are shown. Groups were comparable on all parameters shown. All participants met the minimum requirement of 8 shifts/15 days to participate in this study. The total number of shifts included in the ambulatory observation (mean ± S.E.M.: 12.2±0.25 and 11.9±0.1) was also comparable between groups. However, the temporal organization of shifts and off days varied according to the habitual staffing practices of the sponsoring hospital. Schedules were as follows: (a) 6 on / 4 off, (b) 3 on/ 1 off / 3 on / 3 off, (c) 9 on / 5 off, (d) 5 on / 2off.

Table 1. Summary of night shift workers participating in this study.

SUBJECT	HOSPITAL SERVICE	SEX	YEARS OF FULL TIME NIGHT WORK	AGE	SHIFT SCHEDULE TYPE	SEASON OF STUDY
			CONTROL GROUP			
s02	Psychiatry	F	9	43.5	a	fall
s03	General medicine, readaptive services	F	8	45.4	b	winter
s05	General medicine, readaptive services	F	24	43.2	b	summer
s06	General medicine, readaptive services	M	16	40.0	b	summer
s07	Cardiovascular medicine	F	20.8	51.5	b	summer
s11	Intensive care	F	5.5	25.9	c	spring
s12	Intensive care	M	0.8	47.7	c	summer
s13	General medicine	F	16	38.2	c	summer
s14	General medicine	M	21	42.5	b	summer
MEAN			**13.5**	**42.0**		
SD			**8.0**	**7.2**		
N			**9**	**9**		
			TREATMENT GROUP			
s02	Psychiatry	F	9.4	43.9	a	spring
s03	General medicine, readaptive services	F	8.7	46.1	b	fall
s04	General medicine, readaptive services	M	0.04	49.1	b	summer
s06	General medicine, readaptive services	M	17.0	41.0	b	summer
s07	Cardiovascular medicine	F	20.0	50.6	b	summer
s08	General medicine, readaptive services	F	9.0	53.6	b	summer
s09	Nephrology	F	9.0	30.6	c	summer
s10	Neurosurgery	F	17.0	38.2	c	spring
s15	Pediatric medicine	M	2.0	25.9	c	summer
s16	General medicine	M	1.0	38.0	d	spring
MEAN			**9.3**	**41.7**		
SD			**7.0**	**8.8**		
n			**10**	**10**		
p			0.2	0.9		

TABLE 2.
BEDTIMES DURING AMBULATORY PERIOD.
Shown are times in and out of bed for control and treatment groups during periods following work days and days off. Times in and out of bed, were determined via sleep-wake logs kept by each subject, and confirmed by the results of actigraphy data. Mean times in and out of bed, and total times in bed were compared between groups (as reflected by p values). Control group subjects spent significantly more time in bed during days off than they did during sleep periods following work days (^{a}). Times in bed on work days and on off days were comparable (^{b}).

Table 2. Mean subject bedtimes during ambulatory period.

	SHIFT DAYS			DAYS OFF		
	Bedtime	**Time out of bed**	**Time in bed**	**Bedtime**	**Time out of bed**	**Total time in bed**
			CONTROL GROUP			
S03	10:21	17:34	7:13	1:46	10:32	8:45
S05	9:11	16:51	7:41	00:50	11:37	10:47
S06	9:31	16:27	6:56	00:54	8:24	7:30
S07	9:59	17:56	7:56	23:27	8:12	8:45
S11	9:33	16:16	6:42	22:41	7:54	9:13
S12	9:04	16:31	7:27	22:00	8:26	10:26
S13	9:24	17:35	8:11	00:00	9:17	9:21
S14	10:37	17:48	7:11	23:54	7:19	7:26
Mean	**9:42**	**17:07**	**7:25**	**23:56**	**8:58**	**9:02** [a]
SEM	**0:12**	**0:14**	**0:11**	**0:26**	**0:30**	**0:26**
			TREATMENT GROUP			
S03	9:51	17:37	7:45	00:30	8:23	8:20
S04	9:28	17:10	7:42	1:26	9:00	7:34
S06	9:23	16:56	7:33	1:18	10:05	8:47
S07	10:00	17:30	7:30	23:35	6:44	7:10
S08	9:30	17:37	8:07	23:44	8:31	8:47
S09	9:51	16:38	6:47	23:28	7:40	8:12
S10	9:11	16:40	7:28	23:26	7:50	8:24
S15	9:50	17:40	7:50	6:21	14:4	7:53
S16	10:08	19:12	9:04	23:59	8:51	8:52
Mean	**9:45**	**17:27**	**7:42**	**00:48**	**9:02**	**8:13**[b]
SEM	**0:08**	**0:15**	**0:12**	**0:44**	**0:43**	**0:12**
p	0.9	0.4	0.3	0.3	0.9	0.1

[a] comparison of sleep lengths on work days and days off within the control group, p=0.01
[b] comparison of sleep lengths on work days and days off within the treatment group, p=0.1

Table 3. Summary of physiological phase markers and their relations to the time of awakening. The phase angle is a measure of circadian entrainment or adjustment to the sleep-wake cycle. It is calculated in decimal hours as a difference between the habitual time of awakening (as reported and confirmed by actigraphy) and circadian phase (time of the fitted minimum of core body temperature, or the midpoint of the peak secretion of salivary melatonin). Statistically significant points (p-values) are shown for between and within group comparisons (initial versus final conditions: *a*, *b*, *c*, *d*, *e*).

Table 3. Summary of physiological phase markers and their relations to the time of awakening (expressed in decimal hours ± S.E.M.)

Core body temperature

	Initial condition			Following night work		
	Time of fitted minimum	Time of awakening	phase angle	Time of fitted minimum	Time of awakening	phase angle
Control group	4.87 ± 0.65	8.22±0.49	3.35 ± 0.46	8.96 ± 2.20 [a]	17.12 ± 0.24	8.16 ± 2.23 [c]
Treatment group	6.20 ± 1.23	8.32±0.40	2.12 ± 1.13	15.53 ± 1.00 [b]	17.44 ± 0.26	1.92 ± 0.88
p	0.5		0.5	0.002		0.002

Melatonin secretion

	Initial condition			Following night work		
	Time of midpoint of secretion	Time of awakening	phase angle	Time of midpoint of secretion	Time of awakening	phase angle
Control group	3.92 ± 0.49	8.22±0.49	4.30 ± 0.28	9.00 ± 2.48 [d]	17.12 ± 0.24	8.12 ± 2.54
Treatment group	3.79 ± 0.47	8.32±0.40	4.53 ± 0.30	15.09 ±0.97 [e]	17.44 ± 0.26	2.35 ± 0.88
p	0.9		0.9	0.003		0.004

[a] within group comparison, $F_{(1,15)}=7.30$, $p=0.02$
[b] within group comparison, $F_{(1,15)}=37.99$, $p<0.0001$
[c] within group comparison, $F_{(1,15)}=8.81$, $p=0.01$
[d] within group comparison, $F_{(1,15)}=8.36$, $p=0.01$
[e] within group comparison, $F_{(1,15)}=41.42$, $p<0.0001$

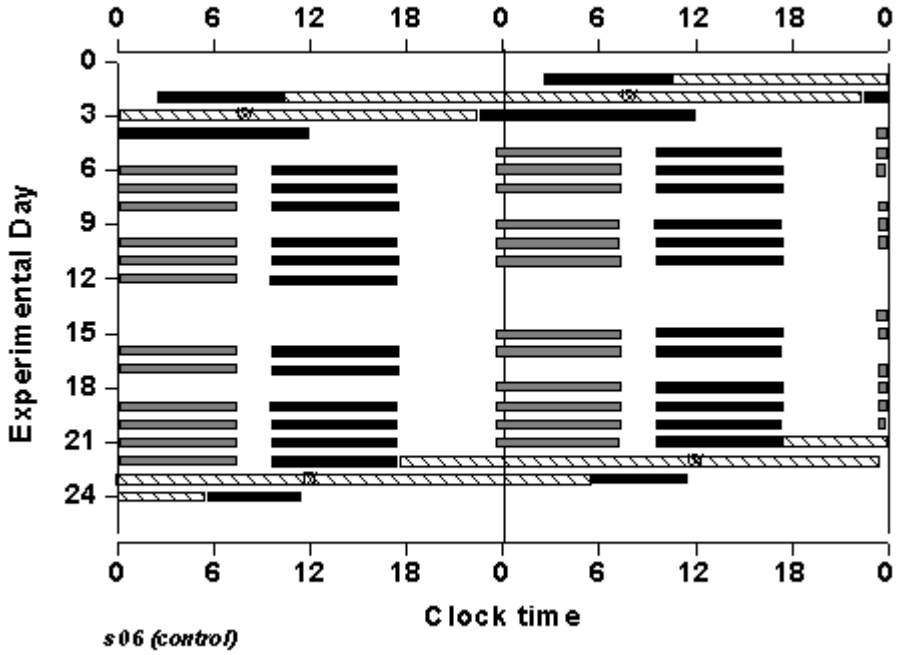


FIGURE 1A.
DOUBLE REPRESENTATION OF THE EXPERIMENTAL PROTOCOL, CONTROL CONDITION.
The course of the experiment for control group subject s06 is shown. The succession of experimental days is shown along the y-axis and side-by-side to aid visualization. Dark bars represent sleep episodes, and gray bars represent night shifts during which subjects were in their habitual lighting environments. Constant routines are indicated by hatched rectangles. Fitted minima of the core body temperature cycle, as determined for this subject during constant routines, are indicated by encircled **X**'s. Subjects, following a vacation period, entered the laboratory on the first experimental day, and slept on their habitual schedule. Upon awakening, subjects underwent a 36-hour constant routine for the determination of the endogenous phase of the circadian pacemaker. An *ad libitum* sleep episode was then scheduled. Subjects then returned to their regular schedule of night shifts, for a total of 12 shifts. They were instructed to remain in the dark and to attempt to sleep during a single 8-hour period beginning 2 hours after the end of the shift. Sleep episodes on nights off are not shown. A final 36-hour constant routine was performed in-laboratory following the period of night work and was followed by an *ad libitum* sleep episode.

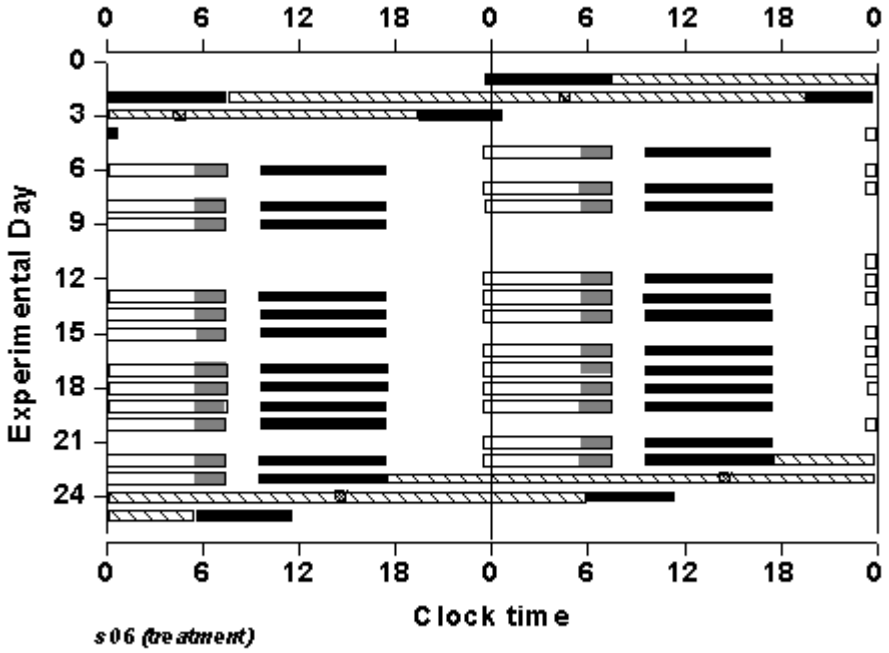


FIGURE 1B

DOUBLE REPRESENTATION OF THE EXPERIMENTAL PROTOCOL, TREATMENT CONDITION.

Legend is as described for **Figure 1A**. The course of the experiment for the treatment phase of investigation for subject s06 is shown. Night shifts are shown as open bars with gray tails to represent the 6-hour light therapy beginning at the start of the shift. The last two hours of the shift were spent in ordinary indoor illumination.

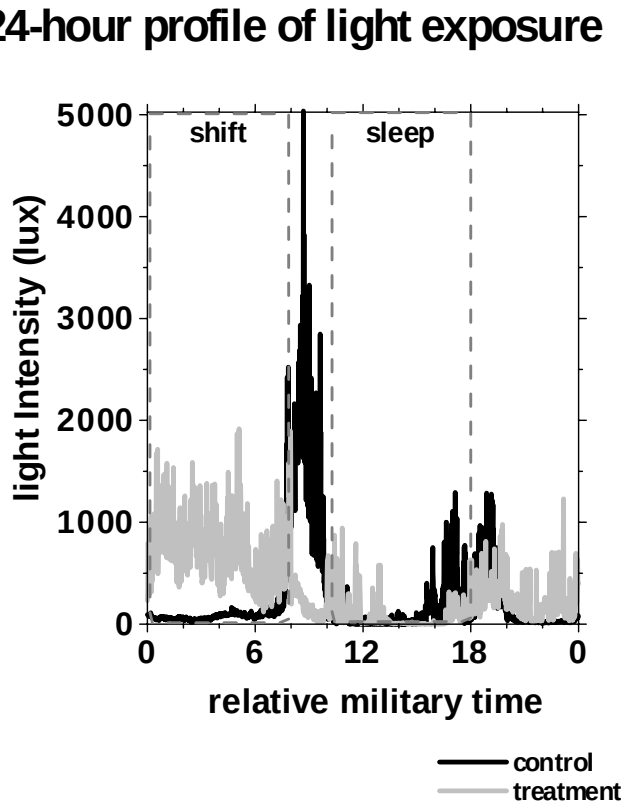


FIGURE 2.
PROFILE OF LIGHT EXPOSURE ON SHIFT DAYS.
The mean 24-hour profile of light exposure for control and treatment groups on shift days is shown. Subjects' light exposure profiles were determined from wrist actigraphy with light sensor, and were averaged after alignment to the time of the start of the night shift. To facilitate visual interpretation, group means are shown here relative to a shift beginning at midnight (relative military time). The eight-hour periods corresponding to the night shift and the daytime sleep period are delineated with dashed lines. Mean light exposure levels for treatment group, with the correction for goggles use at hours 6-8, are in gray. The light exposure profile for the control group is in black.

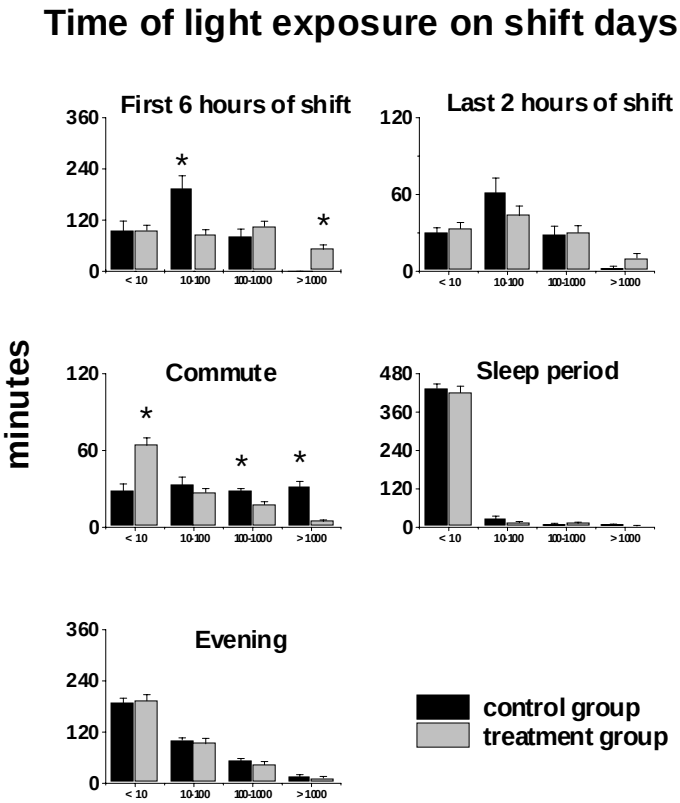


FIGURE 3.
MEAN EXPOSURE TO LIGHT LEVELS ON SHIFT DAYS.
As described in the Methods section, light exposure levels, divided into 4 bins of intensity, were quantified over 5 periods of the day. Average minutes of exposure to light per bin within a given intensity range, as determined from actigraphy and light sensor, are represented for each group. The five time periods represented here are (A) the first 6 hours of the night shift (the time during which subjects in the treatment group would have received bright light); (B) the last two hours of the shift; (C) the 2-hour commute window; (D) the time of the day sleep episode; (E) the period between the time of awakening and the time of start of the next night shift. Points of significant between-group differences are indicated (*).

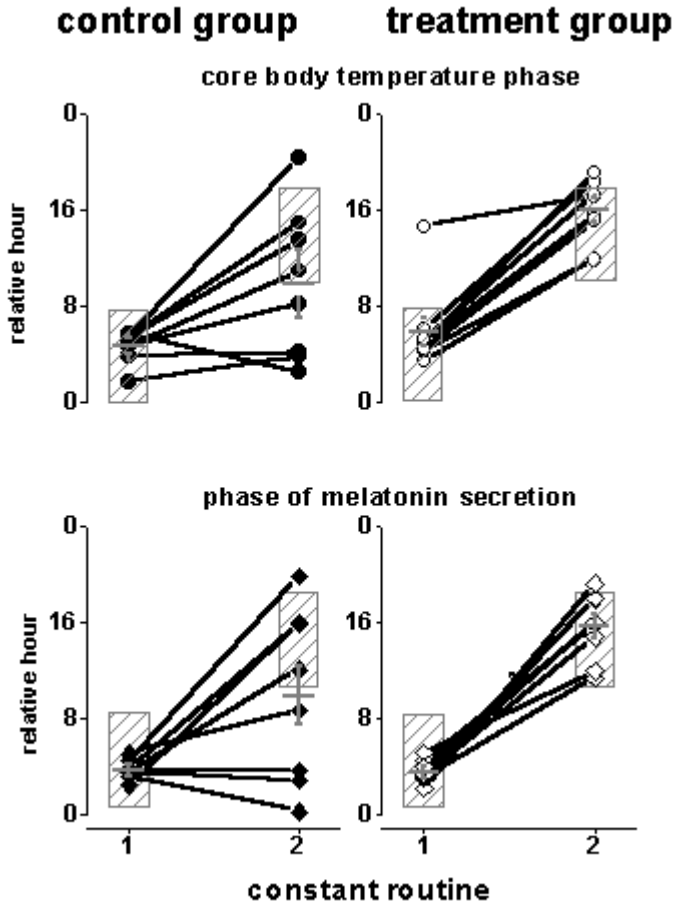


FIGURE 4.
PROGRESSION OF THE CIRCADIAN PHASE FROM A DAY TO A NIGHT-ORIENTED SCHEDULE.
The time of circadian phase, determined via the fitted minimum of core body temperature (upper panels) and the midpoint of melatonin concentration (lower panels) are plotted for each subject and are expressed relative to in-bed times (hatched rectangles). In order to facilitate interpretation, all subjects were assigned a relative bedtime of 00:00 for evening sleep episodes and 10:00 for morning sleep episodes. Control group subjects are represented with closed symbols, treatment group subjects are represented as open symbols. Mean circadian phase, plotted for the groups, is expressed as a horizontal bar (± S.E.M.).

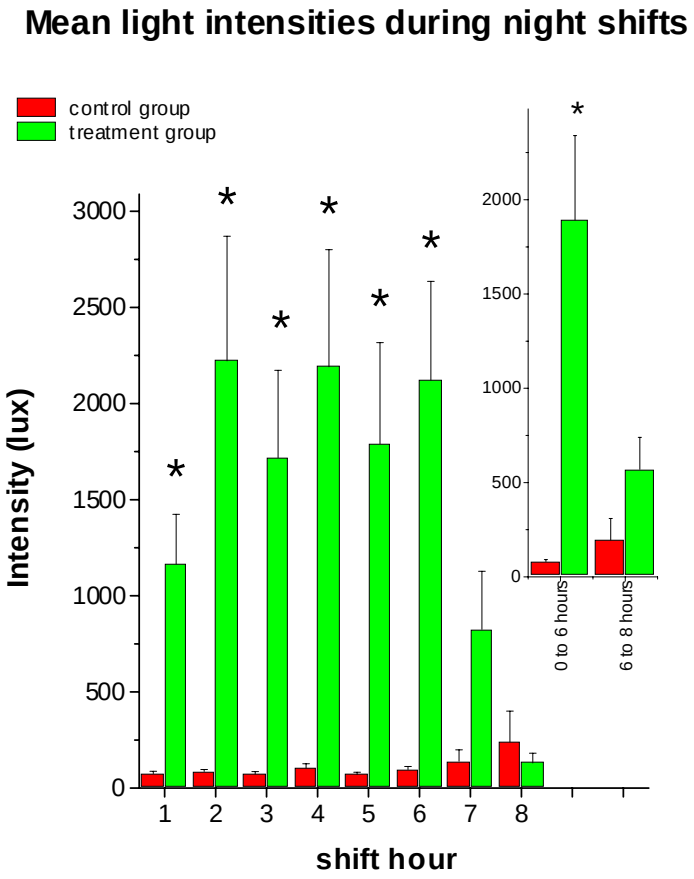


FIGURE 5.
MEAN LIGHT INTENSITY PER WORK HOUR.
Mean light intensities, as measured with research photometers at the level of the eye, are displayed per hour of the night shift. Statistically significant comparisons are shown with a (*). Mean light exposure for workers in the treatment group are shown with light bars, while those of the control group subjects are represented as dark bars. Error bars represent S.E.M. Group means for the first 6 hours and the last 2 hours of the shift are also represented.

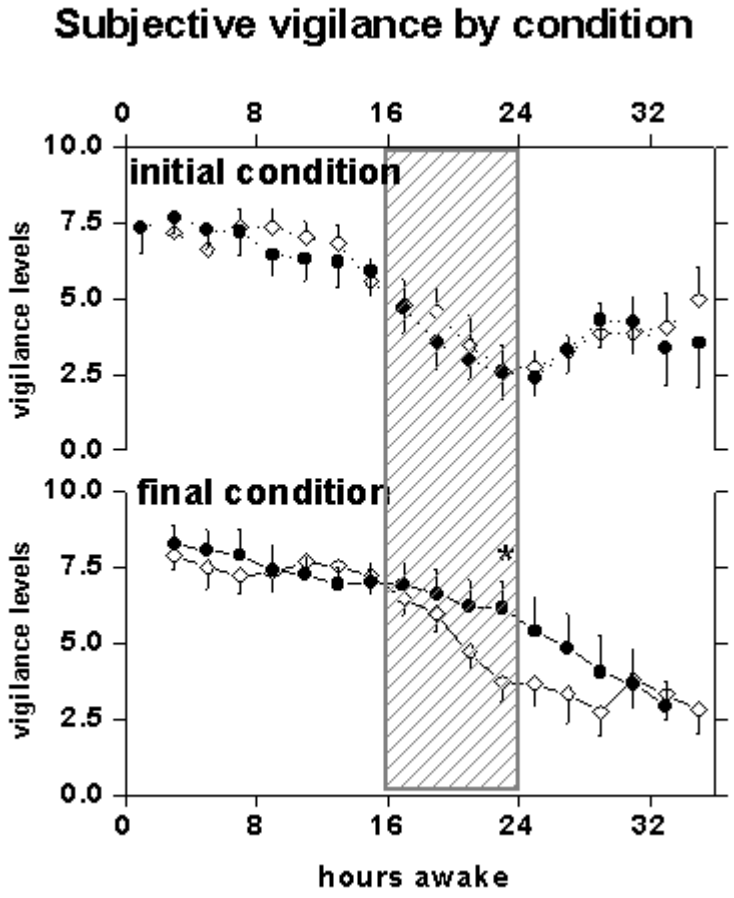


FIGURE 6.
SUBJECTIVE VIGILANCE BY CONDITION.
Self-rated alertness scores during the initial constant routine (upper panel) are expressed as a function of hours awake and are plotted in the middle of 2-hour bins. The variation of subjective alertness following the period of night shifts (lower panel) is plotted since the time of awakening from day sleep episodes following night shifts. The time of nocturnal or diurnal sleep episodes, projected into the constant routine, is shown as a hatched rectangle in the initial and final conditions, respectively. In the final condition, a significant difference in alertness (*) was detected between scores at the 23rd hour of awakening, ($p=0.04$).

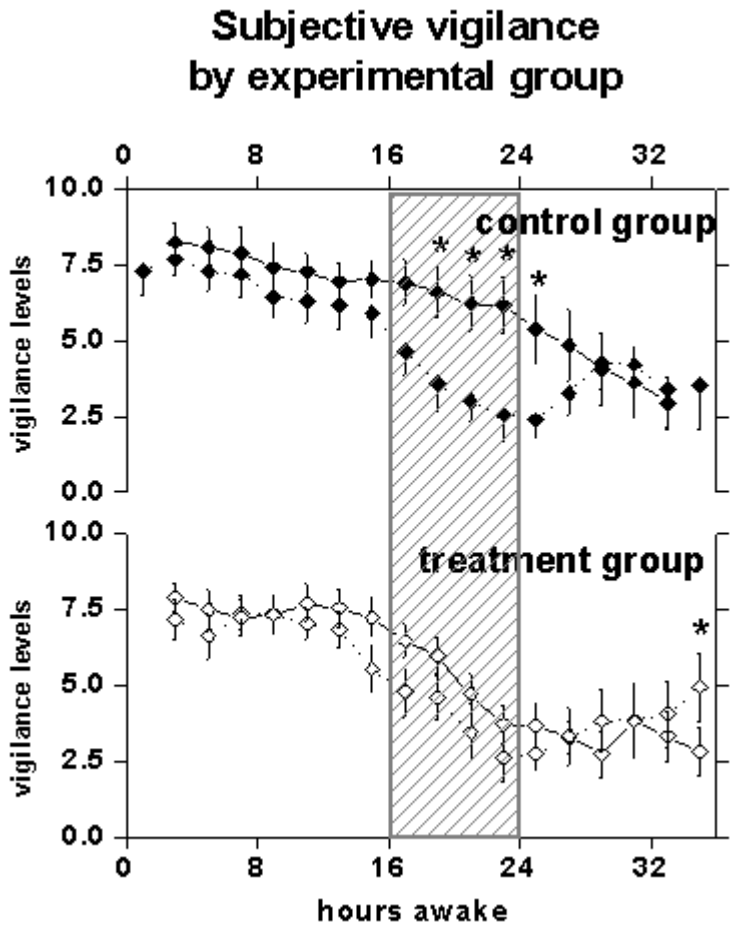


FIGURE 7.
SUBJECTIVE VIGILANCE BY EXPERIMENTAL GROUP.
The variation of self-rated alertness during the initial and final constant routines are expressed as a function of hours awake for the control group (upper panel) and the treatment group (lower panel). Legend is as in Figure 6 except the initial conditions of both group are shown as joined with dotted lines, and the final condition is joined with solid lines. Significant difference in alertness (*) was detected between the scores for the control group at hours at hours 19 (p=0.02), 21 (p=0.01), 23 (p=0.005), and 25 (p=0.02)

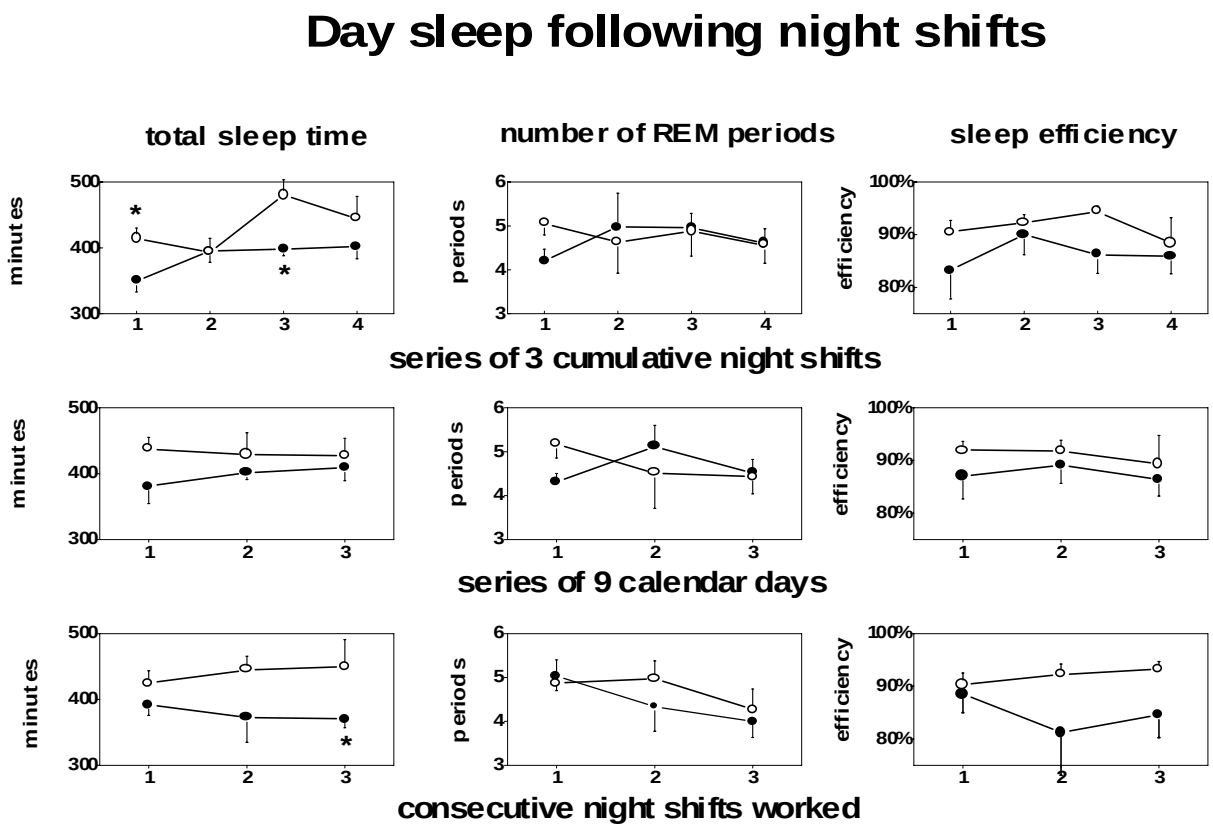


FIGURE 8.

DAY SLEEP FOLLOWING NIGHT SHIFTS.

The quality of daytime sleep episodes following night shifts is quantified as total sleep time in minutes (left column), number of REM periods (center column) and sleep efficiency as a percentage (right column) are shown. The variation of sleep quality per group is expressed according to the number of cumulative shifts organized in series of 3 (top row), sections of 9 calendar days (center row), and as function of the number of shifts worked in a row prior to the sleep episode (bottom row). Mean sleep parameters for the control group are shown as filled symbols while the treatment group is shown with open symbols. Error bars represent S.E.M. Points of statistical significance are indicated (*).

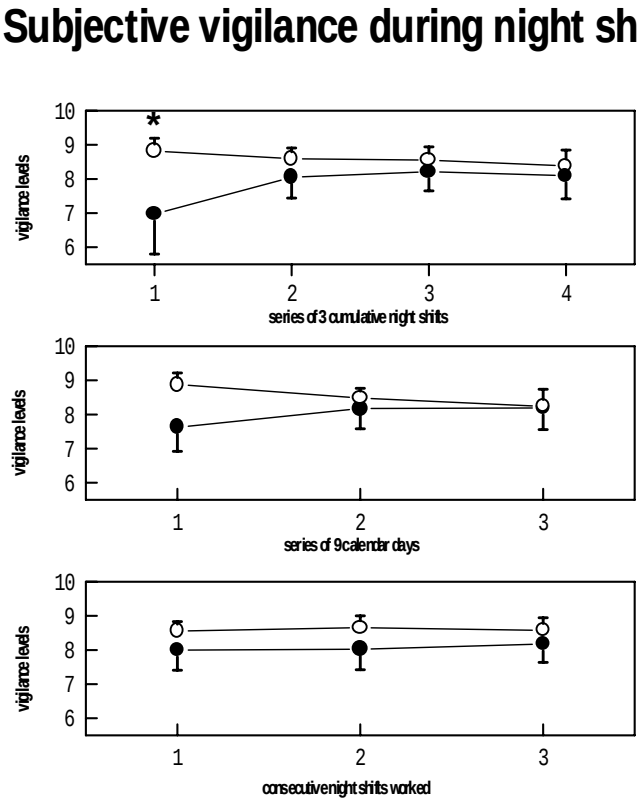


FIGURE 9.
SUBJECTIVE VIGILANCE DURING NIGHT SHIFTS.
Vigilance levels during night shifts are reported for the control (closed symbols) and treatment (open symbols) groups. Mean scores (± S.E.M.) are plotted as described in **Figure 8**.

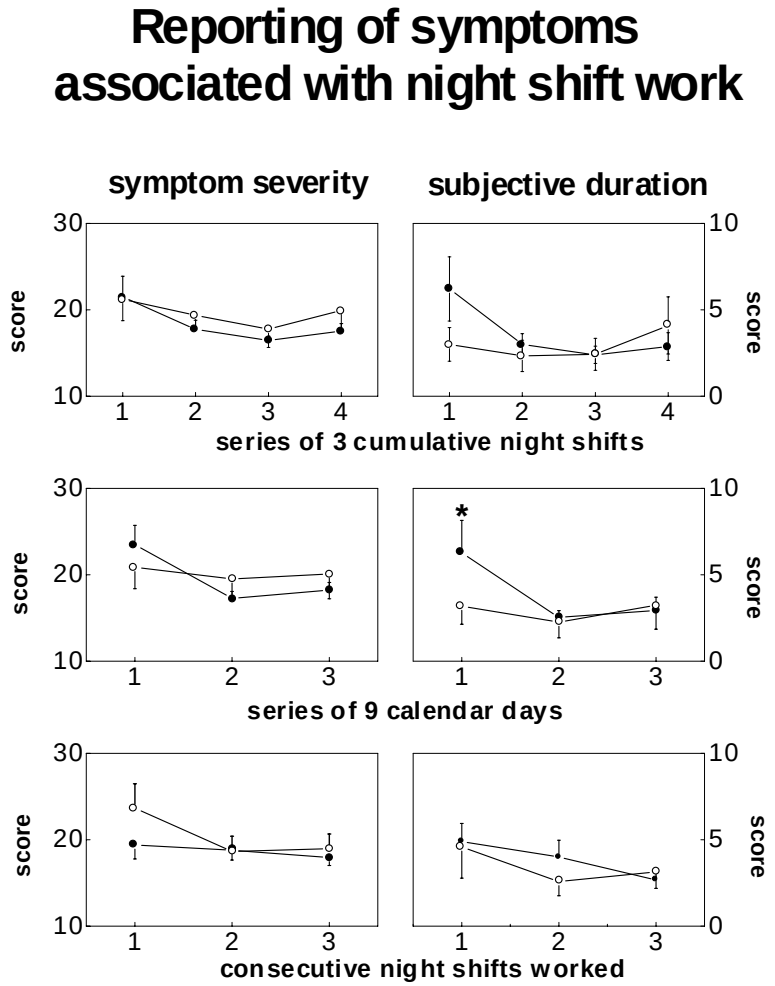


FIGURE 10.
MEDICAL SYMPTOMS ASSOCIATED WITH NIGHT SHIFT WORK.
Results from questionnaires describing the intensity and subjective duration of medical symptoms associated with night work given after each shift are shown here as described for **Figures 8**. Results for treatment group subjects are shown with open symbols; those for the control group are shown with closed symbols. All values are means ± S.E.M.. Statistically significant points are indicated (*).

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APPENDIX

A1. Consent form
A2. Sleep-wake log
A3. Symptom severity questionnaire
A4. Subjective symptom duration questionnaire
A5. Scientific Publications

A1. Consent form

McGill

July 5, 1999

RESEARCH CONSENT FORM

RESEARCH TITLE

Prevention of physiologic maladaptation to night-shift work by phototherapy

PRINCIPAL INVESTIGATOR: Diane B. Boivin, M.D., Ph.D.

PURPOSE

We would like permission to enroll you as a participant in a research study. The purpose of this study is to investigate how the lighting environment influences your daily rhythms of body temperature, hormone levels, urine production, vigilance, and sleep organization. It has been shown that these daily rhythms reflect the output of a biological clock, which is adjusted to its environment by exposure to light.

These studies in normal volunteers will help us understand how your biological clock is influenced by light. The results of this study will allow us to develop potential treatments for disorders of human biological rhythms such as misadaptation to jet lag and night work. This consent form asks for your permission to undertake the actual experimental procedures.

SCREENING

Before the start of study, you will be asked to undergo a series of routine medical procedures to ensure that you can safely participate in the study. These procedures may include: a detailed medical history and physical examination, questions about your family members, routine blood and urine tests, an ovulation test and documentation at home of your body temperature, a pregnancy test, an electrocardiogram, a chest x-ray, various questionnaires and/or interviews with a psychologist or psychiatrist. Before you give your consent, you will have the opportunity to visit the research facilities.

It is important to realize that your participation in any of these screening procedures does not guarantee you a place in the study, something, which will be determined on the basis of results from the above tests. If you successfully complete these screening procedures, you will be admitted to the laboratory as a research subject.

Throughout the course of the screening procedure and of the laboratory protocol, small samples of urine will be frequently collected to test for the presence of any prescription or non-prescription drugs, and street drugs, including alcohol. If any blood or urine tests indicate the use of any of these substances, you will be immediately excluded from the experiments. If you are currently smoking and drinking beverages containing caffeine, you should limit your consumption to the amount authorized by the research team and maintain your consumption stable throughout the study; you will also be asked to keep a log of your smoking and drinking habits.

OVERVIEW OF THE EXPERIMENTS

The study is made up of two phases separated by one year each. Each phase will be planned after at least 2 weeks of vacation time in order to allow you to return to a conventional daytime schedule before the start of the experiments. Each phase of the study is detailed as follows: one week of ambulatory monitoring at home during your last week of vacation; 3-day initial assessment in the laboratory; 3-week ambulatory monitoring on your usual night-shift schedule; 3-day final reassessment in the laboratory. During one of these two phases, you will be exposed to ordinary room light during your work hours, whereas during the other phase you will receive a 3-week treatment of bright light exposure in your work place. Each year, you will thus be admitted 2 times in the laboratory (during 3 consecutive days) and will have a total of 4 weeks of ambulatory monitoring.

AMBULATORY MONITORING:

During your last week of vacation and during your 3-week night shift on your usual schedule, a small device worn day and night will monitor your activity levels at home. You will also be requested to maintain a regular sleep-wake schedule during this week and the preceding one, and to document this schedule by filling out a sleep-wake log and calling in to the laboratory. During your 3-week period on your nighttime schedule, luminance levels will be monitored by a portable device worn during your waking episodes and you will record your sleep at home by a special procedure. The recording of your sleep involves the use of specialized electrodes and of a head ban worn on your head during your sleep and connected to a small box next to your bed. You will be given a special training to operate this equipment adequately. You will also be requested to fill out a form daily to report any symptoms associated with night-shift work. During your nighttime shifts, you will be asked to fill out short paper-and-pencil alertness tests every 20-60 minutes. In all 24 hour periods that include work shifts, you will be asked to provide saliva samples, every 30-60 minutes by moistening a filter paper that will be provided for you. Before and after sleep episodes during this 3 week ambulatory period, you will also be asked to collect small samples of urine in laboratory tubes for analysis.

LABORATORY PROCEDURES:

You will be admitted twice each year for a 2 to 3-day assessment (about 48-56 hours) at the Center for Study and Treatment of Circadian Rhythms of the Douglas Hospital Research Centre. During this period, you will live in a private room, specially designed to monitor your sleep and circadian rhythms. Research technicians will be available at all time to ensure your comfort and to supervise all aspects of the experiments.

This assessment will start after a 2-week vacation period or after a night shift, a few hours before your habitual bedtime. After awakening from this sleep episode, you will start a special procedure during which you will be asked to remain awake and relatively inactive while lying down in bed for up to 30-40 hours. You will be given the opportunity to sleep before and after these periods of extended wakefulness. These sections of extended wakefulness are important to measure the internal time of your biological clock. They represent the most difficult and delicate sections of these experiments, and a technician will be present with you at all times in order to help you stay awake.

During this procedure, your temperature will be recorded by a flexible and thin plastic tube, called a rectal sensor, that you will insert 10 cm into your rectum. Your success staying awake will be verified by the recording of your cerebral waves and by vigilance tests as during your normal days. These consist of short pencil-and-paper tests and/or computerized tests. The total duration of these tests can vary from 10 to 40% of your waking periods. Your meals and snacks will be replaced by frequent snacks provided to you such that the quantity of food and liquid you receive will be equal to that of your normal days. Each time you urinate, you will be requested to use a urinal and a small quantity of urine will be collected for analyses. Finally, saliva samples will be collected by asking you to spit in a test tube.

This section of extended wakefulness will be followed by a recuperative sleep episode. Before each sleep episode, a technician will proceed with the installation of a standardized montage designed to record your brain activity while you are sleeping. This montage consists of small electrodes applied to the face and scalp, and held in place by pieces of tape and special glue; these electrodes will be removed upon awakening from the last sleep episode. All lights will be turned off during each sleep episode and you will be awakened after each episode according to the laboratory schedule.

The light levels will be controlled during the entire experiment. You may not always live under ordinary room illumination and may be asked to remain under an environment of different luminance levels for a substantial portion of your experimental protocol (up to the entire duration of your waking episodes). The intensity of light in your room may vary from very dim illumination to ordinary luminance levels. A dim light environment has a similar level of intensity as a room which is lighted by candle lights; an ordinary room light environment has a similar intensity to that produced by ordinary indoor lamps.

RISKS AND DISCOMFORTS

1. All battery-operated monitoring devices, used to record your levels of activity and light exposure, your body temperature, and sleep patterns are safe and electrically insulated. The tape and special paste used to attach the electrodes for the sleep recordings and the adhesive pads for the electrocardiogram may cause some minor discomfort or skin irritation; if irritation occurs, you should mention it and their placement will be changed. The glue used to hold electrodes to the scalp may leave a flaky residue, which will disappear after several days.

2. The procedures of extended waking involve the following risks and discomforts:

a) You will probably become sleepy during this procedure and a member of the staff will be with you at all times to assist you in remaining awake; he (she) may ask you to converse or not to read at some times. This experience is similar to that of a night shift worker who works all night. Should you feel that you are unable to remain awake during this procedure, as at other times during the course of the study, you are free to interrupt this experiment and to go to sleep. There are no known lasting adverse effects from missing nighttime sleep.

b) You will be asked to remain in bed continuously for 30-40 hours, with minimal levels of activity, and not to stand up. A bedpan and/or urinal will be available to you. Because saliva samples will be collected, you won't be allowed to brush your teeth or use a mouth wash; however, you may rinse your mouth with salted water. Since you will be chewing on a thin layer of paraffin or cotton to stimulate saliva production, a small irritation of the gums may occur. If this is the case, you should report it and saliva collection will be interrupted.

c) You will be asked to be prudent if you are driving a vehicle or using machinery the days following your investigation in the laboratory. Sometimes, discomforts such as upset stomach, insomnia, irritability, or sleepiness may occur. These discomforts are frequently experienced by night-workers or airline crew members. These symptoms may last for 1-2 weeks, although most people report readjustment after only a few days.

3. During your work shifts, you will be exposed to controlled levels of light, which may range in intensity from ordinary indoor room light to bright light. You may be inconvenienced by the glare from the bright light, which may irritate your eyes. However, the brightest intensity level you would be exposed to is only one tenth that of a blue sky at midday**.** The lamps used for the phototherapy sessions(s**)** are safe and the plexiglass diffuser lenses covering the boxes filter out UV rays.

4. During this study, you will be asked to wear a portable device for ambulatory monitoring, to record your sleep at home, to maintain a sleep-wake log according to a

predetermined schedule, to collect urinary and saliva samples, and to fill out questionnaires during several consecutive weeks. As well, you will have to be admitted to the laboratory on several occasions.

5. The researchers reserve the right to terminate the study at any time they feel it is necessary for your physical or psychological welfare, or for research purposes.

BENEFITS

1. The proposed experiments will allow us to evaluate your degree of physiologic adaptation to night-shift work and your response to a treatment of bright light exposure in the workplace. It will be possible, upon completion of the protocol and analysis of the data, to make some of the information we have gathered from the physiological testing available to you.

2. There is a chance that the pre-study screening or the various blood and urine samples taken during the study will reveal some medical abnormality. This information will be conveyed to you and a recommendation to a local physician will be made.

3. As a monetary compensation, you will be reimbursed for any loss of income or expenses secondary to your participation to these studies. However, no additional financial gain will result from your participation as a research subject.

GENERAL INFORMATION

In the event that at any time during the course of this project you feel you have not been adequately informed as to the risks, benefits, or alternative procedures, or your rights as a research subject, or feel under duress to continue this study against your wishes, the Ombudsman of the Douglas Hospital is available to speak to you during normal working hours (8 a.m. to 4:30 p.m.) at 514-762-3010.

Confidential information contained in your medical/research records may not be furnished to anyone unaffiliated with the Douglas Hospital without your written consent, except as required by law or regulation.

A signed copy of this consent form will be made available to you.

You are free to withdraw your consent and to discontinue participation in this study at any time, and such discontinuance will not affect your regular treatments or medical care in any way.

STATEMENT OF INVESTIGATOR

I have fully explained the procedures, identifying those, which are experimental, and have explained their purpose. I have asked whether or not any questions have arisen regarding the procedures and have answered these questions to the best of my ability.

_____ _____
DATE INVESTIGATOR

STATEMENT OF SUBJECT

I have been fully informed as to the procedures to be followed, including those which are experimental, and have been given a description of the attendant discomforts, risks and benefits to be expected and the appropriate alternate procedures. In signing this consent form, I agree to participate in this project, and I understand that I am free to withdraw my consent and have this study discontinued at any time. I understand also that if I have any questions at any time, they will be answered.

Finally, I understand that as a subject participating in this study, I am expected to abstain from the use of all drugs or medications, prescription or non-prescription, throughout the course of the experiments. I also understand that my blood and urine will be periodically tested for the presence of any drugs or other substances and that I will be excluded from the experiments if any of these substances is detected.

_____ _____
DATE SUBJECT

STATEMENT OF WITNESS

I have witnessed the statements made by the investigator listed above, and have heard his (her) responses to questions.

_____ _____
DATE WITNESS

A2. Sleep-wake log

SLEEP-WAKE LOG

NAME:_____ **PHONE:**_____ **PAGE:**_____

Target Bed Time:_____ **Target Wake Time:**_____

INSTRUCTIONS: Please make your form entry every night just before going to bed and every morning upon wakening in addition to calling (514) 761-6131 ext. 2398 (unless you are keeping a post-study log, in which case, you do not have to call). If you run out of forms or have any questions, please call the number listed below.

Date at bedtime	Day of the week	Time into bed	Est time to fall asleep	Awakening time and length	Day at wake time	Final wake time	Time out of bed	Naps time and length

Please Return to: McGill-Douglas Hospital Research Center,
c/o Dr. Diane Boivin
6875, boul. LaSalle, Verdun (Québec) H4H-1R3
Telephone: (514) 761-6131 ext 2395

A3. Symptom severity questionnaire

Subject code: _____ Date: _____

Circle one rating for each symptom. Rate all symptoms shown.

Scale:	Mild				Moderate					Severe
	1	2	3	4	5	6	7	8	9	10
Loss of appetite	1	2	3	4	5	6	7	8	9	10
Nausea	1	2	3	4	5	6	7	8	9	10
Diarrhoea	1	2	3	4	5	6	7	8	9	10
Upset stomach	1	2	3	4	5	6	7	8	9	10
Tired eyes	1	2	3	4	5	6	7	8	9	10
Headaches	1	2	3	4	5	6	7	8	9	10
Muscular aches	1	2	3	4	5	6	7	8	9	10
Muscular weakness	1	2	3	4	5	6	7	8	9	10
Lack of co-ordination	1	2	3	4	5	6	7	8	9	10
Difficulty falling asleep	1	2	3	4	5	6	7	8	9	10
Disturbed sleep	1	2	3	4	5	6	7	8	9	10
Premature awakening	1	2	3	4	5	6	7	8	9	10
Non-restful sleep	1	2	3	4	5	6	7	8	9	10
Difficulty waking up	1	2	3	4	5	6	7	8	9	10
Waking sleepiness	1	2	3	4	5	6	7	8	9	10
Difficulty concentrating	1	2	3	4	5	6	7	8	9	10
Difficulty remembering	1	2	3	4	5	6	7	8	9	10
Anxiety	1	2	3	4	5	6	7	8	9	10
Sadness	1	2	3	4	5	6	7	8	9	10
Irritability	1	2	3	4	5	6	7	8	9	10

Commentaires:

_____

_____

_____

A4. Subjective symptom duration questionnaire

Subject		**Shift date:**		**Shift code**	

Rate the extent to which you suffered from the symptoms below during your shift.

	No symptoms	**A few minutes**	**10 to 30 minutes**	**1 hour**	**1 to 2 hours**	**Half of the shift**	**Almost the entire shift**
Tired eyes	❒	❒	❒	❒	❒	❒	❒
Heavy eyelids	❒	❒	❒	❒	❒	❒	❒
Difficulty focussing	❒	❒	❒	❒	❒	❒	❒
Forcing to keep eyes open	❒	❒	❒	❒	❒	❒	❒
Periods during which I am fighting sleep	❒	❒	❒	❒	❒	❒	❒
Difficulty paying attention	❒	❒	❒	❒	❒	❒	❒

A5. Scientific Publications

ADAPTATION TO NIGHT SHIFT WORK VIA A REGULAR SCHEDULE OF SLEEP/DARKNESS. F.O. James and D.B. Boivin. Douglas Hospital Research Centre, Department of Psychiatry, McGill University, Montréal, Québec, Canada.

One of the most serious occupational hazards facing the night shift worker is the state of persistant misalignment that exists between the worker's environment and the internal clock. Early lines of evidence suggest that a state of internal desynchronisation persists between several diurnal rhythms in night shift workers, even after many years on a permanent schedule. Here, we report results from an ongoing field study of shift workers and their circadian adaptation to night shift work in ordinary illumination. Five full-time ($8 shifts/15 days) night shift hospital workers were recruited for this study. Subjects passed physical and psychological examination and were admitted to the laboratory after having kept a daytime schedule for at least 10 days while on vacation. Upon admission to the laboratory, assessment of circadian phase was performed using a constant routine (CR) protocol of enforced extended wakefulness in constant dim light. Subjects then returned to their habitual night shifts for a minimum 12 shifts in 20 days, and were asked to keep regular sleep habits on days following night shifts. Schedules were confirmed by actimetry and sleep logs. Following the period of night shifts a second circadian evaluation was planned using the CR protocol. Circadian phase was determined via dual harmonic regression to core body temperature data. Initial circadian phase was consistent with a daytime schedule and comparable between all subjects (mean $\pm$ SD: 5.96 "1.56 hours p=0.56). After the period of night shifts, the endogenous circadian pacemaker adjusted to a night time schedule (group mean: 18.89 " 5.88): significantly different from the initial condition (p=0.013 two-tailed paired t-test). The endogeneous circadian curve of salivary melatonin varied in parallel with that of the core body temperature. These results are consistent with the sensitivity of the human circadian pacemaker to ordinary levels of light. They imply that keeping a regular schedule of sleep/darkness and exposure to light may substantially improve the adaptation to an inverse work schedule.

IMPACT DE LA RÉGULARITÉ DE L'HORAIRE DE SOMMEIL SUR L'ADAPTATION AU TRAVAIL DE NUIT

Francine O. James* et Diane B. Boivin
Centre de Recherche de l'Hôpital Douglas,
Département de Psychiatrie, Université McGill

Des troubles chroniques de sommeil et d'éveil sont rapportés par les travailleurs de nuit. La majorité des études antérieures indiquent qu'un état de désynchronisation interne persiste chez la plupart des travailleurs de nuit entre plusieurs rythmes diurnes. Ces observations pourraient expliquer les troubles d'adaptation au travail de nuit. Nous présentons les résultats préliminaires d'une étude en cours auprès d'infirmiers(ères) de nuit et leur adaptation circadienne en milieu de travail.

À ce jour, cinq travailleurs de nuit à temps plein ($8 quarts/15 jours) ont participé à un protocole de recherche à trois étapes. Après une période d'adaptation ($ 10 jours) à un horaire régulier de jour, les travailleurs furent admis en laboratoire pour une investigation de 60 heures dans un environnement sans repère temporel. Après l'évaluation initiale de leur oscillation circadienne, les sujets ont travaillé sur leur horaire régulier de nuit pour $12 quarts/ 20jours. Durant cette période d'étude ambulatoire, les sujets ont maintenu un horaire régulier de sommeil de jour faisant suite aux quarts de travail de nuit. Cet horaire fut confirmé par actigraphie et agendas de sommeil. Finalement, ils ont été réadmis en laboratoire pour une évaluation finale de leur oscillation circadienne.

La phase circadienne fut déterminée à l'aide d'une routine constante (RC) de 36 heures qui vise à dégager l'oscillation circadienne endogène des facteurs qui en masquent l'expression. La RC consiste en un éveil forcé, en position semi-couchée, avec niveaux d'activité physique et apport alimentaire contrôlés. La phase de l'oscillation circadienne endogène de la température rectale fut déterminée à l'aide d'un modèle de régression nonlinéaire à double harmoniques.

Au début de l'étude, un rythme circadien endogène significatif et normalement ajusté à un horaire de jour fut observé pour tous les sujets. La phase circadienne moyenne initiale (" D.S.M.) de 5.96 h " 1.5 était comparable entre tous les sujets (p=0.56). Suivant la période d'étude ambulatoire, l'oscillateur circadien endogène a démontre un délai de phase de –12.93 h " 6.82h. Le changement de phase est significativement différent entre les évaluations (test de t pairé; p=0.013). L'oscillation circadienne endogène de la mélatonine salivaire s'est déplacée en parallèle avec celle de la température corporelle.

Ces résultats préliminaires suggèrent qu'un horaire régulier de sommeil et d'exposition à la lumière peut améliorer significativement l'adaptation au travail de nuit. Ils supportent l'hypothèse selon laquelle l'oscillateur circadien humain est sensible à de faibles niveaux de luminosité.

Circadian readaptation to full time night shift work with bright light treatment in the workplace.

Francine O. James and Diane B. Boivin

Department of Psychiatry, McGill University
Centre for Study and Treatment of Circadian Rhythms
Douglas Hospital Research Centre
Montreal, Québec, CANADA

INTRODUCTION

Shiftworkers on a full-time schedule of night work suffer from a chronic state of internal desynchrony with their work schedule. Daytime sleep of poor quality, and limited alertness during night work, as typically observed in the night shift worker, may be caused in part by this circadian misalignment [1]. The results from numerous studies have suggested that a regimen of bright light may be effective in the promotion of circadian adaptation to the inverted sleep-wake schedule [2;3]. In this combined laboratory and field study, we examined the effectiveness of a bright light treatment in circadian adaptation of full time night shift workers to their inverted sleep-wake schedule.

EXPERIMENTAL PROTOCOL

The experiment followed a three-tiered design:

Following an adaptation period (≥ 10 days on a regular daytime schedule), subjects were admitted to the laboratory for an initial circadian assessment.

Subjects returned to their regular night work schedule for a total of 12 shifts. During this ambulatory observation, all subjects maintained regularly timed day sleep episodes. Participants assigned to the treatment group received a 6-hour bright light (2000-7000 lux) treatment at the start of each night shift.

Subjects are re-admitted to the laboratory for a final assessment of circadian phase

EXPERIMENTAL CONDITIONS

LABORATORY ASSESSMENT

At the beginning and end of the experimental period, subjects were admitted to the laboratory for a 60-hour observation. During each laboratory stay, a constant routine was performed for the determination of endogenous circadian phase (see Constant Routine). Subjects remained in an environment free of time cues, and in constant contact with research assistants trained to avoid the communication of temporal cues.

FIELD STUDY

Subjects returned to a schedule of regular night work for a minimum of 12 shifts. They were requested to keep regular sleep-wake habits such that an eight-hour sleep episode begins each morning two hours after the end of the night shift.

TREATMENT

Subjects assigned to the treatment group received a 6-hour regimen of bright light (2000-7000 lux) at the beginning of each night shift. They were instructed to look at the light as much as possible, but were free to move around. To control for exposure to morning natural light, these subjects wore dark goggles on their journeys home at the termination of the night shift.

CONSTANT ROUTINE

The constant routine is a procedure of enforced wakefulness, designed to unmask the oscillation of the endogenous circadian pacemaker. The subject, in a semi-recumbent position, has limited activity, and is kept in dim light (<10 lux). Nutritional requirements are met via timed snacks. Core body temperature for each subject is recorded throughout the constant routine at 1-minute intervals. Saliva samples are collected at 30-minute intervals.

ANALYSIS

The phase of the endogenous circadian pacemaker is determined via a dual-harmonic regression model [4] applied to core body temperature data collected during the constant routine. Regression analyses did not incorporate the serial correlated noise factor. Circadian phase is defined as the fitted minimum of the core body temperature oscillation. The first five hours of data are removed from analysis to compensate for the masking effect of the sleep episode preceding the constant routine.

Shifts in circadian phase are defined as the difference between the initial and final phase of fitted minimum of core body temperature, thus:

$$\Delta\text{Phase} = \text{Phase}_{\text{initial}} - \text{Phase}_{\text{final}}$$

RESULTS

15 workers participated in this protocol, and were observed over a total of 19 experimental conditions.

Initial circadian phase was comparable between both groups ($p=0.36$, two-tailed). Initial phases for the treatment and non-treatment groups were ($\pm$ SD) 5:54 $\pm$ 3:37 and 4:40 $\pm$ 1:51 hours, respectively.

Following the period of ambulatory study, mean circadian phase was assessed in the treatment group at 16:14 $\pm$ 3:41 hours, implying adjustment to a nocturnal schedule. Mean phase in the non-treatment group was determined at 9:49 $\pm$ 6:42 hours. Final phases for the two experimental groups were significantly different ($p=0.03$).

CONCLUSIONS

The results suggest that bright light treatment in the workplace may significantly contribute to the realignment of the endogenous circadian pacemaker to a night-oriented schedule.

Moreover, the partial shift in mean circadian phase of subjects studied in typical illuminance conditions may be a result of the potent effect of light even in ordinary lighting conditions [5].

ACKNOWLEDGEMENTS

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1287.E

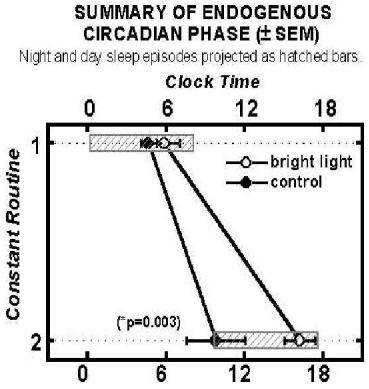
Circadian Adjustment to Night Shift Work with a Bright Light Intervention Regimen in the Workplace

James FO, Boivin DB
(1) Department of Psychiatry, McGill University (2) Centre for Study and Treatment of Circadian Rhythms (3) Douglas Hospital Research Centre, Montreal, Quebec, CANADA

Introduction: Laboratory simulations and field studies have revealed that phototherapy may be a powerful approach in helping the shiftworker adjust to an inverted sleep/wake schedule (1,2). The present combined field and laboratory investigation aims to accurately assess the effects of an intervention regimen on the adjustment of the endogenous circadian system of night shift workers.

Methods: A total of 15 nurses (6 male, 9 female; mean age ± SD: 40.8 ± 8.4 years) working regular night shifts (³ 8 shifts/15 days) were recruited from area hospitals. Following a vacation period including ³ 10 days on a daytime schedule, workers were admitted to the laboratory for a 36-hour constant routine procedure (CR). Workers then returned to their regular night shift work schedule for an average of 12 shifts, under one of two experimental conditions: treatment or control. Workers assigned to the treatment condition were exposed to bright light (2000-7000 lux) during the first 6 hours of each night shift, and wore dark goggles on the commute home. Control group workers were observed in their habitual lighting conditions. Subjects maintained regular 8-hour day sleep/dark periods beginning 2 hours after the end of their night shifts. At the end of the ambulatory period, workers were readmitted to the laboratory for a final 36-hour CR. Endogenous circadian phase was determined from CR temperature data via a dual-harmonic regression model without serial correlated noise.

Results: At the start of the study, both groups were adjusted to a day-oriented schedule and no between-group differences were observed ($F(1,34)=0.39$, $p=0.54$). Mean initial circadian phase of the treatment and control groups were (± SEM) 5:54 ± 1:09 and 4:40 ± 0:37, respectively. Following the period of night shifts, mean circadian phase (± SEM) was assessed at 16:14 ± 1:10 and 9:49 ± 2:14 hours for the treatment and control groups, respectively. An ANOVA for repeated measures revealed that these final values differed significantly between groups ($F(1,34)=10.56$, $p=0.003$).



Conclusions: In the treatment group, the shift in endogenous phase was one that allowed the maintenance of a harmonious relationship between the circadian pacemaker and the inverted sleep schedule. These results suggest that judicious control of exposure to bright light and darkness can hasten the adjustment to night shift work in the field. Further, the partial adjustment of the endogenous circadian pacemaker as observed in the control group may be the result of the strong resetting effects exerted in low levels of light (3), and in the maintenance of a regular schedule of sleep/darkness.

References:

(1) Czeisler CA, Johnson MP, Duffy JF, Brown EN, Ronda JM, Kronauer RE. Exposure to bright light and darkness to treat physiologic maladaptation to night work. N Engl J Med 1990;322:1253-1259.
(2) Bjorvatn B, Kecklund G, Akerstedt T. Bright light treatment used for adaptation to night work and

re-adaptation back to day life. A field study at an oil platform in the North Sea. J Sleep Res 1999;8:105-112.
(3) Boivin DB, Duffy JF, Kronauer RE, Czeisler CA. Dose-response relationships for resetting of human circadian clock by light. Nature 1996;379:540-542.

Institut de Recherche en Santé et en Sécurité du Travail du Québec

15TH APSS ANNUAL MEETING

JUNE 5 - 10, 2001

HYATT REGENCY • CHICAGO, ILLINOIS

A Joint Meeting of the American Academy of Sleep Medicine and the Sleep Research Society

PRELIMINARY PROGRAM

5:00pm - 6:00pm POSTER VIEWING

Friday, June 8

7:00am - 8:00am MEET THE PROFESSOR SESSIONS
Pre-registration is required.

Symposia

8:00am - 10:00am

THE NEUROBIOLOGY OF STRESS AND ADAPTATIONS TO STRESS: THERE'S NO SLEEPING ON IT
CHAIR - Israel L. Lederhendler, Ph.D.
Steven F. Maier, Ph.D.
Paul Plotsky, Ph.D.
Rita J. Valentino, Ph.D.
Eve Van Cauter, Ph.D.

AROUSALS: WHAT ARE THEY AND WHAT DO THEY MEAN?
CO-CHAIRS - Mario Giovanni Terzano, M.D. and Christian Guilleminault, M.D.
Jamie MacFarlane, Ph.D.
Liborio Parrino, M.D.

CIRCADIAN ADJUSTMENT TO SHIFTWORK: HOW MUCH SHOULD BRIGHT LIGHT INTEREST US?
CHAIR - Diane Boivin, M.D., Ph.D.
Torbjorn Akerstedt, Ph.D
Marie Dumont, Ph.D.
Charmane Eastman, Ph.D.
Todd S. Horowitz, Ph.D.

NHLBI PROGRAMS FOR GENOMIC APPLICATIONS
CHAIR - Michael Twery, Ph.D.
Atul J. Butte, M.D.
Fernando Martinez, M.D.
Allan I. Pack, M.B., Ch.B., Ph.D.
John Quackenbush, Ph.D.

Oral Presentations

8:00am - 10:00am SLEEP IN MEDICAL/NEUROLOGICAL DISORDERS

PHYLOGENY/BRAINSTEM

10:00am - 10:15am EXHIBIT HALL OPENS/COFFEE BREAK

Oral Presentations

10:15am - 12:15pm SLEEP AND DEPRESSION

MECHANISMS OF SLEEP REGULATION

SLEEP DISORDERED BREATHING: GENETICS AND CONSEQUENCES

Judicious Control of the Pattern of Light Exposure in Circadian Readaptaion to Night Shift Work.

Francine O. James, B.Sc. and Diane B. Boivin, M.D., Ph.D.
Department of Psychiatry, McGill University; Centre for Study and Treatment of Circadian Rhythms, Douglas Hospital Research Centre, Montreal, Quebec, CANADA.

Introduction

As demonstrated in laboratory and field studies of shift work, bright light phototherapy in the workplace may be effective in helping the shift worker adjust to an inverted sleep/wake schedule (1,2). Investigations have also demonstrated that morning bright light may impede the circadian adjustment to a night-oriented schedule (4). This field and laboratory study investigated the efficacy of an intervention regimen in the adjustment of the endogenous circadian system of night shift workers.

Methods

Fifteen full-time night shift workers (6 male, 9 female; mean age ± SD: 40.8 ± 8.4 years) were recruited for this study. Following a vacation period including ≥ 10 days on a daytime schedule, workers were admitted to the laboratory for a 36-hour constant routine procedure (CR). Workers then returned to their regular night shift work schedule for an average of 12 shifts, under one of two experimental conditions: treatment or control. Workers assigned to the treatment condition were exposed to bright light (2000-7000 lux) during the first 6 hours of each night shift, and wore dark goggles on the commute home. Control group workers were observed in their habitual lighting conditions. Subjects maintained regular 8-hour day sleep/dark periods beginning 2 hours after the end of their night shifts. At the end of the ambulatory period, workers were readmitted to the laboratory for a final 36-hour CR. Endogenous circadian phase was determined from CR temperature data via a dual-harmonic regression model without serial correlated noise.

Results

At the start of the study, both groups were adjusted to a day-oriented schedule and no between-group differences were observed ($F_{(1,34)}$=0.36, p=0.4). Mean initial circadian phase of the treatment and control groups were (± SEM) 4.72 ± 0.60 and 5.90 ± 1.14 hours, respectively. Following the period of night shifts, the treatment group displayed a -10.37±1.41 hour phase delay. The observed phase delay in the control group was of only -5.33±2.11 hours. Final circadian phase in the control and treatment groups were 10.06±2.23 and 16.27±1.16 hours, and were significantly different, ($F_{(1,34)}$=9.97, p=0.003).

Conclusions

Mean final phase in the treatment group was aligned with a night-oriented rest/activity cycle. These results suggest a practical means of promoting circadian adjustment in the night shift worker. Moreover, they emphasise the importance of the pattern of exposure to light throughout the day, in the process of circadian entrainment to an inverted schedule (3).

References

(1) Czeisler CA et al. N Engl J Med 1990;322:1253-1259. (2) Bjorvatn B et al. J Sleep Res 1999;8:105-112. (3) Jewett ME et al. Am J Physiol. 273:R1800-R1809. (4) Eastman CI et al. Sleep 1994;17:535-543.