Circadian countermeasures in the high Arctic during winter

Michel A. Paul
Ryan J. Love
Andrea M. Hawton
Donald R. McCreary
DRDC

Kaighley D. Brett
Michael J. Jerrott
Canadian Forces Health Services

Joesphine Arendt
University of Surrey, UK

Defence Research and Development Canada

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Abstract

Background. DRDC Toronto has optimized the ability to manipulate circadian rhythms with supplementary melatonin and/or light treatment, as appropriate, to reduce or eliminate the circadian desynchrony that is inherent in jetlag and shiftlag. For the past 3 years we have collected Arctic circadian baselines at CFS Alert to establish the impact on human circadian physiology during each of the extremes of arctic winter and arctic summer photoperiod. The work described herein is our first attempt at implementing Arctic circadian countermeasures for the treatment of discordant human circadian rhythms that are apparent in personnel of CFS Alert during the Arctic winter. **Methods.** This data collection commenced on Jan 18, 2014 at CFS Alert. To qualify for the study, subjects had to have been at Alert for at least three weeks prior to commencement of the study. Subjects filled out questionnaires regarding sleep difficulty and psychosocial parameters, and wore motion logging devices (Actigraphs) to obtain objective sleep data. Saliva was collected at regular intervals on two occasions, two weeks apart, to measure melatonin and assess melatonin onset. Individuals with a melatonin rhythm that was in disaccord with their sleep schedule were given a light treatment visor to use daily. Treatment efficacy was evaluated using the questionnaire data, actigraphic data, and endogenous melatonin profiles. **Results.** The light treatment prescribed to eight of the thirteen subjects was effective, to a statistically significant degree, at improving sleep quality both subjectively, based on the questionnaire results, and objectively, based on the actigraphic data. Circadian system effects from the light treatment were less definite, but the melatonin profile of many of the subjects improved. **Conclusions.** The light treatment significantly improved sleep quality in our subject population. Since the treatment is non-invasive and has no associated side-effects, our results support the use of the light visors at CFS Alert and other northern outposts during the winter for individuals that are experiencing some difficulty adapting to the lack of daylight (i.e., mild sleep trouble or increased negative affectivity). However, due to the low statistical power of this study, more research on the effectiveness of treatment is certainly warranted before any firm recommendations can be made.

Significance to defence and security

The study described herein found a statistically significant benefit of light treatment on the quality of sleep obtained among residents of CFS Alert during the winter. Improved sleep quality increases cognitive performance [1]. Therefore, these results support the use of the light visors for individuals that are experiencing difficulty adapting to the arctic winter (i.e., mild sleep trouble or increased negative affectivity).

Résumé

Contexte. RDDC Toronto a maximisé la capacité de manipulation du rythme circadien au moyen de suppléments de mélatonine ou de séances de photothérapie, selon le cas, pour réduire ou éliminer la désynchronisation du rythme circadien provoquée par le décalage horaire ou le décalage lié au travail par roulement. Depuis trois ans, nous avons recueilli des données de référence sur le rythme circadien dans l'Arctique, à la SFC Alert, pour connaître les effets sur la physiologie humaine des variations extrêmes de chacune des photopériodes de l'hiver et de l'été dans cette région. Les travaux décrits ici constituent notre première tentative visant à mettre en œuvre des contre-mesures afin de traiter les perturbations du rythme circadien humain observées parmi le personnel de la SFC Alert pendant l'hiver en Arctique. **Méthodes.** La collecte de données a commencé le 18 janvier 2014 à la SFC Alert. Pour participer à l'étude, les sujets devaient être à la SFC Alert depuis au moins trois semaines avant le début de l'étude. Les sujets ont rempli des questionnaires sur leur difficulté à dormir et sur des paramètres psychosociaux. De plus, ils portaient un dispositif d'enregistrement du mouvement (ActiGraph), qui permet d'obtenir des données objectives sur le sommeil. La salive a été recueillie à intervalles réguliers à deux occasions, à deux semaines d'intervalle, pour mesurer la mélatonine et déterminer le début de sa sécrétion. On a remis aux personnes dont le rythme de sécrétion de mélatonine ne correspondait pas à leur horaire de sommeil une visière de photothérapie pour usage quotidien . Les données du questionnaire, les données actigraphiques et les profils de sécrétion de mélatonine endogène ont servi à évaluer l'efficacité du traitement. La photothérapie prescrite à huit des treize sujets s'est avérée efficace, à un degré statistiquement significatif, pour améliorer la qualité du sommeil, d'un point de vue subjectif, au moyen des résultats du questionnaire, et d'un point de vue objectif, au moyen des données actigraphiques. Les effets de la photothérapie sur le rythme circadien étaient moins évidents, mais la sécrétion de mélatonine a augmenté chez de nombreux sujets. **Conclusions**. La photothérapie a considérablement amélioré la qualité du sommeil chez les sujets ciblés. Comme le traitement est non invasif et qu'il n'a aucun effet secondaire, nos résultats permettent d'appuyer l'utilisation de visières de photothérapie à la SFC Alert et dans les autres postes nordiques éloignés pendant l'hiver pour les personnes qui éprouvent de la difficulté à s'adapter au manque de lumière (p. ex., troubles légers du sommeil ou augmentation de l'affectivité négative). Toutefois, étant donné le faible poids statistique de cette étude, il serait certainement justifié de mener d'autres recherches sur l'efficacité du traitement avant de pouvoir formuler des recommandations fermes à ce sujet.

Importance pour la défense et la sécurité

L'étude décrite ici a révélé les bienfaits statistiquement significatifs de la photothérapie sur la qualité du sommeil parmi des résidents de la SFC Alert pendant l'hiver. L'amélioration de la qualité du sommeil augmente le rendement cognitif [1]. Par conséquent, les résultats permettent d'appuyer l'utilisation de visières de photothérapie pour les personnes qui éprouvent de la difficulté à s'adapter à l'hiver dans l'Arctique (p. ex., troubles légers du sommeil ou augmentation de l'affectivité négative).

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1 Background

In recent years, DRDC Toronto has optimized the ability to manipulate circadian rhythms either forwards or backwards as appropriate to reduce or eliminate the circadian desynchrony that is inherent in jetlag and shiftlag [2-6]. Eliminating or reducing jetlag allows deployment of military personnel across multiple time zones without the normal attendant impact on human performance upon arrival in the new theatre of operations. Eliminating or reducing shiftlag allows personnel to adapt to their work shifts, and reduces the circadian desynchrony that arises when an individual changes work hours from day to night or the reverse.

The two treatment modalities used in the manipulation of circadian rhythms are appropriately-timed ingestion of supplementary melatonin and appropriately-timed light treatment. Further, exposure to light at the wrong time is counter-productive since it can impair the desired circadian phase shift, whether it be phase advance or phase delay. For example, if one is seeking phase advance, early morning light is used, but evening light has to be avoided. Similarly, for phase delay, evening light treatment is taken but morning light is avoided.

Each day, during physiologic night the pineal gland in the brain produces melatonin and releases it into the circulation. This rhythm is governed by the activity of the suprachiasmatic nucleus of the hypothalamus (SCN, central circadian clock) and persists in constant darkness, albeit with a period which usually deviates from 24h, on average 24.1-24.3h. Normally the light dark cycle dictates the activity of the SCN such that the rhythm is synchronised to 24h and the length of the photoperiod (daylength) influences the duration of melatonin secretion via the SCN, which is longer in long nights and shorter in short nights. It is unusual to observe the propensity of the SCN to influence the duration of human melatonin secretion due to length of night, unless strict control is exercised over exposure to long nights or short nights (1, 2), or subjects are exposed to an extreme environment such as in polar regions (3-5). This particular aspect of circadian physiology has led some people to refer to melatonin as ‘a biochemical expression of darkness’, a ‘biochemical manifestation of darkness’ or, succinctly, the 'Darkness Hormone'.

The profile of secretion is species-dependent but in humans melatonin increases approximately 2h before normal bedtime/darkness, unless exposed to evening artificial light, which could suppress melatonin production. Arctic intensity natural light in the evening is more than sufficient to suppress melatonin production. Melatonin begins to decline before wake up and exposure to morning light - the point at which this is initiated has been called Melatonin synthesis offset, or 'SynOff' (6, 7). Exposure to sufficiently bright morning light can advance the timing of the rhythm and/or suppress melatonin production.

The time at which melatonin begins to be released into the circulation in a dim light environment prior to sleep is called “Dim Light Melatonin Onset” or DLMO. DLMO is the best biologic marker for assessing an individual’s circadian rhythm. Thus, circadian treatments are best developed after establishing the timing of DLMO. For people who regularly retire to bed between 2300 h and 2400 h and remain in bed for 7 to 8 hours DLMO will typically occur between 2000 h to 2200 h. The timing of DLMO in the northern hemisphere will be somewhat earlier in the winter since the sun goes down earlier, whereas in the summer DLMO will be somewhat later since sundown is delayed relative to winter.

All circadian phase shifting treatments, whether with light or ingestion of supplementary melatonin, are relative to DLMO. Thus, the most effective circadian treatments are made after establishment of the exact timing of DLMO. For phase advance, melatonin is usually given 2 to 5 hours before DLMO (or 1600 h to 1900 h clock time for those with a normal DLMO of 2100 h), depending on the size of the melatonin dose. For phase delay, melatonin is taken 9 to 11 hours after DLMO (or 0600 h to 0800 h clock time for those with a normal 2100 h DLMO. When light treatment is given during physiologic night (i.e., when the body is producing melatonin) the light transforms physiologic night into physiologic day by suppressing the body's production of melatonin. To phase delay with light, treatment is given 4 to 6 hours after DLMO (i.e., 0100 to 0300 h clock time) for those with a 2100 h DLMO. To phase advance with light, treatment is given 9 to 11 hours after DLMO (i.e., 0600 h to 0800 h clock time) for those with a normal DLMO.

In the southern cities of Canada (Halifax, Montreal, Toronto, Calgary, Vancouver, etc.) a significant number of people develop winter depression or SAD (Seasonal Affective Disorder) due to the shorter duration of sunlight during winter. In these locations winter brings about 8 hours of light each day, compared to about 16 hours of daily light in the summer. SAD is usually successfully treated with supplementary exposure to morning light. SAD could be much worse at the polar extremes of the Arctic and Antarctic since there are months without any daylight and also months without darkness which can create different problems for circadian physiology.

For the past 3 years we have collected Arctic circadian baselines mainly at CFS Alert to assess how human circadian physiology is impacted during each of the extremes of the Arctic winter and Arctic summer photoperiod [7]. This data suggests that personnel deployed to the Arctic in summer obtain less sleep than their Arctic winter counterparts. When Arctic sleep is modeled with FAST (Fatigue Avoidance Scheduling Tool) software, it is evident that Arctic summer personnel would not be expected to perform as well as Arctic winter personnel, due to their reduced sleep duration.

The work described here is our first attempt at implementing Arctic circadian countermeasures in the Arctic winter. We expect to conduct a corresponding study in the next Arctic summer, which we will report in a separate publication.

2 Methods

2.1 Dim Light Melatonin Onset (DLMO)

DLMO is found by sampling melatonin concentration in blood or saliva at uniform intervals under dim light conditions (<10 lux; (8-11)), where the first sample that exceeds a prescribed threshold is designated as DLMO.

2.2 Subject inclusion/exclusion criteria/age/gender demographics

Subjects were 13 Regular Force subjects stationed at CFS Alert in January 2014, whose ages ranged from 22 to 42 years, with a mean age and standard deviation of 31.2 ± 6.3. There were 8 males and 5 female subjects. To qualify, all subjects had to be at CFS Alert for at least 2 weeks prior to commencement of the study.

Exclusion criteria included:

1. Medications – beta-blockers, SSRIs, sleep aids/hypnotics.

2. Use of supplementary melatonin in the 30 days prior to the study.

3. Use of light treatment for circadian adjustment for 30 days prior to the study.

2.3 Procedures

2.3.1 Study design

The study took place over 23 days. Each subject wore an Actigraph (a wrist-worn device to measure movement and quantify sleep [16] and kept a daily sleep log. The study comprised two phases.

Phase 1. The protocol began with a 7-day baseline period, at the end of which subjects underwent a 24-hour salivary melatonin assessment. Based on the information from the initial salivary melatonin assessment, subjects were divided into 2 groups:

1. An adapted group, who did not receive any interventions. These 5 control subjects had normal melatonin secretion curves.

2. An unadapted group , who had abnormal baseline melatonin secretion curves, and who were prescribed light treatment protocols. Phase 2 lasted 11 days, at the end of which all subjects (control and treatment groups) again underwent a 24-hour salivary melatonin assessment.

2.3.2 Melatonin assays/DLMO

All subjects underwent a 24-hour baseline salivary melatonin profile by providing samples (one sample every 2 hours for 24 hours). The saliva was collected in test tubes configured for that purpose. These saliva samples were analyzed for melatonion content at CFS Alert by DRDC, Toronto Research Center staff using ELISA kits from Buhlmann Laboratories AG (Schönenbuch, Switzerland). These salivary melatonin levels were used to calculate the timing of DLMO in each of the participating subjects. DLMO is found by sampling melatonin concentration in blood or saliva at uniform intervals under dim light conditions (<10 lux; (8-11)), where the first sample that exceeds a prescribed threshold is designated as DLMO. Based on our own data, a normal DLMO occurs 2.54 h ± 1.18 h before sleep onset (12-15). A DLMO occurring after sleep onset or more than 2 SDs before mean sleep onset is considered abnormal. Subjects whose onset timing of endogenous melatonin (i.e., their DLMO) is normal, were not given a countermeasure treatment. For subjects whose DLMO was either significantly advanced or delayed (relative to a normal DLMO for their particular work schedule), their own unique DLMO was used to craft an intervention countermeasure using a light visor (Physician Engineered Products, Bangor, Maine USA). Post-treatment salivary melatonin samples were also analyzed via ELISA at CFS Alert. The difference in timing of the pre-treatment to post-treatment DLMO provided the magnitude and direction (advance or delay) and thus the efficacy of the phase shift for those participants who received a treatment.

During both pre- and post-treatment salivary melatonin profile assessments, subjects remained in a darkened room with illumination set to a maximum of 5 lux, as normal room lighting levels can suppress melatonin production. Based on our previous findings a 5 lux light level did not suppress endogenous melatonin. All subjects were positioned on lounge chairs and remained in a semi-recumbent posture for at least 15 minutes immediately prior to each sampling of salivary melatonin, to avoid hemo-concentration of the melatonin that can occur across different postures (16). The subjects were provided with bottled water, and were served similar meals during both 24-hour assessments. They provided 13 saliva samples with one sample every 2 hours for the 24-hour period. The samples were collected by the study investigators and technicians from DRDC, Toronto Research Center. Immediately prior to each saliva sample time, the subjects were handed a salivette (a small test tube which contains a cotton plug) by the data collectors. The subjects were instructed to drop the cotton plug from the salivette into their mouths without touching it with their hands, and to chew it for 45 seconds. The cotton plug was then held in their mouth for a further 45 seconds to ensure an adequate saliva sample was obtained. At the end of 90 seconds, the subjects deposited the cotton plug (now laden with saliva) back into the salivette. The salivettes were centrifuged to extract the saliva from the cotton plug. The subjects were allowed to arise from semi-recumbent posture to use an adjacent washroom (also kept at about 5 lux illumination), eat, and socialize as desired, except during the 15 minutes prior to a saliva sample. During this 24-hour period, subjects were allowed to relax in their lounge chairs watching a series of videos with the video monitor set at least 20 ft away from the subjects to keep the eye-level light from the monitor down to the level of ambient room lighting (i.e., 5 lux). During the 24-h salivary melatonin sampling, the subjects were allowed to sleep between 2300 h and 0700 h, except when samples were being collected. Subjects were awakened 5 minutes prior to the time for each saliva sample. The subjects were required to remain awake between 0700 h and 2300 h.

Immediately prior to each of the pre- and post-treatment salivary melatonin profile assessments, all subjects completed several questionnaires to measure the psychological parameters of interest (depression symptoms, anxiety, sleep disturbance, negative and positive affect). A questionnaire to establish chronotype (i.e., morningness or eveningness) was completed prior to the first 24-hr salivary melatonin collection (i.e., the pre-treatment salivary melatonin collection). All questionnaires used in this study have undergone rigorous validation and are commonly used in the psychological literature.

2.3.2.1 Affect

Positive and negative affect were assessed using the Positive and Negative Affect Scales (17, 18). Responses are summed or averaged separately for each subscale.

2.3.2.2 Symptoms of depression and anxiety

These were measured using items from the Patient Health Questionnaire(19). Responses are summed separately for the depression and anxiety scales and higher scores indicate a greater degree of depression- or anxiety-related symptomatology. Note that clinical assessment of the presence of depression or an anxiety disorder cannot be made with this instrument.

2.3.2.3 Sleep disturbance

This is measured using the Sleep Disturbance subscale of the Pittsburgh Sleep Quality Index (20). Responses are summed and higher scores are associated with greater degrees of sleep disturbance.

2.3.2.4 Chronotype

To establish chronotype (i.e., morningness or eveningness) preference for each of our subjects, the Horne and Ostberg questionnaire (1968) was used.

2.3.3 Wrist actigraphs

A wrist actigraph is a watch-like device worn on the wrist. The actigraph can discriminate a sleeping state from a waking state, and the associated software can quantify daily sleep to the nearest minute. Wrist actigraphs have been used in many previous studies(21).

The wrist actigraph data files were downloaded and analysed together with sleep diaries at CFS Alert by DRDC Toronto Research Centre staff. The wrist Actigraph data and the work times for each subject were input to the Fatigue Avoidance Scheduling Tool (FAST^{TM}) program to generate cognitive effectiveness models which were analysed on an individual basis. The questionnaire data were linked to the Actigraph sleep findings and were analyzed using standard univariate data analysis.

2.3.4 Statistical power

The powers of the various two-tailed statistical tests we estimated for $p = 0.05$, an effect size of 1 standard deviation, and a test-retest reliability for repeated measures of $r = 0.50$. The estimate of power is thus 68% (22). Generally, 2 x 5 repeated-measures ANOVAs were used to analyze the data (2 levels of pre vs. post-treatment X 5 days). Where a pre- to post-treatment comparison involved only 2 cells, paired t-tests were used to assess significance.

3 Results

Of the 13 subjects in this data collection, the pre-treatment salivary melatonin data indicated that 5 subjects were adapted to the Arctic environment and did not require treatment. The remaining 8 subjects had not yet adapted and were given customized treatment with light (based on their individual pre-treatment salivary melatonin profiles) with the Light Visor (Physician Engineered Products, in Bangor Maine, USA).

Of the 5 subjects who did not require circadian countermeasures, their arrival time on Station prior to the pre-treatment salivary melatonin profile ranged from 50 to 71 days and averaged 59 days. Of the 8 subjects who required circadian interventions, their arrival time on Station prior to the pre-treatment salivary melatonin profile ranged from 19 to 44 days and averaged 38.25 days. See Table 1 and 2, and Figure 1 below.

Table 1: *Date of arrival of subjects not requiring treatment.*

Subject #	Date arrived at CFS Alert	Days before pre-treatment melatonin profile
4	2013-11-20	58
5	2013-11-28	50
6	2013-11-07	71
7	2013-11-20	58
10	2013-11-20	58
		Mean days = 59

Table 2: *Date of arrival of subjects requiring treatment.*

Subject #	Date Arrived at CFS Alert	Days before pre-treatment melatonin profile
1	2013-12-04	44
2	2013-12-11	37
3	2013-12-05	43
8	2013-12-05	43
9	2013-12-05	43
11	2013-12-12	36
12	2013-12-07	41
13	2013-12-29	19
		Mean days = 38.25

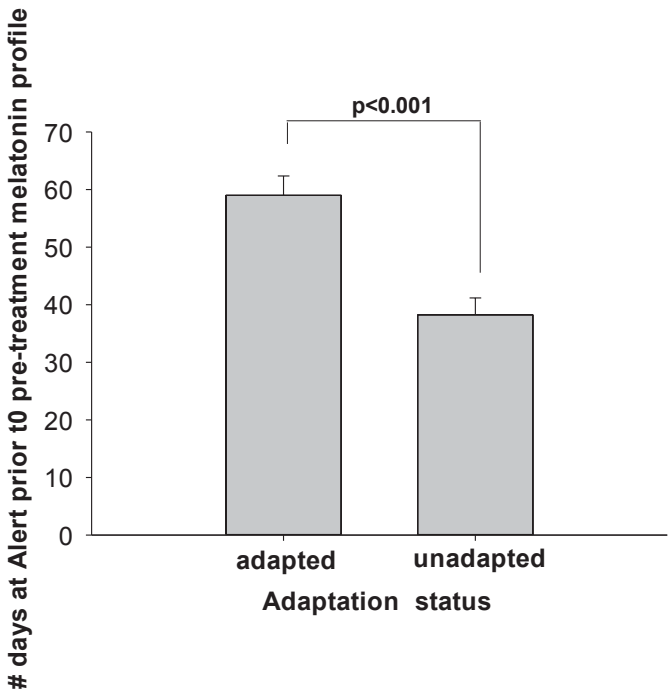

Figure 1: *Number of days at CFS Alert prior to pre-treatment salivary melatonin profile.*

3.1 Psychosocial questionnaire data

The Pittsburgh sleep scale scores were significantly lower following treatment for the 8 treated subjects, indicating that they subjectively felt that their sleep quality improved due to the treatment (Figure 2) (20). This was supported by a statistically significant improvement in the question found on Patient Health Questionnaire that asked if subjects had 'difficulty falling or staying asleep' over the last two weeks (Figure 3) (19). Lower scores of negative affectivity were also observed for the 8 treated subjects following treatment (Figure 4) (17, 18). There were no significant changes in pre-post intervention scores on the overall positive affect, depression, or anxiety scales.

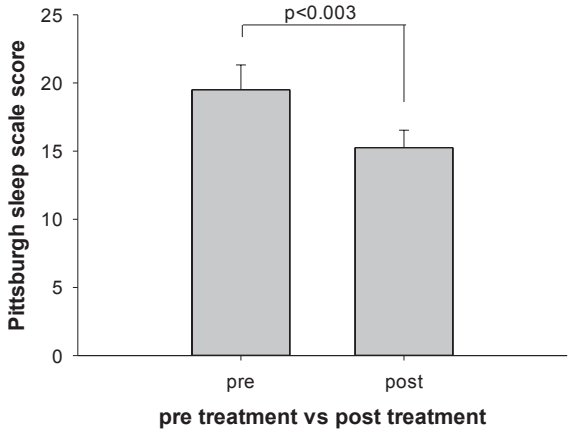

Figure 2: *Pre- vs. post-treatment differences in the Pittsburgh sleep scale score. Values are mean ± sem.*

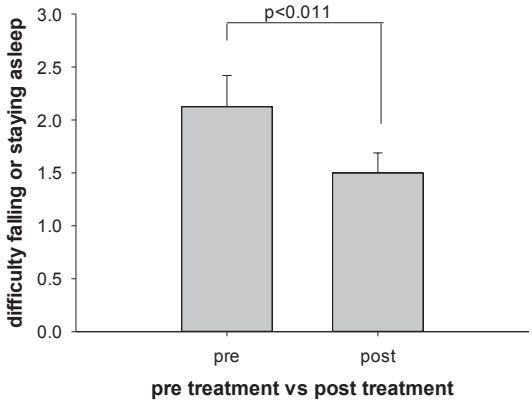

Figure 3: *Pre- vs. post-treatment 'difficulty falling or staying asleep'. Values are mean ± sem.*

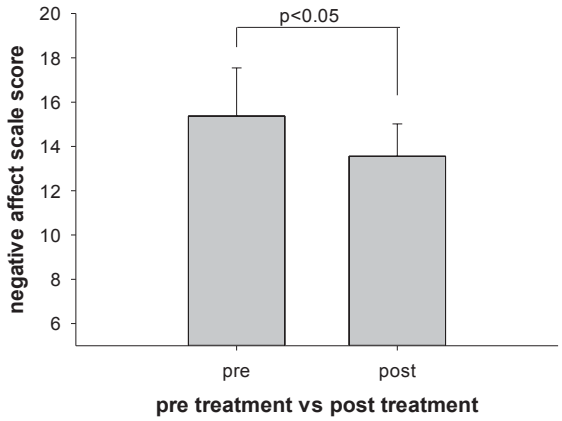

Figure 4: *Pre- vs. post-treatment negative affect scale score. Values are ± sem.*

3.2 Sleep data

The sleep data from Subject 2 (who was suffering from insomnia secondary to a medical condition) was excluded from the analysis of the treated subjects since this subject's data was in excess of 2SD difference relative to the other 7 treated subjects. His data is shown separately in Section 3.3.

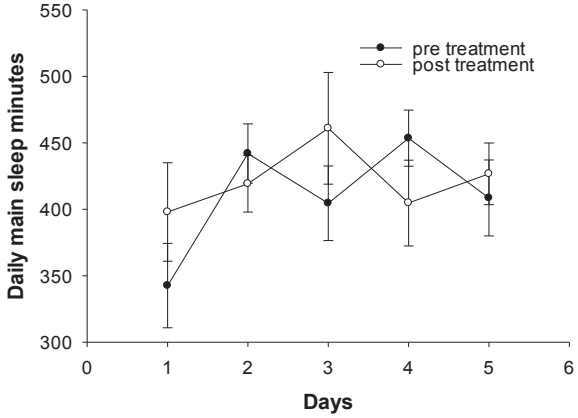

Figure 5: *Main sleep period (minutes) for the five days immediately prior to each of the pre- and post-treatment 24-hour melatonin profile collections. Values are means ± sem.*

The repeated measures ANOVA (2 levels of 2 pre- vs. post-treatment x 5 days) to evaluate the daily mean sleep period is illustrated in Figure 4 which indicates the main effect of pre- vs. post-treatment is not significant [$F(1,6) = 0.53$, $p= 0.49$], the main effect of days is not significant [$F(3,24) = 1.47$, $p = .24$], and the pre- vs. post-treatment x days interaction was also not significant [$F(4,24) = 1.76$, $p = .17$].

Except for the first pre-treatment day, where subjects averaged less than 6 hours (360 minutes) of sleep, subjects generally attained on average 7 hours (420 minutes) of daily sleep or better.

Comparison of the last night of sleep prior to each of the pre- and post-treatment salivary melatonin data collections shows that sleep quality improved on several parameters including: Wake After Sleep Onset (WASO), number of sleep episodes, sleep efficiency (the percentage of time spent in sleep after sleep onset) and percent sleep (the percentage of the sleep period spent in sleep).

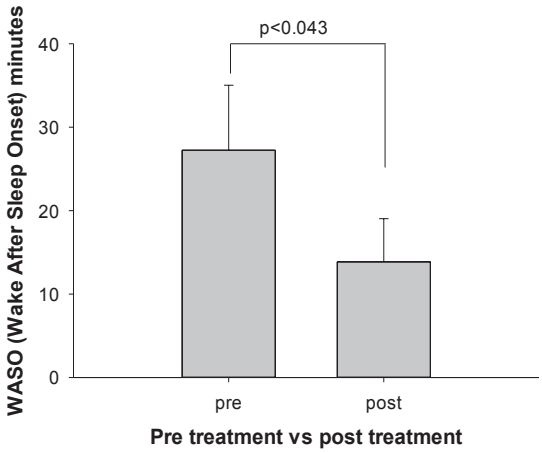

Figure 6: *Wake after sleep onset for the night prior to each of the pre- and post-treatment salivary melatonin profile collection. Values are mean ± sem.*

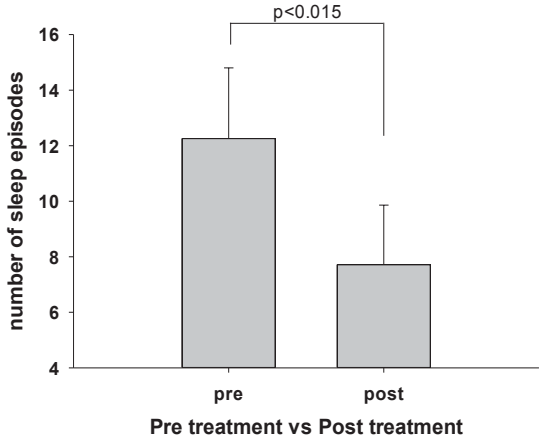

Figure 7: *Number of sleep episodes for the night prior to each of the pre- and post-treatment salivary melatonin profile collection. Values are mean ± sem.*

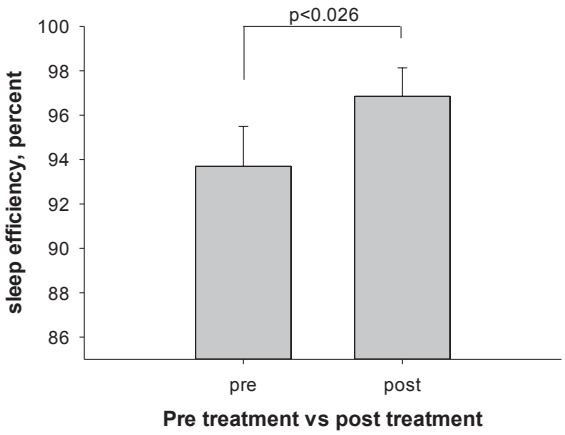

Figure 8: *Sleep efficiency (percentage of time spent in sleep after sleep onset) for the night prior to each of the pre- and post-treatment salivary melatonin profile collection. Values are mean ± sem.*

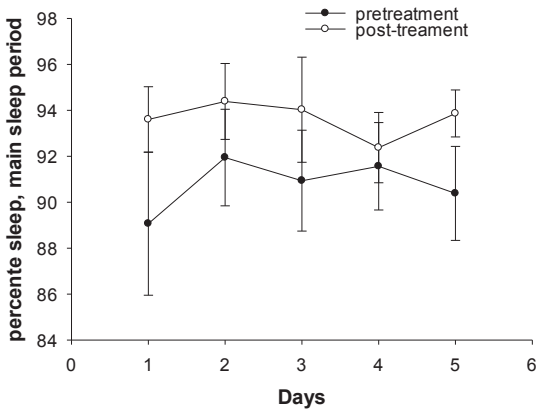

Figure 9: *Percent sleep for the five days immediately prior to each of the pre- and post-treatment 24-hour melatonin profile collections. Values are means ± sem.*

The repeated measures ANOVA to evaluate the daily mean sleep periods illustrated in Figure 4 (2 levels of 2 pre- vs. post-treatment x 5 days) indicates that the main effect of pre- vs. post-treatment is significant [$F(1,6) = 6.08$, $p= 0.048$], the main effect of days is not significant [$F(3,24) = 0.48$, $p = .75$], and the pre-treatment vs. post-treatment x days interaction was also not significant [$F(4,24) = 0.57$, $p = .68$]. The main effect of pre- vs post-treatment for percent sleep is plotted below in Figure 9.

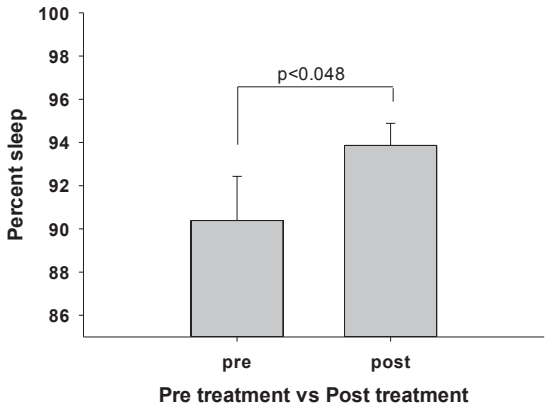

Figure 10: *Percent sleep (percentage of time spent in sleep throughout the entire sleep period) for the night prior to each of the pre- and post-treatment salivary melatonin profile collection. Values are mean ± sem.*

3.3 Sleep and cognitive effectiveness data for Subject 2

3.3.1 Pre-treatment

As mentioned above, Subject 2 was exceptional due to his insomnia. Shown below is the Actigram for Subject 2 (Figure 11), illustrating that of the 4 nights of sleep shown, he hardly slept on nights 2 and 4. The resulting modeled cognitive effectiveness for this individual (Figure 12) shows very worrisome levels of modeled performance prior to the prescription of light treatment.

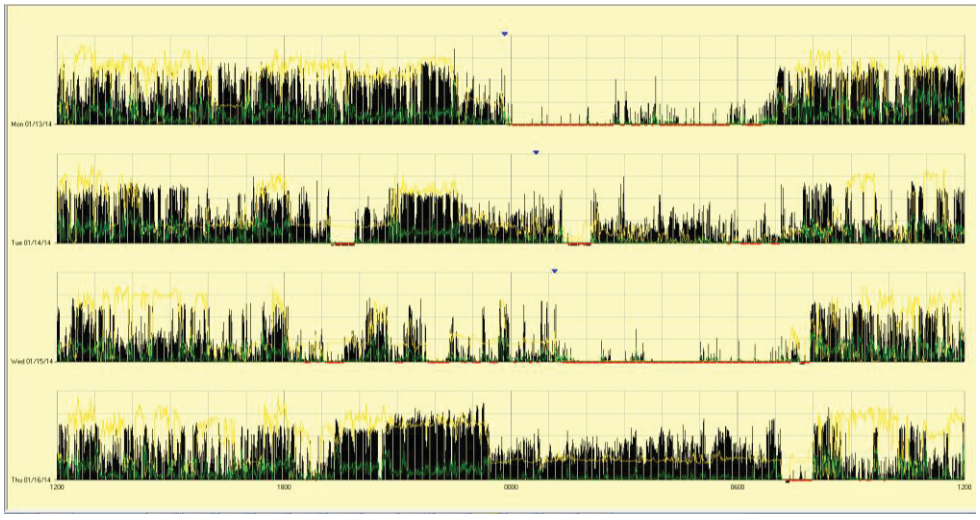

Figure 11: *Pre-treatment actigram for Subject 2. Note lack of sleep on nights 2 and 4.*

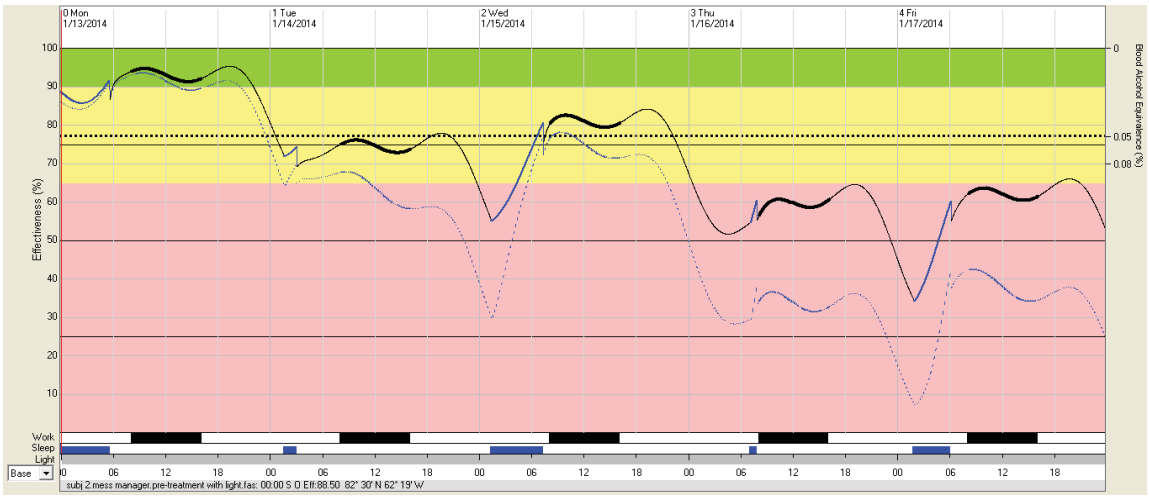

Figure 12: *FAST model of cognitive effectiveness based on pre-treatment actigraph shown in Figure 11. Cognitive effectiveness is extremely compromised by lack of sleep.*

3.3.2 Post-treatment

In contrast to the actigram and resulting modeled cognitive performance before the prescription of light treatment shown above, Subject 2's post-treatment actigram showed very significant improvements in sleep (Figure 13) and modeled cognitive effectiveness (Figure 14). This indicates that although we were not able to include Subject 2 in the analysis of sleep data for the study pre- and post-treatment, due to his outlying data, this subject clearly benefitted from the treatment.

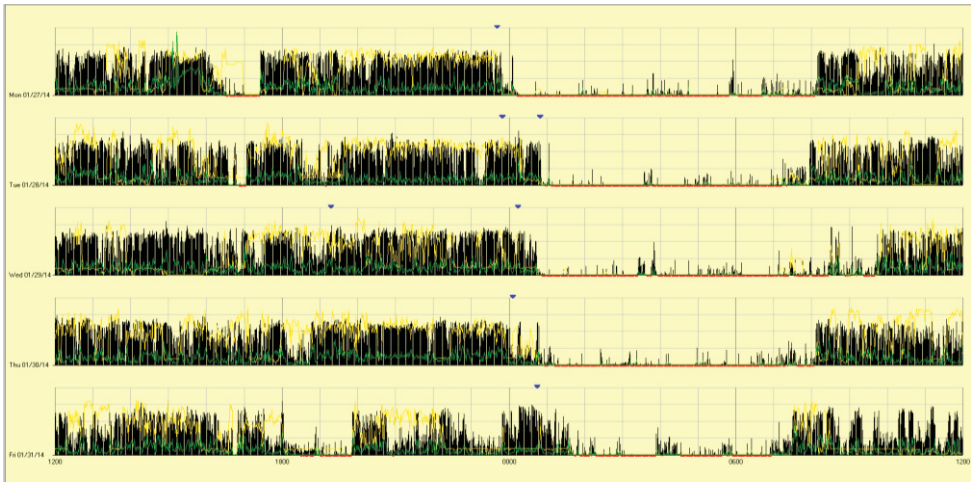

Figure 13: *Post-treatment actigram for Subject 2. Dramatically better sleep evident over the last five days of his treatment period.*

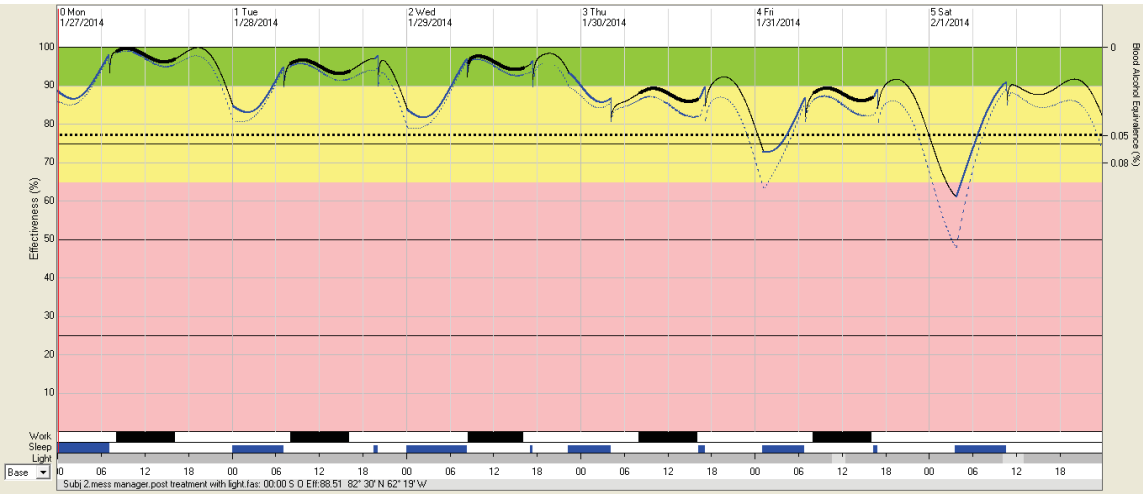

Figure 14: *FAST model of cognitive effectiveness based on post-treatment actigraph shown in Figure 13. Note the corresponding dramatic improvement in cognitive effectiveness relative to the pre-treatment period.*

3.4 Circadian data

3.4.1 Adapted subjects

The melatonin profile of the non-treated subjects remained quite consistent from pre-treatment to post-treatment saliva collection and analysis. Melatonin onset timing did not change for Subject 4 (Figure 15), advanced slightly for Subject 7 (Figure 18), and delayed slightly for subjects 5, 6, and 10 (Figures 16, 17, 19). Small drifts in the melatonin profiles of non-treated individuals are to be expected over a two week stretch of time, and we consider this finding to be natural and normal.

3.4.1.1 Subject 4

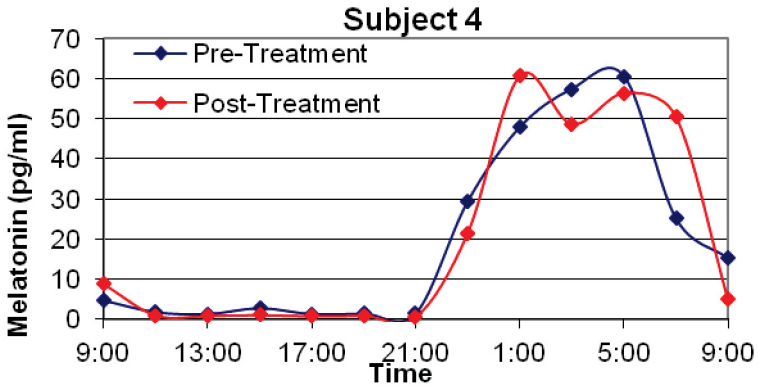

Figure 15: *Subject 4 pre- and post-treatment melatonin profiles.*

3.4.1.2 Subject 5

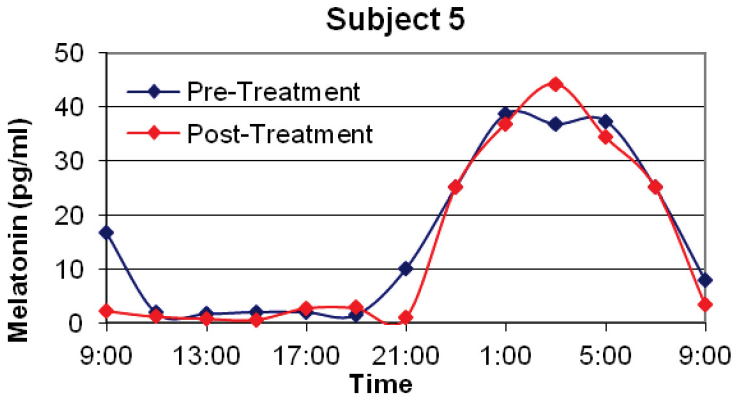

Figure 16: *Subject 5 pre- and post-treatment melatonin profiles.*

3.4.1.3 Subject 6

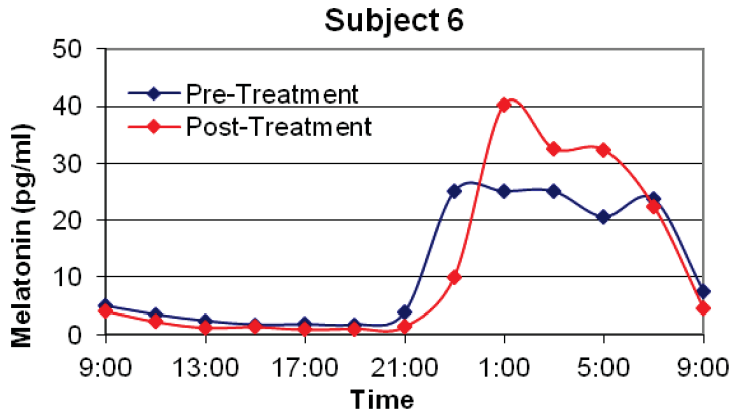

Figure 17: *Subject 6 pre- and post-treatment melatonin profiles.*

3.4.1.4 Subject 7

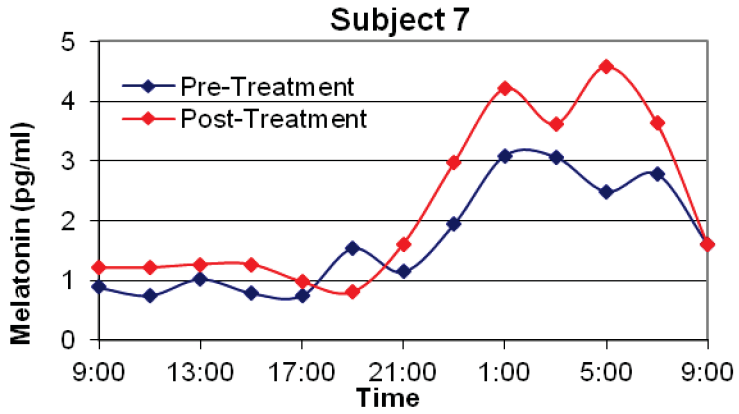

Figure 18: *Subject 7 pre- and post-treatment melatonin profiles.*

3.4.1.5 Subject 10

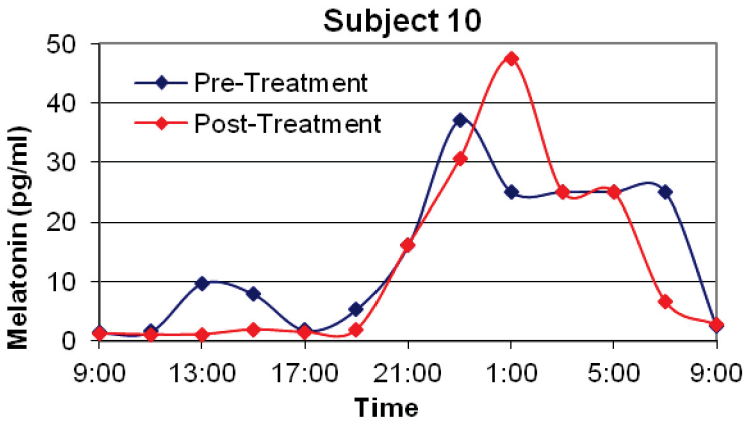

Figure 19: *Subject 10 pre- and post-treatment melatonin profiles.*

3.4.2 Unadapted Subjects

The melatonin profile of the treated subjects varied more between pre- and post-treatment compared to the non-treated subjects, but not to the degree that we had expected. The melatonin profiles (pre- and post-treatment) of the individual subjects are shown and discussed below. The treatments that were prescribed to the subjects are shown below each subject's melatonin profile.

3.4.2.1 Subject 1

Pre-treatment analysis of Subject 1's melatonin profile revealed that his pineal gland was producing melatonin for 18 to 20 hours each day (Figure 20, blue line). The normal duration of melatonin production is closer to 12 hours, so the treatment goal for Subject 1 was to shorten this subject's melatonin profile with light treatment each evening (see Figure 21). Post-treatment

analysis of his melatonin profile indicated that we were not successful with our treatment goal (Figure 20, red line). One possible reason is that this subject stopped daily treatment during the weekend (treatment days 5 and 6).

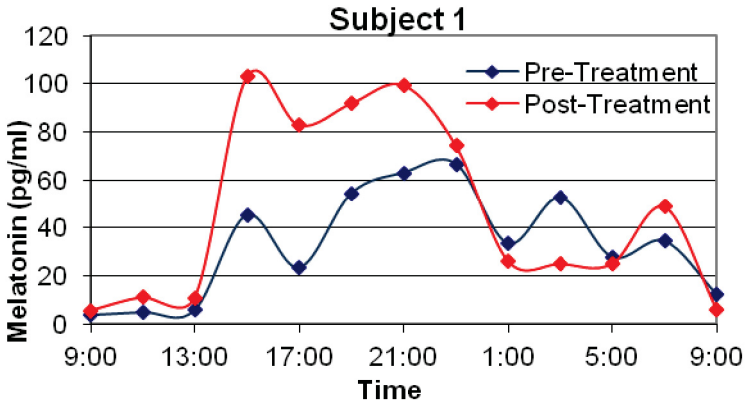

Figure 20: *Subject 1 pre- and post-treatment melatonin profiles.*

	Subject 1 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 21: *Treatment goal: shorten profile with 1-hr daily light commencing at 1400 h day 1, 1500 h day 2, 1600 h day 3, continuing to delay light treatment by 1 hour each day until reaching 1900 h and then holding at 1900 h for remaining treatment days.*

3.4.2.2 Subject 2

Subject 2 was found to be producing melatonin late into the morning (Figure 22, blue line). Therefore, the treatment goal for Subject 2 was to suppress morning melatonin production with light treatment from 9:00 to 10:00 on the first day, and 8:00 to 9:00 each subsequent day (Figure 23). Post-treatment analysis showed that we were successful in decreasing his melatonin production in the late morning.

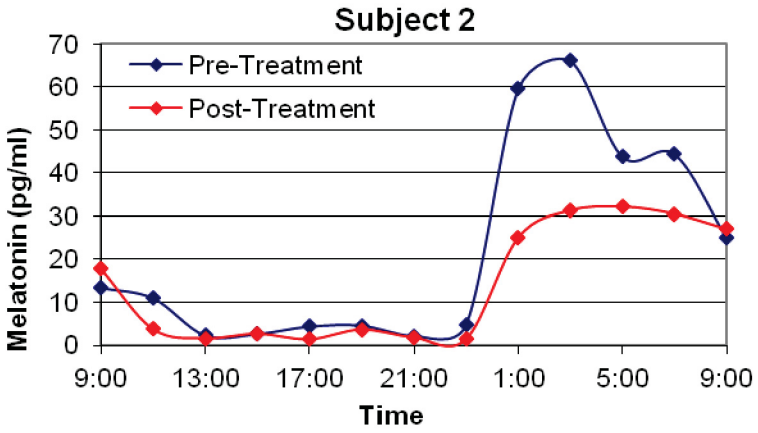

Figure 22: *Subject 2 pre- and post-treatment melatonin profiles.*

	Subject 2 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 23: *Treatment goal: suppress morning melatonin with 1-hour light treatments commencing at 0900 h on day1, advancing to 0800 h on day 2 and remaining at 0800 h for the remaining treatment days.*

3.4.2.3 Subject 3

Pre-treatment analysis of Subject 3's melatonin profile revealed evening melatonin production was too early, with a spike of melatonin production occurring at 1900 h (Figure 24, blue line). Therefore, the light treatment for Subject 3 was prescribed between 1800 to 1900 h, with the intention of suppressing early evening melatonin production (Figure 25). Post-treatment analysis showed that the prescribed light treatment was successful in suppressing early evening melatonin production (Figure 24, red line).

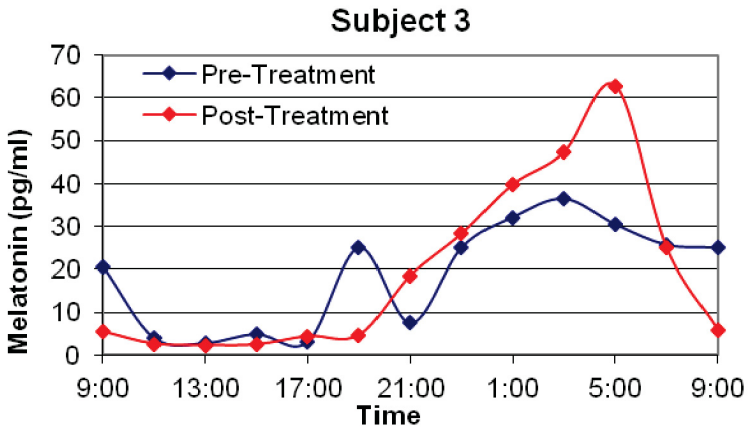

Figure 24: *Subject 3 pre- and post-treatment melatonin profiles.*

	Subject 3 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 25: *Treatment goal: suppress early evening melatonin with 1 hour of light treatment at 1800 h each day.*

3.4.2.4 Subject 8

An early afternoon peak of melatonin production was evident in Subject 8's pre-treatment melatonin profile (Figure 26, blue line). Therefore, the light treatment prescription for Subject 8 was intended to suppress the early afternoon melatonin (Figure 27). Post-treatment analysis revealed that the early afternoon melatonin production was no longer occuring. (Figure 26, red line).

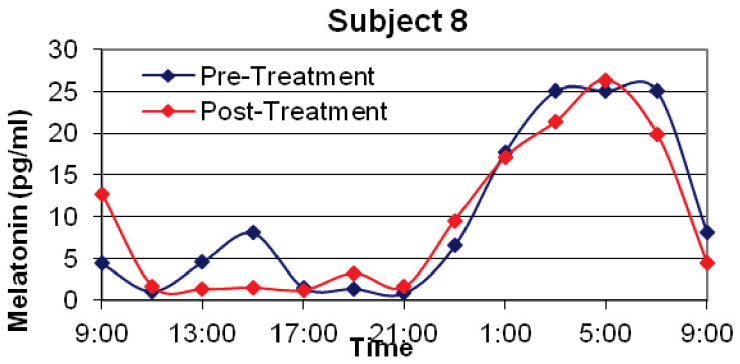

Figure 26: *Subject 8 pre- and post-treatment melatonin profiles.*

	Subject 8 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 27: *Treatment goal: suppress afternoon melatonin peak with light from 1100 h to 1200h for all treatment days.*

3.4.2.5 Subject 9

A peak of melatonin production at 1300 h was evident in the pre-treatment melatonin profile of Subject 9 (Figure 28). Therefore, the light treatment goal for Subject 9 was to suppress this mid-day melatonin (see Figure 29). Post-treatment analysis revealed that the light treatment was not successful in suppressing this individual's mid-day melatonin production; however, this may have been due to subject compliance issues as this subject consistently delayed assigned light treatment times by up to 2 hours and missed one treatment entirely.

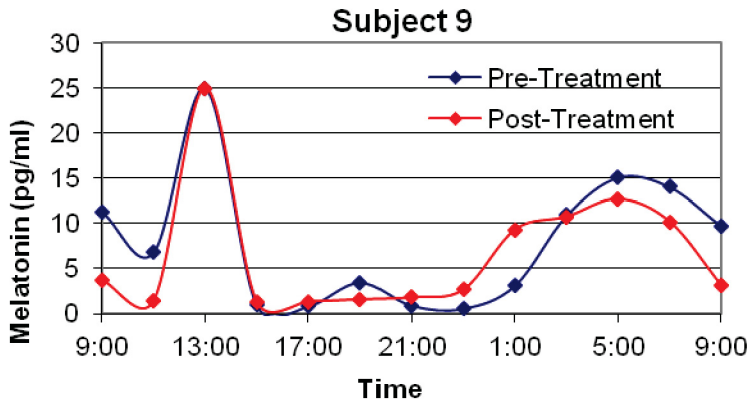

Figure 28: *Subject 9 pre- and post-treatment melatonin profiles.*

	Subject 9 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 29: *Treatment goal: supress mid-day melatonin with 1-hour of daily light treatments starting at 1100 h to 1200 h on day 1, advancing by an hour each day until reaching 0800 h to 0900 h and holding at 0800 h to 0900 h for the balance of the treatment period.*

3.4.2.6 Subject 11

The pre-treatment melatonin profile for Subject 11 showed quite a significant amount of melatonin present during the day, but a late rise in production in the evening (Figure 30, blue line). Therefore, light treatment was prescribed with the intention of advancing this subject's circadian system (i.e., earlier melatonin production in the evening, earlier melatonin clearance in the morning; see Figure 31). Post-treatment analysis showed that this individual's afternoon melatonin production was advanced to a late morning position, which is still a problem since there would still be potential sleepiness in the late morning (Figure 30, red line). This late morning melatonin production could probably have been eliminated by shifting the original 0800 h to 0900 h treatment, after a few days, to 0700 h to 0800 h. Earlier light treatment would have also been more effective at advancing his circadian system.

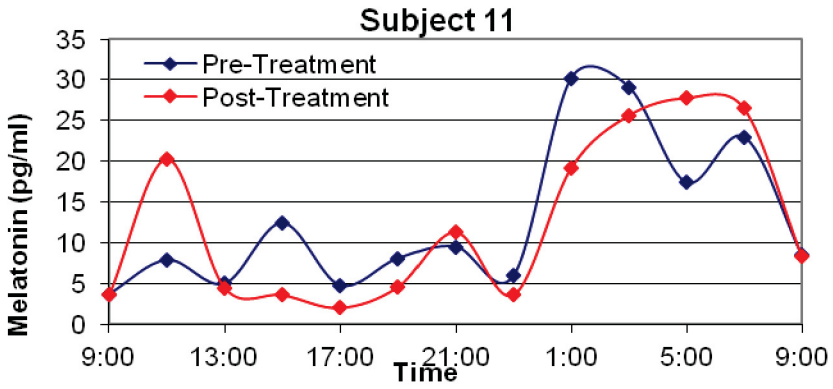

Figure 30: *Subject 11 pre- and post-treatment melatonin profiles.*

	Subject 11 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 31: *Treatment goal: to advance the circadian system with 1 hour daily light treatment from 0800 h to 0900 h for all treatment days.*

3.4.2.7 Subject 12

Subject 12 was found to produce a surge of melatonin between 1300 h and 1700 h during pre-treatment analysis (Figure 32, blue line). Light treatment was prescribed with the intention of suppressing this afternoon melatonin production (Figure 33). The intended suppression of afternoon melatonin production by this individual was marginally effective in that the afternoon melatonin was pushed to the late morning (Figure 32, red line).

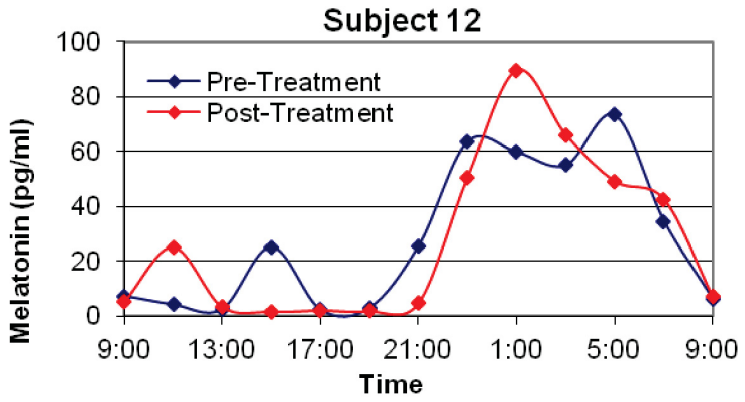

Figure 32: *Subject 12 pre- and post-treatment melatonin profiles.*

	Subject 12 - Time of Day													
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 33: *Treatment goal: To suppress afternoon melatonin with daily 1-hr light treatments from 1400 h to 1500 h on day 1 delaying by 1 hour each day for the next 5 days until reach 1900 h to 2000 h and keep treatment at 1900 h to 2000 h for remaining treatment days.*

3.4.2.8 Subject 13

The pre-treatment melatonin analysis for Subject 13 revealed that she was producing a high quantity of melatonin for a long duration during the day (Figure 34, blue line). Pre-treatment melatonin concentration only fell below 10pg/ml at 1700 h, and reached 60 pg/ml only 2 hours afterwards (at 1900 h). Therefore, the light treatment goal for Subject13 was to eliminate inappropriate melatonin production in the morning and the afternoon, and delay the onset of production in the evening (see Figure 35). Post-treatment melatonin production revealed that the prescribed morning light treatment caused attenuation of the morning peak of melatonin (Figure 34, red line). Overall, the light treatments seemed to increase the quantity of melatonin that was produced through the night.

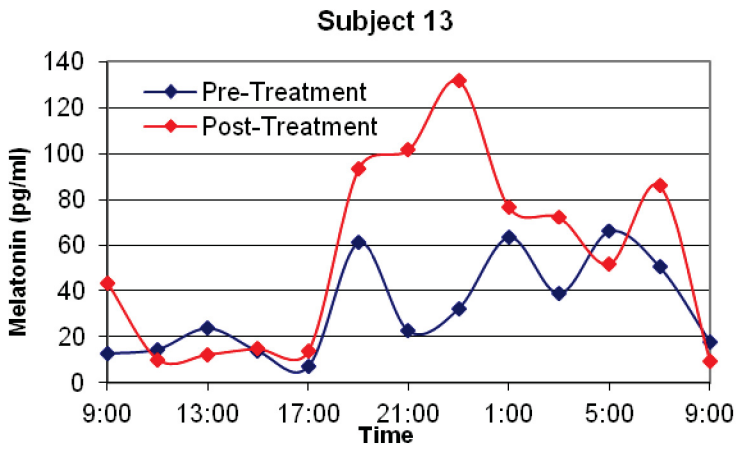

Figure 34: *Subject 13 pre- and post-treatment melatonin profiles.*

	Subject 13 - Time of Day														
Day	07h-08h	08h-09h	09h-10h	10h-11h	11h-12h	12h-13h	13h-14h	14h-15h	15h-16h	16h-17h	17h-18h	18h-19h	19h-20h	20h-21h	21h-22h
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Figure 35: *Treatment goal: To suppress morning melatonin production, take l-hour light treatment from 0800 h to 0900 h each morning. To suppress afternoon melatonin, take 1-hr light treatment from 1400 h to 1500 h on day 1 and delay daily afternoon light by 1 hour until reaching 1900 h to 2000 h and remain at 1900 h to 2000 h for the remaining treatment days.*

4 Discussion

The decision on who would receive circadian adjustment was strictly based on the melatonin profiles obtained from the subjects. Subsequently we learned that the five subjects who did not require any circadian adjustments were the five individuals who had been on station the longest: two months, on average (Table 1 and Figure 1). In contrast, the eight subjects that required circadian intervention with daily light treatments were on station for the shortest amount of time: five weeks, on average (Table 2 and Figure 1). The differences in 'time on station' between the adapted and unadapted subjects indicates that there is an adjustment by the circadian system that occurs in response to the (lack of) light intensity in the Arctic during the winter. An important outstanding question is "How much time would have to elapse before these subjects would fully adapt to Arctic winter conditions at CFS Alert?" It is very possible that some of the subjects that we treated had already entered a period of adaptation, but were not yet fully adapted to the light levels in the Arctic environment. Our study is the first study ever to report adaptation to the Arctic environment, and thus, further elucidation of the circadian system adaptation that occurs due to the lack of light in the arctic winter is warranted.

Based on data from our psychosocial questionnaires, the Pittsburgh sleep scale score (Figure 2), the 'difficulty falling or staying asleep' item from the PHQ depression scale (Figure 3), and the negative affect scale score (Figure 4), it is evident that our treated subjects perceived benefits from the light treatments. The subjective improvement in sleep reported by the subjects through the questionnaires was objectively supported by the significant improvements in quality of sleep, as measured by the actigraphic data. Specifically, the treated subjects woke less after sleep onset, as measured by the Wake after Sleep Onset (WASO) parameter (Figure 6), and had fewer awakenings, as measured by the number of sleep episodes (Figure 7). Furthermore, sleep efficiency improved (Figure 8), as did the percent of time spent asleep during the daily main sleep periods (Figures 9 and 10). Notably, the quantity of sleep obtained by the subjects did not increase in response to the light treatment. However, we learned from our baseline studies (23) conducted at CFS Alert that the quantity of sleep obtained during the winter in the Arctic generally seems to be sufficient. Therefore, it appears that the subjects were already obtaining sufficient sleep, and the light treatment lead to qualitatively better sleep (i.e., more efficient sleep with fewer awakenings, etc.). As we discuss below, the efficacy of treatment on the circadian system was not as definite, and we suspect that this may be due to the timing in which the treatment was given to some of the subjects. Timing was based on the assumption that light treatment would both suppress (immediately) and phase shift melatonin (according to the Phase Response Curve [PRC]). However the baseline profiles obtained from many of the treated subjects were unusual in showing high daytime 'spikes' not normally seen in controlled laboratory conditions in our data and that of others. These 'spikes' made the definition of DLMO difficult in several cases. It is possible that some of these values might be due to salivary substances interfering with the ELISA. However the only way of confirming the identity of the 'spikes', and indeed the very high levels seen in subjects 1 and 13, would be to re-assay the samples with a mass-spectrometric method and this is now impossible. While the circadian system requires very specifically-timed light treatment (4 to 6 hours after DLMO for phase delay and 9 to 11 hours after the DLMO for phase advance), or a complete day of bright light, there seems to be an apparent psychosocial benefit of morning or evening light to suppress early circadian spikes of melatonin that seem to be produced by many of the subjects in the winter

Arctic environment. Since light treatment is non-invasive, relatively unimposing, and has no associated side-effects, the use of the light visors is appropriate for individuals that are experiencing some difficulty adapting to the arctic winter (i.e., mild sleep trouble or increased negative affectivity). Due to the small subject population in this study, more research on the effectiveness of treatment is certainly warranted before any firm recommendations can be made. Even though treatment timing may not be as important for psychosocial benefit as it is for circadian system benefit, use of a light visor within two hours of a person's normal bedtime will suppress the melatonin that helps that individual fall asleep.

The efficacy of treatment for shifting the circadian system was very specific to the individual and treatment that they were prescribed. Therefore, the effectiveness of treatment on each subject's circadian system is discussed below. Among our non-treated subjects, melatonin onset timing pre-treatment vs. post-treatments either didn't change (Subject 4, Figure 15), advanced slightly (Subject 7, Figure 18), or delayed slightly (Subjects 5, 6, and 10), illustrated in Figures 16, 17, and 19 respectively. Note the very low melatonin production of Subject 7 (Figure 18) relative to the other subjects. Among our treated subjects, the daily delaying light treatment designed to shorten the melatonin profile of Subject 1 was not effective. One possible reason is that Subject 1 stopped daily treatment during the weekend (treatment days 5 and 6), because it was not convenient for him Light treatment for Subject 3 was intended to suppress early evening melatonin and was successful (Figure 24). Light treatment for Subject 8 was intended to suppress afternoon melatonin and was successful (Figure 26). The light treatment goal for Subject 9 was to suppress mid-day melatonin and was not successful. Subject 9 consistently delayed assigned light treatment times by up to 2 hours and missed one treatment entirely. Light treatment prescribed for Subject 11 was intended to suppress afternoon melatonin. The afternoon melatonin was advanced to a late morning position, which is still a problem as the potential since late morning sleepiness is still present. The late morning melatonin could probably have been eliminated by shifting the original 0800 h treatment to 0700 h after a few days. The intended suppression of afternoon melatonin for Subject 12 using sequentially delayed light treatments was marginally effective in that the afternoon melatonin was pushed into the late morning (Figure 32) where it would potentially result in late morning sleepiness. In retrospect, a more effective plan might have been to begin the sequentially delayed light treatments an hour earlier on day 1 and continuing to delay until reaching light treatments at 2000 h to 2100 h and holding at that time for the remaining 5 treatment days. The light treatment goal for Subject 13 was to eliminate inappropriate melatonin peaks in the morning and the afternoon. Consequently, this subject received fixed morning light and a schedule of sequentially delayed afternoon light. The morning light did attenuate the morning peak of melatonin but did not entirely eliminate it. The afternoon light actually increased melatonin levels through the evening and night, similar to the response of Subject 1. These subjects both received sequentially delayed light treatments but whether or not this is relevant remains to be seen.

Subject 2 was exceptional due to insomnia secondary to a medical condition. Of the 4 nights of sleep shown in his actigram (Figure 11), Subject 2 hardly slept on nights 2 and 4. Note also that this individual's modeled cognitive effectiveness prior to light treatment (Figure 12) was at very worrisome levels of modeled performance. In contrast, this individual's post-treatment actigram showed very significant improvements in sleep (Figure 13) and in modeled cognitive effectiveness (Figure 14). The daily light treatment for Subject 2 was intended to suppress his morning melatonin and was partially successful in that regard (Figure 22). Note the drop in

melatonin post-treatment at 1100 h. Light treatment also very significantly improved this individual's ability to sleep (Figures 11 and 13).

While repeated exposures to day-time light treatments are effective in manipulating circadian phase timings, they have also been shown to result in increases to the peak levels of nocturnal melatonin (24). Subjects 1, 3, 12 and 13 show increases in peak melatonin levels after treatment, although Subjects 6, 7 and 10 (who did not receive treatment) also showed increases in peak melatonin levels in the 2nd (post-treatment) salivary melatonin profile.

The reader should make note of the limited statistical power of the experiment described herein due to the low number of treated subjects. We hope to continue these Arctic countermeasures over the next one to two years for each of the Arctic winter and summer extremes of daylight. This would allow us to pool data in order to increase statistical power and thus improve our understanding of the relative efficacy of our circadian countermeasures.

The simplest approach to circadian countermeasures would be to increase light levels throughout the working day. This has been successfully implemented on an Antarctic base with improvements in sleep and circadian phase (4, 25)**.** One possible method of achieving this at CFS Alert would be the installation of the latest LED high intensity/high efficiency lighting systems.

5 Conclusions/Recommendations

In summary, the light treatments prescribed were effective at improving sleep quality both subjectively, based on the questionnaire results, and objectively, based on the actigraphic data. Circadian system effects from the light treatment were less definite, but the melatonin profile of many of the subjects certainly improved. Since light treatment is non-invasive, relatively unimposing, and has no associated side-effects, we recommend the use of the light visors at CFS Alert and other northern outposts during the winter for individuals that are experiencing some difficulty adapting to the lack of daylight (i.e., mild sleep trouble or increased negative affectivity). Since statistical power of the experiment described herein was limited due to the low number of unadapted subjects, we hope to perform similar studies in the near future to improve our understanding of the relative efficacy of our circadian countermeasures. Future studies could clarify the time-course of the adaptation period, whether general lighting improvements could accelerate this adaptation, and whether rapid individual salivary melatonin assays (when they become available) would allow identification of problematic melatonin rhythms by the attending CFS Alert Physician Assistants or Medical Officers.

It is evident from this study that can be individuals suffering from sleep disorders who are deployed to the high Arctic. Perhaps pre-deployment screening for sleep pathologies would preclude such deployments and thus eliminate unnecessary suffering of these individuals in the high Arctic environment.

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6 References

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List of symbols/abbreviations/acronyms/initialisms

CFS	Canadian Forces Station
DND	Department of National Defence
DRDC	Defence Research and Development Canada
DSTKIM	Director Science and Technology Knowledge and Information Management
ELISA	Enzyme-linked Immunosorbent Assay
FAST	Fatigue Avoidance Scheduling Tool
PRC	Phase Response Curve
R&D	Research & Development
SCN	Suprachiasmatic Nucleus

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Background. DRDC Toronto has optimized the ability to manipulate circadian rhythms with supplementary melatonin and/or light treatment, as appropriate, to reduce or eliminate the circadian desynchrony that is inherent in jetlag and shiftlag. For the past 3 years we have collected Arctic circadian baselines at CFS Alert to establish the impact on human circadian physiology during each of the extremes of arctic winter and arctic summer photoperiod. The work described herein is our first attempt at implementing Arctic circadian countermeasures for the treatment of discordant human circadian rhythms that are apparent in personnel of CFS Alert during the Arctic winter. **Methods.** This data collection commenced on Jan 18, 2014 at CFS Alert. To qualify for the study, subjects had to have been at Alert for at least three weeks prior to commencement of the study. Subjects filled out questionnaires regarding sleep difficulty and psychosocial parameters, and wore motion logging devices (Actigraphs) to obtain objective sleep data. Saliva was collected at regular intervals on two occasions, two weeks apart, to measure melatonin and assess melatonin onset. Individuals with a melatonin rhythm that was in disaccord with their sleep schedule were given a light treatment visor to use daily. Treatment efficacy was evaluated using the questionnaire data, actigraphic data, and endogenous melatonin profiles. **Results.** The light treatment prescribed to eight of the thirteen subjects was effective, to a statistically significant degree, at improving sleep quality both subjectively, based on the questionnaire results, and objectively, based on the actigraphic data. Circadian system effects from the light treatment were less definite, but the melatonin profile of many of the subjects improved. **Conclusions.** The light treatment significantly improved sleep quality in our subject population. Since the treatment is non-invasive and has no associated side-effects, our results support the use of the light visors at CFS Alert and other northern outposts during the winter for individuals that are experiencing some difficulty adapting to the lack of daylight (i.e., mild sleep trouble or increased negative affectivity). However, due to the low statistical power of this study, more research on the effectiveness of treatment is certainly warranted before any firm recommendations can be made.

Contexte. RDDC Toronto a maximisé la capacité de manipulation du rythme circadien au moyen de suppléments de mélatonine ou de séances de photothérapie, selon le cas, pour réduire ou éliminer la désynchronisation du rythme circadien provoquée par le décalage horaire ou le décalage lié au travail par roulement. Depuis trois ans, nous avons recueilli des données de référence sur le rythme circadien dans l'Arctique, à la SFC Alert, pour connaître les effets sur la physiologie humaine des variations extrêmes de chacune des photopériodes de l'hiver et de l'été dans cette région. Les travaux décrits ici constituent notre première tentative visant à mettre en œuvre des contre-mesures afin de traiter les perturbations du rythme circadien humain observées parmi le personnel de la SFC Alert pendant l'hiver en Arctique. **Méthodes.** La collecte de données a commencé le 18 janvier 2014 à la SFC Alert. Pour participer à l'étude, les sujets devaient être à la SFC Alert depuis au moins trois semaines avant le début de l'étude. Les sujets ont rempli des questionnaires sur leur difficulté à dormir et sur des paramètres psychosociaux. De plus, ils portaient un dispositif d'enregistrement du mouvement (ActiGraph), qui permet d'obtenir des données objectives sur le sommeil. La salive a été recueillie à intervalles réguliers à deux occasions, à deux semaines d'intervalle, pour mesurer la mélatonine et déterminer le début de sa sécrétion. On a remis aux personnes dont le rythme de sécrétion de mélatonine ne correspondait pas à leur horaire de sommeil une visière de photothérapie pour usage quotidien . Les données du questionnaire, les données actigraphiques et les profils de

sécrétion de mélatonine endogène ont servi à évaluer l'efficacité du traitement. La photothérapie prescrite à huit des treize sujets s'est avérée efficace, à un degré statistiquement significatif, pour améliorer la qualité du sommeil, d'un point de vue subjectif, au moyen des résultats du questionnaire, et d'un point de vue objectif, au moyen des données actigraphiques. Les effets de la photothérapie sur le rythme circadien étaient moins évidents, mais la sécrétion de mélatonine a augmenté chez de nombreux sujets. **Conclusions**. La photothérapie a considérablement amélioré la qualité du sommeil chez les sujets ciblés. Comme le traitement est non invasif et qu'il n'a aucun effet secondaire, nos résultats permettent d'appuyer l'utilisation de visières de photothérapie à la SFC Alert et dans les autres postes nordiques éloignés pendant l'hiver pour les personnes qui éprouvent de la difficulté à s'adapter au manque de lumière (p. ex., troubles légers du sommeil ou augmentation de l'affectivité négative). Toutefois, étant donné le faible poids statistique de cette étude, il serait certainement justifié de mener d'autres recherches sur l'efficacité du traitement avant de pouvoir formuler des recommandations fermes à ce sujet.

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endogenous melatonin; circadian desynchrony; fatigue; sleep hygiene; modeled cognitive effectiveness