

Effect of phototherapy on sleep disorders

[Health & Medicine](#), [Sleep Disorders](#)



In the natural world, the light - dark cycle entrains our rhythm. Light is a very effective 'Zeitgeber'. In the presences of environmental time cues, sleep-wake physiology, and gene expression continue to exhibit a near-24-hour circadian rhythm regulated by the Suprachiasmatic Nucleus in the Hypothalamus. Phototherapy is an accepted modality for non-pharmacological management of Circadian Disorders such as Delayed Sleep Phase Syndrome, Insomnia etc. This review discusses the physiological principle and highlights evidence based literature of phototherapy and its management in Sleep Disorders.

Introduction;

Living organism's exhibit a biological periodicity, this rhythm when occurs on a 24 hour cycle is known as 'Circadian Rhythm'.

A rhythmic biological cycle that displays an endogenous entrainable oscillation of less than 24 hours is known as ultradian rhythm. and that last for more than 24 hours is known as Infradian rhythms.

Circadian Rhythms generate rhythmic cycling of sleep patterns, food intake, sexual behavior, core body temperature and secretion & release of hormones such as ACTH, Prolactin, Gonadotrophin and Melatonin.

Circadian Rhythms are generated by the Suprachiasmatic Nucleus (SCN) of the Anterobasal Hypothalamus. Pineal gland regulates the rhythmic production and release of melatonin. The duration, phase and amplitude of melatonin and cortisol secretion, are influenced by changes in light-dark cycles. The plasma levels are low during day time and are high at night. This

rhythm is maintained by the SCN and is entrained by the light-dark cycle. Low light intensities like 100 to 500 lux also have been shown to suppressed levels of melatonin.

Phototherapy or light therapy utilizes light boxes which are typically LED square bright lights, ranging from 8-12 x 12-24 inches that emit 10, 000 Lux (highest Lux) light, “ cool” color temperature light acts as natural sunlight without the harmful effect of UV rays. This mode of entraining the sleep wake cycle is an accepted modality and mainstay treatment in the non-pharmacotherapeutic management of Circadian Rhythm Disorders.

Principles of Phototherapy

The goal of the Circadian Rhythm is to maintain a bridge between sleep patterns and the internal clock that is set at a optimally synchronized time. This results in a normal sleep-wake pattern.

The Biological Model-Phase response curve

The Phase Response curve is modulated by two efficacious modalities i. e. light and melatonin, both of which are exploited to entrain the circadian cycle. Bright light is very helpful in synchronizing the human rhythms and the melatonin serves as a “ dark pulse” helping to induce night-time behaviors. Bright morning light advances circadian rhythms; bright evening light delays them. Melatonin in the evening advances circadian rhythms; melatonin in the morning delays them.

Circadian Disturbances and Insulin Resistance

Type 2 Diabetes Mellitus is a multifactorial disorder, of which Circadian Disturbances is one of the lifestyle factors that contribute to it.

Sleep disturbances including sleep insufficiency, sleep loss, sleep fragmentation, are connected to abnormal Glucose Metabolism and thus, increase the risk of Type 2 Diabetes Mellitus. Studies in rodent models suggest that disruption of Circadian Rhythms leads to impaired glucose homeostasis and beta-cell failure, culminating in increased susceptibility to Type 2DM. Disturbed Circadian Rhythm is causative factor in the recent epidemic “ Obesity”. In controlled clinical studies, acute 1-3 week circadian misalignment (alone) or in combination with sleep restriction results in dysregulation of glucose homeostasis and consequent glucose intolerance attributed in part to loss of beta-cell function as well as decline in insulin sensitivity.

CIRCADIAN RHYTHM PROBLEM CONTRIBUTES TO INFLAMMATORY DISEASES.

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn’s disease (CD), is a chronic and recurrent inflammatory disorder of the intestinal tract. Study says that sleep disturbances are one of the main reasons of pathogenesis of the patients with IBD. In addition melatonin plays a vital role in regulation of inflammation as well as immune system and antioxidant system in the intestinal disorders. (16, 17)

CIRCADIAN RHYTHM and visually Impaired

Bright light has been shown to suppress Melatonin secretion even in visually impaired subjects which substantiates the fact that non-visual

photoreceptors in the eye mediate the Circadian Rhythm regulating effects of light

CIRCADIAN RHYTHM AND IMMUNITY

Sleep restriction and sleep deficit increase your vulnerability to disease. The immune system is connected to the sleep regulatory system and actions of the immune system to fight disease. Sleep is regulated partly by immune system components called cytokines. Blood counts of T-cells and levels of proinflammatory cytokines are high during the night while leukocytes and the anti-inflammatory cytokine IL-10 go up during daytime.

Changes in the immune system seem associated with the onset of narcolepsy, which has a neurological cause (brain cell death) inflammatory diseases increase cytokine levels and make people feel fatigued. This is a good thing during a short-term injury or illness, as it drives the person to rest. For those with chronic inflammation, however, the immune system keeps them tired for long periods, which may explain symptoms of fibromyalgia and chronic fatigue disorder. The trouble in sleeping that people with those conditions experience is not due to just the discomforts of the illnesses, but because the sleep regulation system is affected.

The different phases of sleep are responsible for different functions within our bodies. The first and second phases involve settling in, resulting in rhythmic breathing and a lowered body temperature. The third and fourth stages are when our bodies are working to restore themselves. During this time our muscles relax and the blood supply going to them increases. Our bodies use this time to repair tissue damage and grow new tissue. Important

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hormones are released and our energy is renewed. These stages appear to be a critical factor in maintaining a healthy immune system and any sleep disturbance that impacts them, impacts our health. It is becoming increasingly evident that disruption of daily rhythms, such as from sleep deprivation, affects the immune response.

Toll-like receptor 9 (TLR9), is an immune system protein that can sense bacterial and viral DNA

Role of Phototherapy

Cognitive Impact

Light intensity has a direct impact on cognitive performance and alertness and on the subjective feeling of sleepiness. The researchers found that volunteers subjected to higher light intensity during the afternoon were more alert all the way into the early evening than those who were not. But when subjected to light intensity 10 times weaker, they showed signs of sleepiness and obtained lower scores on the memory tests.

Artificial light is used to phase shift circadian rhythm and help improve performance, sleep, and well-being during shiftwork simulations , this was proved in study designed for NASA personals during t he prelaunch week. The treated subjects were self exposed to 10, 000 Lux. The treated personnel showed a positive result reporting better sleep, performance, and physical and emotional well-being than control subjects and rated the treatment as highly effective for promoting adjustment to their work schedules for the study. Nocturnal alertness, performance, and daytime

sleep could be improved by light exposure of tolerable intensity and duration in a real work place. This was proved in a cross-over design study conducted on 12 night Shift nurses with three different treatment procedures: Room Light (RL) exposure in the night followed by a 1hr sunlight or 10, 000 lux light next morning(08: 30 to 09: 30), Bright Light (BL) a 4-hour nocturnal light exposure of 4, 000-6, 000 lux (from 01: 00 to 05: 00) and Bright Light with Sunglasses (BL/S) the same nocturnal light exposure as in BL was done with light attenuation in the morning. Nocturnal alertness was measured by a visual analog scale. Daytime sleep was recorded with actigraphy. Nocturnal alertness was the highest in the BL/S. The improvement was maximized by attenuating morning light.

Sun-Downing phenomenon

Sundowning is a clinical phenomenon characterized by the emergence or increment of neuropsychiatric symptoms such as confusion, disorientation, anxiety, agitation, aggression, pacing, wandering, resistance to redirect screaming, yelling and so forth observed late afternoon, evening or at night and occurs among cognitively impaired, demented, or institutionalized elderly patients. In a 6-week, double-blind, placebo-controlled, cross-over trial the effects of bright light therapy combined with melatonin on motor restless behavior in demented patients had been evaluated. This study concluded that bright light therapy (10, 000 lux bright light) has a positive effect on motor restlessness in subjects with dementia.

Mood disturbances

Manic-Depressive Illness (MDP): MDP is recurrent illness in which episodes of Mania and Depression occur and remit spontaneously. Several clinical studies say that disturbance in the Circadian Rhythms play a crucial role in its pathophysiology. Melatonin secretion shows abnormal levels in some bipolar patients (MDP). Patients with MDP exhibit circadian sleep wake rhythm in which patients spent one complete sleepless night in between two nights of normal sleep. In a study, 143 patients with a major depressive episode in the course of bipolar disorder (DSM-IV criteria) treatment with 3 consecutive total sleep deprivation cycle (each composed of a period of 36 hours awake followed by recovery sleep), light therapy, and lithium rapidly decreased the depressive suicidality and prompt antidepressant response in patients with drug-resistant major depression in the course of bipolar disorder. Borderline personality disorder (BPD) is typically characterized by instability and impaired behaviour, affectivity, interpersonal relations and lifestyle. This open study assessed 13 female patients for the effectiveness of the application of bright light (10,000 lux, 6:30 to 7:30 a.m. for 6 weeks) added to SSRIs in drug-resistant depressed patients with comorbid BPD who did not show any improvement to 6-week administration of antidepressants. The participants were regularly evaluated using the CGI, HAMD and MADRS scales and the BDI and BDI self-report inventories. All the assessments proved that the application of Bright light leads to a significant improvement.

SAD: Phototherapy acts through Retinal Melatonin or Rhodopsin, which regulates Dopamine release in the eye where it acts as the main neurotransmitter. The retina-SC'Nvpineal gland forms a link, which is

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disturbed in SAD. By suppressing retinal Melatonin, Phototherapy has been suggested to correct the underlying biochemical abnormality seen in SAD and thereby inducing clinical remission. In Non- Demented people, light therapy is an accepted and validated treatment for seasonal affective disorder, but has also been reported to be effective in Non -Seasonal Depression(15).

Recently it has been noted that exposure of SAD patients to natural sunlight in the morning hours resulted in complete remission of depressive symptoms. In the study, N= 24(12 SAD patients and 12 controls) were exposed to morning light therapy in the winter and the melatonin profiles being sensitive to light were measured before and after treatment. The SAD Patients showed a phase advance of melatonin rhythms in response to phototherapy which showed an association between phase position and phase shift in the SAD patients. This instability may be secondary to impaired serotonergic function in the afferent pathways to the suprachiasmatic nuclei. This seems to be a significant advancement in the etiology of SAD that links light with Mood Disorders. In Seasonal Affective Disorder (SAD) is common when vitamin D stores are typically low. wavelengths between 280-320 nm which are Broad-spectrum light therapy that allow the skin to produce vitamin D. In a prospective, randomized controlled trial was conducted N= 15 subjects with SAD (8 subjects-100, 000 I. U. of vitamin D and 7 subjects-phototherapy).

At the onset of treatment and after 1 month of therapy subjects different depression scale were administered. Vitamin D status improved in both

groups (74% vitamin D group, $p < 0.005$ and 36% phototherapy group, $p < 0.01$). Subjects vitamin D improved in all outcome measures. The phototherapy group showed no significant change in depression scale measures. Improvement in 25-OH D was significantly associated with improvement in depression scale scores ($r^2 = 0.26$; $p = 0.05$). Vitamin D may be an important treatment for SAD

ADHD

Morning bright light therapy is associated helps reduce both subjective and objective measures of core ADHD pathology, improves mood symptoms, and phase advance in circadian preference. Multiple regressions showed that the shift toward an earlier circadian preference with LT was the strongest predictor of improvement on both subjective and objective ADHD measures.

In the Elderly

The risk of developing depression increases with old age. The occurrence of a major depressive episode in Alzheimer's disease is as high as 20-25% and minor depressive symptoms occur in an additional 20-30% (9, 10).

In a randomized double-blind placebo-controlled trial, patients with early Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and Subjective Memory Complaints (SMC) ($N = 79$, Age = between 50 - 75). Patients were exposed to $\sim 10,000$ lux for two years, the active condition or ~ 300 lux in the placebo condition, daily, for two half-hour sessions at fixed times in the morning and evening. Neuropsychological, behavioral, physiological and endocrine measures are assessed at baseline and follow-up every five to six

months. The evaluation showed long-term daily bright light prevented worsening of sleep-wake rhythms and depressive symptoms in elderly people with memory complaints. Elderly experience increased difficulties with sleeping, and thus could be one of the contributing factor for mood problems.(11)

Factors contributing in Aging process

Aging process

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Impaired Ocular light transmission due to age related eye deficiencies

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Requires high demand of light intensities inorder to maintain a sufficient input to SCN

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Diminished SCN input

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Arrhythmia in the Sleep Wake cycle

Studies report that it is possible to reactivate the SCN and improve ' Sleep - Wake Rhythm' by applying extra light. Light therapy provides a safe treatment option(13). It's reported that, bright light therapy is decreasing common health issues(14). In 10 Alzheimer's patients with sundowning behavior and sleep disturbances were studied for a week who received 2 hours/day of exposure to bright light between 7: 00 p. m. and 9: 00 p. m. The results showed that the proportion of total daily activity occurring during the nighttime decreased during the light-treatment week. The relative amplitude of the circadian locomotor activity rhythm, a measure of its stability, increased during the light-treatment week. This kind of effect mediated through a chronobiological mechanism.

Artificial light is used to phase shift circadian rhythm and help improve performance, sleep, and well-being during shiftwork simulations , this was proved in study designed for NASA personals during t he prelaunch week. The treated subjects were self exposed to 10, 000 Lux. The treated personnel showed a positive result reporting better sleep, performance, and physical and emotional well-being than control subjects and rated the treatment as highly effective for promoting adjustment to their work schedules for the study.

In study bright light exposure improved sleep quality in 7-18% subjects, the study consisted of 13 interventional studies with 1154 participants.

Jet lag causes distress to the number of travelers impairing sleep, mood and cognitive performance. Timed exposure to bright light and melatonin administration can help to reduce symptoms. Specific recommendations

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using bright light and melatonin for eastward and westward travel before and after departure are provided for time zone changes of up to 6, 7-9 and 10 or more hours. Timed bright light and melatonin administration, by helping to adjust underlying circadian rhythms to the new time zone, can serve to mitigate the symptoms of jet lag. Reducing the symptoms of jet lag by this methods can lessen the mood, cognitive and behavioral symptoms resulting from these desynchronized rhythms.(