



**Research abstracts of  
Light therapy in treating  
emotional, mental and physical disorders**



Clinical intervention study's with bright light therapy have been done for a small group of disorders, which are listed below. Based on the multidimensional physiological effects of sunlight on the brain and our body, one can distract multiple other indications for bright light therapy in various clinical applications.

#### Table of content

Light therapy general	4
Emotional Disorders	6
Seasonal affective disorder (SAD)	6
Depression	9
Bipolar depression	13
Schizophrenic disorders	15
Eating Disorders	15
Mental Disorders	18
Mild traumatic brain injury	18
Attention deficit hyperactivity disorder (ADHD)	19
Alzheimer's disease (AD)	19
Dementia	22
Intellectual disabilities	25
Prevention of Delirium	26
Physical Disorders	26
Parkinson's disease (PD)	26
Multiple sclerosis	28
Epilepsy	29
Chronic nonspecific back pain	29
Fibromyalgia	30
Breast cancer during chemotherapy	31
Cancer related fatigue	33
Pre-menstrual syndrome	35
Pregnancy	35
Postpartum depression	37
Sleep problems	37
Shiftwork disorder and jet lag disorder	40

### Light therapy general

#### Evolving applications of light therapy.

Terman M., Sleep Med Rev. 2007 Dec;11(6)

The psychiatric intervention, light therapy, grew from an intensive 25-year research focus on seasonal affective disorder (SAD). Dosing and timing strategies have been honed to optimize the antidepressant effect, and efficacy relative to placebo has provided the evidence base for widespread implementation. A persistent question has been whether the model system for SAD has wider utility for psychiatric disturbance, even beyond depression. The circadian phase-shifting capacity of timed light exposure is universal, and chronobiological factors are at play across the disease spectrum. Recent promising initiatives extend to light treatment for nonseasonal major depressive disorder and bipolar depression, including drug- and electroconvulsive therapy-resistant cases. With light therapy, patients with antepartum depression may find an alternative to medication during pregnancy. Cognitive improvement under light therapy has been noted in adult attention deficit hyperactivity disorder. Motor function in Parkinson's disease has improved in parallel with the antidepressant effect of light therapy. The rest-activity disturbance of elderly dementia has been partially allayed under light therapy. In a new initiative, three major chronotherapeutic inventions—light therapy, sleep deprivation (wake therapy) and sleep time displacement (sleep phase advance therapy) are being combined to snap hospitalized patients out of deep depression and maintain long-term improvement.

#### Bright light therapy.

Prasko J, Neuro Endocrinol Lett. 2008 Nov;29

Bright light is a treatment of choice for seasonal affective disorder. Other indications for bright light therapy have also been tested. These include non-seasonal depression, bipolar depression, chronic depressive disorder, ante- and postpartum depression, late luteal phase dysphoric disorder, circadian phase sleep disorders, jet lag, shift work problems, and behavioral disturbance and insomnia in organic dementia. Future studies should focus on exploring the use of light therapy in combination with sleep deprivation, other classes of antidepressants, and with psychotherapy and their possible combined effect on subtypes of depression or other mentioned diagnoses,

light treatment duration, and the applicability and efficacy of adjunct light treatment for in-patients.

#### Bright light therapy

Poirrier R1, Cambron L. Rev Med Liege. 2007;62 Spec No:25-32.

Bright light therapy is a treatment that emerged in the eighties of the last century. It can be used in different pathologies such as seasonal affective disorders, major depressions, and many disorders of the wake-sleep rhythm, whether they are of primary or secondary origin. Important progress made at the basic neuroscience levels, allows today a sound understanding of the bright light mode of action. Moreover, the main indications are now the subject of consensus reports and meta-analyses which show good levels of evidence-based medicine. Bright light therapy constitutes a first choice indication in seasonal affective disorder. It is also perfectly possible to prescribe bright light therapy in the major depression disorders. It has been demonstrated that the effect size is the same as with antidepressants of reference. It is admitted nowadays that bright light therapy may be at least, an adjunct to pharmacotherapy, in order to accelerate the antidepressant effect onset, or to prolong this effect after withdrawal of the drug. Bright light therapy can also be viewed as an alternative to the pharmacological approach especially when this one is impossible, not tolerated or not accepted by the patient. The contraindications are rare.

#### Light therapy: is it safe for the eyes?

Brouwer A1, Nguyen HT, Snoek FJ, van Raalte DH, Beekman ATF, Moll AC, Bremmer MA. Acta Psychiatr Scand. 2017 Dec;136(6):534-548.

**OBJECTIVE:** Light therapy has become an increasingly popular treatment for depression and a range of other neuropsychiatric conditions. Yet, concerns have been raised about the ocular safety of light therapy.

**METHOD:** We conducted the first systematic review into the ocular safety of light therapy. A PubMed search on January 4, 2017, identified 6708 articles, of which 161 were full-text reviewed. In total, 43 articles reporting on ocular complaints and ocular examinations were included in the analyses.

**RESULTS:** Ocular complaints, including ocular discomfort

and vision problems, were reported in about 0% to 45% of the participants of studies involving light therapy. Based on individual studies, no evident relationship between the occurrence of complaints and light therapy dose was found. There was no evidence for ocular damage due to light therapy, with the exception of one case report that documented the development of a maculopathy in a person treated with the photosensitizing antidepressant clomipramine.

**CONCLUSION:** Results suggest that light therapy is safe for the eyes in physically healthy, unmedicated persons. The ocular safety of light therapy in persons with pre-existing ocular abnormalities or increased photosensitivity warrants further study. However, theoretical considerations do not substantiate stringent ocular safety-related contraindications for light therapy.

#### Towards a uniform specification of light therapy devices for the treatment of affective disorders and use for non-image forming effects: Radiant flux.

Aarts MPJ, Rosemann ALP., J Affect Disord. 2018 Aug 1;235:142-149.

**BACKGROUND:** For treating affective disorders like SAD, light therapy is used although the underlying mechanism explaining this success remains unclear. To accelerate the research on defining the light characteristics responsible for inducing a specific effect a uniform manner for specifying the irradiance at the eye should be defined. This allows a genuine comparison between light-affect studies. An important factor impacting the irradiance at the eye are the radiant characteristics of the used light therapy device.

**METHOD:** In this study the radiant fluxes of five different light therapy devices were measured. The values were weighted against the spectral sensitivity of the five photopigments present in the human eye. A measurement was taken every five minutes to control for a potential stabilizing effect.

**RESULTS:** The results show that all five devices show large differences in radiant flux. The devices equipped with blue LED lights have a much lower spectral radiant flux than the devices equipped with a fluorescent light source or a white LED. The devices with fluorescent lamps needed 30 min to stabilize to a constant radiant flux.

**LIMITATIONS:** In this study only five devices were meas-

ured. Radiant flux is just the first step to identify uniform specifications for light therapy devices.

**CONCLUSIONS:** It is recommended to provide all five  $\alpha$ -opic radiant fluxes. Preferably, the devices should come with a spectral power distribution of the radiant flux. For the devices equipped with a fluorescent lamp it is recommended to provide information on the stabilization time.

#### Illuminating rationale and uses for light therapy.

Shirani A1, St Louis EK., J Clin Sleep Med. 2009 Apr 15;5(2):155-63.

Light therapy is increasingly applied in a variety of sleep medicine and psychiatric conditions including circadian rhythm sleep disorders, seasonal affective disorder, and dementia. This article reviews the neural underpinnings of circadian neurobiology crucial for understanding the influence of light therapy on brain function, common mood and sleep disorders in which light therapy may be effectively used, and applications of light therapy in clinical practice.

#### Current state of research in bright light therapy

Bassa D1, Canazei M, Hinterhuber H, Weiss EM., Neuropsychiatr. 2013;27(3):142-8

The significance of light for the human organism and especially for the mental health is well-established for a long time. Therefore, the impact of light on mood and the use of bright light as a treatment-option for affective disorders have been studied extensively by scientists. Today bright light therapy is the treatment of choice for seasonal affective disorders. In the last years several clinical trials could demonstrate the therapeutic efficacy of bright light therapy for different neurological and psychiatric disorders such as sleep disorders, non-seasonal affective disorders or dementia. This article will give an overview about the neurobiological basis for light therapy and discuss different disorders responsive to light therapy. Finally a short overview about technical aspects of light therapy and new developments in light engineering will be presented.

**Bright light therapy in focus: lamp emission spectra and ocular safety.**

Remé CE, Rol P, Grothmann K, Kaase H, Terman M. *Technol Health Care.* 1996 Dec;4(4):403-13.

In recent years, bright light treatment of seasonal affective disorder (SAD), recurrent depressions in fall and winter, has been discovered. Newer applications include circadian sleep phase disorder, shift work and jet lag. Apart from creating the visual signal, light can modify retinal structure and physiology. UV and visible light lead to distinct lesions of ocular tissues under certain experimental and naturalistic conditions. In light therapy, a large variety of fixtures is used but the spectral emission of lamps is mostly unknown to the user and clinician leading to the potential hazard of ocular lesions. Therefore, we have analyzed a wide selection of light sources commonly used for treatment. We measured the spectral emission and calculated irradiant doses for several light therapy regimens. Based on these measurements, potential hazards are analyzed, physiological mechanisms of light action are discussed and safety measures for bright light therapy are proposed. They include recommendations for lamps devoid of damaging spectral emissions and standardized therapy fixtures, ophthalmological monitoring of patients with eye diseases and control by optometrists for patients with healthy eyes who are likely to undergo light treatment for extended periods.

**Side effects of short-term 10,000-lux light therapy.**

Kogan AO, Guilford PM. *Am J Psychiatry.* 1998 Feb;155(2):293-4.

**OBJECTIVE:** Previous reports of side effects from light therapy were mostly based on administration of 2,500-lux treatments. It has become common practice to use brighter, 10,000-lux exposure when treating seasonal affective disorder. The authors studied side effects produced by short-term 10,000-lux light therapy.

**METHOD:** Seventy subjects with seasonal affective disorder who underwent brief 10,000-lux light therapy were asked to report side effects.

**RESULTS:** Of the 70 subjects, 32 (45.7%) experienced side effects, and nine (12.9%) reported two or more apiece. Headaches and eye or vision problems were the most common. Almost all were mild, were transient, and did not interfere with treatment.

**CONCLUSIONS:** Short-term 10,000-lux light therapy often produces side effects early in treatment. These are not serious or prolonged, however, confirming findings from earlier studies that used dimmer light.

**Emotional Disorders**
**Seasonal affective disorder (SAD)**
**Bright Light as a Personalized Precision Treatment of Mood Disorders.**

Maruani J, Geoffroy PA. *Front Psychiatry.* 2019 Mar 1;10:85.

**Background:** The use of light for its antidepressant action dates back to the beginnings of civilization. Three decades ago, the use of bright-light therapy (BLT) for treating Seasonal Affective Disorder (SAD) was officially proposed. Since then, a growing scientific literature reports its antidepressant efficacy in both unipolar and bipolar disorders (BD), with or without seasonal patterns. This review aims to examine the management of BLT as a personalized and precision treatment in SAD, unipolar, and BD.

**Methods:** We conducted a narrative review using Medline and Google Scholar databases up to June 2018.

**Results:** BLT has physiological effects by resynchronizing the biological clock (circadian system), enhancing alertness, increasing sleep pressure (homeostatic system), and acting on serotonin, and other monoaminergic pathways. Effects of BLT on mood depend on several factors such as light intensity, wavelength spectrum, illumination duration, time of the day, and individual circadian rhythms. A growing body of evidence has been generated over the last decade about BLT evolving as an effective depression treatment not only to be used in SAD, but also in non-seasonal depression, with efficiency comparable to fluoxetine, and possibly more robust in patients with BD. The antidepressant action of BLT is fast (within 1-week) and safe, with the need in BD to protect against manic switch with mood stabilizers. Side effects might be nausea, diarrhea, headache, and eye irritation, and are generally mild and rare. This good safety profile may be of particular interest, especially in women during the perinatal period or for the elderly. The management of BLT needs to be clarified across mood disorders and

future studies are expected to compare different dose-titration protocols, to validate its use as a maintenance treatment, and also to identify predictive biomarkers of response and tolerability. We propose clinical guidelines for BLT use in SAD, non-seasonal depression, and BD.

**Conclusions :** BLT is an efficient antidepressant strategy in mono- or adjunct-therapy, that should be personalized according the unipolar or bipolar subtype, the presence or absence of seasonal patterns, and also regarding its efficacy and tolerability.

**Light therapy for preventing seasonal affective disorder.**

Nussbaumer, B., Kaminski-Hartenthaler, A., Forneris, C. A., Morgan, L. C., Sonis, J. H., Gaynes, B. N., ... Gartlehner, G. (2015). *The Cochrane Database of Systematic Reviews*, 11, CD011269.

Evidence on light therapy as preventive treatment for people with a history of SAD is limited. Methodological limitations and the small sample size of the only available study have precluded review author conclusions on effects of light therapy for SAD. Given that comparative evidence for light therapy versus other preventive options is limited, the decision for or against initiating preventive treatment of SAD and the treatment selected should be strongly based on patient preferences.

**Seasonal affective disorder and light therapy**

Matías J1, Manzano JM, Santalla JL, Carrasco JL, Llorca G, Ledesma A.

Seasonal affective disorders (SAD) represents a subgroup of major depression with a regular occurrence of symptoms in autumn and winter and full remission in spring and summer. Light therapy or phototherapy has become the standard treatment of this type of depression. The phototherapy is affective therapy for depressive symptoms of SAD. However, the action mechanism of light therapy is uncertain. Finally, new lines of the investigation of light therapy are aforementioned.

**Patterns of depressive symptom remission during the treatment of seasonal affective disorder with cognitive-behavioral therapy or light therapy.**

Meyerhoff, J., Young, M. A., & Rohan, K. J. (2018). *Depression and Anxiety*, 35(5), 457–467.

**BACKGROUND:** To elucidate mechanisms related to remission in winter seasonal affective disorder (SAD), we explored the course of individual depressive symptom offset across two distinct treatment modalities that show comparable outcomes at treatment endpoint: cognitive-behavioral therapy for SAD (CBT-SAD) and light therapy (LT).

**METHOD:** One hundred seventy-seven adults with SAD in a depressive episode were randomized to 6-weeks of CBT-SAD (n = 88) or LT (n = 89). Symptoms were assessed via the 29-item Structured Interview Guide for the Hamilton Rating Scale for Depression-SAD Version (SIGH-SAD) at pretreatment and weekly during treatment. Survival analyses were conducted for the 17 SIGH-SAD items endorsed by more than 40 participants at pretreatment. Within each of the included symptoms, data from participants who endorsed the symptom at pretreatment and who had 3 or fewer weeks missing were included.

**RESULTS:** For most (13/17; 76%) symptoms, CBT-SAD and LT did not differ in time to remission. However, for four symptoms (early insomnia, psychic anxiety, hypersomnia, and social withdrawal), LT led to symptom remission more quickly than CBT-SAD.

**CONCLUSIONS:** Symptom remission progressed comparably across CBT-SAD and LT for most symptoms. Despite the fact that the two treatments led to similar remission rates and improvements at treatment endpoint, for early insomnia, psychic anxiety, hypersomnia, and social withdrawal, LT led to symptom remission faster than CBT-SAD. These results suggest different mechanisms and pathways to the same therapeutic end. Speedier remission of early insomnia and hypersomnia is consistent with the theory that SAD is related to a pathological circadian phase-shift that can be corrected with LT.

**Changes of sleep quality and mood disorders under the influence of phototherapy in patients with seasonal affective disorders SAD**

Ciesielczyk K1, Pracka D, Pracki T, Tafil-Klawe M, Ziolkowska-Kochan M. *Psychiatr Pol.* 2004 Nov-Dec;38(6):1105-14.

Major depression, seasonal pattern (seasonal affective disorder SAD) characterize the winter recurrence depressive episodes with remission of symptoms in spring and

summer. Patients with winter depression report hypersomnia, fatigue, loss of energy, carbohydrate craving, appetite and weight gain.

**AIM:** The aim of this study was to assess the effect of phototherapy on the quality of sleep parameters and subjective estimation of mood disorders in patients with seasonal affective disorders.

**METHOD:** The investigated group consisted of 17 patients with SAD (15 female, 2 male) aged 18-64 (mean 38+/-12) years. Phototherapy (bright light therapy) was applied for 14 days, everyday morning--30 minutes, between 6.00 to 10.00--exposition to light of about 10,000 lux intensity. Polysomnogram (sleep EEG) was recorded before and after treatment.

**RESULTS:** After phototherapy patients reported a significant mood improvement (57%) measured by the Seasonal Pattern Assessment Questionnaire. Sleep investigation showed: increased sleep efficiency, decreased sleep latency, decreased slow wave sleep latency and increased of sleep spindles in the first hour of sleep.

**CONCLUSIONS:** Research confirms that phototherapy is an effective method of treatment of choice for patients with SAD. The result indicates that phototherapy markedly improved mood and sleep quality.

#### **Bright light therapy: side effects and benefits across the symptom spectrum.**

Terman M1, Terman JS. Department of Psychiatry, Columbia University, New York

**BACKGROUND:** Bright light therapy has been established for treatment of winter depression, or seasonal affective disorder (SAD). Analysis of side effects most often have focused on a narrow set of suspected symptoms, based on clinical observation (e.g., headache, eyestrain, nausea, insomnia, and hyperactivity). This study broadens the purview to a set of 88 physical and subjective symptoms that might emerge, remit, or remain unchanged relative to baseline, thus reducing bias toward assessment of presumed side effects.

**METHOD:** Eighty-three patients with SAD (DSM-III-R criteria for mood disorders with seasonal pattern [winter type] and National Institute of Mental Health criteria for SAD) received bright light therapy at 10,000 lux for 30 minutes daily in the morning or evening for 10 to 14 days. They completed a questionnaire (Systematic

Assessment for Treatment Emergent Effects), rating symptom severity before and after treatment. Results were compared for morning or evening treatment and for responders and nonresponders.

**RESULTS:** Several side effects emerged--mostly mildly--including jumpiness/jitteriness (8.8%), headache (8.4%), and nausea (15.9%), mirroring findings of past studies with a less inclusive scope. In most cases, remission rate equalled or exceeded emergence rate. Several nondepressive symptoms also showed large improvement, including poor vision and skin rash/itch/irritation. Being overactive/excited/elated showed greater emergence under morning light and greater remission under evening light. Emergence of nausea was greater than remission in responders.

**CONCLUSION:** The dominant effect of light treatment was improvement in bothersome symptoms. Although patients should be advised of side effects and guided in dose manipulations to reduce them, attention also should be drawn to the substantial benefit-to-risk ratio. Improvement of symptoms outside the depressive cluster, seen in both responders and nonresponders, may point to new therapeutic uses of light therapy.

#### **Winter depression and phototherapy. The state of the art**

Gysin F, Gysin F, Gross F. Acta Med Port. 1997 Dec;10(12):887-93.

Winter depression (seasonal affective disorder, SAD) is characterised by a seasonal major depressive episode in the last 2 years. Hypersomnia, carbohydrate-craving and weight-gain are specific traits. These patients preferentially seek help from their General Practitioner. Current research on the aetiology of SAD covers fields such as retinal deficiency, phase-disturbance of the internal circadian rhythms given by internal oscillators and neuroendocrinologically expressed disorders, assuming that melatonin is the main mediator of human circadian systems in the CNS. Disorders of neurotransmitters (serotonin) are another cue. Recent longitudinal studies show a prevalence of seasonal depressive symptoms in up to 10% of the general population. Among patients treated for depression, the prevalence of SAD is even higher. The SAD sex-ratio of women to men of 3 to 1 is found repeatedly. SAD becomes rare above the age of 50. Effectiveness of phototherapy is showed in nearly all con-

trolled studies. Bright light appears to be most effective for patients with mild SAD. Hypersomnia and hyperphagia seem to be predictors of response to bright light therapy. To enable evaluation of unspecific therapeutic factors in phototherapy a true placebo for bright light-studies is still to be found. Possible new indications for photo therapy are currently being explored. Bright light for non- seasonal depression has been tested with encouraging results; panic disorders seem to have features in common with SAD; effectiveness in bulimia has been suggested and recently sleep disorders in elderly patients have been successfully and substantially diminished.

#### **Phototherapy in psychiatry: clinical update and review of indications.**

Gross F1, Gysin F. Encephale. 1996 Mar-Apr;22(2):143-8.1 Clinique de Psychiatrie II, Institutions universitaires de Psychiatrie, Genève, Suisse.

Phototherapy introduced in 1984 by Rosenthal as a treatment for SAD (Seasonal Affective Disorder) is the first therapeutic answer to season-related psychopathology. Findings in chronobiology have largely contributed to pathophysiological theories of disorders in the internal circadian system. Actual researches on the etiology of SAD covers fields as retinal deficiency (i.e. disorder of photoreceptors), phase disturbance of the internal circadian rhythms given by internal oscillators and neuroendocrinologically driven disorders, supposing that melatonin is the main mediator of human circadian systems in the CNS. Disorders of the neurotransmitters are an other explored cue. Recent longitudinal studies show a prevalence of seasonal depressive symptoms in general population up to 10%. In populations treated for depression the prevalence of SAD is up to 20%. The SAD sex-ratio (women/men) of 3/1 is found repeatedly. Above 55 years SAD get rare. Effectiveness of phototherapy is showed in nearly all controlled studies. Bright light for patients with mild SAD appears to be most effective as is also the authors clinical impression through the practice of phototherapy in Geneva since 1991. A true placebo for bright light is still to be found according to enable evaluation of potentially important impact that unspecific therapeutic factors may trigger in phototherapy. Actually possible new indications for phototherapy are being explored: bright light for non

seasonal depression has been tested with features with SAD; effectiveness in bulimia has been suggested and recently sleep disorders in psychogeriatric patients have been improved. Non seasonal circadian disorders such as jet lag might be sensitive to light.

#### **Depression**

##### **Bright-Light Therapy in the Treatment of Mood Disorders**

Pail G. · Huf W. · Pjrek E. · Winkler D. · Willeit M. · Praschak-Rieder N. (2011) Kasper S.. Neuropsychobiology ;

Bright-light therapy (BLT) is established as the treatment of choice for seasonal affective disorder/winter type (SAD). In the last two decades, the use of BLT has expanded beyond SAD: there is evidence for efficacy in chronic depression, antepartum depression, premenstrual depression, bipolar depression and disturbances of the sleep-wake cycle. Data on the usefulness of BLT in non-seasonal depression are promising; however, further systematic studies are still warranted. In this review, the authors present a comprehensive overview of the literature on BLT in mood disorders. The first part elucidates the neurobiology of circadian and seasonal adaptive mechanisms focusing on the suprachiasmatic nucleus (SCN), the indolamines melatonin and serotonin, and the chronobiology of mood disorders. The SCN is the primary oscillator in humans. Indolamines are known to transduce light signals into cells and organisms since early in evolution, and their role in signalling change of season is still preserved in humans: melatonin is synthesized primarily in the pineal gland and is the central hormone for internal clock circuitries. The melatonin precursor serotonin is known to modulate many behaviours that vary with season. The second part discusses the pathophysiology and clinical specifiers of SAD, which can be seen as a model disorder for chronobiological disturbances and the mechanism of action of BLT. In the third part, the mode of action, application, efficacy, tolerability and safety of BLT in SAD and other mood disorders are explored.

##### **Efficacy of light therapy in nonseasonal depression: a systematic review.**

Even C1, Schröder CM, Friedman S, Rouillon F., J Affect Disord. 2008 May;108(1-2):11-23.

**BACKGROUND:** The efficacy of bright light therapy is well established for winter depression but its status in depression without seasonal pattern is unclear.

**METHODS:** We systematically evaluated available data on the efficacy of light therapy in nonseasonal depression.

**RESULTS:** We identified 62 reports among which 15 met our predefined selection criteria. The available data show evidence for the efficacy of light therapy as an adjuvant treatment to antidepressants. Trials that evaluated light therapy alone (without antidepressants) in nonseasonal depression yielded inconsistent results.

**LIMITATIONS:** Most of the studies extracted poorly controlled the issue of blindness and were limited by small sample sizes. Publication bias may have distorted our estimation of the effect of light therapy.

**CONCLUSIONS:** Overall, bright light therapy is an excellent candidate for inclusion into the therapeutic inventory available for the treatment of nonseasonal depression today, as adjuvant therapy to antidepressant medication. Future clinical trials of light therapy should distinguish homogenous subgroups of depressed patients in order to evaluate whether light therapy may eventually be considered as stand-alone treatment for specific subgroups of patients with nonseasonal depression.

#### **Bright Light as a Preventive Intervention for Depression in Late-Life: A Pilot Study on Feasibility, Acceptability, and Symptom Improvement.**

Leggett AN, Conroy DA, Blow FC, Kales HC. *Am J Geriatr Psychiatry*. 2018 May;26(5):598-602.

**OBJECTIVES:** We examined the feasibility and acceptability of a portable bright light intervention and its impact on sleep disturbance and depressive symptoms in older adults.

**METHODS:** One-arm prevention intervention pilot study of the Re-Timer (Re-Timer Pty Ltd, Adelaide, Australia) bright light device (worn 30 minutes daily for 2 weeks) in 1 older adults (age 65+ years) with subsyndromal symptoms of depression and poor sleep quality. Participants were assessed on intervention acceptability and adherence, depressive symptoms (Patient Health Questionnaire- 9), and sleep (Pittsburgh Sleep Quality Index, Insomnia Severity Index, actigraphy and daily diary reports).

**RESULTS:** The Re-Timer device was rated positively by

participants, and, on average, participants only missed 1 day of utilization. Although depressive symptoms declined and self-reported sleep improved, improvement was seen largely before the start of intervention.

**CONCLUSIONS:** An effective preventive intervention that is targeted towards a high risk group of older adults has the potential to reduce distress and costly health service use.

#### **The Efficacy of Light Therapy in the Treatment of Mood Disorders: A Review and Meta-Analysis of the Evidence.**

Golden, R. N., Gaynes, B. N., Ekstrom, R. D., Hamer, R. M., Jacobsen, F. M., Suppes, T., ... Nemeroff, C. B. (2005). *American Journal of Psychiatry*, 162(4), 656–662.

**OBJECTIVE:** The purpose of this study was to assess the evidence base for the efficacy of light therapy in treating mood disorders.

**METHOD:** The authors systematically searched PubMed (January 1975 to July 2003) to identify randomized, controlled trials of light therapy for mood disorders that fulfilled predefined criteria. These articles were abstracted, and data were synthesized by disease and intervention category.

**RESULTS:** Only 13% of the studies met the inclusion criteria. Meta-analyses revealed that a significant reduction in depression symptom severity was associated with bright light treatment (eight studies, having an effect size of 0.84 and 95% confidence interval [CI] of 0.60 to 1.08) and dawn simulation in seasonal affective disorder (five studies; effect size=0.73, 95% CI=0.37 to 1.08) and with bright light treatment in nonseasonal depression (three studies; effect size=0.53, 95% CI=0.18 to 0.89). Bright light as an adjunct to antidepressant pharmacotherapy for nonseasonal depression was not effective (five studies; effect size=-0.01, 95% CI=-0.36 to 0.34). **CONCLUSIONS:** Many reports of the efficacy of light therapy are not based on rigorous study designs. This analysis of randomized, controlled trials suggests that bright light treatment and dawn simulation for seasonal affective disorder and bright light for nonseasonal depression are efficacious, with effect sizes equivalent to those in most antidepressant pharmacotherapy trials. Adopting standard approaches to light therapy's specific issues (e.g., defining parameters of active versus placebo

conditions) and incorporating rigorous designs (e.g., adequate group sizes, randomized assignment) are necessary to evaluate light therapy for mood disorders.

#### **Chronotherapeutic treatments for depression in youth.**

Gest S, Holtmann M, Bogen S, Schulz C, Pniewski B, Legenbauer T., *Eur Child Adolesc Psychiatry*. 2016 Feb;25(2):151-61.

Chronotherapeutics such as wake therapy and bright light therapy are well-established methods in treating adults with depressive disorders and are additionally beneficent for sleep regulation. Few studies concerning chronotherapeutics in juvenile depression exist, though the established treatments are insufficient and sleep disorders often co-occur. In this study, we investigate the impact of two types of chronotherapeutics on depressive symptoms and sleep behavior in a juvenile setting. Juvenile inpatients (n = 62) with moderate to severe depressive symptoms took part in either a combined setting consisting of one night wake therapy followed by 2 weeks bright light therapy or in a setting of bright light therapy alone. Depressive symptoms, general psychopathology, clinical impression and sleep behavior were measured before (T1), directly after (T2) and 2 weeks after intervention (T3). Depressive symptoms decreased while sleep quality increased in both groups. The bright light therapy alone group showed further improvement at T3 in regards to depressive symptoms. Correlation analyses indicated significant negative correlations between sleep quality and awaking after restorative sleep with the depressive symptoms. However, only awaking after restorative sleep had a predictive impact on treatment outcome. The present study provides first evidence for a positive impact of chronotherapeutic interventions on treatment outcome in depressed juvenile inpatients. Bright light therapy seems to stabilize and further enhance reduction of depressive symptoms during follow-up, whereas one night wake therapy does not have an additional long-lasting impact on depressive symptoms and sleep parameters.

#### **Light Therapy for Depressive Disorders: Indications and Efficacy**

Lam R.W. · Terman M. Wirz-Justice A. · *Mood Disorders* 1997, vol 25, pp 215-234

#### **Efficacy of Bright Light Treatment, Fluoxetine, and the Combination in Patients With Nonseasonal Major Depressive Disorder: A Randomized Clinical Trial.**

Lam, R. W., Levitt, A. J., Levitan, R. D., Michalak, E. E., Cheung, A. H., Morehouse, R., ... Tam, E. M. (2016). *JAMA Psychiatry*, 73(1), 56–63.

Bright light treatment, both as monotherapy and in combination with fluoxetine, was efficacious and well tolerated in the treatment of adults with nonseasonal MDD. The combination treatment had the most consistent effects.

#### **Light therapy for non-seasonal depression: systematic review and meta-analysis.**

Perera, S., Eisen, R., Bhatt, M., Bhatnagar, N., de Souza, R., Thabane, L., & Samaan, Z. (2016). *BJPsych Open*, 2(2), 116–126.

The overall quality of evidence is poor due to high risk of bias and inconsistency. However, considering that light therapy has minimal side-effects and our meta-analysis demonstrated that a significant proportion of patients achieved a clinically significant response, light therapy may be effective for patients with non-seasonal depression and can be a helpful additional therapeutic intervention for depression.

#### **A systematic review of light therapy on mood scores in major depressive disorder: light specification, dose, timing and delivery.**

Alotaibi, M., Halaki, M., & Chow, C.-M. (2015). *International Journal of Basic and Applied Sciences*, 5(1), 30.

**Background:** Depression is associated with prolonged disability, mortality, and morbidity. Ninety percent of patients with Major depressive disorder (MDD) have sleep problems. Light therapy has been shown to be effective in treating sleep disorders and MDD. This review aims to assess the characteristics (colour, intensity), exposure dose (duration and timing) and the mode of delivery (light boxes, visor etc) of light in reducing depression, measured by mood scores, in MDD.

**METHOD:** a systematic literature search was performed on 6 major databases. The Physiotherapy Evidence Database (PEDro) Scale was applied to assess study quality.

**RESULT:** Twenty-four articles satisfied the inclusion criteria. Effective light intensities varied from 176 -10,000 lux. Effective modes of delivery included light box, table lamp, visor and light emitting diode (LED) glasses. Effective light colours included white, green, and blue with the white colour being the most commonly used. The duration of light treatment ranged from 30 min to 2 h, and evening light generally improved mood.

**CONCLUSION:** Light therapy, with exposure durations in the range of 30 min to 2 h per day, intensity range of 176 to 10,000 lux, in any of blue, green, or white light colour and exposure during morning mostly demonstrated a positive change in mood effects. Factors other than the light properties, such as anti-depressant medication use, depression episodes and severity, natural light exposure and sleep deprivation may confound the effects of light therapy.

#### **Efficacy of light therapy on nonseasonal depression among elderly adults: a systematic review and meta-analysis.**

Chang, C.-H., Liu, C.-Y., Chen, S.-J., & Tsai, H.-C. (2018). *Neuropsychiatric Disease and Treatment*, Volume 14, 3091–3102.

Our results highlighted the significant efficacy of light therapy in the treatment of geriatric depression. Additional well-designed, controlled studies are necessary to adopt standard parameters, adequate group sizes, and randomized assignment to evaluate more thoroughly the efficacy of light therapy for treating geriatric depression.

#### **Feasibility and Efficacy of Bright Light Therapy in Depressed Adolescent Inpatients.**

Kirschbaum-Lesch, I., Gest, S., Legenbauer, T., & Holtmann, M. (2018). *Zeitschrift Für Kinder- Und Jugendpsychiatrie Und Psychotherapie*, 46(5), 423–429.

Bright light therapy (BLT) has recently come into increasing focus in the treatment of adolescent depression, whereby light glasses today appear to be more feasible than light therapy boxes. This study investigated the feasibility and efficacy of 4 weeks of BLT with light glasses. It also analyzed whether a treatment duration of 4 weeks of BLT yields larger effects than the 2 weeks of BLT investigated in previous studies.

**METHODS:** This first open-label, single-arm, prospective clinical trial pursued a naturalistic approach: 39 inpatients aged 12–18 years with moderate or severe depression received 4 weeks of morning BLT with light glasses in addition to usual treatment. Depressive symptoms, sleep problems, circadian phase, and the clinical global impression were assessed at several timepoints. In a second analysis, the data of the present study were compared to those from a previous pilot trial.

**RESULTS:** Depressive symptoms, sleep problems, and the global clinical impression improved significantly after BLT with light glasses, whereas the circadian phase did not change over time. Light glasses showed similarly positive effects on sleep parameters and depressive symptoms as light boxes. Contrary to expectation, prolonging BLT to 4 weeks did not yield larger effects on depressive symptoms and sleep complaints compared to 2 weeks of intervention.

**CONCLUSIONS:** Light glasses seem to be a feasible and highly acceptable method for the treatment of adolescent depression. Further randomized controlled trials are needed to obtain sufficient evidence regarding the efficacy of BLT as an add-on intervention to psychological and pharmacological approaches for adolescent depression.

**Bright Light as a Preventive Intervention for Depression in Late-Life: A Pilot Study on Feasibility,** Amanda N., Leggett Ph.D.a, Deirdre A., Conroy Ph.D.b, Frederic C., Blow Ph.D.c, Helen C., Kales M.D.ad. Acceptability, and Symptom Improvement. *The American Journal of Geriatric Psychiatry* Volume 26, Issue 5, May 2018, Pages 598-

Participants found the Re-Timer bright light intervention acceptable with 91% reporting it very easy to use. Participants had 93% adherence to the intervention with no adverse events reported. Evidence points toward potential for improvement in mood with the intervention.

**OBJECTIVES:** We examined the feasibility and acceptability of a portable bright light intervention and its impact on sleep disturbance and depressive symptoms in older adults.

**METHODS:** One-arm prevention intervention pilot study of the Re-Timer (Re-Timer Pty Ltd, Adelaide, Australia) bright light device (worn 30 minutes daily for 2 weeks)

in 1 older adults (age 65+ years) with subsyndromal symptoms of depression and poor sleep quality. Participants were assessed on intervention acceptability and adherence, depressive symptoms (Patient Health Questionnaire- 9), and sleep (Pittsburgh Sleep Quality Index, Insomnia Severity Index, actigraphy and daily diary reports).

**RESULTS:** The Re-Timer device was rated positively by participants, and, on average, participants only missed 1 day of utilization. Although depressive symptoms declined and self-reported sleep improved, improvement was seen largely before the start of intervention.

**CONCLUSIONS:** An effective preventive intervention that is targeted towards a high risk group of older adults has the potential to reduce distress and costly health service use.

#### **Bipolar depression**

##### **Light therapy in the treatment of patients with bipolar depression: A meta-analytic study**

Ping-Tao Tseng, Yen-Wen Chen, Kun-Yu Tu, Weilun Chung, Pao-Yen Lin (2016) *European Neuropsychopharmacology*, 26,1037-1047

Light therapy (LT) has been widely used in the treatment of seasonal affective disorder. Recently some evidence indicated that LT may play a role in bipolar depression, either as monotherapy or in combination with total sleep deprivation (TSD). However, the studies examining the treatment effect of LT in bipolar depression resulted in inconsistent findings. To clarify the role of LT in the disorder, we conducted a meta-analysis to compare the efficacy of LT in the treatment of bipolar depression. The results of individual studies were synthesized by a random effects model. Nine studies including 489 patients with bipolar depression were included in this current meta-analysis. We found that disease severity was significantly decreased after LT, in both with and without TSD, and with concomitant medication ( $p < 0.001$ ). Augmentation treatment with LT significantly decreased disease severity compared to treatment without LT ( $p = 0.024$ ). Our results highlight the significant efficacy of LT, either as monotherapy or in combination with TSD, in the treatment of bipolar depression. However, the detailed mechanism of LT still remains elusive. Further well-designed controlled trials are required

to investigate the optimal intensity and frequency of LT in the treatment of bipolar depression.

#### **Use of "Lights" for Bipolar Depression.**

Sit D, Haigh S. *Curr Psychiatry Rep*. 2019 May

**PURPOSE:** In this review, we will review the background and diagnosis of bipolar disorder (BD); describe the efficacy data and potential circadian and neural mechanisms underlying the effects of bright light for bipolar depression; and discuss the implementation of light therapy in clinical practice.

**RECENT FINDINGS:** To date, morning bright light is the most widely tested form of light therapy for all mood disorders. Clinical trial reports suggest that midday or morning bright light treatment and novel chronotherapeutic interventions are effective for bipolar depression. Mechanisms of response may relate to effects on the circadian system and other changes in neural functioning. Using bright light to manage depressive symptoms in BD is reasonable but also requires concurrent antimanic treatment and careful clinical monitoring for response, safety, and mood polarity switch.

#### **Clinical efficacy, onset time and safety of bright light therapy in acute bipolar depression as an adjunctive therapy: A randomized controlled trial.**

Zhou, T., Dang, W., Ma, Y., Hu, C., Wang, N., Zhang, G., ... Yu, X. (2018). *Journal of Affective Disorders*, 227, 90–96.

BLT can be considered as an effective and safe adjunctive treatment for patients with acute bipolar depression.

#### **Combined sleep deprivation and light therapy: Clinical treatment outcomes in patients with complex unipolar and bipolar depression.**

Sikkens, D., Riemersma - Van der Lek, R. F., Meesters, Y., Schoevers, R. A., & Haarman, B. C. M. (2019). *Journal of Affective Disorders*, 246, 727–730.

#### **Highlights**

In depression, treatment resistant patients or patients with psychiatric comorbidity are often difficult to treat. Combined chronotherapy consists of sleep deprivation and light therapy. These procedures, along with the continuation of antidepressant medication, may be a valuable

treatment modality in patients with depression.

Chronotherapy appears to have a rapid effect that lasts for at least several weeks, even in patients with psychiatric comorbidity or treatment resistant depression.

**BACKGROUND:** The combination of sleep deprivation and light therapy, called combined chronotherapy, may yield positive short- and long-term results, even in patients with treatment resistant depression (TRD). The implementation of combined chronotherapy in daily clinical practice is rare. This study describes the implementation and the effectiveness in a clinical setting.

**METHODS:** Twenty six depressed patients with unipolar or bipolar depression received combined chronotherapy consisting of three nights of sleep deprivation with alternating recovery nights, light therapy, and continuation of antidepressant medication. Inventory of Depressive Symptoms C (IDS-C) scores were determined before chronotherapy and at week 1, 2, and 4. Paired t-tests were used to compare the IDS-C scores over time.

**RESULTS:** The mean pre-treatment IDS-C score was  $39.3 \pm 9.6$ , the mean score in week 2 was  $28.4 \pm 10.2$ , and  $28.6 \pm 14.0$  in week 4. A subsample of patients with psychiatric co-morbidities showed a reduction in depression severity from a mean score of  $42.9 \pm 11.0$  to a mean score of  $34.9 \pm 13.0$  after 4 weeks. The overall response rate was 34.6%, the remission rate 19.2%.

**LIMITATIONS:** This open label case series has a relative small sample size and no control group

**CONCLUSION:** In a clinical setting patients with major depressive disorder or bipolar disorder benefited significantly from combined chronotherapy. This chronotherapeutic intervention appears to have a rapid effect that lasts for at least several weeks, even in patients with psychiatric comorbidity or TRD. Indicating that chronotherapy can be a valuable treatment addition for depressed patients.

#### **Adjunctive Bright Light Therapy for Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Trial.**

Sit, D. K., McGowan, J., Wiltrout, C., Diler, R. S., Dills, J. J., Luther, J., ... Wisner, K. L. (2018). *The American Journal of Psychiatry*, 175(2), 131–139.

**OBJECTIVE:** Patients with bipolar disorder have recurrent major depression, residual mood symptoms, and limited treatment options. Building on promising pilot data, the

authors conducted a 6-week randomized double-blind placebo-controlled trial to investigate the efficacy of adjunctive bright light therapy at midday for bipolar depression. The aims were to determine remission rate, depression symptom level, and rate of mood polarity switch, as well as to explore sleep quality.

**METHOD:** The study enrolled depressed adults with bipolar I or II disorder who were receiving stable dosages of antimanic medication (excluding patients with hypomania or mania, mixed symptoms, or rapid cycling). Patients were randomly assigned to treatment with either 7,000-lux bright white light or 50-lux dim red placebo light (N=23 for each group). Symptoms were assessed weekly with the Structured Interview Guide for the Hamilton Depression Scale With Atypical Depression Supplement (SIGH-ADS), the Mania Rating Scale, and the Pittsburgh Sleep Quality Index. Remission was defined as having a SIGH-ADS score of 8 or less.

**RESULTS:** At baseline, both groups had moderate depression and no hypomanic or manic symptoms. Compared with the placebo light group, the group treated with bright white light experienced a significantly higher remission rate (68.2% compared with 22.2%; adjusted odds ratio=12.6) at weeks 4–6 and significantly lower depression scores (9.2 [SD=6.6] compared with 14.9 [SD=9.2]; adjusted  $\beta$ =-5.91) at the endpoint visit. No mood polarity switches were observed. Sleep quality improved in both groups and did not differ significantly between them

**CONCLUSIONS:** The data from this study provide robust evidence that supports the efficacy of midday bright light therapy for bipolar depression.

#### **Efficacy of light therapy versus antidepressant drugs, and of the combination versus monotherapy, in major depressive episodes: a systematic review and meta-analysis**

Geoffroy P.A., Carmen M., Schroder C.M., Reynaud E., Bourgin P. (2019)

Although light therapy (LT) has been shown to be efficient in the treatment of seasonal and non-seasonal depression, it is underused in clinical settings and antidepressant drugs (AD) remain so far the usual first line treatment. The aim of this systematic review and weighted random effect meta-analysis is to examine the randomized controlled trials that compared directly

light therapy and antidepressant drugs, as well as their combination (LT+AD). A total of 397 participants were included, with a moderate to severe major depressive episode, from seven independent populations. The median duration of intervention was 5 weeks (range 2-8 weeks). The superiority (lower depression score) of LT+Placebo compared to AD+Placebo was non-significant (SMD=0.19[-0.08-0.45];  $p=0.17$ ). The combination LT+AD was superior to AD+Placebo (SMD=0.56[0.24-0.88];  $p<0.001$ ). This superiority was confirmed in the subgroup of patients with non-seasonal depression (SMD=0.55[0.16-0.93];  $p=0.005$ ). Meta-analyses showed no or small heterogeneity between studies ( $I^2=0\%$ , 18.41%, and 39.23% respectively). No potential publication biases were observed by statistical tests and visual inspection of the funnel plots. No differences were observed between LT and AD, with a clear superiority of the combination, thus both LT monotherapy and combination may be proposed as a first line treatment in seasonal and non-seasonal depression.

#### **The psychiatry of light** Schwartz

RS1, Olds J.. *Harv Rev Psychiatry*. 2015 May-Jun;23(3)

Bright light therapy and the broader realm of chronotherapy remain underappreciated and underutilized, despite their empirical support. Efficacy extends beyond seasonal affective disorder and includes nonseasonal depression and sleep disorders, with emerging evidence for a role in treating attention-deficit/hyperactivity disorder, delirium, and dementia. A practical overview is offered, including key aspects of underlying biology, indications for treatment, parameters of treatment, adverse effects, and transformation of our relationship to light and darkness in contemporary life.

#### **Schizophrenic disorders**

##### **Bright light therapy in schizophrenic diseases.**

Heim M. *Psychiatr Neurol Med Psychol (Leipzig)*. 1990 Mar;42(3):146-50.

20 patients with schizophrenic disorders, displaying a depressive syndrome, were given bright-light therapy, and compared with 11 patients treated by means of partial deprivation of sleep. Against a figure of 27% in the case

of sleep-deprivation, syndrome remittance was 55% in the case of bright-light therapy. Psychometric data were obtained by use of three external-assessment schemes (HAMD, BPRS, and NOSIE) and two self-assessment procedures (TSD, POMS). As depressive syndromes improve under bright-light therapy, schizophrenic symptoms also recede, which suggests close syndromatologic links in the sense of a universal genesis of psychoses.

#### **Eating Disorders**

##### **A Systematic Review of Bright Light Therapy for Eating Disorders.**

Beauchamp, M. T., & Lundgren, J. D. (2016). *The Primary Care Companion For CNS Disorders*, 18(5). <https://doi.org/10.4088/PCC.16r02008>

**OBJECTIVE:** Bright light therapy is a noninvasive biological intervention for disorders with nonnormative circadian features. Eating disorders, particularly those with binge-eating and night-eating features, have documented nonnormative circadian eating and mood patterns, suggesting that bright light therapy may be an efficacious stand-alone or adjunctive intervention. The purpose of this systematic literature review, using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, was (1) to evaluate the state of the empirical treatment outcome literature on bright light therapy for eating disorders and (2) to explore the timing of eating behavior, mood, and sleep-related symptom change so as to understand potential mechanisms of bright light therapy action in the context of eating disorder treatment.

**DATA SOURCES:** A comprehensive literature search using PsycInfo and PubMed/MEDLINE was conducted in April 2016 with no date restrictions to identify studies published using bright light therapy as a treatment for eating disorders. Keywords included combinations of terms describing disordered eating (eating disorder, anorexia nervosa, bulimia nervosa, binge eating, binge, eating behavior, eating, and night eating) and the use of bright light therapy (bright light therapy, light therapy, phototherapy). After excluding duplicates, 34 articles were reviewed for inclusion.

**Study Selection and Data Extraction:** 14 published studies of bright light therapy for eating disorders met inclusion criteria (included participants with an eating disorder/

disordered-eating behaviors; presented as a case study, case series, open-label clinical trial, or randomized/nonrandomized controlled trial; written in English; and published and available by the time of manuscript review).

**RESULTS:** Results suggest that bright light therapy is potentially effective at improving both disordered-eating behavior and mood acutely, although the timing of symptom response and the duration of treatment effects remain unknown.

**CONCLUSIONS:** Future research should systematically control for placebo response, assess symptom change frequently and across a broad range of systems, and evaluate the longer-term efficacy of bright light therapy for eating disorders.

#### **Bright light therapy for the treatment of night eating syndrome: A pilot study**

Ashley M. McCune, Jennifer D. Lundgren (2015) *Psychiatry Research*, 229, 577-579

- Bright light therapy improves symptoms of night eating syndrome.
- Bright light therapy improves mood.
- Bright light therapy improves sleep quality.

The effect of bright light therapy (BLT) on the symptoms of night eating syndrome was evaluated. Fifteen adults completed two weeks of daily 10,000 lux BLT administered in the morning. Significant reductions were found pre-to-post treatment in night eating symptomatology, mood disturbance, and sleep disturbance. This pilot trial provides preliminary support for the efficacy of BLT for the treatment of night eating syndrome.

#### **A controlled study of light therapy for bulimia nervosa.**

Lam RW, Goldner EM, Solyom L, Remick RA. *Am J Psychiatry*. 1994 May;151(5):744-50.

**OBJECTIVE:** Winter worsening of mood and eating symptoms, similar to that of seasonal affective disorder, has recently been reported in patients with bulimia nervosa. To assess the effectiveness of light therapy for treatment of bulimia nervosa, the authors conducted a study of light therapy during winter comparing an active (bright white light) condition to a control (dim red light)

condition in bulimic patients who were not selected for a seasonal pattern of bulimia.

**METHOD:** After a 2-week baseline assessment, 17 female patients with a DSM-III-R diagnosis of bulimia nervosa underwent early morning light treatment with 2 weeks of bright white light exposure (10,000 lux for 30 min/day) and 2 weeks of dim red light exposure (500 lux for 30 min/day) in a counterbalanced, crossover design. Outcome measures included daily binge/purge diaries, objective and subjective measures of mood, and the Eating Attitudes Test. Expectation of response for each condition was also assessed before treatment.

**RESULTS:** Although pretreatment expectation ratings were similar for each condition, the bright white light condition was superior to the dim red light condition for all mood and eating outcome measures. Patients with "seasonal" bulimia (N = 7) had significantly greater improvement after the bright white light treatment than patients with nonseasonal bulimia (N = 10). No significant order effects were noted, nor differential effects for patients taking concurrent antidepressant medications (N = 4). **CONCLUSIONS:** These data suggest that bright white light therapy is an effective short-term treatment for both mood and eating disturbances associated with bulimia nervosa, although the therapeutic effect may be greater in those patients with a seasonal pattern.

**Bright light therapy decreases winter binge frequency in women with bulimia nervosa: a double-blind, placebo-controlled study.** Braun DL, Sunday SR, Fornari VM, Halmi KA. *Compr Psychiatry*. 1999 Nov-Dec;40(6):442-8.

The study objective was to determine the effect of winter bright light therapy on binge and purge frequencies and depressive symptoms in subjects with bulimia nervosa. Thirty-four female bulimic outpatients were treated with either 10,000 lux bright white light or 50 lux dim red light (placebo control) during the winter months. In this double-blind study, the placebo group (n = 18) and the bright light group (n = 16) were matched for age, degree of seasonality (measured by the Seasonal Patterns Assessment Questionnaire [SPAQ]), and concurrent depression (measured by Structured Clinical Interview for DSM-IV [SCID]). Three weeks of baseline data collection were followed by 3 weeks of half-hour daily morning light

treatment and 2 weeks of follow-up evaluation. There was a significant light-treatment by time interaction (Wilks' lambda = .81, F(2,28) = 3.31, P = .05). The mean binge frequency decreased significantly more from baseline to the end of treatment for the bright light group (F(1,29) = 6.41, P = .017) than for the placebo group. The level of depression (measured by daily Beck Depression Inventory [BDI] scores) did not significantly differ between the groups during any phase, and neither depression nor seasonality affected the response to light treatment. In this double-blind study, bulimic women who received 3 weeks of winter bright light treatment reported a reduced binge frequency between baseline and the active treatment period in comparison to subjects receiving dim red light.

#### **Light therapy in bulimia nervosa: a double-blind, placebo-controlled study.**

Blouin AG1, Blouin JH, Iversen H, Carter J, Goldstein C, Goldfield G, Perez E. *Psychiatry Res*. 1996 Feb 28;60(1):1-9.

The effects of light therapy on food intake and affective symptoms of bulimia nervosa (BN) were examined in a double-blind study. Eighteen women who met DSM-III-R criteria for BN were randomly assigned to receive either 2500 lux of bright light (experimental condition) or < 500 lux of dim light (placebo condition) daily in the early evening for a 1-week period. The Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorder Version (SIGH-SAD), the Beck Depression Inventory (BDI), and the Bulimic Symptoms Checklist were administered to subjects before light exposure, after 1 week of light exposure, and after 7 days of withdrawal of light exposure. Throughout the study, the Profile of Mood States and the Daily Binge Record were completed daily. Compared with subjects in the dim light condition, subjects in the bright light condition showed a significant improvement in depressed mood during light exposure, as measured by both the BDI and the SIGH-SAD. There was a return to pretreatment levels of depression after withdrawal of light exposure. No changes in depression were noted in the placebo group. No effect of light therapy was found on the frequency, size, or content of binge-eating episodes. The results are discussed in terms of the physiological processes associated with light therapy and seasonal affective disorder that may underlie the affective and food intake symptoms of BN.

#### **An open trial of light therapy for women with seasonal affective disorder and comorbid bulimia nervosa.**

Lam RW, Lee SK, Tam EM, Grewal A, Yatham LN. *J Clin Psychiatry*. 2001 Mar;62(3):164-8.

**OBJECTIVE:** Many patients with seasonal affective disorder (SAD) have dysfunctional eating behaviors. Conversely, many women with bulimia nervosa have marked winter worsening of mood and bulimic symptoms. Controlled studies of light therapy in SAD and in bulimia nervosa have shown beneficial effects on mood and binge/purge symptoms. We explored the clinical use of light therapy in women with SAD who also had comorbid bulimia nervosa. **METHOD:** Twenty-two female patients diagnosed using DSM-IV criteria with both bulimia nervosa and major depressive disorder with a seasonal (winter) pattern were treated with an open design, 4-week trial of light therapy (10,000 lux fluorescent light box with an ultraviolet filter, 30 to 60 minutes per day in the early morning). Patients were assessed before and after treatment with depression scales and with binge/purge diaries.

**RESULTS:** Light therapy resulted in significant improvement in mood, with a mean 56% reduction in 29-item Hamilton Rating Scale for Depression scores following treatment (p < .001). The frequency of binges and purges per week also significantly decreased (p < .001) from baseline by a mean of 46% and 36%, respectively. Two (9%) of 22 patients became abstinent of binge/purge episodes, compared with 10 (45%) of 22 patients who met criteria for remission of depressive symptoms. The light therapy was well tolerated by patients.

**CONCLUSION:** These results suggest that therapeutic effects of light therapy on mood and bulimic symptoms in patients with SAD and comorbid bulimia nervosa are sustained over at least 4 weeks. However, the low abstinence rate in bulimic symptoms indicates that light therapy may be most effectively used as an adjunctive treatment to medications and/or psychotherapy for bulimia nervosa.

#### **Bright light treatment of depressive symptoms in patients with restrictive type of anorexia nervosa.**

Janas-Kozik M, Krzystanek M, Stachowicz M, Krupka-Matuszczyk I, Janas A, Rybakowski JK. *J Affect Disord*. 2011 May;130(3):462-5.

**BACKGROUND:** Light therapy refers to two different categories of treatment. One of them is used in common medical practice and the other in complementary medicine. The aim of the study was to assess the effect of short time (6 weeks) bright light treatment (BLT) on depressive symptoms in female patients with the restrictive type of anorexia nervosa (AN-R).

**METHODS:** Twenty-four girls, aged 15-20 (mean 17.4±1) years, diagnosed as AN-R, with concomitant depressive symptoms ≥17 points on the 21-item Hamilton Depression Rating Scale (HDRS) were studied. All girls received cognitive behavioral therapy. Among them, twelve were randomly assigned to additional treatment with BLT for 6 weeks (10,000 lux, 30 min daily). Both groups did not differ on baseline demographic and clinical parameters. The assessments of depression by means of HDRS and measuring of body mass index (BMI) were done weekly throughout the treatment.

**RESULTS:** Improvement of depression was significantly greater in the group receiving BLT, with a significant difference between groups in depression intensity after 5 and 6 weeks. There was no difference in the increase of BMI between groups after 6 weeks, although such increase started earlier in patients treated with BLT.

**LIMITATIONS:** Six weeks of treatment may be an insufficient duration to draw the conclusion about the efficacy of BLT and a follow-up is needed to assess the maintenance of the effect.

**CONCLUSIONS:** The results obtained may suggest that BLT could be an effective non-pharmacological modality for the treatment of depression in patients with AN-R.

#### **Reducing symptoms in women with chronic anorexia nervosa. A pilot study on the effects of bright light therapy.**

Daansen PJ1, Haffmans J. *Neuro Endocrinol Lett.* 2010;31(3):290-6.

**OBJECTIVE:** To examine the effect of bright light therapy on the sleep-wake rhythm, the menstrual cycle, mood, and key eating pathology symptoms in chronic anorexia nervosa.

**METHODS:** Five chronic anorectic women (mean duration of illness: 15.3 years) received 5 daily sessions of 30 minutes bright light therapy (10,000 LUX). Participants completed a diagnostic interview and questionnaires at

pre-test, post-test and at a three month follow-up.

**RESULTS:** At follow up there was a slight improvement on core eating pathology, a fair decrease of depressive symptoms and an clinically important improvement on global distress.

**CONCLUSIONS:** Bright light therapy has on short term a positive effect on the physiological and psychological well being of chronic anorectic women. However, at follow-up the effects were partly lost. It is recommended to enhance the exposure period and repeat the treatment after 3 months.

### **Mental Disorders**

#### **Mild traumatic brain injury**

##### **Potential for the development of light therapies in mild traumatic brain injury**

A.C. Raikes, W.D. Killgore 2018

Light affects almost all aspects of human physiological functioning, including circadian rhythms, sleep-wake regulation, alertness, cognition and mood. We review the existing relevant literature on the effects of various wavelengths of light on these major domains, particularly as they pertain to recovery from mild traumatic brain injuries. Evidence suggests that light, particularly in the blue wavelengths, has powerful alerting, cognitive and circadian phase shifting properties that could be useful for treatment. Other wavelengths, such as red and green may also have important effects that, if targeted appropriately, might also be useful for facilitating recovery. Despite the known effects of light, more research is needed. We recommend a personalized medicine approach to the use of light therapy as an adjunctive treatment for patients recovering from mild traumatic brain injury.

##### **A randomized, double-blind, placebo-controlled trial of blue wavelength light exposure on sleep and recovery of brain structure, function, and cognition following mild traumatic brain injury**

William D.S.Killgore, John R.Vanuk, Bradley R.Shane, Maureen Weber, Sahil Bajaj. *Neurobiology of Disease* Volume 134, February 2020, 104679

- Mild traumatic brain injury (mTBI) is associated with sleep problems.
- Morning blue light may re-entrain the circadian rhythm and improve sleep problems.
- Compared 6-weeks of morning blue light therapy versus placebo in mTBI patients.
- Blue light improved sleep timing, daytime sleepiness, and executive functioning.
- Blue light increased thalamic volume and functional and structural connectivity.

Sleep and circadian rhythms are among the most powerful but least understood contributors to cognitive performance and brain health. Here we capitalize on the circadian resetting effect of blue-wavelength light to phase shift the sleep patterns of adult patients (aged 18–48 years) recovering from mild traumatic brain injury (mTBI), with the aim of facilitating recovery of brain structure, connectivity, and cognitive performance. During a randomized, double-blind, placebo-controlled trial of 32 adults with a recent mTBI, we compared 6-weeks of daily 30-min pulses of blue light (peak  $\lambda = 469$  nm) each morning versus amber placebo light (peak  $\lambda = 578$  nm) on neurocognitive and neuroimaging outcomes, including gray matter volume (GMV), resting-state functional connectivity, directed connectivity using Granger causality, and white matter integrity using diffusion tensor imaging (DTI). Relative to placebo, morning blue light led to phase-advanced sleep timing, reduced daytime sleepiness, and improved executive functioning, and was associated with increased volume of the posterior thalamus (i.e., pulvinar), greater thalamo-cortical functional connectivity, and increased axonal integrity of these pathways. These findings provide insight into the contributions of the circadian and sleep systems in brain repair and lay the groundwork for interventions targeting the retinohypothalamic system to facilitate injury recovery.

### **Attention deficit hyperactivity disorder (ADHD)**

##### **Correcting delayed circadian phase with bright light therapy predicts improvement in ADHD symptoms: A pilot study.**

Rachel E. Fargason, Aaron D. Fobian, Lauren M. Hablitz,

Jodi R. Paul, Karen L. Gamble (2017) *Journal of Psychiatric Research*, 91

Attention-deficit/hyperactivity disorder (ADHD) is a common condition with comorbid insomnia reported in >70% of children and adults. These patients demonstrate delays in sleep-wake rhythms, nocturnal rise in melatonin, and early morning rise in cortisol. Given that standard psychopharmacologic treatments for ADHD often do not completely control symptoms in participants with circadian rhythm delay, we sought to test whether bright light therapy (BLT) advances circadian rhythms and further reduces ADHD symptoms over standard treatments. In addition to standard of care, participants with ADHD diagnosis underwent 1 week of baseline assessment followed by 2-weeks of 30-min morning 10,000-lux BLT beginning 3 h after mid-sleep time. Participants minimized overhead light after 4 p.m., wore an actigraphy watch, and recorded BLT time on daily sleep logs. Dim Light Melatonin Onset (DLMO) was assessed at baseline and after 2-week treatment. ADHD symptoms were measured by the ADHD-Rating Scales (ADHD-RS). BLT significantly advanced the phase of DLMO by 31 min [mean time (SEM), 20:36 (0:21) advanced to 20:05 (0:20)] and mid-sleep time by 57 min [4:37 (0:22) advanced to 3:40 (0:16); paired t-tests,  $p = 0.002$  and  $0.004$ , respectively]. Phase advances (in DLMO or mid-sleep time) were significantly correlated with decreased ADHD-RS total scores ( $p = 0.027$  and  $0.044$ ) and Hyperactive-Impulsive subscores ( $p = 0.014$  and  $0.013$ , respectively). Actigraphy analysis for a subset of 8 participants with significant DLMO phase advance revealed no significant changes in total sleep time, sleep efficiency, wake after sleep onset, or percent wake during sleep interval. This is the first successful use of BLT for advancing melatonin phase and improving ADHD symptoms in adults. BLT may be a complementary treatment for both delayed sleep timing and ADHD symptoms in adults.

### **Alzheimer's disease (AD)**

##### **Effects of Light Treatment on Sleep, Cognition, Mood, and Behavior in Alzheimer's Disease: A Systematic Review.**

Mitolo, M., Tonon, C., La Morgia, C., Testa, C., Carelli, V.,

& Lodi, R. (2018). *Dementia and Geriatric Cognitive Disorders*, 46(5–6), 371–384.

**BACKGROUND:** Bright light treatment is a therapeutic intervention mainly used to treat sleep and circadian disturbances in Alzheimer's disease (AD) patients. Recently, a handful of studies also focused on the effect on cognition and behavior. Conflicting findings are reported in the literature, and no definite conclusions have been drawn about its specific therapeutic effect.

**SUMMARY:** The aim of this review is to provide a critical evaluation of available evidence in this field, highlighting the specific characteristics of effective bright light treatment. Eligible studies were required to assess at least one of the following outcome measures: sleep, cognition, mood, and/or behavior (e.g., depression, agitation). A total of 32 articles were included in this systematic review and identified as research intervention studies about light treatment in AD. The quality of the papers was evaluated based on the US Preventive Service Task Force guidelines.

**KEY MESSAGES:** Overall, the current literature suggests that the effects of light treatment in AD patients are mixed and may be influenced by several factors, but with a general trend toward a positive effect. Bright light seems to be a promising intervention treatment without significant adverse effects; therefore, further well-designed randomized controlled trials are needed taking into account the highlighted recommendations.

#### **Light therapy and Alzheimer's disease and related dementia: past, present, and future.**

Hanford N1, Figueiro M., *J Alzheimers Dis*. 2013

Sleep disturbances are common in persons with Alzheimer's disease or related dementia (ADRD), resulting in a negative impact on the daytime function of the affected person and on the wellbeing of caregivers. The sleep/wake pattern is directly driven by the timing signals generated by a circadian pacemaker, which may or may not be perfectly functioning in those with ADRD. A 24-hour light/dark pattern incident on the retina is the most efficacious stimulus for entraining the circadian system to the solar day. In fact, a carefully orchestrated light/dark pattern has been shown in several controlled studies of older populations, with and without ADRD, to be a

powerful non-pharmacological tool to improve sleep efficiency and consolidation. Discussed here are research results from studies looking at the effectiveness of light therapy in improving sleep, depression, and agitation in older adults with ADRD. A 24-hour lighting scheme to increase circadian entrainment, improve visibility, and reduce the risk of falls in those with ADRD is proposed, and future research needs are discussed.

#### **Bright light therapy for elderly.**

Okawa M. *Nihon Rinsho*. 2015 Jun;73(6):997-1005.

Bright light therapy (BLT) holds considerable promise for sleep problems in the elderly. BLT for community-dwelling patients with Alzheimer's disease showed significant improvement in sleep parameters. In the institutional setting, BLT was effective in reducing daytime nap duration. Morning BLT was found to advance the peak circadian rhythm and increase activity level in daytime and melatonin level at night. Light therapy could be used in combination with other nonpharmacological methods such as social activities, outside walking, physical exercises, which showed greater effects than independent BLT on sleep and cognitive function. BLT treatment strategy was proposed in the present paper. We should pay more attentions to BLT in community setting for mental and physical well-being.

#### **Light, sleep and circadian rhythms in older adults with Alzheimer's disease and related dementias.**

Figueiro MG, *Neurodegener Dis Manag*. 2017 Apr;7(2):119-145, Lighting Research Center, USA.

Alzheimer's disease and related dementias (ADRD) can cause sleep and behavioral problems that are problematic for ADRD patients and their family caregivers. Light therapy has shown promise as a nonpharmacological treatment, and preliminary studies demonstrate that timed light exposure can consolidate and improve nighttime sleep efficiency, increase daytime wakefulness and reduce evening agitation without the adverse effects of pharmacological solutions. Compliance with light treatment and the accurate measurement of light exposures during treatment, however, have presented barriers for the adoption of light therapy for ADRD. Recent research showing that the circadian system is maximally sensitive to short-wavelength light opens the way for the potential

application of lower, more-targeted light intensities to maximize compliance and individualize light dose/timing in therapeutic settings.

#### **Bright light treatment of behavioral and sleep disturbances in patients with Alzheimer's disease.**

Satlin A, Volicer L, Ross V, Herz L, Campbell S. *Am J Psychiatry*. 1992 Aug;

**OBJECTIVE:** The authors tested the hypothesis that evening bright light pulses would improve sleep-wake patterns and reduce agitation in patients with Alzheimer's disease who have severe sundowning (a syndrome of recurring confusion and increased agitation in the late afternoon or early evening) and sleep disorders. **METHOD:** Ten inpatients with Alzheimer's disease on a research ward of a veterans' hospital were studied in an open clinical trial. All patients had sundowning behavior and sleep disturbances. After a week of baseline measurements, patients received 2 hours/day of exposure to bright light between 7:00 p.m. and 9:00 p.m. for 1 week. During the baseline week, the treatment week, and a posttreatment week, patients were rated by nurses for agitation, sleep-wake patterns, use of restraints, and use of prescribed-as-needed medication. On the last 2 days of each week, patients wore activity monitors. Activity counts were analyzed for circadian rhythmicity.

**RESULTS:** Clinical ratings of sleep-wakefulness on the evening nursing shift improved with light treatment in eight of the 10 patients. 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. More severe sundowning at baseline predicted greater clinical improvement.

**CONCLUSIONS:** Evening bright light pulses may ameliorate sleep-wake cycle disturbances in some patients with Alzheimer's disease. This effect may be mediated through a chronobiological mechanism.

#### **Effect of timed bright light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease.**

Dowling GA, Mastick J, Hubbard EM, Luxenberg JS, Burr RL. *Int J Geriatr Psychiatry*. 2005 Aug;20(8):738-43.

**BACKGROUND:** Disturbances in rest-activity rhythm are prominent and disabling symptoms in Alzheimer's disease (AD). Nighttime sleep is severely fragmented and daytime activity is disrupted by multiple napping episodes. In most institutional environments, light levels are very low and may not be sufficient to entrain the circadian clock to the 24-hour day.

**METHOD:** The purpose of this randomized clinical trial was to test the effectiveness of timed bright light therapy in reducing rest-activity (circadian) disruption in institutionalized patients with AD. The experimental groups received either morning (9.30-10.30 am) or afternoon (3.30-4.30 pm) bright light exposure (> or = 2500 lux in gaze direction) Monday through Friday for 10 weeks. The control group received usual indoor light (150-200 lux). Nighttime sleep, daytime wake, and rest-activity parameters were determined by actigraphy. Repeated measures analysis of variance was employed to test the primary study hypotheses.

**RESULTS:** Seventy institutionalized subjects with AD (mean age 84) completed the study. No significant differences in actigraphy-based measures of nighttime sleep or daytime wake were found between groups. Subjects in either experimental light condition evidenced a significantly ( $p < 0.01$ ) more stable rest-activity rhythm acrophase over the 10-week treatment period compared to the control subjects whose rhythm phase delayed by over two hours.

**CONCLUSIONS:** One hour of bright light, administered to subjects with AD either in the morning or afternoon, did not improve nighttime sleep or daytime wake compared to a control group of similar subjects. However, exposure to one-hour of bright light in either the morning or afternoon may provide sufficient additional input to the circadian pacemaker to facilitate entrainment to the 24-hour day.

#### **Effect of morning bright light treatment for rest-activity disruption in institutionalized patients with severe Alzheimer's disease.**

Dowling GA, Hubbard EM, Mastick J, Luxenberg JS, Burr RL, Van Someren EJ. *Int Psychogeriatr*. 2005 Jun;17(2):221-36.

**BACKGROUND:** Disturbances in rest-activity rhythm are prominent and disabling symptoms in Alzheimer's disease (AD). Nighttime sleep is severely fragmented

and daytime activity is disrupted by multiple napping episodes. In most institutional environments, light levels are very low and may not be sufficient to enable the circadian clock to entrain to the 24-hour day. The purpose of this randomized, placebo-controlled, clinical trial was to test the effectiveness of morning bright light therapy in reducing rest-activity (circadian) disruption in institutionalized patients with severe AD.

**METHOD:** Subjects (n = 46, mean age 84 years) meeting the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke--the Alzheimer's Disease and Related Disorders Association) AD diagnostic criteria were recruited from two large, skilled nursing facilities in San Francisco, California. The experimental group received one hour (09:30-10:30) of bright light exposure (> or = 2500 lux in gaze direction) Monday through Friday for 10 weeks. The control group received usual indoor light (150-200 lux). Nighttime sleep efficiency, sleep time, wake time and number of awakenings and daytime wake time were assessed using actigraphy. Circadian rhythm parameters were also determined from the actigraphic data using cosinor analysis and nonparametric techniques. Repeated measures analysis of variance (ANOVA) was used to test the primary study hypotheses.

**RESULTS AND CONCLUSION:** Although significant improvements were found in subjects with aberrant timing of their rest-activity rhythm, morning bright light exposure did not induce an overall improvement in measures of sleep or the rest-activity in all treated as compared to control subjects. The results indicate that only subjects with the most impaired rest-activity rhythm respond significantly and positively to a brief (one hour) light intervention.

**Melatonin and bright-light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease.**

Dowling GA1, Burr RL, Van Someren EJ, Hubbard EM, Luxenberg JS, Mastick J, Cooper BA. *J Am Geriatr Soc.* 2008 Feb

**OBJECTIVES:** To test whether the addition of melatonin to bright-light therapy enhances the efficacy in treating rest-activity (circadian) disruption in institutionalized patients with Alzheimer's disease (AD).

**DESIGN:** Randomized, controlled trial.

**SETTING:** Two nursing homes in San Francisco, California.

**PARTICIPANTS:** Fifty subjects (mean age 86) with AD.

**INTERVENTION:** Experimental subjects received 1 hour of morning light exposure (> or = 2,500 lux in gaze direction) Monday to Friday for 10 weeks and 5 mg melatonin (LM, n=16) or placebo (LP, n=17) in the evening. Control subjects (n=17) received usual indoor light (150-200 lux).

**MEASUREMENTS:** Nighttime sleep variables, day sleep time, day activity, day:night sleep ratio, and rest-activity parameters were determined using actigraphy.

**RESULTS:** Linear mixed models were employed to test the primary study hypotheses. No significant differences in nighttime sleep variables were found between groups. At the end of the intervention, the LM group showed significant improvement in daytime somnolence as indicated by a reduction in the duration of daytime sleep, an increase in daytime activity, and an improvement in day:night sleep ratio. The LM group also evidenced a significant increase in rest-activity rhythm amplitude and goodness of fit to the cosinor model.

**CONCLUSION:** Light treatment alone did not improve nighttime sleep, daytime wake, or rest-activity rhythm. Light treatment plus melatonin increased daytime wake time and activity levels and strengthened the rest-activity rhythm. Future studies should resolve the question of whether these improvements can be attributed to melatonin or whether the two zeitgebers interact to amplify efficacy.

**Dementia**

**Treatments for Sleep Disturbances in Individuals With Dementia.**

Deschenes CL, McCurry SM. *Current Curr Psychiatry Rep.* 2009 February; 11(1): 20-26.

Sleep disturbances are widespread among older adults. Degenerative neurologic disorders that cause dementia, such as Alzheimer's disease and Parkinson's disease, exacerbate age-related changes in sleep, as do many common comorbid medical and psychiatric conditions. Medications used to treat chronic illness and insomnia have many side effects that can further disrupt sleep and place patients at risk for injury. This article reviews the neurophysiology of sleep in normal aging and sleep

changes associated with common dementia subtypes and comorbid conditions. Current pharmacologic and nonpharmacologic evidence-based treatment options are discussed, including the use of light therapy, increased physical and social activity, and multicomponent cognitive-behavioral interventions for improving sleep in institutionalized and community-dwelling adult with dementia.

**Bright light therapy for sleep disturbance in dementia is most effective for mild to moderate Alzheimer's type dementia: a case series.**

Sekiguchi H, Iritani S, Fujita K *Psychogeriatrics.* 2017 Sep;17(5):275-281

**BACKGROUND:** Sleep problems in people with dementia are common and place a high burden on caregivers. Although hypnotic agents are often used to treat sleep disturbances, their use is associated with a considerable number of high-risk side-effects such as daytime sleepiness, amnesia, and an increased frequency of falling. The administration of bright light therapy (BLT) in the morning was a non-pharmacological remedy that was expected to treat sleep disorders in patients with dementia by entraining the circadian rhythm to ameliorate disturbances to the normal sleep-wake cycle. However, there are some unsolved issues related to the application of BLT, including the types of dementia for which it is effective and its efficacy in the different stages of cognitive decline and dementia. Furthermore, a protocol for effective BLT has not yet been proposed.

**METHODS:** In this study, we explored the efficacy of BLT in the treatment of 17 participants, including those with Alzheimer's type dementia (AD) (n=8), vascular dementia (n=4), and dementia with Lewy bodies (n=5). Patients sat in front of the light box for 1h/day from 0900 to 1000. The patients underwent treatment every day for 2 weeks.

**RESULTS:** BLT led to the improvement of sleep disturbance in four participants, all of whom were AD patients. The four AD patients showed a shorter duration of illness and/or had mild to moderate AD.

**CONCLUSION:** BLT could be an effective strategy for treating dementia patients, depending on their type and grade of their dementia. To confirm this hypothesis, it would be necessary to study a larger number of cases. Non-pharmaco-

logical therapies for sleep disorders should be emphasized as a safe form of treatment for patients with dementia.

**Methodological challenges in studies of bright light therapy to treat sleep disorders in nursing home residents with dementia.**

van der Ploeg, E. S & O'Connor, DW. (2014). *Psychiatry and Clinical Neurosciences*, 68(11), 777-784.

**AIM:** Numerous studies have explored the effectiveness of bright light therapy as a treatment of sleep disorders in nursing home and long-stay geriatric hospital residents, most of whom have dementia. A recent Cochrane Collaboration meta-analysis of 10 selected studies concluded that there was insufficient evidence to assess its therapeutic efficacy as most available studies had methodological problems. We sought to remedy this situation by developing proposals to guide research methods in future studies.

**METHODS:** Based on the literature and our own clinical and research experience, we developed a series of proposals relating to study design, participant selection, light delivery modalities and outcome measures that we believe will maximize the chances of identifying a bright light treatment effect. We then checked adherence to these proposals in all relevant published experimental studies.

**RESULTS:** Of the 18 studies published in the last two decades that met our selection criteria, only half the studies had selected participants with a sleep disorder. Eleven studies excluded people with severe vision loss; seven included a clinical rating of sleep, and five measured baseline lighting levels. Most checked psychoactive medication prescriptions but few reported changes in prescriptions over the course of the study. Most also checked treatment adherence and included some control for differences in amount of social contact.

**CONCLUSIONS:** Evidence for the effectiveness of bright white light treatment in people residing in nursing homes is equivocal. We anticipate that the quality of this evidence will be improved if researchers refine their study methods and adopt a more uniform approach.

**Light therapy for behavioural and psychological symptoms of dementia.**

Skjerve A, Bjorvatn B. *Int J Geriatr Psychiatry.* 2004;19(6):516-22.

**OBJECTIVES:** To review literature concerning the efficacy, clinical practicability and safety of light treatment for behavioural and psychological symptoms of dementia (BPSD). **METHOD:** Data collection included computer literature searches (MEDLINE, PsycINFO and Cochrane) and checks of references, covering the period of January 1980–September 2003. Trials were searched for evidence for treatment efficacy and for their consideration of the treatment's clinical practicability and evidence of adverse effects.

**RESULTS:** Results from randomised controlled trials (RCT) indicated some evidence of improvement in aspects of sleep disturbances and circadian activity rhythmicity. One RCT study indicated better response in patients with vascular dementia compared to Alzheimer's disease. By and large, non-RCT studies reported improvement in BPSD including sleep disturbances, agitation and activity rhythm disturbances. Few studies commented on the treatment's practicability and safety.

**CONCLUSION:** Although there is some evidence for influence of light therapy on sleep and circadian activity rhythmicity, it is not possible to draw any conclusion about efficacy of light therapy for BPSD, or about practicability in clinical settings and safety. There are still too few well designed studies. Suggestions for further research are presented.

#### **Tailored Lighting Intervention for Persons with Dementia and Caregivers Living at Home.**

Figueiro MG, Hunter CM, Higgins P, Hornick T, Jones GE, Plitnick B, Brons J, Rea MS. *Sleep Health*. 2015 Dec 1;1(4):322-330.

**OBJECTIVES:** Light therapy has shown promise as a non-pharmacological treatment to help regulate abnormal sleep-wake patterns and associated behavioral issues prevalent among individuals diagnosed with Alzheimer's disease and related dementia (ADRD). The present study investigated the effectiveness of a lighting intervention designed to increase circadian stimulation during the day using light sources that have high short-wavelength content and high light output.

**METHODS:** Thirty-five persons with ADRD and 34 caregivers completed the 11-week study. During week 1, subjective questionnaires were administered to the study participants. During week 2, baseline data were collected

using Daysimeters and actigraphs. Researchers installed the lighting during week 3, followed by 4 weeks of the tailored lighting intervention. During the last week of the lighting intervention, Daysimeter, actigraph and questionnaire data were again collected. Three weeks after the lighting intervention was removed, a third data collection (post-intervention assessment) was performed. **RESULTS:** The lighting intervention significantly increased circadian entrainment, as measured by phasor magnitude and sleep efficiency, as measured by actigraphy data, and significantly reduced symptoms of depression in the participants with ADRD. The caregivers also exhibited an increase in circadian entrainment during the lighting intervention; a seasonal effect of greater sleep efficiency and longer sleep duration was also found for caregivers.

**CONCLUSIONS:** An ambient lighting intervention designed to increase daytime circadian stimulation can be used to increase sleep efficiency in persons with ADRD and their caregivers, and may also be effective for other populations such as healthy older adults with sleep problems, adolescents, and veterans with traumatic brain injury.

#### **Effect of home-based light treatment on persons with dementia and their caregivers.**

Sloane PD, Figueiro M, Garg S, Cohen LW, Reed D, Williams CS, Preisser J, Zimmerman S. *Light Res Technol*. 2015 Apr;47(2):161-176.

Sleep disorders are problematic for persons with dementia and their family caregivers. This randomized controlled trial with crossover evaluated the effects of an innovative blue-white light therapy on 17 pairs of home-dwelling persons with dementia and their caregivers. Subjects with dementia received blue-white light and control ('red-yellow' light) for six weeks separated by a four-week washout. Neither actigraphic nor most self-reported sleep measures significantly differed for subjects with dementia. For caregivers, both sleep and role strain improved. No evidence of retinal light toxicity was observed. Six weeks of modest doses of blue-white light appear to improve sleep in caregivers but not in persons with dementia. Greater or prolonged circadian stimulation may be needed to determine if light is an effective treatment for persons with dementia.

#### **Effect of Bright Light and Melatonin on Cognitive and Noncognitive Function in Elderly Residents of Group Care Facilities A Randomized Controlled Trial**

Rixt F. Riemersma-van der Lek, MD, Dick F. Swaab, MD, PhD, Jos Twisk, PhD, Elly M. Hol, PhD, Witte J. G. Hoogendijk, MD, PhD, Eus J. W. Van Someren, PhD

**CONTEXT:** Cognitive decline, mood, behavioral and sleep disturbances, and limitations of activities of daily living commonly burden elderly patients with dementia and their caregivers. Circadian rhythm disturbances have been associated with these symptoms.

**OBJECTIVE:** To determine whether the progression of cognitive and noncognitive symptoms may be ameliorated by individual or combined long-term application of the 2 major synchronizers of the circadian timing system: bright light and melatonin. **Design, Setting, and Participants** A long-term, double-blind, placebocontrolled, 22 factorial randomized trial performed from 1999 to 2004 with 189 residents of 12 group care facilities in the Netherlands; mean (SD) age, 85.8 (5.5) years; 90% were female and 87% had dementia.

**INTERVENTIONS:** Random assignment by facility to long-term daily treatment with whole-day bright ( $\pm 1000$  lux) or dim ( $\pm 300$  lux) light and by participant to evening melatonin (2.5 mg) or placebo for a mean (SD) of 15 (12) months (maximum period of 3.5 years). **Main Outcome Measures** Standardized scales for cognitive and noncognitive symptoms, limitations of activities of daily living, and adverse effects assessed every 6 months.

**RESULTS:** Light attenuated cognitive deterioration by a mean of 0.9 points (95% confidence interval [CI], 0.04-1.71) on the Mini-Mental State Examination or a relative 5%.

Light also ameliorated depressive symptoms by 1.5 points (95% CI, 0.24-2.70) on the Cornell Scale for Depression in Dementia or a relative 19%, and attenuated the increase in functional limitations over time by 1.8 points per year (95% CI, 0.61-2.92) on the nurse informant activities of daily living scale or a relative 53% difference. Melatonin shortened sleep onset latency by 8.2 minutes (95% CI, 1.08-15.38) or 19% and increased sleep duration by 27 minutes (95% CI, 9-46) or 6%. However, melatonin adversely affected scores on the Philadelphia Geriatric Centre Affect Rating Scale, both for positive affect ( $-0.5$  points; 95% CI,  $-0.10$  to  $-1.00$ ) and negative

affect (0.8 points; 95% CI, 0.20-1.44). Melatonin also increased withdrawn behavior by 1.02 points (95% CI, 0.18-1.86) on the Multi Observational Scale for Elderly Subjects scale, although this effect was not seen if given in combination with light. Combined treatment also attenuated aggressive behavior by 3.9 points (95% CI, 0.88-6.92) on the Cohen-Mansfield Agitation Index or 9%, increased sleep efficiency by 3.5% (95% CI, 0.8%-6.1%), and improved nocturnal restlessness by 1.00 minute per hour each year (95% CI, 0.26-1.78) or 9% (treatment time effect).

**CONCLUSIONS:** Light has a modest benefit in improving some cognitive and noncognitive symptoms of dementia. To counteract the adverse effect of melatonin on mood, it is recommended only in combination with light.

#### **Intellectual disabilities**

##### **The applicability of bright light therapy in adults with moderate, severe or profound intellectual disabilities: a brief report.**

Hermans H, Soerokromo N, Evenhuis H. *J Intellect Disabil Res*. 2017 Jun;61(6):618-623.

**BACKGROUND:** Bright light therapy (BLT) is effective in the treatment of depression in the general population. It may be a good treatment option for adults with intellectual disabilities (ID) too. However, its applicability and effectiveness are not studied in groups of adults with ID, yet. Our aim was to study the applicability of BLT in adults with ID.

**METHODS:** Bright light therapy was offered for 2 weeks, using a 10 000 lux light box, to 14 adults with moderate, severe or profound ID. Applicability of BLT and change in depressive symptoms were studied with questionnaires. **RESULTS:** Bright light therapy was successfully applied for  $\geq 10$  days in 10 participants. It was also applicable in participants with rather severe challenging behaviour. Before BLT, nine participants scored above the cut-off score of the ADAMS' depressive mood subscale. After BLT, six of them scored below cut-off.

**CONCLUSIONS:** Bright light therapy is applicable in adults with moderate, severe or profound ID. Its effectiveness as a treatment for depression in adults with ID should be further studied.

### Prevention of Delirium

#### Increasing Light Exposure for the Prevention of Delirium: A Systematic Review.

Groves, R. L. (2019).

*Dimensions of Critical Care Nursing : DCCN*, 38(2), 96–107.

**BACKGROUND:** Delirium is a neurological disorder with correlations to increased hospital length of stays and higher morbidity and mortality rates, particularly in the growing elderly population, making prevention strategies key in improving patient outcomes and health care systems. **OBJECTIVES:** Does increased exposure to light, by artificial or natural means, decrease the incidence of delirium?

**METHODS:** A systematic review was conducted of 4 revered databases, CINAHL, PubMed, PsycINFO, and Scopus, for articles related to key words “delirium” and “lighting” or “daylight” or “natural light” or “bright light” or “sunlight.” Results were narrowed to adult inpatients, defined as age older than 18 years. After limiting for quality of the study and content that addressed the objective, 7 articles were selected for review: 4 related to artificial means of light therapy and 3 consistent with increased exposure to natural light.

**RESULTS:** Two studies examined the effects of bright light therapy and reported a decreased incidence of delirium. Two studies researched whether increased lighting via a lighting system with varying degrees of intensity throughout the day would prevent delirium, and neither reported a decrease in delirium. The remaining 3 studies focused on whether increased natural light via windows decreased the occurrence of delirium and uncovered no correlation.

**DISCUSSION:** It is recommended that the study by Potharajaroen et al, which demonstrated significant findings for bright light therapy preventing delirium, be replicated as well as new pilot studies to enrich the growing body of research. Bright light therapy is a low-cost and easy-to-institute intervention that should be utilized on a case-to-case basis.

#### High bright light therapy may reduce delirium incidence in critically ill patients.

Shen, Y., Yan, J., & Cai, G. (2019, May). *Intensive Care Medicine*. United States.

In a recent meta-analysis [ 1], Dr. Bannon reported that bright light therapy (BLT) could not reduce delirium incidence in critically ill patients (Fig. 2, four trials, RR 0.45, 99% CI 0.10–2.13). Despite the well-designed analysis, this conclusion may be biased by the significant heterogeneity ( $I^2=69\%$ ) which we thought was caused by inclusion of the Simons trial. First, compared to the other three trials, the lighting intensity was quite low in the Simons trial (Table 1. 1500 lx vs. 5000 lx). Whether the effect of BLT was mediated by the lighting intensity remains unclear. Second, the BLT therapy only lasted for 2 h in the morning in all three trials, whereas the duration was much longer in the Simons study (from 9:00 am to 16:00 pm). According to Burgess et al.’s finding [2], the BLT only had antidepressant effect in the morning, but not in the evening. Whether the prolonged duration played a role in the inconsistent findings...

### Physical Disorders

#### Parkinson’s disease (PD)

##### Light Therapy for Sleep and Daytime Sleepiness Associated With Parkinson Disease

##### A Randomized Clinical Trial,

Aleksandar Videnovic, MD, MSc1,2; Elizabeth B. Klerman, MD, PhD2,3; Wei Wang, PhD2; et al., Angelica Marconi, MS4; Teresa Kuhta, DO4; Phyllis C. Zee, MD, PhD4 *Timed JAMA Neurol.* 2017;74(4):411-418. doi:10.1001/jama-neurol.2016.5192

Conclusions, free article

Light therapy is a well-tolerated, feasible intervention for impaired sleep-wake cycles associated with PD. Bright LT was associated with improvements in EDS, sleep fragmentation, and sleep quality. Light therapy may also be beneficial for motor symptoms of PD. Based on these results, the next logical step is to optimize various parameters of LT (eg, intensity, duration, and wavelength) not only for impaired sleep and alertness but also for other motor and nonmotor manifestations of PD. Such chronobiological treatment strategies would be highly desirable because pharmacological interventions for sleep disturbances in PD have been of modest benefit and may cause unacceptable side effects.

With great interest, we read the work of Videnovic and

colleagues.<sup>1</sup> They assessed the effects of timed light therapy on sleep and alertness and explored light therapy’s effects on motor and nonmotor manifestations and the quality of life for patients with Parkinson disease (PD). The results showed that bright light therapy could improve the sleep-wake cycles, enhance daytime alertness and sleep quality, and also have positive effects on activities of daily living. Although similar findings have been reported before,<sup>2</sup> this study further emphasizes the relationship between circadian disruption and PD, and sets a new standard for future studies of sleep-wake cycles and daytime function in PD.

##### Light Therapy Promoting Dopamine Release by Stimulating Retina in Parkinson

Disease. Li, Z., & Tian,

T. (2017). *JAMA Neurology*, 74(10), 1267.

Their letter centers on the potential novel mechanism of action of light therapy in Parkinson disease (PD). Specifically, they highlight the possibility that light therapy may promote dopamine release by stimulating cells within the retina, which translates to improvements of PD symptoms. We agree that this is a sound scientific hypothesis based on the current understanding of the intricate relationship between the retinal dopaminergic function in PD and the circadian system.

##### Polychromatic Light Exposure as a Therapeutic in the Treatment and Management of Parkinson’s Disease: A Controlled Exploratory Trial.

Willis, G. L., Boda, J., &

Freelance, C. B. (2018). *Frontiers in Neurology*. Switzerland.

Parkinson’s disease (PD) is a disorder characterized by loss of dopamine (DA) in the nigro-striatal dopamine (NSD) system with the primary symptoms of bradykinesia, rigidity, tremor, and altered gate. Secondary symptoms including depression, insomnia, involuntary movement, and psychiatric side effects are also commonly observed. While the treatment focus for the past 50 years has been aimed at replacing deficient DA, to relieve the primary symptoms, more recent studies have suggested that the circadian system plays a critical role in the etiology and treatment of this disorder. Several case studies and open label trials have implemented

bright light therapy (BT) in an attempt to repair sleep, depression and even the primary motor symptoms of this disorder, however controlled studies are yet to be fully implemented. In this controlled trial, patients that had been maintained on BT daily for 4 months to 5 years previously were assigned to one of three groups: continued polychromatic light, continued with red light or discontinued polychromatic light for a 2 week period. The Movement Disorder Society-Unified Parkinson’s Disease Rating Scale (MDSUPDRS), The Parkinson’s Disease Questionnaire (PDQ-39), The Beck Depression Inventory II, The Beck Anxiety Inventory, The Epworth Sleep Scale (ESS) and a global rating scale were used to assess patients prior to and at 1 and 2 weeks after commencing the trial. Patients continuing polychromatic BT showed significant improvement on the MDSUPDRS Rating Scale (12 points;  $p = 0.028$ ), the PDQ-39 (10 points;  $p = 0.011$ ), ESS (4 points;  $p = 0.013$ ), and numerous motor and secondary symptoms on a global rating scale. Performance on standardized motor tests also incrementally improved in this group while those exposed to red light and those that discontinued BT treatment deteriorated. These results demonstrate that strategically applied polychromatic light was beneficial in reducing many primary motor and secondary symptoms of PD. Further work investigating the role of light in mitigating PD symptoms and involvement of the circadian system will provide further advances in the treatment of PD.

##### Bright light therapy for depression in Parkinson disease: A randomized controlled trial.

Rutten, S., Vriend, C., Smit, J. H., Berendse, H. W., van Someren, E. J. W., Hoogendoorn, A. W., ... van den Heuvel, O. A. (2019). *Neurology*, 92(11), e1145–e1156.

Conclusion BLT was not more effective in reducing depressive symptoms than a control light. Mood and subjective sleep improved in both groups. BLT was more effective in improving subjective sleep quality than control light, possibly through a BLT-induced decrease in cortisol levels.

##### Light Therapy in Parkinson’s Disease: Towards Mechanism-Based Protocols

Fifel K., Videnovic A., *Neurosciences, Volume 41, Issue 5, May 2018, Pages 252-254*

A growing body of work is investigating the safety and efficacy of light in Parkinson's disease (PD). Here we discuss the potential of this emerging therapy to improve both motor and non-motor symptoms of PD. We also highlight directions for future basic, translational, and clinical research that are critical for the development of mechanism-based protocols of light therapy in PD.

#### **Timed Light Therapy for Sleep and Daytime Sleepiness Associated With Parkinson Disease: A Randomized Clinical Trial.**

Videnovic A, Klerman EB, Wang W, Marconi A, Kuhta T, Zee PC. *JAMA Neurol.* 2017 Apr 1;74(4):411-418

**IMPORTANCE:** Impaired sleep and alertness are some of the most common nonmotor manifestations of Parkinson disease (PD) and currently have only limited treatment options. Light therapy (LT), a widely available treatment modality in sleep medicine, has not been systematically studied in the PD population.

**OBJECTIVE:** To determine the safety and efficacy of LT on excessive daytime sleepiness (EDS) associated with PD.

**DESIGN< SETTING AND PARTICIPANTS:** This randomized, placebo-controlled, clinical intervention study was set in PD centers at Northwestern University and Rush University. Participants were 31 patients with PD receiving stable dopaminergic therapy with coexistent EDS, as assessed by an Epworth Sleepiness Scale score of 12 or greater, and without cognitive impairment or primary sleep disorder. Participants were randomized 1:1 to receive bright LT or dim-red LT (controlled condition) twice daily in 1-hour intervals for 14 days. This trial was conducted between March 1, 2007, and October 31, 2012. Data analysis of the intention-to-treat population was conducted from November 1, 2012, through April 30, 2016.

**MAIN OUTCOMES AND MEASURES:** The primary outcome measure was the change in the Epworth Sleepiness Scale score comparing the bright LT with the dim-red LT. Secondary outcome measures included the Pittsburgh Sleep Quality Index score, the Parkinson's Disease Sleep Scale score, the visual analog scale score for daytime sleepiness, and sleep log-derived and actigraphy-derived metrics.

**RESULTS:** Among the 31 patients (13 males and 18 females; mean [SD] disease duration, 5.9 [3.6] years), bright LT resulted in significant improvements in EDS, as

assessed by the Epworth Sleepiness Scale score (mean [SD], 15.81 [3.10] at baseline vs 11.19 [3.31] after the intervention). Both bright LT and dim-red LT were associated with improvements in sleep quality as captured by mean (SD) scores on the Pittsburg Sleep Quality Index (7.88 [4.11] at baseline vs 6.25 [4.27] after bright LT, and 8.87 [2.83] at baseline vs 7.33 [3.52] after dim-red LT) and the Parkinson's Disease Sleep Scale (97.24 [22.49] at baseline vs 106.98 [19.37] after bright LT, and 95.11 [19.86] at baseline vs 99.28 [16.94] after dim-red LT). Bright LT improved several self-reported mean (SD) sleep metrics, including sleep fragmentation (number of overnight awakenings, 1.51 [1.03] at baseline vs 0.92 [0.97] after the intervention), sleep quality (sleep diary score, 3.03 [1.01] at baseline vs 3.53 [0.91] after the intervention), and ease of falling asleep (sleep diary score, 2.32 [0.89] at baseline vs 1.83 [0.88] after the intervention). Light therapy was associated with increased daily physical activity as assessed by actigraphy (average activity [SD] counts, 165.01 [66.87] at baseline vs 194.59 [87.81] after the intervention).

**CONCLUSIONS AND RELEVANCE:** Light therapy was well tolerated and may be a feasible intervention for improving the sleep-wake cycles in patients with PD. Further studies are required to determine optimal parameters of LT for PD.

#### **Multiple sclerosis**

##### **Light therapy for multiple sclerosis-associated fatigue: Study protocol for a randomized controlled trial.**

Mateen FJ, Manalo NC, Grundy SJ, Houghton MA, Hotan GC, Erickson H, Videnovic A. *Medicine (Baltimore).* 2017 Sep;96(36):e8037.

**BACKGROUND:** Fatigue is the most commonly reported symptom among multiple sclerosis (MS) patients, more than a quarter of whom consider fatigue to be their most disabling symptom. However, there are few effective treatment options for fatigue. We aim to investigate whether supplemental exposure to bright white light will reduce MS-associated fatigue.

**METHODS:** Eligible participants will have clinically confirmed multiple sclerosis based on the revised McDonald criteria (2010) and a score  $\geq 36$  on the Fatigue Severity Scale (FSS). Participants will be randomized 1:1 to bright

white light (10,000 lux; active condition) or dim red light (<300 lux; control condition) self-administered for 1 hour twice daily. The study will include a 2-week baseline period, a 4-week treatment period, and a 4-week wash-out period. Participants will record their sleep duration, exercise, caffeine, and medication intake daily. Participants will record their fatigue using the Visual Analogue Fatigue Scale (VAFS) 4 times every third day, providing snapshots of their fatigue level at different times of day. Participants will self-report their fatigue severity using FSS on 3 separate visits: at baseline (week 0), following completion of the treatment phase (week 6), and at study completion (week 10). The primary outcome will be the change in the average FSS score after light therapy. We will perform an intention-to-treat analysis, comparing the active and control groups to assess the postintervention difference in fatigue levels reported on FSS. Secondary outcome measures include change in global VAFS scores during the light therapy and self-reported quality of life in the Multiple Sclerosis Quality of Life-54.

**DISCUSSION:** We present a study design and rationale for randomizing a nonpharmacological intervention for MS-associated fatigue, using bright light therapy. The study limitations relate to the logistical issues of a self-administered intervention requiring frequent participant self-report in a relapsing condition. Ultimately, light therapy for the treatment of MS-associated fatigue may provide a low-cost, noninvasive, self-administered treatment for one of the most prevalent and burdensome symptoms experienced by people with MS.

#### **Epilepsy**

##### **Bright light therapy for symptoms of anxiety and depression in focal epilepsy: randomised controlled trial.**

Baxendale S1, O'Sullivan J, Heaney D., *Br J Psychiatry.* 2013

**BACKGROUND:** Bright light therapy is an effective treatment for seasonal affective disorder and non-seasonal depression. Depression and anxiety are common psychiatric comorbidities in epilepsy.

**AIMS:** To examine the efficacy of bright light therapy for symptoms of anxiety and depression in adults with focal epilepsy (trial registration at ClinicalTrials.gov: NCT01028456).

**METHOD:** We recruited 101 adults with medically intractable focal epilepsy. Participants completed the Hospital Anxiety and Depression Scale (HADS) at the beginning (T1) and end of a 12-week baseline period (T2) and again after 12 weeks of daily light therapy (T3), with 51 participants using a high-intensity light box and 50 using a low-intensity one. Seizure diaries were kept throughout the baseline and trial period.

**RESULTS:** A total of 58 patients completed the trial. Anxiety and depression scores were significantly reduced following the light therapy at T3 in both the high- and low-intensity groups.

**CONCLUSIONS:** Light therapy resulted in a significant reduction in symptoms of anxiety and depression but we did not find any differences between high- v. low-intensity treatment. This may, therefore, be an effective treatment for symptoms of low mood in epilepsy at lower intensities than those typically used to treat seasonal affective disorder. Further work is needed to investigate this possibility with an adequate placebo condition

#### **Chronic nonspecific back pain**

##### **Short-term effects of bright light therapy in adults with chronic nonspecific back pain: a randomized controlled trial.**

Leichtfried V, Matteucci Gothe R, Kantner-Rumplmair W, Mair-Raggautz M, Bartenbach C, Guggenbichler H, Gehmacher D, Jonas L, Aigner M, Winkler D, Schobersberger W. *Pain Med.* 2014 Dec;15(12):2003-12

**OBJECTIVE:** The present trial evaluated incorporation of bright light therapy in the treatment of chronic nonspecific back pain (CNBP).

**DESIGN:** A prospective, randomized, controlled, multicenter, open design with three parallel trial arms was used. **SETTING:** Subjects received a novel therapeutic, an expected therapeutic ineffective low dose, or no light exposure at three different medical centers.

**PATIENTS:** A total of 125 CNBP patients reporting pain intensity of  $\geq 3$  points on item 5 of the Brief Pain Inventory (BPI) were included.

**INTERVENTION:** Over 3 weeks, 36 active treatment, 36 placebo controls, and 33 controls received 3 or no supplementary light exposures of 5.000 lx or 230 lx, respectively.

**OUTCOME MEASURES:** Changes in self-reported scores of pain intensity (BPI sub-score 1) and depression (Hospital Anxiety and Depression Questionnaire) were the primary outcome measures. Secondary outcome measures were changes in self-reported overall pain sensation (BPI total score), grade of everyday life impairment (BPI sub-score 2), mood (visual analog scale), and well-being (World Health Organization-Five Well-Being Index).

**RESULTS:** Changes in pain intensity were higher (1.0 [0.8-1.6]) in the bright light group compared with controls (0.3 [-0.1-0.8]; effect size  $D=0.46$ ). Changes in the depression score were also higher in the intervention group (1.5 [0.0-2.5]) compared with controls (0.0 [0.0-2.0]; effect size  $D=0.86$ ). No differences were seen in change scores between intervention vs sham group.

**CONCLUSION:** The present randomized controlled trial shows that light therapy even in low dose could improve depressive symptoms and reduce pain intensity in CNBP patients. Further research is needed for optimizing parameters of frequency, dose, and duration of therapeutic light exposure.

#### **An Open Trial of Morning Bright Light Treatment Among US Military Veterans with Chronic Low Back Pain: A Pilot Study.**

Burgess HJ, Rizvydeen M, Kimura M, Pollack MH, Hobfoll SE, Rajan KB, Burns JW., *Pain Med.* 2019 Apr 1;20(4):770-778

**OBJECTIVE:** To examine the feasibility, acceptability, and effects of a home-based morning bright light treatment on pain, mood, sleep, and circadian timing in US veterans with chronic low back pain.

**DESIGN:** An open treatment trial with a seven-day baseline, followed by 13 days of a one-hour morning bright light treatment self-administered at home. Pain, pain sensitivity, mood, sleep, and circadian timing were assessed before, during, and after treatment.

**SETTING:** Participants slept at home, with weekly study visits and home saliva collections.

**PARTICIPANTS:** Thirty-seven US veterans with medically verified chronic low back pain.

**METHODS:** Pain, mood, and sleep quality were assessed with questionnaires. Pain sensitivity was assessed using two laboratory tasks: a heat stimulus and an ischemia stimulus that gave measures of threshold

and tolerance. Sleep was objectively assessed with wrist actigraphy. Circadian timing was assessed with the dim light melatonin onset.

**RESULTS:** Morning bright light treatment led to reduced pain intensity, pain behavior, thermal pain threshold sensitivity, post-traumatic stress disorder symptoms, and improved sleep quality ( $P < 0.05$ ). Phase advances in circadian timing were associated with reductions in pain interference ( $r=0.55$ ,  $P < 0.05$ ).

**CONCLUSIONS:** Morning bright light treatment is a feasible and acceptable treatment for US veterans with chronic low back pain. Those who undergo morning bright light treatment may show improvements in pain, pain sensitivity, and sleep. Advances in circadian timing may be one mechanism by which morning bright light reduces pain. Morning bright light treatment should be further explored as an innovative treatment for chronic pain conditions.

#### **Fibromyalgia**

##### **Morning Versus Evening Bright Light Treatment at Home to Improve Function and Pain Sensitivity for Women with Fibromyalgia: A Pilot Study.**

Burgess HJ, Park M, Ong JC, Shakoor N, Williams DA, Burns J., *Pain Med.* 2017 Jan 1;18(1):116-123.

**OBJECTIVE:** To test the feasibility, acceptability, and effects of a home-based morning versus evening bright light treatment on function and pain sensitivity in women with fibromyalgia.

**DESIGN:** A single blind randomized study with two treatment arms: 6 days of a 1 hour morning light treatment or 6 days of a 1 hour evening light treatment. Function, pain sensitivity, and circadian timing were assessed before and after treatment.

**SETTING:** Participants slept at home, except for two nights in Sleep Center.

**PARTICIPANTS:** Ten women meeting the American College of Rheumatology's diagnostic criteria for fibromyalgia, including normal blood test results.

**METHODS:** Self-reported function was assessed with the Fibromyalgia Impact Questionnaire (FIQ). Pain sensitivity was assessed using a heat stimulus that gave measures of threshold and tolerance. Circadian timing was assessed with the dim light melatonin onset.

**RESULTS:** Both morning and evening light treatments

led to improvements in function and pain sensitivity. However, only the morning light treatment led to a clinically meaningful improvement in function ( $>14\%$  reduction from baseline FIQ) and morning light significantly increased pain threshold more than evening light ( $P < 0.05$ ). Phase advances in circadian timing were associated with an increase in pain tolerance ( $r=0.67$ ,  $P < 0.05$ ).

**CONCLUSIONS:** Bright light treatment appears to be a feasible and acceptable adjunctive treatment to women with fibromyalgia. Those who undergo morning light treatment may show improvements in function and pain sensitivity. Advances in circadian timing may be one mechanism by which morning light improves pain sensitivity. Findings can inform the design of a randomized controlled trial.

#### **Breast cancer**

##### **Light therapy and mood in breast cancer.**

Dallaspezia S, Cantamessa S, Benedetti F. *Int J Cancer.* 2018 Apr 15;142(8):1723-1724.

As found by White et al.,<sup>1</sup> inadequate or poor quality sleep is associated with an increased risk of breast cancer. In patients, sleep can interfere immune function, alter responses to stress, and impact daytime activities and quality of life which is not only a target in the treatment of patients affected by cancer but also a predictor of response to therapy. Moreover, circadian rhythm alterations strongly influence the development of depressive symptoms and fatigue syndrome. Not only breast cancer patients perceive fatigue before they begin chemotherapy, but the syndrome worsens during treatment<sup>2</sup> and a large proportion of patients continue to experience it for months after therapy is completed. Morning bright light treatment has been found to prevent overall fatigue from worsening during chemotherapy<sup>3</sup> and to protect women from circadian activity rhythm deterioration during chemotherapy.<sup>4</sup> No study so far focused on the effect of light therapy on mood in breast cancer patients.

We confirmed the usefulness of dawn simulation light therapy in preventing fatigue from worsening during chemotherapy, with an improvement in emotional well-being. A trend in decrease in PSQI total score was found after treatment. Moreover, a reduction of sleep latency and of the ratio between time asleep and time in bed

was observed, suggesting an improvement in patients' quality of sleep.

We also found that dawn light therapy induced an amelioration in patient perceived mood, which is influenced by the improvement of quality of sleep and in fatigue syndrome.

##### **Light treatment prevents fatigue in women undergoing chemotherapy for breast cancer.**

Ancoli-Israel S, Rissling M, Neikrug A, Trofimenko V, Natarajan L, Parker BA, Lawton S, Desan P, Liu L. *Support Care Cancer.* 2012 Jun;20(6):1211-9.

**PURPOSE:** Fatigue is one of the most disturbing complaints of cancer patients and is often the reason for discontinuing treatment. This randomized controlled study tested the hypothesis that increased morning bright light, compared to dim light, would result in less fatigue in women with breast cancer undergoing chemotherapy.

**METHODS:** Thirty-nine women newly diagnosed with stage I-III breast cancer were randomized to either bright white light (BWL) or dim red light (DRL) treatment and were instructed to use the light box for 30 min every morning throughout the first four cycles of chemotherapy. The Multidimensional Fatigue Symptom Inventory was administered prior to the start of chemotherapy (baseline), during the chemotherapy treatment week of cycle 1 (C1TW), the last week (recovery week) of cycle 1 (C1RW), the chemotherapy treatment week of cycle 4 (C4TW), and the last week (recovery week) of cycle 4 (C4RW).

**RESULTS:** The DRL group reported increased fatigue at C1TW ( $p=0.003$ ) and C4TW ( $p < 0.001$ ) compared to baseline, while there was no significant change from baseline in the BWL group. A secondary analysis showed that the increases in fatigue levels in the DRL group were not mediated through nor associated with changes in sleep or in circadian rhythms as measured with wrist actigraphy.

**CONCLUSIONS:** The results of this study suggest that morning bright light treatment may prevent overall fatigue from worsening during chemotherapy. Although our hypothesis that overall fatigue would improve with bright light treatment was not supported, the lack of deterioration in total fatigue scores suggests that bright morning light may be a useful intervention during chemotherapy for breast cancer.

**Prevention of quality-of-life deterioration with light therapy is associated with changes in fatigue in women with breast cancer undergoing chemotherapy.**

Jeste N, Liu L, Rissling M, Trofimenko V, Natarajan L, Parker BA, Ancoli-Israel S. *Qual Life Res.* 2013 Aug;22(6):1239-44

**PURPOSE:** During chemotherapy, women with breast cancer not only experience poor quality of life (QOL), they also have little exposure to bright light, which has been shown to be associated with depression, fatigue, and poor sleep in other chronic illnesses. This study examined whether increased light exposure would have a positive effect on QOL.

**METHODS:** Thirty-nine women with stage I-III breast cancer scheduled to receive  $\geq 4$  cycles of chemotherapy were randomized to a bright white light (BWL,  $n = 23$ ) or dim red light (DRL,  $n = 16$ ) treatment group. Data were collected before (baseline) and during cycles 1 and 4 of chemotherapy. Light was administered via a light box (Litebook<sup>®</sup>, Ltd.). QOL was assessed with the Functional Assessment of Cancer Therapy-Breast (FACT-B) and the Functional Outcomes of Sleep Questionnaire (FOSQ).

**RESULTS:** Compared with baseline, the DRL group demonstrated significant decline in QOL during the treatment weeks of both cycles (all  $ps < 0.02$ ), whereas the BWL group had no significant decline (all  $ps > 0.05$ ). Mixed model analyses revealed that there was a group-by-time interaction for FOSQ at the treatment week of cycle 4, and this interaction was mediated by fatigue. **CONCLUSION:** The data suggest that increased exposure to bright light during chemotherapy may prevent the decline in QOL via preventing the increase in fatigue.

**Bright light therapy protects women from circadian rhythm desynchronization during chemotherapy for breast cancer.**

Neikrug AB, Rissling M, Trofimenko V, Liu L, Natarajan L, Lawton S, Parker BA, Ancoli-Israel S. *Behav Sleep Med.* 2012;10(3):202-16.

Circadian rhythms (CRs) are commonly disrupted in women undergoing chemotherapy for breast cancer (BC). Bright light improves and strengthens CRs in other populations. This randomized controlled study examined

the effect of morning administration of bright light therapy on CRs in women undergoing chemotherapy for BC. It was hypothesized that women receiving bright light therapy would exhibit more robust rhythms than women exposed to dim light. Thirty-nine women newly diagnosed with BC and scheduled for chemotherapy were randomized into 2 groups: bright white light (BWL) or dim red light (DRL). Women were instructed to use the light box every morning for 30 min during their first 4 cycles of chemotherapy. Wrist actigraphy was recorded at 5 time points: prior to chemotherapy (baseline), Cycle-1 treatment week (C1TW), Cycle-1 recovery week (C1RW), Cycle-4 treatment week (C4TW), and Cycle-4 recovery week (C4RW). There was a Group  $\times$  Time interaction at C4TW compared to baseline such that the DRL group showed significant deterioration in the mean of the activity rhythm (mesor) and amplitude, whereas the BWL group exhibited a significant increase in both mesor and amplitude. The DRL group also exhibited significant deterioration in overall rhythm robustness at C1TW, C4TW, and C4RW. Women in the BWL group also showed significant decreases in overall rhythm robustness at C1TW and C4TW, but returned to baseline levels at both recovery weeks. The results suggest that morning administration of bright light may protect women from experiencing CR deterioration during chemotherapy.

**Moderators of Cognitive Therapy and Bright Light Therapy Effects on Depressive Symptoms in Patients with Breast Cancer.**

Maruani, J., Geoffroy, P. A., O’Caoimh, R., Mannion, H., Sezgin, D., O’Donovan, M. R., ... Gartlehner, G. (2019). *Chronobiology International*, 36(7), 45. <https://link.springer.com/article/10.1007/s12529-019-09802-6>

**BACKGROUND:** Cognitive therapy (CT) and bright light therapy (BLT) have been found to be effective to treat depressive symptoms in breast cancer patients. No study has investigated the baseline patients’ characteristics that are associated with better outcomes with CT vs. BLT in this population. This study aimed to assess, in breast cancer patients, the moderating role of eight clinical variables on the effects of CT and BLT on depressive symptoms. **METHODS:** This is a secondary analysis of a randomized controlled trial conducted in 59 women who received an 8-week CT or BLT and completed questionnaires evaluat-

ing depression and possible moderating variables. **RESULTS:** Patients benefited more from BLT when they had no prior history of major depressive disorder, higher depression scores on the Hospital Anxiety and Depression Scale (HADS-D) at baseline, a greater initial preference for BLT, and when they received BLT during spring or summer. Patients benefited more from CT when they had a lower initial preference for receiving CT, higher depression scores on the HADS-D, and seasonal depressive symptoms.

**CONCLUSIONS:** Although replication is needed, findings of this study suggest the existence of different profiles of patients more likely to benefit from CT and BLT.

**Cancer related fatigue**

**Bright light therapy improves cancer-related fatigue in cancer survivors: a randomized controlled trial.**

Johnson JA, Garland SN, Carlson LE, Savard J, Simpson JSA, Ancoli-Israel S, Campbell TS. *J Cancer Surviv.* 2018 Apr;12(2):206-215

**PURPOSE:** Cancer-related fatigue (CRF) is a common and distressing symptom that can persist after cancer treatment has concluded. Bright light therapy has shown preliminary efficacy in reducing CRF, but its impact on other psychosocial factors is unclear. The purpose was to examine the impact of a 1-month light therapy intervention on fatigue, mood, and quality of life in cancer survivors with fatigue.

**METHODS:** This 4-week blinded randomized controlled trial recruited cancer survivors who met diagnostic criteria for CRF. Participants were randomly assigned to receive a light therapy device that produced either bright white light (BWL; intervention) or dim red light (DRL; active control). Participants were instructed to use the device daily for 30 min upon waking for 28 days. The primary outcome, fatigue, was assessed weekly. Secondary outcomes assessed pre- and post-intervention included mood, depressive symptoms, and quality of life.

**RESULTS:** A total of 81 participants were randomly assigned to receive BWL ( $n = 42$ ) or DRL ( $n = 39$ ). Analyses revealed a group-by-time interaction for fatigue ( $p = .034$ ), wherein the BWL condition reported a 17% greater reduction in fatigue than those in the DRL condition (between group  $d = .30$ ). There were also significant improve-

ments over time for both groups on measures of mood, depressive symptoms, and quality of life ( $p's < .01$ ). **CONCLUSIONS:** BWL was associated with greater improvements in fatigue and both groups displayed improvements on secondary psychosocial outcomes. **IMPLICATIONS FOR CANCER SURVIVORS:** These findings, along with previous reports of light therapy for CRF, support the use of this intervention to improve fatigue in cancer survivors.

**The LITE study: Rationale and protocol for a randomized controlled trial of light therapy for cancer-related fatigue in cancer survivors.**

Johnson JA, Garland SN, Carlson LE, Savard J, Simpson JS, Ancoli-Israel S, Campbell TS. *Contemp Clin Trials.* 2016 Jul;49:166-73.

**BACKGROUND:** Fatigue is a common and distressing symptom that can last for months or years in up to one-third of cancer survivors. Despite its prevalence, the nature and mechanisms of cancer-related fatigue are poorly understood and the available treatments may not provide sufficient relief. Fatigue has been identified as a significant contributor to decreased quality of life, making it an important target for intervention. One approach that may be a safe and inexpensive treatment is bright light therapy.

**METHODS:** This study is a 4-week blinded randomized controlled trial. Subjects will be men and women who meet criteria for cancer-related fatigue and have completed cancer treatment. Subjects will be randomly assigned to receive a Litebook treatment device that produces either bright white light (treatment) or dim red light (active control). The devices will be used daily for 30min upon waking for a period of four weeks. The primary outcome, fatigue, will be measured with the Multidimensional Fatigue Symptom Inventory-SF. Secondary outcomes include mood disturbance, sleep quality, quality of life, diurnal cortisol, and inflammatory biomarkers. Fatigue assessments will be completed weekly and secondary outcomes will be assessed at pre- and post-intervention.

**CONCLUSIONS:** The current research will examine the effect of light exposure on cancer-related fatigue and its potential psychological, behavioral, and biological mechanisms. If successful, this research would support the use of

light therapy for the management of persistent fatigue in cancer survivors, expanding existing treatment options. It may also improve upon the current understanding of the mechanisms that underlie cancer-related fatigue.

**Light therapy as a treatment of cancer-related fatigue in (non-)Hodgkin lymphoma survivors (SPARKLE trial): study protocol of a multicenter randomized controlled trial.**

Starreveld DEJ1, Daniels LA, Valdimarsdottir HB, Redd WH, de Geus JL, Ancoli-Israel S, Lutgendorf S, Korse CM, Kieffer JM, van Leeuwen FE, Bleiker EMA. BMC Cancer. 2018 Sep 10;18(1):880.

**BACKGROUND:** Cancer related fatigue (CRF) is one of the most prevalent and distressing long-term complaints reported by (non-) Hodgkin survivors. To date there has been no standard treatment for CRF in this population. A novel and promising approach to treat CRF is exposure to bright white light therapy. Yet, large scale randomized controlled trials testing its efficacy in these patients and research on potential mechanisms is lacking. The objective of the current study is to investigate the efficacy of light therapy as a treatment for CRF and to explore potential mechanisms.

**METHODS/DESIGN:** In a multicenter, randomized controlled trial we are evaluating the efficacy of two intensities of light therapy in reducing CRF complaints and restrictions caused by CRF in survivors of Hodgkin lymphoma or diffuse large B-cell lymphoma. Secondary outcomes include sleep quality, depression, anxiety, quality of life, cognitive complaints, cancer worries, fatigue catastrophizing, self-efficacy to handle fatigue, biological circadian rhythms of melatonin, cortisol and activity, and biomarkers of inflammation. We will recruit 128 survivors, with fatigue complaints, from academic and general hospitals. Survivors are randomized to either an intervention (exposure to bright white light) or a comparison group (exposure to dim white light). The longitudinal design includes four measurement points at baseline (T0), post-intervention at 3.5 weeks (T1), 3 months post-intervention (T2) and 9 months post-intervention (T3). Each measurement point includes self-reported questionnaires and actigraphy (10 days). T0 and T1 measurements also include collection of blood and saliva samples.

**DISCUSSION:** Light therapy has the potential to be an

effective treatment for CRF in cancer survivors. This study will provide insights on its efficacy and potential mechanisms. If proven to be effective, light therapy will provide an easy to deliver, low-cost and low-burden intervention, introducing a new era in the treatment of CRF.

**The Effect of Systematic Light Exposure on Sleep in a Mixed Group of Fatigued Cancer Survivors.**

Wu LM, Amidi A, Valdimarsdottir H, Ancoli-Israel S, Liu L, Winkel G, Byrne EE, Sefair AV, Vega A, Bovbjerg K, Redd WH. J Clin Sleep Med. 2018 Jan 15;14(1):31-39

**STUDY OBJECTIVES:** Sleep disturbances are commonly reported by cancer survivors. Systematic light exposure using bright light has been used to improve sleep in other populations. In this secondary data analysis, the effect of morning administration of bright light on sleep and sleep quality was examined in a mixed group of fatigued cancer survivors.

**METHODS:** Forty-four cancer survivors screened for cancer-related fatigue were randomized to either a bright white light or a comparison dim red light condition. Participants were instructed to use a light box every morning for 30 minutes for 4 weeks. Wrist actigraphy and the Pittsburgh Sleep Quality Index were administered at 4 time points: prior to light treatment (baseline), 2 weeks into the intervention, during the last week of the intervention, and 3 weeks postintervention. Thirty-seven participants completed the end-of-intervention assessment. **RESULTS:** Repeated-measures linear mixed models indicated a statistically significant time x treatment group interaction effect with sleep efficiency improving more in the bright light condition over time compared with the dim light condition ( $F_{3,42} = 5.55$ ;  $P = .003$ ) with a large effect size (partial  $\eta^2 = 0.28$ ). By the end of the intervention and 3 weeks postintervention, mean sleep efficiency in the bright light group was in the normal range. Medium to large effect sizes were also seen in sleep quality, total sleep time, and wake after sleep onset for participants favoring the bright light condition. **CONCLUSIONS:** The results suggest that systematic bright light exposure in the morning may have beneficial effects on sleep in fatigued cancer survivors. Larger scale efficacy trials are warranted.

**Pre-menstrual syndrome**

**A controlled study of light therapy in women with late luteal phase dysphoric disorder.**

Lam RW1, Carter D, Misri S, Kuan AJ, Yatham LN, Zis AP. Psychiatry Res. 1999 Jun 30;86(3):185-92.

Previous studies suggest that light therapy, as used to treat seasonal affective disorder, may be beneficial for pre-menstrual depressive disorders. We conducted a six-menstrual cycle randomized, double-blind, counter-balanced, crossover study of dim vs. bright light therapy in women with late luteal phase dysphoric disorder (LLPDD). Fourteen women who met DSM-III-R criteria for LLPDD completed two menstrual cycles of prospective baseline monitoring of pre-menstrual symptoms, followed by two cycles of each treatment. During the 2-week luteal phase of each treatment cycle, patients were randomized to receive 30 min of evening light therapy using: (1) 10000 lx cool-white fluorescent light (active condition); or (2) 500 lx red fluorescent light (placebo condition), administered by a light box at their homes. After two menstrual cycles of treatment, patients were immediately crossed over to the other condition for another two cycles. Outcome measures were assessed at the mid-follicular and luteal phases of each cycle. Results showed that the active bright white light condition significantly reduced depression and pre-menstrual tension scores during the symptomatic luteal phase, compared to baseline, while the placebo dim red light condition did not. These results suggest that bright light therapy is an effective treatment for LLPDD.

**Light therapy of late luteal phase dysphoric disorder: an extended study.**

Parry BL, Mahan AM, Mostofi N, Klauber MR, Lew GS, Gillin JC. Am J Psychiatry. 1993 Sep;150(9):1417-9.

Nineteen patients with late luteal phase dysphoric disorder (LLPDD) and 11 healthy comparison subjects underwent a 3-month crossover trial of bright (more than 2500 lux) white morning, bright white evening, and placebo dim (less than 10 lux) red evening light, administered daily for 1 week during the premenstrual phase of the menstrual cycle. All light treatments significantly reduced depressive ratings from baseline levels.

**Pregnancy**

**Bright light therapy in pregnant women with major depressive disorder: study protocol for a randomized, double-blind, controlled clinical trial.**

Bais B, Kamperman AM, van der Zwaag MD, Dieleman GC, Harmsen van der Vliet-Torij HW, Bijma HH, Lieveverse R, Hoogendijk WJ, Lambregtse-van den Berg MP. BMC Psychiatry. 2016 Nov 8;16(1):381.

**BACKGROUND:** Depression during pregnancy is a common and high impact disease. Generally, 5-10 % of pregnant women suffer from depression. Children who have been exposed to maternal depression during pregnancy have a higher risk of adverse birth outcomes and more often show cognitive, emotional and behavioural problems. Therefore, early detection and treatment of antepartum depression is necessary. Both psychotherapy and antidepressant medication, first choice treatments in a non-pregnant population, have limitations in treating depression during pregnancy. Therefore, it is urgent and relevant to investigate alternative treatments for antepartum depression. Bright light therapy (BLT) is a promising treatment for pregnant women with depressive disorder, for it combines direct availability, sufficient efficacy, low costs and high safety, taking the safety for the unborn child into account as well.

**METHODS:** In this study, 150 pregnant women (12-18 weeks pregnant) with a DSM-V diagnosis of depressive disorder will be randomly allocated in a 1:1 ratio to one of the two treatment arms: treatment with BLT (9.000 lux) or treatment with dim red light therapy (100 lux). Both groups will be treated for 6 weeks at home on a daily basis for 30 min, within 30 min of habitual wake-up time. Follow-up will take place after 6 weeks of therapy, 3 and 10 weeks after end of therapy, at birth and 2, 6 and 18 months postpartum. Primary outcome will be the average change in depressive symptoms between the two groups, as measured by the Structured Interview Guide for the Hamilton Depression Scale - Seasonal Affective Disorder version and the Edinburg Postnatal Depression Scale. Changes in rating scale scores of these questionnaires over time will be analysed using generalized linear mixed models. Secondary outcomes will be the changes in maternal cortisol and melatonin levels, in maternal sleep quality and gestational age, birth weight, infant behaviour, infant cortisol exposure and infant cortisol stress response.

**DISCUSSION:** If BLT reduces depressive symptoms in pregnant women, it will provide a safe, cheap, non-pharmacological and efficacious alternative treatment for psychotherapy and antidepressant medication in treating antepartum depression, without any expected adverse reactions for the unborn child.

#### **Bright light therapy in pregnant women depression--3 case studies.**

Krzystanek M, Krupka-Matuszczyk I. *Psychiatr Pol.* 2006 Mar-Apr;40(2):261-7.

**AIM:** Bright light therapy (BLT) is a new method of biological treatment in psychiatry. Good tolerance makes it an attractive method used not only in seasonal affective disorder. An episode of depression during pregnancy may be a new indication. The study aimed to describe effects of treatment of depression in 3 pregnant women.

**METHOD:** The women were out-patients in their 6-th, 7-th and 8-th months of pregnancy and diagnosed with depression according to ICD-10 criteria. The treatment was a morning exposure to 1 hour 5 000 LUX bright light from Monday to Friday. The antidepressant effect was assessed after the 2nd and 4th week of BLT. Side effects of BLT were monitored over the whole BLT treatment period.

**RESULTS:** The mean improvement of depressive symptoms after 2 and 4 weeks of BLT was 33% and 55%, respectively. Side effects were not observed in any of the patients.

**CONCLUSIONS:** Morning BLT seems to be an effective and a very well tolerated mode of treatment of pregnant women suffering from non-seasonal depression. The manner and length of BLT maintenance treatment requires further studies.

#### **An open trial of morning light therapy for treatment of antepartum depression.**

Oren DA, Wisner KL, Spinelli M, Epperson CN, Peindl KS, Terman JS, Terman M., *Am J Psychiatry.* 2002 Apr;159(4):666-9.

**OBJECTIVE:** About 5% of pregnant women meet criteria for major depression. No pharmacotherapy is specifically approved for antepartum depression; novel treatment approaches may be welcome. The authors explored the use of morning bright light therapy for

antepartum depression.

**METHOD:** An open trial of bright light therapy in an A-B-A design was conducted for 3-5 weeks in 16 pregnant patients with major depression. The Hamilton Depression Rating Scale, Seasonal Affective Disorders Version, was administered to assess changes in mood. A follow-up questionnaire was used to assess outcome after delivery.

**RESULTS:** After 3 weeks of treatment, mean depression ratings improved by 49%. Benefits were seen through 5 weeks of treatment. There was no evidence of adverse effects of light therapy on pregnancy.

**CONCLUSIONS:** These data provide evidence that morning light therapy has an antidepressant effect during pregnancy. A randomized controlled trial is warranted to test this alternative to medication.

#### **A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression.**

Wirz-Justice A, Bader A, Frisch U, Stieglitz RD, Alder J, Bitzer J, Hösl I, Jazbec S, Benedetti F, Terman M, Wisner KL, Riecher-Rössler A., *J Clin Psychiatry.* 2011 Jul;72(7):986-93.

**OBJECTIVE:** Affective disorder during pregnancy is a common condition requiring careful judgment to treat the depression while minimizing risk to the fetus. Following up on promising pilot trials, we studied the efficacy of light therapy.

**METHOD:** Twenty-seven pregnant women with nonseasonal major depressive disorder according to DSM-IV (outpatients, university polyclinic) were randomly assigned to 7,000 lux fluorescent bright white or 70 lux dim red (placebo) light administered at home in the morning upon awakening for 1 h/d in a 5-week double-blind trial carried out between October 2004 and October 2008. Clinical state was monitored weekly with the 29-item Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS) with Atypical Depression Supplement (SIGH-ADS). Changes of rating scale scores over time were analyzed with the general linear model. Differences from baseline of SIGH-ADS and 17-item HDRS scores at every time point were the dependent variables, time was the within-subjects factor, and treatment was the between-subjects factor. The model also included baseline score of depression and gestational age at intervention start.

**RESULTS:** The superiority of bright light over dim light placebo was shown for both SIGH-ADS ( $R^2 = 0.251$ ;  $F(3,23) = 3.91$ ;  $P < .05$ ) and HDRS ( $R^2 = 0.338$ ;  $F(3,23) = 5.42$ ;  $P < .01$ ) when analyzing the week-by-week change from baseline, and HDRS scores showed a significant interaction of treatment with time ( $F(4,92) = 2.91$ ;  $P < .05$ ). Categorical analysis revealed that the response rate (HDRS  $\geq 50\%$  improvement) at week 5 was significantly greater for bright light (81.3%,  $n = 16$ ) than for placebo light (45.5%,  $n = 11$ ) ( $P < .05$ ). Remission (final score  $\leq 8$ ) was attained by 68.6% versus 36.4%, respectively ( $P < .05$ ). Expectation ratings did not differ significantly between groups.

**CONCLUSIONS:** Bright white light treatment for 5 weeks improved depression during pregnancy significantly more than placebo dim red light. The study provides evidence that light therapy, a simple, cost-effective antidepressant modality with minimal side effects for the mother and no known risk for the unborn child, may be a useful nonpharmacologic approach in this difficult situation.

#### **Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings.**

Epperson CN, Terman M, Terman JS, Hanusa BH, Oren DA, Peindl KS, Wisner KL. *J Clin Psychiatry.* 2004 Mar;65(3):421-5.

**BACKGROUND:** Bright light therapy was shown to be a promising treatment for depression during pregnancy in a recent open-label study. In an extension of this work, we report findings from a double-blind placebo-controlled pilot study.

**METHOD:** Ten pregnant women with DSM-IV major depressive disorder were randomly assigned from April 2000 to January 2002 to a 5-week clinical trial with either a 7000 lux (active) or 500 lux (placebo) light box. At the end of the randomized controlled trial, subjects had the option of continuing in a 5-week extension phase. The Structured Interview Guide for the Hamilton Depression Scale-Seasonal Affective Disorder Version was administered to assess changes in clinical status. Salivary melatonin was used to index circadian rhythm phase for comparison with antidepressant results.

**RESULTS:** Although there was a small mean group advantage of active treatment throughout the randomized controlled trial, it was not statistically significant. How-

ever, in the longer 10-week trial, the presence of active versus placebo light produced a clear treatment effect ( $p = .001$ ) with an effect size (0.43) similar to that seen in antidepressant drug trials. Successful treatment with bright light was associated with phase advances of the melatonin rhythm.

**CONCLUSION:** These findings provide additional evidence for an active effect of bright light therapy for antepartum depression and underscore the need for an expanded randomized clinical trial.

#### **Postpartum depression**

##### **Efficacy of light therapy for perinatal depression: a review.**

*J Physiol Anthropol.* 2012 Jun 6;31:15 Crowley SK, Youngstedt SD.

Perinatal depression is an important public health problem affecting 10% to 20% of childbearing women. Perinatal depression is associated with significant morbidity, and has enormous consequences for the wellbeing of the mother and child. During the perinatal period, treatment of depression, which could affect the mother and child during pregnancy and lactation, poses a complex problem for both mother and clinician. Bright light therapy may be an attractive treatment for perinatal depression because it is low cost, home-based, and has a much lower side effect profile than pharmacotherapy. The antidepressant effects of bright light are well established, and there are several rationales for expecting that bright light might also be efficacious for perinatal depression. This review describes these rationales, summarizes the available evidence on the efficacy of bright light therapy for perinatal depression, and discusses future directions for investigation of bright light therapy as a treatment for perinatal depression.

#### **Sleep problems**

##### **The effects of light therapy on sleep problems: A systematic review and meta-analysis.**

van Maanen, A., Meijer, A. M., van der Heijden, K. B., & Oort, F. J. (2016). *Sleep Medicine Reviews*, 29, 52–62. <https://doi.org/10.1016/j.smrv.2015.08.009>

Although bright light therapy seems a promising treatment for sleep problems, research shows inconclusive results. This meta-analysis is the first to systematically review the effect of light therapy on sleep problems in general and on specific types of sleep problems in particular (circadian rhythm sleep disorders, insomnia, sleep problems related to Alzheimer's disease and dementia). Fifty-three studies with a total of 1154 participants were included. Overall effects and effects on separate circadian and sleep outcomes were examined. We calculated Hedges' g effect sizes and we investigated the effects of twelve moderators (design-related, treatment-related, participant-related). Light therapy was found effective in the treatment of sleep problems in general ( $g = 0.39$ ), and for circadian rhythm sleep disorders ( $g = 0.41$ ), insomnia ( $g = 0.47$ ), and sleep problems related to Alzheimer's disease/dementia ( $g = 0.30$ ) specifically. For circadian rhythm sleep disorders, effects were smaller for randomised controlled trials. For insomnia, we found larger effects for studies using a higher light intensity, and for sleep problems related to Alzheimer's disease/dementia larger effects were found for studies with more female participants. There was indication of publication bias. To conclude, light therapy is effective for sleep problems in general, particularly for circadian outcomes and insomnia symptoms. However, most effect sizes are small to medium.

**Effect of light therapy on the night sleep of children with sleep problems.**

Wessolowski N, Barkmann C, Stuhmann LY, Schulte-Markwort M. *Z Kinder Jugendpsychiatr Psychother.* 2019 Aug 8:1-9

Effect of light therapy on the night sleep of children with sleep problems Abstract. Studies on the effect of light therapy on the nighttime sleep of adolescents revealed earlier sleep onset and longer sleep periods. The present study examines the corresponding effects in children. A group of 28 children ( $M = 10.0$ ;  $SD = 1.65$  years) with difficulties falling asleep and sleeping through the night received a light therapy device for home application. The effect was investigated by an A-B-A-B design with four measurement points. We detected significant, small-to medium-sized effects on the children's sleep-onset problems and ability to sleep through the night as well

as mood. Sleep onset was reduced by approximately 10 minutes. The representativeness of the sample is limited, but the results largely correspond to the findings in adolescents. Because of the weekly switch between application and nonapplication, the true circadian effects might be underestimated. In principle, however, the effects found in adolescents appear to be transferable to children, though further research is necessary.

**Light therapy for insomnia in older adults.** Gammack JK. *Clin Geriatr Med.* 2008 Feb;24(1):139-49, viii.

Exposure to bright light suppresses the production of melatonin and contributes to the regulation of the circadian rhythm. Because of environmental and medical conditions, older adults are less likely than younger adults to receive the prolonged, high intensity, daily bright light needed to promote a satisfactory sleep-wake cycle. The best available evidence for bright light therapy is in the management of seasonal affective disorder, which is relatively infrequent in the elderly population. For older adults with chronic insomnia, dementia, and nonseasonal depression, there is no consensus on the optimum treatment protocol for bright light therapy. However, in addition to sleep improvement, bright light therapy may be used to reduce unwanted behavioral and cognitive symptoms associated with dementia and depression in the elderly.

**A randomized controlled trial of cognitive-behavior therapy plus bright light therapy for adolescent delayed sleep phase disorder.**

Gradisar M, Dohnt H, Gardner G, Paine S, Starkey K, Menne A, Slater A, Wright H, Hudson JL, Weaver E, Trenowden S. *Sleep.* 2011 Dec 1;34(12):1671-80.

OBJECTIVE: To evaluate cognitive-behavior therapy plus bright light therapy (CBT plus BLT) for adolescents diagnosed with delayed sleep phase disorder (DSPD). DESIGN: Randomized controlled trial of CBT plus BLT vs. waitlist (WL) control with comparisons at pre- and post-treatment. There was 6-month follow-up for the CBT plus BLT group only. SETTING: Flinders University Child & Adolescent Sleep Clinic, Adelaide, South Australia. PATIENTS: 49 adolescents (mean age  $14.6 \pm 1.0$  y, 53%

males) diagnosed with DSPD; mean chronicity 4 y 8 months; 16% not attending school. Eighteen percent of adolescents dropped out of the study (CBT plus BLT:  $N = 23$  vs. WL:  $N = 17$ ).

INTERVENTIONS: CBT plus BLT consisted of 6 individual sessions, including morning bright light therapy to advance adolescents' circadian rhythms, and cognitive restructuring and sleep education to target associated insomnia and sleep hygiene.

MEASUREMENTS AND RESULTS: DSPD diagnosis was performed via a clinical interview and 7-day sleep diary. Measurements at each time-point included online sleep diaries and scales measuring sleepiness, fatigue, and depression symptoms. Compared to WL, moderate-to-large improvements ( $d = 0.65-1.24$ ) were found at post-treatment for CBT plus BLT adolescents, including reduced sleep latency, earlier sleep onset and rise times, total sleep time (school nights), wake after sleep onset, sleepiness, and fatigue. At 6-month follow-up ( $N = 15$ ), small-to-large improvements ( $d = 0.24-1.53$ ) continued for CBT plus BLT adolescents, with effects found for all measures. Significantly fewer adolescents receiving CBT plus BLT met DSPD criteria at post-treatment (WL = 82% vs. CBT plus BLT = 13%,  $P < 0.0001$ ), yet 13% still met DSPD criteria at the 6-month follow-up.

CONCLUSIONS: CBT plus BLT for adolescent DSPD is effective for improving multiple sleep and daytime impairments in the immediate and long-term. Studies evaluating the treatment effectiveness of each treatment component are needed.

**Light Therapy With Scheduled Rise Times in Young Adults With Delayed Sleep Phase Disorder: Therapeutic Outcomes and Possible Predictors.**

Danielsson K, Jansson-Fröjmark M, Broman JE, Markström A. *Behav Sleep Med.* 2018 Jul-Aug;16(4):325-336

Clinical trials with light therapy (LT) for delayed sleep phase disorder (DSPD) are sparse and little is known about factors that are favorable for improvements. In this study, LT with scheduled rise times was conducted at home for 14 days by 44 participants with DSPD aged 16-26 years. Primary outcomes were sleep onset and sleep offset. Potential predictors were demographic characteristics, chronotype, dim light melatonin onset, the number of days the LT lamp was used, the daily duration of LT, daytime

sleepiness, anxiety, depression, worry, and rumination. Significant advances were observed in sleep onset and sleep offset from baseline to the end of treatment. The number of days of LT predicted earlier sleep onset and sleep offset.

**The treatment of early-morning awakening insomnia with 2 evenings of bright light.**

Lack L, Wright H, Kemp K, Gibbon S. *Sleep.* 2005 May;28(5):616-23.

STUDY OBJECTIVE: To assess the effectiveness of brief bright-light therapy for the treatment of early-morning awakening insomnia.

PARTICIPANTS: Twenty-four healthy adults with early-morning awakening insomnia were assigned to either the bright-light condition (2,500-lux white light) or the control (dim red light) condition.

MEASUREMENTS AND RESULTS: The circadian phase of rectal temperature and urinary melatonin rhythms were assessed with 26-hour constant routines before and after 2 evenings of light therapy. Sleep and daytime functioning were monitored using sleep diaries, activity monitors, and mood scales before light therapy and for 4 weeks during the follow-up period. While there were no significant circadian phase changes in the dim-light control group, the bright-light group had significant 2-hour phase delays of circadian temperature and melatonin rhythm. Compared to pretreatment measures, over the 4-week follow-up period, the bright-light group had a greater reduction of time awake after sleep onset, showed a trend toward waking later, and had a greater increase of total sleep time. Participants in the bright-light condition also tended to report greater reductions of negative daytime symptoms, including significantly fewer days of feeling depressed at the 4-week follow-up, as compared with the control group.

CONCLUSION: Two evenings of bright-light exposure phase delayed the circadian rhythms of early-morning awakening insomniacs. It also improved diary and actigraphy sleep measures and improved some indexes of daytime functioning for up to 1 month after light exposure. The study suggests that a brief course of evening bright-light therapy can be an effective treatment for early-morning awakening insomniacs who have relatively phase advanced circadian rhythms.

#### Non-pharmacological interventions for sleep and quality of life: a randomized pilot study

Santos, M. A. dos, Conceição, A. P. da, Ferretti-Rebustini, R. E. de L., Ciol, M. A., Heithkemper, M. M., & Cruz, D. de A. L. M. da. (2018). *Revista Latino-Americana de Enfermagem*, 26(0), e3079.

Phototherapy refers to regular exposure to light and can be used to improve sleep. There is evidence that exposure to morning light benefits individuals with delayed sleep problems and/or seasonal sleep disorders<sup>21-22</sup>. One study conducted with institutionalized elderly individuals shows that light exposure during the morning improves total time of sleep during night<sup>23</sup>. Phototherapy is well-tolerated and presents very few adverse effects<sup>22</sup>.

#### Effects of bright light at lunchtime on sleep of patients in a geriatric hospital I.

Kobayashi R1, Fukuda N, Kohsaka M, Sasamoto Y, Sakakibara S, Koyama E, Nakamura F, Koyama T. *Psychiatry Clin Neurosci*. 2001 Jun;55(3):287-9.

The effects of lunchtime bright light exposure in patients of a geriatric hospital were investigated. Ten inpatients (six women and four men; mean age +/- SD: 81.2 +/- 8.8 years) with sleep disturbances were studied for 9 weeks. Nurses performed daily ratings for sleep-wakefulness disturbances. Approximately 8000 lx bright light exposure was performed for 3 weeks in the light therapy room. Before and after exposure, ocular function was evaluated. Clinical ratings of sleep-wakefulness improved in eight patients. The score of difficulty in falling asleep and drowsiness in the morning declined during the light exposure. The score of drowsiness in the afternoon decreased during the post-light exposure. Post-exposure ocular disturbances were not found.

#### Shiftwork disorder and jet lag disorder

##### Evidence based interventions using light to improve circadian adaptation to working hours.

Lowden, A., Ozturk, G., Reynolds, A., & Bjorvatn, B. (2019). Working Time Society consensus statements: *Industrial Health*, 57(2), 213–227.

Interventions and strategies to improve health through the management of circadian (re) adaptation have been explored in the field, and in both human and animal laboratory manipulations of shiftwork. As part of an initiative by the Working Time Society (WTS) and International Committee on Occupational Health (ICOH), this review summarises the literature on the management of circadian (re) adaption using bright light treatment. Recommendations to maximise circadian adaptation are summarised for practitioners based on a variety of shiftwork schedules. In slowly rotating night shift schedules bright light appears most suitable when used in connection with the first three night shifts. These interventions are improved when combined with orange glasses (to block blue-green light exposure) for the commute home. Non-shifting strategies involve a lower dosage of light at night and promoting natural daylight exposure during the day (also recommended for day shifts) in accordance with the phase and amplitude response curves to light in humans.

##### Effect of bright light therapy on delayed sleep/wake cycle and reaction time of athletes participating in the Rio 2016 Olympic Games.

Rosa JPP, Silva A, Rodrigues DF, Simim MA, Narciso FV, Tufik S, Bichara JJ, Pereira SRD, Da Silva SC, de Mello MT. *Chronobiol Int*. 2018 Aug;35(8):1095-1103

This study investigated the effect of using an artificial bright light on the entrainment of the sleep/wake cycle as well as the reaction times of athletes before the Rio 2016 Olympic Games. A total of 22 athletes from the Brazilian Olympic Swimming Team were evaluated, with the aim of preparing them to compete at a time when they would normally be about to go to bed for the night. During the 8-day acclimatization period, their sleep/wake cycles were assessed by actigraphy, with all the athletes being treated with artificial light therapy for between 30 and 45 min (starting at day 3). In addition, other recommendations to improve sleep hygiene were made to the athletes. In order to assess reaction times, the Psychomotor Vigilance Test was performed before (day 1) and after (day 8) the bright light therapy. As a result of the intervention, the athletes slept later on the third ( $p = 0.01$ ), seventh ( $p = 0.01$ ) and eighth ( $p = 0.01$ ) days after starting bright light therapy. Regarding

reaction times, when tested in the morning the athletes showed improved average ( $p = 0.01$ ) and minimum reaction time ( $p = 0.03$ ) when comparing day 8 to day 1. When tested in the evening, they showed improved average ( $p = 0.04$ ), minimum ( $p = 0.03$ ) and maximum reaction time ( $p = 0.02$ ) when comparing day 8 to day 1. Light therapy treatment delayed the sleep/wake cycles and improved reaction times of members of the swimming team. The use of bright light therapy was shown to be effective in modulating the sleep/wake cycles of athletes who had to perform in competitions that took place late at night.

##### Treatment of circadian rhythm sleep disorders with light.

Gooley JJ. *Ann Acad Med Singapore*. 2008 Aug;37(8):669-76.

The human circadian system is normally synchronised with the solar day, insuring that alertness and performance peak during daytime hours and consolidated sleep occurs during the night. In circadian rhythm sleep disorders, the pattern of sleep-wake is misaligned with the patient's circadian system or the external environment, resulting in insomnia, fatigue, and deterioration in performance. Appropriately-timed exposure to bright light can reset the timing of sleep and wake to the desired times, and improve sleep quality and daytime alertness. The efficacy of bright light therapy, however, is dependent on the time-of-day of the circadian cycle that the light is administered. In this article, we examine the physiological basis for bright light therapy, and we discuss the application of light in the treatment of circadian rhythm sleep disorders including advanced and delayed sleep-phase disorder, free-running disorder (nonen-trained type), shiftwork disorder and jet lag disorder. We review the laboratory and field studies which have established bright light therapy as an effective treatment for sleep-wake and circadian misalignment, and we also provide guidelines for the appropriate timing and safe use of bright light therapy.