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Light-therapy applications for DSM-IV-TR disease entities

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ABSTRACT – *Background and Objectives*: Recent decades have seen significant advances in the knowledge of pathogenesis of mood disorders, as well as of other conditions directly or indirectly related to such diseases. Such progress has led to the emergence of new treatments, such as bright light therapy, based on the discovery of the therapeutic effects of exposure to bright light with the so-called *seasonal affective disorder* (SAD), a DSM seasonal pattern specifier linked to major depression and bipolar disorder recurrent describing the course of illness during seasons. The goal of the present work is to review the potential clinical applications of phototherapy, including SAD, obsessive-compulsive disorder, bulimia, premenstrual syndrome, non seasonal major depression, sleep disorders, jet-lag, dementia, normal populations and in primary care.

Methods: A systematic review of the literature about this matter since the early Rosenthal's group observations has been carried out.

Results: A considerable number of studies has been published about this therapeutic approach, pointing that not only depression but also other pathologies that may follow a seasonal pattern could benefit from phototherapy integrated with more standard treatments, as well as other disorders directly or indirectly related to mood, and even another conditions without a seasonal pattern.

Conclusions: The data about the different uses of this treatment neither confirm nor dismiss its efficacy, stating that the therapy should still be regarded as experimental. Future studies should continue investigating to draw reliable conclusions about the usefulness of bright light therapy on mood disorders and other conditions to provide an alternative to standard treatments almost exclusively based on psychoactive drugs.

Seasonal affective disorder (SAD)

The therapeutic effects of exposure to bright light are by no means a phenomenon of recent discovery. As early as the 1920s, thanks primarily to the work of Kraepelin¹, attention was drawn to the presence of certain depressive disorders which, in contrast to other affective disorders, would begin in a more or less regular way in the autumn/winter, with remission in the spring/summer. These initial observations led Rosenthal's² team to define what was known as seasonal affective disorder (SAD) or seasonal depression, after demonstrating the antidepressant effect of exposure to bright light in this type of patient^{3,4}. Thus, the condition would consist in recurrent depressive episodes occurring annually, tending this "winter" depression to be characterised by anergy, hypersomnia, hyperphagia, increased appetite, weight gain and compulsive consumption of carbohydrates^{5,6}.

The first symptoms of SAD usually occur in adulthood, and the severity of the syndrome often increases with geographical latitude^{2,7}; it is more common in women, and in the age range 35 to 508. However, SAD is not considered as a separate diagnostic category: the DSM-III-R9 refers to "specification of seasonal pattern" to apply to Bipolar disorders I and II and to Recurrent Major Depressive Disorder, the principal characteristic of this pattern being the onset and remission of major depressive episodes at certain times of the year.

Given the characteristics of SAD, the reduction in exposure to daylight has been hypothesised as its principal aetiological triggering factor, based on population surveys carried out from the 1990s onwards which explored changes in the prevalence of the disorder in relation to geographical latitude

in countries such as the USA¹⁰, Japan¹¹, Finland¹² and Australia¹³, as well as in samples from polar expeditions¹⁴ and from military personnel and their families¹⁵.

Numerous alternative explanations of the pathogenic mechanisms of SAD have been proposed. The early theories receiving the most empirical support were those related to a psychophysical alteration in light sensitivity due to a retinal or hypothalamic deficit¹⁶. But the discovery that treatment with bright light improved depressive symptoms in such patients has led researchers to focus their attention on the circadian system and the regulatory role of melatonin in it for explaining not only the cause of the disorder but also the therapeutic mechanism of phototherapy^{17,18}.

Light therapy

By the 1990s, the effectiveness of treatment with bright light for "winter depression" had been described in over 30 controlled studies, with more than 300 patients at 14 different research centres¹⁹: recent reviews have confirmed the success of this treatment^{20,21}, due primarily to its rapid and well-tolerated antidepressant effect.

Numerous studies have used the Hamilton Depression Rating Scale-Seasonal Affective Disorders Version (HDRS-SAD)22 in an effort to identify possible predictors of response to treatment. The results of these studies indicate that non-responders to treatment with light for SAD displayed different clinical profiles when they were depressed^{6,23,24}, with higher scores on the Hamilton scale and lower scores on the complementary atypical symptoms scale; the more severe the atypical symptoms of depression (i.e., hypersomnia,

fatigability or carbohydrate craving) the more likely they were to respond to phototherapy, while greater severity of melancholic ("endogenous") symptoms (i.e., suicide, feelings of guilt, motor retardation, insomnia, anxiety, typical diurnal variation morning worse- or despersonalization) predict a poor response. Other studies have identified specific symptoms as potential predictors of response to light therapy (see Table I), and a current research line attempts to relate personality variables and the response to phototherapy²⁵⁻²⁷.

Types of light

The original design for research on phototherapy with SAD used a system of full-spectrum fluorescent bulbs, giving off light containing all the wavelengths of sunlight from behind a plastic diffusing screen inside

a rectangular box³². Since then, there has been speculation as to whether full-spectrum light is actually an essential requirement for the treatment of SAD³³, leading to research on the efficacy of different light spectra³⁴⁻³⁶, including full-spectrum light with or without ultraviolet rays, cool-white light (i.e., fluorescent light with a substantial production of energy in the green and yellow wave bands, and a small quantity of ultraviolet emission), red light, green light and incandescent light (vellow waves with negligible ultraviolet emission). However, and in spite of considerable research efforts, the properties of the light spectrum most suitable for use in phototherapy for SAD have not yet been clearly identified, though it does seem to be clear that ultraviolet wavelengths are not necessary for the antidepressant effect in SAD, so that, given its potentially harmful effects, it should not be used in phototherapy for this disorder³⁷.

Table I Summary of predictor and non-predictor variables of respons to light treatment

Study	Predictors	Non-predictors
Oren et al. ²⁸	Hypersomnia Craving for carbohydrates Sucidal ideation	
Lam et al. ²⁹	Hypersomnia Increased ingestion Youth	
Kräuchi et al. ³⁰	High sweet intake late in the day	Mood swings during the day Sleep-related symptoms
Meesters et al. ³¹		Diurnal variation Hypersomnia

Clinical applications of light therapy

In the early 1990s, Rosenthal's ³⁸ group set out to explore the extent to which seasonality might be a feature of other neuropsychiatric entities, and to study the effectiveness of light therapy for different disorders. From then on, a range of studies have focused on the seasonal pattern and light-therapy applications for diverse conditions:

a) Obsessive-compulsive disorder (OCD)

Initially, seasonal variation in the symptoms of 34 patients with OCD was explored³⁸. Of these patients, who used a retrospective self-report scale measuring mood and behavioural changes, a considerable proportion with obsessive-compulsive disorder (53%) reported a marked seasonal variation in their symptoms. Furthermore, evidence that serotoninergic brain systems are altered in both OCD and SAD lends theoretical support to the use of light therapy for obsessive-compulsive disorder, and in practice a reduction in obsessive-compulsive symptoms through its use has indeed been demonstrated³⁹.

b) Bulimia

There is growing evidence that some patients with bulimia nervosa display a marked seasonal pattern in mood and in symptoms related to ingestion⁴⁰, estimating a prominent worsening of the mood and the symptoms related to ingestion in winter in a high percentage of these patients, percentages varying among the different studies from 10% to as much as 42%. Treatment with light has been shown to be effective and well tolerated in patients with SAD, achieving a rapid improvement of mood state and eating-disorder symptoms, as well as in patients with seasonal patterns of bulimia nervosa^{41,42}, though in the case of these bulimic patients it is recommended that phototherapy be used in conjunction with other treatments of a pharmacological and/or psychological nature.

c) Premenstrual syndrome

Premenstrual syndrome is characterised by cyclical mood changes that correspond to the menstrual cycle⁴³, and it has been shown how women with SAD frequently also present premenstrual syndrome⁴⁴, as well as other common symptoms, such as over-sleeping, carbohydrate craving and lethargy^{2,43}. Very recent studies with large samples of women with premenstrual syndrome, moreover, have reported a reduction in depressive symptoms and premenstrual tension as a result of light therapy^{45,46}.

d) Panic disorder

Panic disorder is characterised by episodes of acute anxiety with intense fear or distress and symptoms of physiological activation. Clinical assessments of patients with this disorder indicate the possibility of a seasonal pattern in a high percentage^{47,48}, with a pronounced peak in their attacks during the winter months. An explanatory model has been proposed by Marriot and cols.⁴⁸ for the development of SAD in patients with panic disorder (Figure 1) which hypothesises a common aetiology for the two disorders related to seasonality, so that light therapy could constitute an appropriate treatment for some of these patients.

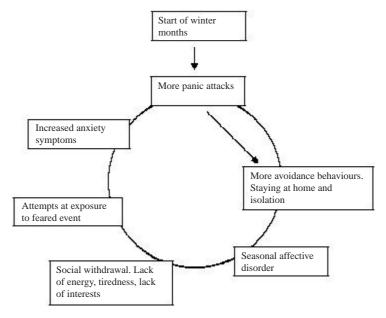


Figure 1. Explanatory model of the development of SAD in patients with Panic disorder⁴⁸.

e) Non-seasonal major depression

Although several investigators have regarded light therapy as a first-line treatment for seasonal affective disorder (SAD), the results of light therapy in nonseasonal major depressive disorder have been non-conclusive⁴⁹. Nevertheless, it seems that major depressed patients can be predicative of beneficial outcome of subsequent light therapy, but since the patients use to be additionally treated with medication, an interaction of the two adjunctive therapies cannot be excluded. Recently accumulated evidence has demonstrated that bright-light therapy in combination with antidepressants is effective in patients with non-seasonal major depression^{50,51}.

f) Sleep disorders

Exposure of the eyes to light of an appropriate intensity and duration and at a certain time of day can have substantial effects on the rhythm, duration and quality of sleep⁵². In patients suffering from SAD accompanied by hypersomnia or delayed sleep phase, normalisation of sleep can be achieved through light therapy, as well as a remission of or improvement in depressive symptoms^{53,54}. Patients without SAD but who experience alterations in their sleep phases, such as initial or terminal insomnia when they try to sleep at normal times, maybe could also be treated with such methods⁵⁵.

Research in this field has revealed differences between patients with SAD and normal controls in the architecture of sleep, the

former displaying higher rapid eye movement (REM) density (though not a shorter latency) throughout the year and a reduction of delta sleep in winter during depressive phases⁵⁶. Light therapy has yielded satisfactory results for stimulating delta sleep and the effectiveness of sleep, at the same time reducing the density of REM sleep.

g) Jet-lag

Jet-lag, or the syndrome resulting from rapid change of time zone, is a complaint affecting travellers and aircrew on long-haul flights from east to west and vice versa. This phenomenon involves a desynchronisation between the endogenous circadian system, which continues to be synchronised with the time markers of the point of departure, and the geo-social system of the point of arrival. Adjustment takes around 4 days, provoking for example, variations in cognitive and athletic performance, body temperature or alcohol metabolism. However, the main symptom being sleep alterations, because of that temporal asynchrony between a sudden change of the time of sleep (owing to the adjustment to the new local day-night cycle) and a progressive readaptation of the circadian system.

Early laboratory studies had not been sufficiently conclusive in support of the hypothesis that bright light could alleviate jet-lag^{57,58}. Nevertheless, the most recent research has attempted to determine the relationship between light therapy and the effects of melatonin, using medication in this context for the treatment of jet-lag^{59,60}. Several laboratory and field experiments with different doses of melatonin, have found that occasional shortterm use of melatonin, taken close to the target bedtime at the destination (i.e., 10 pm to midnight), decreased jet-lag from flights

crossing five or more time zones^{59,61,62}. However, trials with just timed exposure to bright light (without melatonin) do not give enough support to it's efficacy for alleviating jet lag symptoms^{63,64}.

h) Dementia

Early research in this area included that of Fontana Gasio's⁶⁵ team in Switzerland, who studied for a period of three weeks the effects of certain light therapy conditions after sunset on the sleep cycles of elderly patients with dementia, finding a marked improvement in sleep quality and cognitive functions. Other studies have confirmed such results in patients with Alzheimer-type dementia^{66,67}, highlighting the effect on sun-downing, the syndrome of confusion and agitation that occurs at dusk in this type of patient.

In a more recent long-term, doubledblind, placebo-controlled study with elderly residents of group care facilities, Riemersma-van der Lek et al.68 had concluded that light has a modest benefit in improving some cognitive and noncognitive symptoms of dementia, recommending it only in combination with light to counteract the adverse effect of melatonin on mood. This work is along the lines of a recent Cochrane review on light and dementia⁶⁹, who concluded that there is insufficient evidence of efficacy of bright light therapy in managing sleep, behaviour, mood, and cognitive disturbances associated with dementia.

Normal population

Seasonal changes in mood and behaviour are frequent among the general population, mainly affecting women of reproductive age. Given the antidepressant and energising effects of light therapy in patients with SAD, research has tried to determine whether other sectors of the population could benefit from phototherapy, especially those presenting so-called subsyndromal SAD, a milder form of the disorder whose sufferers do not fulfil the criteria for the diagnosis of SAD per se. People presenting this seasonal subsyndrome have been found to respond favourably to treatment with bright light, especially in conditions of long exposure^{70,71}. Likewise, research has shown the utility of exposure to bright light during the winter months for relieving stress and improving vitality in healthy people⁷².

j) Applications in primary care

Between 10 and 15% of primary care patients in industrialised countries express some complaint about certain behavioural alterations and low mood state during the winter months, year on year. In spite of these percentages, just 0.2% of all patients and 3% of depressed patients who consult their GP are diagnosed with SAD. Attempts to assess the efficacy of light therapy in primary care patients have yielded positive results, and this could point the way to a treatment alternative for SAD patients seeking help in the primary care context⁷³.

Conclusions

The significant progress in the area of mood disorders and other pathologies in recent decades, including advances in diagnostic, pathogenetic and epidemiological knowledge, has been accompanied by the emergence of new treatments, among them that of light therapy. The goal of the present

work was to review the potential clinical applications of phototherapy for different defined disease entities on the DSM-IV-TR, as well its possible use with normal populations and in primary care. Although treatment with light therapy is well established since the very first studies on its application to SAD, it must be heeded for recent conclusions of the Swedish Council on Technology Assessment in Health Care's (SBU) report on light therapy for depression⁷⁴; they declare that, although a considerable number of studies has been published about the use of this treatment for SAD, it's efficacy can be neither confirmed nor dismissed. stating that the therapy should still be regarded as experimental, because of the lack of significant difference between placebo and light therapy with regard to the number of patients who improve bay at least 50%. In keeping with this point of view, the present overview of the results obtained from different studies indicates that the effectiveness of this treatment for the revised conditions still remains unconfirmed, because of the lack of satisfactory controlled studies.

Nevertheless, it has been pointed that not only depression but also other pathologies may follow a seasonal pattern, and therefore could benefit from phototherapy, primarily as an approach integrated with more standard treatments. In fact, many potential areas of application of this therapy have to do with disorders directly or indirectly related to mood. Apart from anything else, it's common knowledge that another conditions without a seasonal pattern, could still be helped with this treatment.

Likewise, seasonal changes in mood and behaviour are common in the general population, and light therapy also might constitute an effective treatment, in spite of some people have reported mild (no substantial) side-effects⁷⁵⁻⁷⁷ usually temporary and generally remedied by reducing exposure time, including: headaches, ocular tension, eye irritation or disturbing sensations of visual glare, mild hypomania and irritability, sleep disturbances in patients that use light at dusk, overactive state, jumpiness, jitteriness or feeling "wired", and also slight nausea.

On the other hand, and despite the potential utility of this therapy, we should not overlook the possible interaction of mood with activities that the person may do during the seasons with more light and where there is more exposure to sunlight, with the resulting synergic effect between light and more reinforcing lifestyles. Furthermore, no satisfactory controlled studies have been published on the subject, reflecting the great need to conduct these studies with enough participants to draw reliable conclusions about the efficacy of bright light therapy on mood disorders and other conditions.

In this line of new treatments it is also relevant to mention the research being carried out on Behavioural Activation Therapy for depression, which has concluded that this therapy produces results equivalent to those of psychoactive drugs in patients with severe depression⁷⁸. The findings of this and other recent studies have reopened the debate on the effectiveness and wisdom of the use of psychoactive drugs in the treatment of some psychological disorders, such as depression^{79,80}, indirectly calling into question the models of mental illness and intervention customarily used by health services in dealing with this type of problem.

Finally, the results pointed out with the new therapies, notably light therapy, lead inevitably to a reappraisal of current approaches to the treatment of disorders involving mood alterations. Given that today the equipment necessary for applying phototherapy can be bought or rented from many medical suppliers, such findings should encourage clinicians to make greater efforts to recognise the types of symptoms and of patients who might benefit from this relatively new form of treatment, and to ensure that it is offered and applied in an appropriate way.

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