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Exploring the role of phototherapy in the management of Seasonal Affective Disorder

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ABSTRACT:
Introduction and Purpose: The aim of this paper is to present biological mechanisms underlying the development of a seasonal affective disorder (SAD), as well as discussing the effectiveness of light therapy as a treatment for this disorder. The paper raises the issues relating to the use of low level light technology, such as red and blue light, and their potential influence on the improvement of mood and circadian rhythm regulation in the treatment of seasonal depression.
Brief Description of the State of Knowledge: Light therapy is an effective treatment for seasonal affective disorder (SAD), based on exposure to 10000 lux. It influences the regulation of the circadian rhythm, the production of serotonin and melatonin, of which serotonin is a precursor. The right light intensity and exposure time are crucial to the therapy effectiveness. Despite promising results, further research of the light therapy mechanisms is still needed.
Summary: Seasonal affective disorder (SAD) mainly affects people living in areas where days are short in winter and there is insufficient time of exposure to sunlight. The disease is more common in younger, middle-aged people and in patients diagnosed with other mood disorders. Light therapy as an alternative to pharmacotherapy can significantly improve the health of patients suffering from SAD by reducing the depression symptoms.

Materials and Methods: The literature review was conducted using the Google Scholar database.

Key words: seasonal affective disorder (SAD); light therapy; phototherapy; circadian rhythm; serotonin production; melatonin regulation; blue light; red light; SAD therapy; light exposure.

INTRODUCTION

Seasonal affective disorder (SAD) is a form of depression, which occurs seasonally, especially in winter, with full remission in spring or summer. Depression symptoms occur cyclically and the disorder is linked to disturbances in circadian rhythm, light exposure and serotonin regulation. [1]

SAD is a mood disorder characterised by recurrent depressive episodes at certain times of the year, most often in winter, which distinguished it from a classic depression, which does not show such a connection with seasons and is characterised by a more consistent course of symptoms throughout the year. [2]

The incidence of the SAD ranges from 0.5% to 2.4% in the general population, but in people with depression, even 10–20% of cases may be seasonal. High-risk groups are women, young people (18–30 years old) and inhabitants of higher latitudes, where access to sunlight is significantly restricted in winter. [3]

Improper eating habits, limited physical activity, chronic stress and social isolation in winter also contribute to the development of the disorder. Failure to recognise SAD symptoms results in many people ignoring these symptoms and not looking for medical help at the right time. Effective treatment methods involve light therapy, lifestyle changes, psychological support and pharmacotherapy. [4]

Light therapy has become one of the methods of SAD treatment. The therapy involves exposing the patient to artificial light of high intensity, which aims to imitate natural sunlight. This allows to regulate the circadian rhythm, serotonin production, and thus reduce the symptoms of the disease. [4]

Biological mechanisms behind SAD: the role of light and serotonin regulation

Natural sunlight plays a key role in the circadian production of hormones and neurotransmitters, such as serotonin, which is a melatonin prohormone – the major circadian rhythm regulator. [5] Melatonin biosynthesis begins with tryptamine and involves the formation of serotonin, which is ultimately converted to melatonin. Serotonin is a neurotransmitter affecting mood and its deficiency is often associated with depressive disorders. Melatonin synthesis dysfunction has a negative impact on the serotonin level, which potentially contributes to the exacerbation of the seasonal depression (SAD). [6]

Light, especially morning light, alters the pineal gland's activity, which affects the production of melatonin, the concentration of which increases in the dark and decreases when light is present. Regular exposure to natural sunlight during the day helps to synchronise the circadian rhythm and decreases the production of melatonin during the day, preventing drowsiness and enabling the body to function better. [7]

During autumn and winter, the access to natural sunlight is significantly reduced, which is one of the reasons for the decrease in the serotonin production; reduced exposure to light exacerbates seasonal depression symptoms, such the decrease in energy levels, concentration difficulties or losing interests. [8]
PET tests have shown a seasonal shift in dopamine activity (DA), with lower levels of tyrosine hydroxylase (TH) (a dopamine transporter) in winter compared to summer, suggesting reduced DA production and reuptake. Tests conducted with PET in patients suffering from seasonal depression (SAD) have shown lower DA transporter availability during winter and higher DA levels in the presynaptic membrane, as well as reduced amounts of D2/D3 receptors. This may indicate increased competition of DA molecules with each other for a receptor-binding spot or a reduced number of receptors. Additionally, a higher number of DA metabolites has been reported in autumn. This phenomenon is observed both in healthy patients and in patients suffering from schizophrenia in winter. [9]
One of the hypotheses explaining the development of a seasonal depression (SAD) is the reduced exposure to light during specific seasons, which leads to a shift in the phases of the biological clock rhythm and a change in serotonin metabolism. [10]

Phototherapy as a treatment of SAD

Light modulates the activity of efferent serotonergic neurons; decreases serotonin reuptake by the serotonin transporter, 5-HTT, and increases reuptake by 5-HT receptors in mood-regulating areas – part of the cingulate cortex and prefrontal cortex. [11]
The lux is a unit of measurement of light intensity that takes into account the area over which the light flux spreads, and depends on the distance from the light source. Classical indoor lighting in a room has an intensity of less than 100 lux, and reaches around 5,000 lux outdoors on a cloudy day, while on a sunny day it can reach up to 50,000 lux. [12]
The standard light therapy scheme for the treatment of depressive disorders (including SAD) recommends the use of 10,000 lux white light every morning for 30 minutes over a period of about six weeks. [13]
Side effects may include nausea, diarrhoea, headaches and eye irritation, however, they are usually mild and rare. Such a good safety profile may be particularly important for in women in the perinatal period or in the elderly. [11]
Main contraindications are eye diseases (a cataract, macular degeneration, glaucoma, retinitis pigmentosa) and retina diseases (retinopathy, diabetes, herpes, etc.); patients from the group of risk (or in case of doubts) should undergo an ophthalmological examination before the treatment. [14]
Exposure to 1,500 lux light for two hours a day would increase the blood flow in the frontal cortex and parietal lobe, which has been confirmed in patients responding to the therapy. In research conducted in the tropics, morning light treatment with 10,000 lux for 30 minutes proved effective in reducing depressive symptoms in all participants. [15] Exposure to 2,500 lux light under similar conditions not only failed to improve, but worsened symptoms in some patients. [16] The results emphasise the key importance of appropriate intensity and exposure time for the effectiveness of phototherapy.

The impact of red and blue light on the human body

Low-level light therapy, which uses red and blue light, has a potential in depression treatment. [17]

Red light (620–810 nm)

Deeper penetration: Red light has the ability to penetrate deeper into tissues, allowing it to affect mitochondria in nerve cells and other body structures. [18] Improving the mitochondria functions may contribute to an increased ATP production, which gives more energy to mood-

regulating cells. Better functioning of nerve cells may support the improvement of neurogenic processes and reduction of depressive symptoms.[17]

Anti-inflammatory effects: Red light also has anti-inflammatory effects, which is important in terms of depression, as more and more studies are pointing to the role of inflammation in the development of this disorder. Reduction of inflammations in brain and other body parts can support the mood improvement and alleviate seasonal depression symptoms. [19]

Blue light (450–495 nm)

Circadian rhythm regulation: Blue light affects the functioning of the suprachiasmatic nucleus (SCN) in the hypothalamus, which is the major biological clock of the body. It stimulates melanopsin receptors in the retina, which inhibits the production of melatonin – sleep hormone – and synchronises the circadian rhythm. As a result, it improves sleep quality, regulates energy levels and alleviates depressive symptoms associated with seasonal affective disorder (SAD). [20]

Improving cognitive function and mood: Melanopsin retinal ganglion cells (ipRGCs) transmit signals to structures in the brain stem, such as the locus coeruleus (LC) and the reticular formation. Activation of LC, the main noradrenaline source in the brain, increases vigilance and concentration. At the same time, stimulation of the reticular formation supports cognitive processes such as memory and sensory processing. Exposure to blue light boosts these processes, which can positively influence cognitive functions and mood. [21]

Phototherapy and the role in BDNF production

The brain-derived neurotrophic factor protein takes part in important neuronal processes in the brain, including supporting the process of neurogenesis (stimulates growth and differentiation of new neurons), and has a protective effect on neurons in the hippocampus stimulated by cortisol in stressful situations. [22]

In depression, excessive oxidative stress is observed, which leads to damaging neurons, lowering the BDNF level and impairing neuroplasticity. [23]

Light therapy has been shown to increase BDNF expression in hippocampal neurons through effects on oxidative stress. [24] Light therapy may decrease oxidative stress by increasing the production of antioxidants in cells, which helps neutralise the excess of reactive oxygen species (ROS). Low level light therapy (LLLT) stimulates mitochondria, which leads to increased production of energy – ATP in cells and further reduction of oxidative stress. This, in turn, activates signalling pathways such as MAPK/ERK and CREB, which are crucial for BDNF expression. [25]

Light therapy also affects the intracellular calcium metabolism. Increased Ca^{2+} levels support the regeneration of cells, reduce inflammations and improve interneuronal connections. It increases the Cytochrome c oxidase (CCO), which leads to the increase in calcium (Ca^{2+}) level in cells. [26] Phototherapy stimulates purinergic receptors (e.g. P2X), which allows calcium ions to flow into the cell. It also activates TRP channels that react to light and makes it possible to release calcium from the endoplasmic reticulum thanks to secondary transmitters, such as inositol trisphosphate (IP3). [27]

Phototherapy vs. SSRI pharmacotherapy: a comparative approach

Phototherapy and antidepressants from the SSRI group, such as fluoxetine, demonstrate a comparable effectiveness in the treatment of a seasonal affective disorder.

In comparative research, both methods yielded similar results in terms of clinical response rate and remission, and were also well tolerated by patients. [28] However, light therapy had a slightly quicker start of action, showing an improvement after a week of treatment, while the effects of fluoxetine were more gradual and occurred after 3-4 weeks.

An advantage of phototherapy is that there are fewer side effects compared to fluoxetine, although it requires more patient's discipline due to the need to be exposed to light every

morning. [29] On the other hand, fluoxetine offers a simpler treatment pattern in the form of one, fixed dose, but it can involve more frequent side effects, such as sleep disorders or agitation. [30]
Both methods are effective and the choice of treatment depends on the individual preferences of patients, their expectations and tolerance of possible side effects. [30]

Classic device and new technologies in light therapy

Classic lamps for light therapy, also called "sunboxes", are stationary devices emitting bright full-spectrum light of 10,000 lux, imitating natural sunlight. Due to their structure, they neither mobile nor easy to travel with, which makes them less convenient in everyday use. Nonetheless, they offer the greatest effectiveness in the SAD treatment, as the light of 10,000 lux they emit is considered to be optimal for the treatment of such disorders. In comparison to other devices emitting light of lower intensity, these lamps offer better therapeutic results.[31]
Litebook is one of the most popular devices used in light therapy that is currently available on the market. It has 60 LEDs emitting a wide spectrum of light of the total brightness at 1,350 lux – significantly less than standard 10,000 lux recommended in the seasonal affective disorder (SAD) treatment. Nevertheless, this intensity may be sufficient for some users. Litebook is a mobile device, which makes it easy to use, but its effectiveness may be limited due to the lower brightness and intensity compared to traditional therapy lamps. [32]
Re-Timer is an innovative therapeutic eyewear with built-in LEDs that emit green light directly into the patient's eyes. Their convenience and practicality make them suitable for everyday use and various social situations. However, similarly to Litebook, the effectiveness of Re-Timer in the SAD treatment still needs further research. The lower light intensity compared to traditional therapeutic devices has a potential impact on the effectiveness of the solution. [33]
Bright Light Headset is a gadget using atypical way of providing light through the in-ear headphones emitting light to the brain. Although the concept is original and innovative, there are limitations that are the subject of scientific research on the effectiveness of this technology. The device could be useful in everyday life, but further research is necessary to confirm its effectiveness in the long-term PTSD treatment. [34]
Wireless, battery-free, flexible, miniaturized dosimeters monitor exposure to solar radiation. This small device is used to monitor the user's exposure to sunlight during the day. It records the daily amount of natural light that the user's body is exposed to and may prove useful in dealing with the seasonal affective disorder (SAD). Even though the device does not emit artificial light, it works as a sensor that alarms and raises awareness of the user on the daily exposure to the sun. [35]
Light Visors have been an alternative since the 90s. They were designed to treat SAD symptoms by emitting light ranging from 96 to 6,000 lux. Although they are comfortable and easy to use, their effectiveness may be limited due to the changing intensity and angles of the light emitted. What's more, their appearance can also affect social acceptance and make some users abandon the regular use of the device, as they are worried about the negative response from the society. [36]
Even though modern therapeutic devices offer convenience and mobility on a higher level than ever before, a standard tool in the SAD treatment is still lamps emitting light of intense brightness of 10,000 lux. Still, innovations such as goggles or light-emitting bands are fascinating alternatives for those who prefer subtle and more flexible treatment solutions. [36]

Summary: The analysed materials highlight the importance if light therapy (phototherapy) as an effective method for treating a seasonal affective disorder (SAD). The paper discussed the

biological mechanisms relating to the regulation of serotonin and circadian rhythm, as well as the impact of exposure to light of proper intensity on the brain functions and the level of neurotransmitters. It also described the benefits of using various wavelengths of light, including red light and blue light, and their positive effect on neurogenic processes and regulation of inflammations. Light therapy was compared with the SSRI pharmacotherapy, which emphasised its high effectiveness and milder side effects.

Conclusions: Light therapy is a well-tolerated and effective method of SAD treatment, especially in patients who prefer avoiding pharmacotherapy. Further research on the optimisation of light therapy parameters, such as exposure intensity and time, is necessary to maximise the effects of the treatment. It is also advisable to continue research on mechanisms of light operation on the cellular level, including on the impact on the BDNF production and calcium metabolism. The effectiveness of phototherapy compared to SSRI shows the possibility of using it as the first-line treatment, while keeping the therapy customized depending on patients' preferences and tolerances.

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