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Risk Factors and Treatment Approaches to Seasonal Affective Disorder: A Review

V. Jurgaitytė*
J. Dijokas**
P. Rimkevičiūtė***
N. Khawaja*

**University College London, Division of Biosciences, London, United Kingdom*

***Vilnius lyceum, Vilnius, Lithuania*

****Vilnius University, Faculty of Medicine, Vilnius, Lithuania*

Summary. Seasonal Affective Disorder (SAD) is a type of depression which emerges seasonally, in winter or summer. This condition affects 1–2% of the general population; however, in regions more than 30 degrees of the equator, a higher proportion (10–20%) of people suffer from SAD. There is a milder form of SAD, subsyndromal SAD (S-SAD), which is known as "winter blues". Besides environmental risk factors, such as day length and sunlight exposure, genetics and neurochemical changes in the brain also play a role in SAD patients showing that this disorder is heterogeneous. Imbalances in the circadian rhythm and dysregulation of neurotransmitters (serotonin, dopamine, and norepinephrine) have been identified as risk factors for symptomatic SAD. SAD symptoms can be diminished by bright light therapy, regulating patients' circadian rhythms, and cognitive-behavioural therapy, which more indirectly focuses on alleviating depressive symptoms by allowing patients to actively manage how they perceive stress and anxiety. The paper compares effectiveness and safety of treatment methods against SAD.

Keywords: seasonal affective disorder, seasonal depression, subsyndromal seasonal affective disorder, bright light therapy, cognitive behavioural therapy.

INTRODUCTION

Seasonal affective disorder (SAD) is a seasonal pattern of recurrent episodes of major depression, mania or hypomania [1]. In the last three editions of the Diagnostic and Statistical Manual (DSM), SAD was defined as a seasonal pattern specifier or subform of major depressive disorder (also known as unipolar major depression), bipolar I or II disorders (BPD I or BPD II), but not as an independent entity [2, 3]. Therefore, it may become less clear and less recognizable to clinicians and influence their choice of treatment [4]. Interestingly, up to half of SAD patients are diagnosed with bipolar illness according to DSM [2].

Although two types of seasonality are reported, winter (or fall/winter) and summer (or spring/summer) [1], we focus on winter-type of SAD since more studies on this type of SAD were conducted [4]. Winter SAD is described as depressive episodes with a regular onset during fall or winter, and remission in spring or summer on an almost yearly basis. Symptoms of SAD are fatigability, depressed mood, difficulties at work, social withdrawal, carbohydrate craving, anxiety, reduction of libido, hypersomnia, hyperphagia (increased appetite), overeating, weight gain, and early insomnia (Table). Most of the symptoms are considered to be reversed vegetative or atypical depressive [2–5].

Table. **The most common symptoms of SAD**

Symptom	Prevalence
Fatigability [3, 5]	95–100%
Depressed mood [3, 5]	90–95%
Difficulties at work [3, 5]	70–95%
Social withdrawal [5]	85–95%
Carbohydrate craving [3, 5]	70–90%
Anxiety [5]	70–80%
Reduction of libido [3, 5]	60–75%
Hypersomnia [3, 5]	50–80%
Hyperphagia [3, 5]	50–60%
Overeating, weight gain [3, 5]	40–60%
Early insomnia [5]	35–40%

Address:
Justas Dijokas
Vilniaus licėjus
Širvintų g. 82, LT-08216 Vilnius
El. paštas justas.dijokas@gmail.com

A milder form of SAD is a subsyndromal type of SAD (S-SAD), also known as "winter blues" [6]. Its symptoms do not substantially impair functioning and are less severe. Summer depression, symptoms of which include insomnia, decreased sleep, decreased appetite, and weight loss, begins in spring or summer and remits during the following fall or winter [1].

The purpose of this review is to raise awareness of SAD so that its characteristics become known and, as a result, SAD is correctly identified and treated more efficiently. Part of the review is aimed at environmental and biological risk factors and how they contribute to the pathophysiology of SAD, since a reduced exposure to them is expected to lower an overall number of patients who experience symptoms of SAD. Specifically, the review focuses on genetic factors and neurochemical imbalances which make an individual more prone to SAD. There are three major methods used to treat SAD: pharmacotherapy, bright light therapy (BLT), and cognitive behavioural therapy (CBT). This paper provides an overview of two major methods used in treating SAD: BLT and CBT.

RISK FACTORS OF SAD

Environmental risk factors

Geography

People who live in territories which are either far North or far South of the equator are more likely to suffer from SAD [7, 8]. As the length of the photoperiod is fully dependent on latitude and date, vulnerability is likely to increase as a result of disturbance of circadian rhythms and deprivation of natural light. This eventually results in lower vitamin D synthesis, poorer immunomodulation, and insufficient sleep [9–11]. A few studies have shown that patients who were diagnosed with SAD had shifted circadian rhythms in winter, with the circadian phase occurring either earlier (phase advanced) or later (phase delayed) when compared to healthy individuals [12, 13]. Stable entrainment to environmental circadian rhythms in healthy individuals corresponds to an optimal phase angle or, in some cases, Phase-Angle Difference (PAD), for example, the time interval between the Dim Light Melatonin Onset (DLMO) and midsleep. In entrained people, DLMO is the time interval from evening rise in melatonin levels above a certain threshold to fall below that threshold (under dim light conditions). As normal PAD between DLMO and midsleep is approximately 6 hours, the severity of SAD condition is associated with a temporal deviation of either decreased or increased number of hours emerging between the circadian and sleep-wake oscillators [13, 14]. Patients experiencing either phase advance (with more than 6 hours PAD) or delay (with less than 6 hours PAD) have a higher SIGH-SAD (Structured Interview Guide for the Hamilton Depression Rating Scale – Seasonal Affective Disorder version) score [13]. SAD occurring in fall or winter is more prevalent in temperate, moderate, and polar regions, while summer-type of SAD predominates in tropical regions [15, 16].

Aeroallergens

Spring/summer-type of SAD is associated with mood sensitivity resulting from aeroallergen exposure [17]. Aeroallergens, such as pollen, evoke an immune response by activating CD4+ T helper type 2 (Th2) cells and inducing secretion of cytokines, including interleukin IL-4 [18]. Therefore, IL-4 from Th2 cells promotes class switching of immunoglobulin G to immunoglobulin E, which later binds to Fc receptors on mast cells [19]. When exposure to an aeroallergen occurs, mast cells degranulate and initiate an early phase of the immune response [20]. It is followed by a late phase of the immune response, during which pro-inflammatory cytokines that can reach the central nervous system are released. As a result, they affect neurotransmitter metabolism, neuroendocrine functions, sleep cycle, memory, and emotional state of an individual [21–23]. Seasonal allergic rhinitis caused by allergens in the air is associated with depression [24]. Air pollutants tend to contribute to allergic exacerbations mediated through neuroinflammation, and increased exposure may contribute to mood sensitivity [25]. Vulnerability to summer-type of SAD might increase due to global warming, which is associated with an elevated pollen production and greater variability of the allergens in the air [26].

Biological risk factors

Genetics

Studies have shown that seasonal changes in mood often run through families. One twin study shows that different genetic factors influence male and female seasonality; while another self-report study found seasonality to be a heritable trait that varied in severity across individuals [27, 28]. Rosenthal et al, who first described SAD, states that it is not known if SAD is inherited as a distinct entity or if it "affects individuals who are genetically susceptible to both seasonality and depression", which is also hereditary [29]. Additionally, several genome-wide association studies of SAD have been conducted using the candidate gene approach to investigate the role of genetic variation within biologically relevant genes in SAD susceptibility [30].

A new study by Provencio et al indicates that SAD may be related to a melanopsin gene (*OPN4*) mutation in the eye, which makes SAD patients to be less sensitive to light and requires increased exposure to maintain normal functioning during wintertime. *OPN4* is a photopigment gene encoding a light-sensitive protein melanopsin contained within the retina in intrinsically photosensitive retinal ganglion cells (ipRGCs). As ipRGCs are linked to non-visual/non-image forming responses, "retinal illumination" acts through them as a potent stimulus for regulating circadian, hormonal, and behavioural systems [30, 31]. The melanopsin mutation, therefore, causes lessened photosensitivity and may underlie circadian rhythm disruption. Retinal illumination also acts as a neurophysiological

stimulant, so the melanopsin mutation may result in aberrant regulation of responses to light, thus increasing the possibility of developing SAD [31, 32]. Cryptochromes (photoactive protein pigments in the mammalian retina) and other photopigments involved in processing the light signals could be another promising research area [33].

Mutations in the circadian clock genes are also theorized to heighten patients' susceptibility to SAD since misalignment between the endogenous circadian system and the sleep-wake cycle might contribute to a variety of psychiatric disorders. For instance, the state-dependent alterations of REM sleep latency and advanced circadian rhythm seen in BPD, for which SAD is a specifier, suggest that circadian phase shift contributes to the pathophysiology of winter SAD. Circadian rhythmicity is an outcome of intracellular molecular mechanisms which involve the so-called clock genes that regulate their own expression via end-product inhibition, and the result of this transcriptional-translational feedback loop is an oscillation of the levels of mRNAs and proteins. These oscillations mainly occur in the suprachiasmatic nucleus of the hypothalamus and are regulated by the interaction of clock genes, such as *CLOCK*, *PER*, *TIM* and *CRY*, with other factors that control the phosphorylation, stability, and localization of clock proteins, like Ror m, Rev-Erb , CKI and CKI . Certain allelic combinations among these proteins, such as NPAS2, PER3, and BMAL1, are theorized to heighten the risk of SAD, while genetic studies have also found SAD associations with *CLOCK*, *PER1*, *PER3* and *TIMELESS* [34, 35].

Catecholamine neurotransmitters are thought to play a role in mood swings, and some studies have revealed a significant role for the dopamine system in the circadian regulation of mood and reward. Using the site specific *Clock* 19 knock-out mouse (with a deletion in exon 19 of the *clock* gene) that expressed a protein with dominant-negative function, researchers were able to strongly implicate dopaminergic activity in the ventral tegmental area in the circadian regulation of mood and reward. Other studies suggest that norepinephrine (NE) may also be involved in the cortical clock regulation of mood [34].

Overall, the linkage of certain clock gene polymorphisms and chronotypes indicates a close relation between single nucleotide polymorphisms and SAD. Further studies into this area of research may prove to be fruitful in proposing genetic therapies as well as new pharmaceuticals [35].

Glycogen synthase kinase 3 (GSK3), a central regulator of the circadian clock, may also play an important role in SAD, as GSK3 activity is associated with BPD. The allelic frequency of GSK3/ -50 T/C SNP appears to impact the onset of BPD: bipolar patients with the T/T allele of GSK3 show an earlier age of onset and improve less from lithium therapy than those with the T/C or C/C alleles. GSK3 inhibition exhibits therapeutic effects, possibly making it an effective target for mood-stabilizing agents, including valproate. Furthermore, it may be a target of antidepressant therapies which act via serotonergic and dopaminergic systems or increase phosphorylation of the GSK3 enzyme [35].

Dysfunctions of serotonergic system also have an underlying genetic basis. Variants of genes related to serotonergic transmission, including the serotonin transporter gene *SLC6A46* and the 5-HT_{2A} receptor gene *HTR_{2A}*, have been associated with SAD [30]. The serotonin-transporter-linked polymorphic region (5-HTTLPR) short allele carrier (S-allele-carrier) is considered a risk factor for SAD: possessing the S-carrier status lowers the chances of reducing cerebral serotonin transporter binding in the winter [29]. Additionally, it seems that the serotonin transporter 5-HTT gene determines the sensitivity of the serotonergic system to light [36].

Neurochemical imbalances

Reduction of monoamine neurotransmitters, such as 5-HT, NE, and DA, seems to be a risk factor for depressive symptoms of SAD. Since the most important monoamine neurotransmitters are closely related to symptoms of mood disorders, we searched for evidence to point serotonergic, dopaminergic, and noradrenergic involvement in SAD [33].

Serotonin (5-HT)

5-HT is a monoamine neurotransmitter which stabilizes mood, reduces stress and, therefore, improves sleep. Its inadequate concentration in the brain is believed to be related to SAD [33]. For example, 5-HT levels are found to be the lowest in December and January when winter depression symptoms usually occur [37].

One relevant study has found evidence that the development of depressive symptoms in winter is due to a failure to appropriately down-regulate serotonin transporter during exposure to the environmental stress of winter, especially in individuals with high-risk profiles for affective disorders [38]. The best indicator of 5-HT release dynamics is biomarker [11C]DASB binding preferentially to the 5-HTT on the cell surface, and this is best interpreted as reflecting a key phenotype of SAD [39]. The biomarker [11C]DASB serotonin transporter binding potential (5-HTT BPND) is significantly elevated in winter as compared to summer in SAD, particularly in severe SAD [38]. Then 5-HT is transported from the synaptic cleft more quickly, and, as a result, 5-HT concentration in the synaptic cleft drops.

Besides 5-HTT seasonal regulation of cerebral 5-HT concentration, monoamine oxidase A (MAO-A) levels also change seasonally in healthy but not in SAD patients. The MAO is a mitochondrial enzyme that is responsible for the degradation of 5-HT in the brain and is useful for maintaining normal 5-HT levels [40]. According to a recent study, MAO-A levels in healthy control group decreased from fall/winter to spring/summer, whereas showed no change in SAD patients. As a result of high MAO-A and 5-HT numbers, SAD patients have abnormally low 5-HT concentration when experiencing SAD symptoms [41].

Moreover, 5-HT may explain the mechanism of summer depression. According to one study, plasma levels of free tryptophan are not only lower in the winter periods, but also in the early summer [42], which may imply changes in 5-HT plasma concentrations during summer depression similar to those occurring during winter depression. However, higher cerebral 5-HT transporter binding in winter may suggest that summer depression has a different mechanism from winter depression [38]. This can be related to results from one study where summer depression occurred more often in the recurrent depression group, whereas winter depression was more common in the bipolar patients' group [43].

Besides low mood, reduced concentration of 5-HT explains diet-related symptoms of SAD. Since high levels of 5-HT suppress appetite [44], low concentration of 5-HT could explain the tendency of SAD patients to crave carbohydrates and gain weight during winter depressive episodes [33]. Dietary carbohydrates are thought to increase 5-HT synthesis and transmission via increased tryptophan (a precursor of 5-HT) uptake into the brain [45]. Thus, SAD patients report elevated activity following high-carbohydrate meals, while healthy controls feel more sedated [46].

Catecholamines

The catecholamines DA and NE are also believed to be involved in the winter SAD mechanism, though their effects are not as pronounced. Two studies showed a relapse of SAD symptoms in patients following BLT [47], as well as during summer remission, corresponding to an artificial depletion of catecholamines in the patients [48].

There seem to be two major roles of DA in SAD, the first being linked to its prominent role in the reward pathway in the brain. The striatal density of dopamine transporter has reduced binding sites in depressed SAD patients [49]. This may synergize with the increased appetite caused by lower 5-HT levels, as the corresponding DA levels may trigger a reward mechanism associated with feeding. Additionally, the D4 dopamine receptor (also found in the regions associated with the reward pathway) is thought to be associated with the optical components of SAD, as DA modulates light/dark adaption of the retina in tandem with melatonin [50]. One study found that D4 knockout mice experienced impaired functioning of the retinal photoreceptors [51], which was reminiscent of the impaired dark adaption ability in SAD patients [52]. It can therefore be concluded that DA plays a significant role in SAD.

Reduced NE levels were observed in symptomatic SAD patients, but increased after BLT [53]. The abnormalities in the NE system found in SAD patients are observed in other psychiatric disorders, such as bipolar disorder, attention deficit hyperactivity disorder, and non-seasonal forms of depression [54]. The presence of NE metabolites in the cerebrospinal fluid is an appropriate measure of the effectiveness of SAD therapies including BLT [55].

Other hormonal imbalances

Women are more prone to affective disorders, with females being affected 2–40 times more often than males with SAD [56]. The highest proportion of patients with SAD are premenopausal women [57]. Moreover, SAD symptoms frequently co-occur with premenstrual symptoms [56]. This suggests that gonadal steroids might influence SAD symptoms. There is data that depressive symptoms were positively associated with net decreases in estradiol levels [57], the lowest in October [58], elevated concentrations of follicle-stimulating hormone, and luteinizing hormone [59].

TREATMENT APPROACHES

Phototherapy

BLT plus pharmacotherapy is recommended as a first-line treatment option following a variety of treatment guidelines, as BLT alone is not considered adequate for severe episodes of winter-type SAD. Experts recommend BLT to patients with milder SAD symptoms, leaving pharmacotherapy for patients with more severe symptoms [1, 60].

BLT is primarily used to treat symptoms of winter-type SAD and is as effective as pharmacotherapy and cognitive behaviour therapy. BLT is partially effective as prophylaxis before upcoming autumn and winter seasons reducing the severity of an episode. However, opinions expressed as to whether starting BLT treatment before the appearance of symptoms prevents the depressive episode vary between sources. The development of a full-blown depressive episode can be prevented by using BLT at the first appearance of symptoms, which also postpones the development of the next episode [4, 61]. If BLT is applied after the spontaneous onset of winter-type SAD, it has to be continued for at least two more weeks. Premature discontinuation of BLT can accelerate the occurrence of a relapse [1].

During BLT, a patient is exposed to bright light while sitting in front of the "bright light unit" (preferably a fluorescent lightbox with intensities greater than 2500 lux) placed at eye level at a comfortable distance, as the antidepressant effect is supposedly mediated by optical stimuli. It is advisable not to look directly at the light source though, as visibility of light in peripheral vision is sufficient [1, 3, 4]. During the therapy, patients are able to perform a range of activities, including reading, eating, working on a computer, watching television or even doing exercise (in an adequate distance from the light source) [1]. It is also reportedly possible to use a head-mounted light source for less constrained movement [4].

The clinical standard for intensity of bright light used for treatment is 10,000 lux, with an optimal starting dose of 10,000 lux for 30 minutes a day. The most important aspect of BLT is the light intensity, as high intensities allow for

shorter exposure durations, but even intensities of 2,500 lux show antidepressant effects with 2 hour long daily exposure periods. Though it is recommended to filter out UV spectrum from the therapeutical light source to protect eyes and skin, the most used is a full-spectrum white light at 10,000 lux or green light at 350 lux. As ipRGCs are most sensitive to blue light, blue/blue-enriched fixtures have become available for SAD patients and are sometimes applied at 2,500 lux. However, there is no evidence that blue light is more efficient than white light in treating SAD or S-SAD. In fact, blue light is considered harmful to the retina [1, 3, 4, 62].

Though BLT can be executed at any time of the day, several randomized trials have proven that it is most effective during the first two hours after waking up in the morning, as it would allow phase correction of the circadian cycle and prevention of adverse side effects, such as sleep disturbances and hypomania. Note that for some patients, evening (or even midday) treatment might be more potent in its efficacy. This is thought to be related to a phase shift, as light in the morning advances the circadian phase and delays it in the evening.

Another effective form of BLT is dawn simulation when the intensity of bedside light is slowly increased in the morning hours before waking. According to a comparison study, dawn simulation ranging from 60 to 90 min every morning was equally effective as morning treatment spanning 2 hours every morning with light intensity of 100–300 lux and 1500–2500 lux, respectively [3, 4]. According to a study with exclusively hypersomnic SAD patients, dawn simulation showed better results than BLT. Dawn simulation also has positive effects on waking up and reducing sleep inertia. Dawn simulation and BLT are often used concomitantly. Patients sometimes prefer dawn simulation to BLT, as the former does not require any time to be dedicated to it. BLT should be administered at approximately the same time daily, including weekends, holidays, and vacations [1, 4]. Light-induced phase resetting of endogenous circadian clocks results in a symptomatic improvement in patients with certain affective disorders, sleep-wake disorders, and circadian rhythm disruptions and stimulates phase-advancement in delayed circadian rhythms [63, 64].

BLT also improves mood in SAD patients and normalizes the functioning of the immune system [4]. Some studies even suggest that BLT might also improve cognitive functions of patients, as serotonin and melatonin also function and interact with light influenced mechanisms [65].

Clinical improvement of winter-type SAD is usually noticeable in one to two weeks after the initiation of treatment, though in some cases this period can extend up to 4 weeks. If symptoms remain unchanged after two weeks, doubling the BLT dose is recommended, for example, by adding evening treatment. It is noteworthy that administration of BLT spanning 2 weeks can be as effective as one spanning 5 weeks, so SAD symptoms might improve after a shorter duration of BLT administration [3, 4]. BLT is usually continued during the winter season until remission of SAD symptoms in spring or summer [61], when the patient is exposed to more natural light [62]. If SAD patients experience relapses in the summer during rainy or cloudy days, BLT should be administered until spontaneous remission of symptoms is observed. A prospective observational study of SAD patients showed that the improvement of symptoms was greater in patients who walked outdoors compared to those who were treated only with BLT. Although the intensity of the lightbox was only 2,800 lux, a clear benefit of exposure to environmental light was observed, so it is strongly advised for patients, as the intensity of sunlight is much higher than light units used in BLT. Walking outside can also incorporate elements of psychotherapy known as behavioural activation. The efficacy of BLT has been proved by more than sixty controlled studies and two meta-analyses. Atypical depressive symptoms like hyperphagia, hypersomnia, and carbohydrate craving determine a less severe symptom profile at baseline (i.e. milder initial symptoms). Younger age is also associated with a favourable response to BLT, unlike comorbid personality disorders. Three observational studies have shown that patients with SAD might experience greater improvement compared to those with non-seasonal depression [1, 3].

BLT is generally well tolerated with few benign side-effects [61], though there were several reports of subjects who attempted suicide or developed suicidal thoughts suggesting that BLT is not connected to the improvement in drive and mood [66]. There is no evidence that BLT causes any ocular or retinal damage in humans, yet an ophthalmological examination is recommended for patients with severe ophthalmological conditions, after recent eye surgery or during courses of photosensitizing medication. Some milder adverse effects were recorded, however, including eyestrain, nausea, dizziness, headaches, anxiety, photophobia, visual disturbance, irritability, fatigue, agitation, and even hypomanic decompensation. These can be mitigated by adjusting doses of BLT, therefore, it is regarded as the preferable method of treatment [1, 3, 4]. Note that some patients do find BLT inconvenient and tedious, having to sit in front of a bright light unit for extended periods, and many discontinue the treatment [62].

As SAD is a specifier for bipolar and unipolar disorders, special precautions should be taken when treating SAD patients with bipolar disorder. Monitoring for signs of manic and hypomanic mood switches and administering mood stabilizers together with BLT is recommended. BLT might also be administered along with pharmacotherapy. This would enhance therapeutic effects, minimize side effects, and optimize treatment of patients with both seasonal and non-seasonal BPD [2].

As traditional BLT treatment may be inconvenient for some patients, a technology allowing Intelligent light therapy has been developed. The Energized biomedical ophthalmic device in some models is comprised of an energized contact lens, an integrated light source, sensors, and

a processor controlling the light source in accordance to the light therapy regimen. The device can provide personalized BLT treatment regimen generated or modified by the processor. The modifications are based on data collected and examined by various sensors. The data includes measured biomarkers of the tear film, patients' exposure to ambient light, circadian rhythms, and their phase changes monitored through melatonin concentration changes in tear film. As the light therapy regimen can also be generated based on user's preferences, the light intensity can be manually adjusted, and the BLT schedule and function can also be programmed [62].

BLT might be used to increase the production of vitamin D3 in the skin during exposure to sunlight or the appropriate wavelength of ultraviolet (UV). RayVio's UV LED might be used to stimulate the production of vitamin D3 without increasing the risk of skin cancer by exposing only the upper parts of arms and legs, the abdomen and back (places that normally have less contact with direct sunlight) to UV LED light [67].

Developing some new daily habits may add to the effectiveness of BLT and further improve the symptoms of SAD. These habits include daily walks outside, sleep hygiene (a regular light-dark cycle may contribute to correcting phase shifts of circadian rhythms), enhanced indoor lighting, and minimal exposure to blue light late in the evening, all of which may facilitate sleep onset [1].

Cognitive Behavioural Therapy (CBT)

As with other forms of depression, counselling or a form of Cognitive Behavioural Therapy devised specifically for SAD patients (CBT-SAD) [68] can also show positive results. SAD is enhanced by many psychological factors, such as stress and anxiety. CBT relies on efforts to actively change the way patients think about the stress-inducing problems they face to try to indirectly alleviate the symptoms of SAD [69] without addressing the cause of the disorder. In keeping with the approach to treating the symptoms, not the disease, the National Health Service (United Kingdom) also recommends maintaining a healthy diet and exercising regularly, actively avoiding stressful situations, and spending a sufficient amount of time outdoors in the sun to complement CBT [69].

Comparison and combination of treatment approaches

BLT and CBT differ not only in the mechanism of action but also in to which patients they are advised or effective. BLT is regarded as a clinical standard, although it alone is not considered adequate for severe episodes of winter-type SAD [3]. CBT is usually advised for patients with severe winter-type SAD who are unresponsive to first- and second-line treatment. If it is not effective (severe depression cases), electroconvulsive therapy is recommended, although no highly-conclusive studies have evaluated its efficacy in treating winter-type SAD [1]. One study comparing the efficacy of CBT and BLT showed that the remission rate was similar in patients treated with 90 minutes of CBT twice a week and those treated with 30 minutes of daily BLT [70].

As for the prevention of relapse and safety, CBT seems to be a better approach than BLT. A study comparing the two forms of therapy together and in isolation, measured on multiple scales, found that CBT-SAD alone provided more significant and longer lasting relief of depressive symptoms than BLT, alone or in combination of the two [71]. This prophylactic effect suggests that direct treatment of depressive symptoms plays a major role in the treatment of SAD. Taking into account low withdrawal rate and absence of severe side effects, CBT is far safer than phototherapy.

CONCLUSION

People residing in areas located far from the equator are more prone to suffer from either summer or winter SAD due to deprivation of natural light which impairs sleep and circadian rhythms. Summer-type of SAD may be affected by increased exposure to aeroallergens or air pollutants.

It is not clear if two types of SAD (summer and winter) arise by the same or different mechanisms. However, SAD symptoms in general are associated with seasonal dynamics of free plasma tryptophan (and 5-HT) levels, the availability of 5-HTT binding sites, and the number of MAO-A enzymes.

Genetic predisposition is a major factor in determining SAD susceptibility. Most of the genetic mutations found to be associated with SAD do not directly affect mood regulating elements in the brain, such as various neurotransmitters. Rather, most mutations occur in photosensitive elements in the retina, like the *OPN4* melanopsin, or *CLOCK* genes and related regulators, such as GSK3. The consequent reduced light sensitivity or disrupted endogenous circadian rhythms are responsible for triggering depressive symptoms of SAD. For SAD patients with these mutations, bright light therapy may be most effective, with a variety of antidepressant drugs and therapies available as a possible second option. Some mutations do directly affect mood regulation mechanisms in the brain, such as in genes related to serotonergic transmission, reducing the sensitivity of the serotonergic system to light.

Besides genetics, neurochemical imbalances are also considered as a cause of SAD symptoms. Specifically, reduced levels of 5-HT, DA, and NE and failure to downregulate 5-HT transporter are found in SAD patients during depressive episodes.

BLT manages to alleviate most SAD symptoms by simulating exaggerated seasonal light exposure and not affecting the symptoms caused directly by neurotransmitter imbalances (except 5-HT since serotonergic system is sensitive to light). This not only suggests that most forms of SAD are directly or indirectly linked to light exposure, but also proposes new avenues for research into the link between the optical and mood-regulating centres of the brain.

Combination of BLT and pharmacotherapy is recommended by many treatment guidelines. Usually, if this fails, psychotherapy is added. When compared to BLT, CBT is a safer and longer-lasting treatment for SAD.

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V. Jurgaitytė, J. Dijokas, P. Rimkevičiūtė, N. Khawaja

SEZONINĖS DEPRESIJOS RIZIKOS FAKTORIAI IR GYDYMAS. APŽVALGA

Santrauka

Sezoninė depresija – depresijos tipas, kuriam būdingas sezoninis simptomų pasireiškimas žiemą arba vasarą. Jos požymiai paprastai pasireiškia 1–2 % bendros populiacijos, tačiau daugiau nei 30 laipsnių nuo pusiaujo nutolusiuose regionuose šis rodiklis siekia net 10–20 %. Kartais išskiriamas ir subsindrominis sezoninės depresijos tipas, kuris pasižymi to paties pobūdžio, tik lengvesniais sezoninio afektinio sutrikimo simptomais. Sezoninės depresijos atsiradimui įtakos turi ne tik aplinkos rizikos faktoriai, pavyzdžiui, dienos trukmė ar laikas, praleistas saulės šviesoje, bet ir genetiniai veiksniai bei neurocheminiai pokyčiai smegenyse – šiam sutrikimui būdinga heterogeniška rizikos veiksnių visuma. Cirkadinių ritmų sutrikimai ir neurotransmiterių, pavyzdžiui, serotonino, dopamino ar noradrenalino, disreguliacija yra vieni iš pagrindinių veiksnių, sukeliančių sezoninio afektinio sutrikimo simptomus. Simptomų remisijai įtakos turi ryškios šviesos terapija, taikoma reguliuojant pacientų cirkadinius ritmus, ir kognityvinė elgesio terapija, kuri netiesiogiai palengvina depresijos simptomus (pacientai mokomi valdyti stresą ir nerimą). Šiame straipsnyje palyginama sezoninės depresijos gydymo metodų veiksmingumas ir saugumas.

Raktažodžiai: sezoninė depresija, subsindrominis sezoninės depresijos tipas, šviesos terapija, kognityvinė elgesio terapija.

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