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Seasonal Affective Disorder and Seasonality: A Review

Leo Sher, M.D.

Abstract

Seasonal affective disorder is a condition where depressions in fall and winter alternate with nondepressed periods in the spring and summer. The degree to which seasonal changes affect mood, energy, sleep, appetite, food preference, or the wish to socialize with other people has been called "seasonality." The author reviews historical aspects, clinical features, epidemiology, genetics, pathophysiology, and treatment of seasonal affective disorder and seasonality. Better understanding of the contemporary concept of seasonal affective disorder, seasonality, and light treatment will improve patient care and promote scientific advances in behavioral sciences.

HISTORICAL ASPECTS

Since ancient times people have known about the seasonal changes in mood and behavior (1). The concept of seasonal mood disorders dates to the dawn of medicine (1,2). Seasonal depressions were described by Hippocrates circa 400 BC (3). In the second century Greco-Roman physicians were treating depression and lethargy with sunlight directed towards the eyes (4,5). About 1500 years ago Posidonius wrote that "melancholy occurs in Autumn, whereas mania in Summer" (6). In 1894 Cook linked seasonal loss of sunlight to a mood disorder (7). Cook described a syndrome characterized by loss of sexual desire, fatigue, loss of energy and profoundly depressed mood. Seasonal changes in mood were also described by Esquirol in 1845 (8) and by Kraepelin in 1921 (9).

DIAGNOSIS

In 1984 Rosenthal and associates described the syndrome of "seasonal affective disorder" (SAD), a condition where depressions in fall and winter alternate with nondepressed periods in the spring and summer (10). Rosenthal and colleagues suggested that in order to be diagnosed as having SAD a patient must meet the following criteria: a history of major affective disorder; at least two consecutive previous years in which the depressions developed during fall or winter and remitted by the following spring and summer; absence of any other Axis I psychiatric disorders; and absence of any clear-cut seasonally changing psychosocial variables that would account for the seasonal variability in mood and behavior (10). Later, an opposite pattern, depressions in the summer and non-depressed periods in the winter ("sum-

mer SAD”), has been described (11). These two types of SAD probably represent a subset of a variety of seasonal behavioral disorders. SAD has been included in the Revised Third Edition and in the Fourth Edition of the “Diagnostic and Statistical Manual of Mental Disorders” of the American Psychiatric Association as “seasonal pattern,” an adjectival modifier of any form of seasonally recurrent mood disorders (12,13).

The onset of winter SAD occurs usually between age 20 years and 30 years, but affected people often do not seek psychiatric help for some years (2,14). Many patients report disliking winter since their teenage years, though the problem usually becomes severe only in adulthood. Sadness, anxiety, irritability, decreased activity, difficulties at work, social withdrawal, changes in appetite, decreased libido, and changes in sleep are characteristic symptoms of winter depression (10). Most winter SAD patients have “atypical” depressive symptoms such as increased sleep duration, increased appetite and weight, and carbohydrate craving. Depressive episodes are generally mild to moderate but some patients need hospitalization. The neurovegetative symptoms of “subsyndromal SAD” are similar to those of SAD but major depression is absent (15). Patients with winter SAD may experience a reversal of their winter symptoms in summer: mild hypomania, elevated mood, increased libido, social activity and energy, and decreased sleep requirements, appetite and weight (2). Most episodes of SAD occur within unipolar major depressive disorder, a substantial minority have accompanying hypomanic episodes (bipolar II disorder), and very few are associated with manic episodes. Patients with summer depression usually report “typical” vegetative symptoms, such as insomnia and loss of appetite and weight (11).

The degree to which seasonal changes affect mood, energy, sleep, appetite, food preference, or the wish to socialize with other people has been called “seasonality” (15). Seasonality can manifest to different degrees in different individuals. Some people experience only very mild seasonal changes while others are severely affected.

SAD in children usually presents with fatigue, irritability, difficulty getting out of bed in the morning and problems in school (16). Sadness and changes in appetite have also been observed in children with SAD. Children with winter SAD tend to blame the external world (parents, teachers, etc.) for treating them poorly.

Identification of a seasonal pattern can only be made if both patient and physician actively look for it (2,17). Clinicians should ask: “When the seasons change, do you 1) Feel down or depressed? 2) Have less energy than usual? 3) Feel less productive or creative? 4) Need more sleep? 5) Have less control over your appetite?” If physicians fail to ask these questions many patients with seasonal depression may be diagnosed as “non-seasonals.”

EPIDEMIOLOGY

Seasonality of mood and behavior is common throughout the population (15,17–19). Surveys suggest that the prevalence of SAD in the USA increases with increasing latitude and ranges from 1.4% in Florida to 9.7% in New Hampshire (18). A survey in the Washington area found that approximately 4% of the population have winter

seasonal affective disorder and over 10% more have sub-syndromal SAD (15). Twenty-seven percent of respondents reported that changes with the seasons were a problem for them, 66% reported seasonal changes in energy level, 64% reported some seasonal changes in mood, and 49% reported seasonal changes in weight. Another survey, in New York City, indicated approximately 6% with potential clinical severity, 18% reporting milder symptoms that are bothersome, and 35% noting symptoms but without complaint (19).

Many clinical studies report that winter SAD mainly affects women (2,14). However, the high proportion of women seen in research clinics may result from selection bias. Blazer et al. suggest that SAD with major depressive episodes is more frequent among men, whereas women more commonly experience minor depression with a seasonal pattern (20).

GENETICS

The study of the genetic basis of SAD has recently received a considerable attention (21). The data on the genetics of seasonal affective disorders are of three types:

1. **Familiality:** studies on the prevalence of psychiatric disorders among relatives of patients with SAD suggested a familial contribution to the development of SAD (22–26);
2. **Heritability:** the surveys of two cohorts of twins showed that genetic susceptibility to sensitivity to seasonal changes runs in families (27,28);
3. **Molecular genetic research:** two genetic variants related to serotonergic transmission, the 5-HTTLPR and the 5-HT2A, -1438G/A, gene promoter polymorphisms, are associated with SAD; the former but not the latter polymorphism is related to seasonality (29–31).

Future research may clarify the role of different genes in the development of SAD. The purpose of molecular genetic studies on SAD includes the development of predictive testing for SAD that can help to establish the correct diagnosis and the identification of target for therapeutic drugs.

PATHOPHYSIOLOGY

Several lines of evidence suggest that disturbed serotonin functioning plays an important role in the development of SAD. Many SAD symptoms such as overeating, carbohydrate craving, weight gain, and oversleeping can be related to serotonergic dysfunction. It has been suggested that dietary carbohydrates increase brain serotonin (32,33). Carbohydrate craving in patients with SAD may be a “self-medication” procedure by which brain serotonin level is increased. In a post-mortem study winter decrease in serotonin concentrations was observed in human hypothalamus (34). Selective serotonin reuptake inhibitors have a beneficial effect in patients with SAD (35,36). Studies on the effect of administering of serotonergic agonist m-chlorophenyl-

piperazine in patients with SAD have shown that the infusion of this substance can activate patients and make them euphoric (37–39). Another serotonergic agonist, d-fenfluramine, has been found to be effective in reversing symptoms of SAD (40). As noted above, polymorphism in two serotonin system genes has been found to be associated with winter SAD (21,29,30).

According to the “melatonin hypothesis,” SAD may be a result of abnormal secretion of or sensitivity to melatonin, and phototherapy may modify melatonin secretion (2,10). However, oral administration of melatonin to SAD patients who had responded to light therapy did not induce return of the depression, and atenolol (the beta-adrenergic receptor blocking drug which suppresses production of melatonin) failed to induce remission in SAD (41). These observations raised questions as to whether melatonin plays an important role in the development of SAD and seasonality.

The “phase-shift” hypothesis suggests that the symptoms of SAD may result from abnormally delayed circadian rhythms (42). This theory is based on the facts that bright light in the evening delays the nocturnal rise of melatonin, and that bright light in the morning advances the melatonin rhythm. Three controlled clinical trials reported recently support the phase-shift hypothesis by demonstrating therapeutic superiority of early morning light exposure over evening exposure or placebo controls (43–45). However, in two trials a minority of patients responded preferentially to evening light (43,44).

Depue and colleagues proposed that the dopaminergic system might be involved in the pathogenesis of SAD (46,47). It has been suggested that a hypodopaminergic state in the nigrostriatal system may be associated with up-regulation of dopamine receptors in the prefrontal cortex. However, a double-blind study showed that the administration of a combination of levodopa plus carbidopa was not superior to placebo in patients with SAD (48).

The study of thyroid function in patients with SAD is of considerable interest, because symptoms of SAD include decreased energy and weight gain (2,10), which are also common in hypothyroidism (49). It is possible that persons with SAD have a subtle decrease in thyroid function similar to that which has been described in some patients with non-seasonal depression (50,51). Results of studies of thyroid function in SAD, however, are inconsistent. Thyroid abnormalities in SAD patients were reported by Kasper et al. (15), Raitiere (52), Coiro et al. (53), and Sher et al. (54) but not by Rosenthal et al. (10), Bauer et al. (55), and Lingjaerde et al. (56). We studied blood levels of free thyroxine (T4) and thyroid-stimulating hormone (TSH) in SAD patients and matched controls in the winter (54). We found that free T4 blood levels were slightly but significantly lower in patients than in healthy volunteers but there was no difference in TSH levels between patients and normal volunteers. Future research will be needed to determine whether the difference in thyroid function between SAD patients and controls is an epiphenomenon or is related to the biological mechanisms that cause symptoms of SAD.

TREATMENT

Many SAD patients seek professional treatment for depression but they are not diagnosed as having SAD. This may be related to the physician's insufficient knowledge about SAD and seasonality and/or the physician's inability to gather the appropriate history because of the patient's uncooperativeness or the physician's failure to conduct the appropriate diagnostic interview. Treatments generally effective for depression including combined psychotherapy and antidepressant medications often do not work until springtime.

Light is the mainstay of treatment for winter depression (2,10,14,17,57). The efficacy of light treatment has been shown in many controlled studies in different countries. Light therapy causes improvement in most SAD patients. For example, Oren and Rosenthal reported that significant improvement in depressive symptoms occurred in at least three-quarters of SAD patients treated with light (2). Many researchers reported that morning is the most effective time for light therapy (2,43-45) whereas others have found patients to respond well to light at other times of the day (58-61). Treatment with 10,000 lux for 30 minutes in the morning appears to be as successful as 2500 lux for 120 minutes (62). Lately, the higher levels of light intensity have been preferred because they allow for shorter daily treatments. Light treatment is easy to administer in outpatient settings, lacks major side effects, and is cost-effective. Caution is recommended when light therapy is used in patients with a tendency toward mania or with photosensitive skin.

Patients initially should be given morning light shortly after awakening at the dose of 10,000 lux for 30 minutes (14,57). If this treatment fails to elicit an antidepressant response within several days the treatment time should be extended and/or evening treatment should be added. Oren and Rosenthal suggested that most SAD patients require at least 45 minutes a day of light therapy at the 10,000 lux illuminance (2).

Sertraline and fluoxetine appeared to be effective in SAD but less effective than light therapy (57,63). For example, Ruhrmann et al. recently conducted a study that directly compared bright light and fluoxetine in the treatment of SAD (63). The remission effect for light was superior to fluoxetine (50% vs. 25%), and light therapy improved Hamilton Depression Rating Scale scores faster than the administration of fluoxetine. Serotonin-agonist d-fenfluramine is effective in treatment of overweight patients with SAD (40). Antidepressive drugs are often combined with light therapy. Lithium, valproic acid, carbamazepine, and gabapentin can be used to control the hypomanic symptoms that affect some SAD patients in spring and summer (17).

Light treatment and medications cannot solve all psychological problems in all cases of SAD. Psychotherapy including cognitive, behavioral, and insight-oriented therapy may be useful for some SAD patients (14,17).

A recent controlled study suggested that high-density negative air ionization may act as an antidepressant in patients with SAD (43). Subjects were randomly assigned to a 3-4 week treatment period with 30 minute negative ion exposure sessions every day, at low and high ion concentration. The reduction in depression

rating scale scores was significantly greater at the higher dose than at the lower dose. The results of this study support previous reports that exposure to negative ions may have a mood-enhancing effect (64–66).

Diet and exercise are important considerations in SAD and should be part of the SAD patient's health maintenance plan (14,17). Possibly, St. John's wort has an antidepressive effect on patients with SAD (17).

CONCLUSION

Seasonal changes in mood, energy, sleep, appetite, food preference, or the wish to socialize with other people are common in the general population. In the past 15 years scientists have established a firm definition of the winter SAD and seasonality, and the efficacy of light therapy for winter SAD. In the past several years researchers have found that genetic factors play an important role in the etiology of SAD and seasonality. We can expect that our knowledge about the etiology and pathogenesis of SAD and seasonality will grow in the years to come.

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