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Is Memory Impaired in Seasonal Affective Disorder? A Review of Literature

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Abstract: Seasonal Affective Disorder (SAD) has symptoms similar to those of mild to moderate clinical depression, and is common in places where there is seasonally less natural light. A probable cause of the disorder is deficient regulation of melatonin secretion. In contrast to what is the case in non-seasonal depression, memory impairments in SAD are insufficiently studied. Similar impairments to those shown in non-seasonal depression have been shown, but studies are generally to small for reaching statistical significance, and tests employed lack resolution to describe impairments in sufficient detail. A review of available literature is herein reported.

Key words: Seasonal Affective Disorder; clinical depression; memory impairments; melatonin secretion

Seasonal Affective Disorder (SAD) is a condition that affects persons living in latitudes where the length of the day varies over the year. It seems that the conditions that are most conducive to the development of SAD-symptoms are those where daily duration of sunlight varies greatly between summer and winter, where there is low presence of reflected light, and where there is low social acceptance of seasonally reduced professional or social performance. In practical terms, this means that SAD is most common in large northerly cities in the northern hemisphere. Presence of artificial light does not seem to attenuate the occurrence of SAD. SAD was first systematically described by Rosenthal and associates in 1984.

Symptoms

Symptoms of SAD are similar to those of mild to moderate clinical depression, i.e. depressed mood, reduced psychomotor ability, anxiety, changed sleeping pattern, changes of appetite, loss of initiative, loss of interest, reduced optimism, feelings of guilt or shame, and loss of feeling of meaningfulness. As with clinical depression, thoughts of death and suicide are common. In contrast to clinical depression in adult populations, SAD in adult populations often presents with increased subjective need for sleep as well as increased time objectively spent asleep. Also more common in SAD than in clinical depression seems to be carbohydrate cravings, i.e. craving specific foods rich in starch or sugar, such as pasta, white rice, potatoes, sweets and candies. Whereas clinical depression commonly presents with reduced sleep and reduced appetite, SAD presents with increased sleep and changed food preferences leading to greater daily caloric intake. In both SAD and clinical depression, activities that normally cause joy or are pleasurable are less attractive. In contrast to clinical depression, persons suffering from SAD are more likely to attribute their symptoms to tiredness whereas persons suffering from clinical depression are more likely to attribute their symptoms to personal shortcomings in general.

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Prevalence

Different studies show different prevalence rates of SAD, between 1-10% (Magnusson & Partonen, 2005). Attempts to explain differing prevalence rates with geographical latitude alone have not been successful. For example, Iceland, at about 64 degrees northerly latitude, shows lower prevalence rates than several more southernly populations studied (Magnusson & Stefansson, 1993). Likely, several factors influence the prevalence rates of SAD. Genetics seem to have an effect, with persons belonging to homogenous ethnical groups that traditionally reside in northern latitudes showing reduced propensity for displaying SAD symptoms (Mersch et al., 1999). Furthermore, individual factors such as short duration of stay in northern latitudes, female gender, and young adult age, all seem to contribute to increased risk of developing SAD (Magnusson & Partonen, 2005).

Biological basis

The initial hypothesis regarding the biological basis of SAD was that SAD symptoms could appear in susceptible individuals as a result of circadian biological processes misaligning with the physical daylight. Susceptible individuals were initially considered to be only those with a previous medical history including bipolar disorder or depression (Rosenthal et al. 1984). Consensus has later been established that previous episodes of non-seasonal depression are not necessary to define the patient group (American Psychiatric Association, 2000).

The initial theory of the biological basis of SAD did not specify in detail which circadian biological processes were misaligned with the physical period of daylight. Candidate substances have, however, always included melatonin. Melatonin is a part of the system that regulates sleep and wakefulness. Melatonin secretion is regulated by light exposure, such that acute melatonin secretion is suppressed by bright light (Lewy et al., 1980), and permitted by darkness. Reduced light-intensity differences between day and night may cause sleep disturbances. These disturbances may be associated to melatonin secretion. SAD patients have been shown to have a delay in the secretion of melatonin in response to low light levels (Sack et al., 1990), such that the increase in melatonin related to low light conditions occurs later at night for SAD patients than healthy controls. Furthermore, SAD patients are more sensitive to light-mediated melatonin release suppression (Nathan, Burrows, & Norman, 1999). It is likely that the overall effect on melatonin in SAD patients is a reduction in circadian variation of secretion under circumstances where there is little difference in light intensity over the day, such that daytime melatonin levels would be increased compared to the non-SAD population, whereas nighttime melatonin levels would be reduced. Evidence of reduced nighttime melatonin levels were reported in Sack et al. (1990), whereas results are mixed with regard to elevated daytime melatonin levels. Karadottir and Axelsson (2001), Danilenko and associates (1994), and Levine and associates (1994) have all shown daytime melatonin level elevation in SAD patients, whereas Koorengevel and associates (2002) have failed to show such elevation.

Treatment

As with clinical depression, drugs affecting serotonin and noradrenaline levels in the brain, such as specific serotonin re-uptake inhibitors (SSRI) and serotonin and noradrenaline re-uptake inhibitors (SNRI), are effective in a large percentage of affected patients. More than 50% improvement on standardized symptom rating scales (such as the Montgomery-Åsberg depression rating scale, [MADRS; Montgomery & Åsberg, 1979]; or the Structured Interview Guide to the Hamilton depression rating scale, SAD version [SIGH-SAD; Williams, Link, Rosenthal, Amira, & Terman, 2002]) occur for 56-59% of patients with SAD treated with SSRI drugs (Lam

et al., 1995; Moskovitch et al., 2004), as compared to about 60% of patients with clinical depression treated with SSRI/SNRI drugs (Statens Beredning för Medicinsk Utvärdering, 2004). A difference in placebo effect is notable, such that 50% improvement occurs for about 30% of patients with clinical depression treated with placebo, compared to 50% of patients with SAD treated with placebo. This is likely an effect of the SAD-patients having lower depression scores at enrollment into study.

Cognitive and behavioral therapy is about as effective for persons with clinical depression as SSRI/SNRI (about 60% halve their symptom scores; Elkin et al., 1989), but has not been systematically studied for SAD.

Since SAD symptoms are believed to be related to circadian disturbances caused by change in natural light, melatonin has been suggested as a target substance for treatment of SAD symptoms. Treatment with orally administered melatonin has, however, not been successful. Agomelatin, an experimental pharmacological substance affecting serotonin uptake and melatonin release, has shown promising results in the treatment of SAD in clinical trials (Pjrek, et al., 2007).

Bright light therapy (BLT) has not been systematically studied, but small uncontrolled studies have shown promising results (see e.g. Eastman et al., 1998; Michalon, Eskes, & Mate-Kole, 1997; and Terman, Terman, & Ross, 1998). Biologically, there is a plausible explanation of the mechanism of action of BLT, and there is a strong clinical impression that BLT is efficient in at least short term evaluations. It seems that BLT administered in the morning is more likely to be efficient than BLT administered at other times of day (Terman et al, 1998). Likely, the SAD symptomatology is not primarily an effect of lack of daylight, but lack of cues to normal circadian regulation. That is, bright mornings help people regulate their sleep-cycles, and persons susceptible to sleep-cycle dysregulation are at risk if external cues are not present.

Memory impairment

The effects of clinical depression on memory performance have been extensively studied (see e.g.Hartledge, Alloy, Vazquez, & Dykman, 1993; Elliot, 1998; Berger, 2004). Generally, the effects of clinical depression on memory performance range from mild loss of cognitive speed, noted at mild levels of clinical depression, to profound pseudo-dementia of severe major depression. Generally, effortful tasks are more pronouncedly affected than less effortful tasks. Tasks requiring the coordination of several cognitive processes are more likely to be affected by depression. Neurological structures related to the ability to coordinate cognitive processes include the prefrontal cortex, and neuroimaging studies have shown affected blood-flow patterns in the anterior cortex cinguli and on the medial aspects of the frontal lobes (Bench et al., 1992; Drevets, 2000), establishing a functional correlate of the behavioral data. Negative feedback, normally associated with improved performance in non-depressed subjects, causes reduced performance in depressed subjects (Farrin, Hull, Unwin, Wikes & David, 2003). Neural correlates of the tendency to perform more poorly when informed of poor performance in a previous part of the test can be visualized. A disturbed blood-flow-pattern affecting the medial caudate nucleus and the venterolateral orbitofrontal cortex[1] is present in depressed patients that receive negative feedback (Elliott, Sahakian, Michael, Paykel, & Dolan, 1998). Relatedly, depressed persons seem to have a depression congruent bias in remembering, such that memories of negative affective content are more likely to be remembered (Blaney, 1986). Pharmacological treatments of

[1] The orbital cortex is a difficult structure to study with functional neuroimaging, because of great interindividual variability in its anatomy. Thus, findings implicating cerebral blood-flow or metabolism changes in the orbital cortex should be interpreted cautiously.

depression have been shown to affect cerebral blood flow in both depressed patients and healthy controls, such that they reduce blood-flow in the frontal, parietal and temporal lobes (Drevets, 2000). Behavioural correlates of this reduction in cerebral blood-flow are difficult to establish, since the blood-flow changes are so diffuse that they do not predict any particular effect on cognition. Conversely, whereas treatment with antidepressants has been shown to improve cognitive function of depressed patients (see e.g. Doraiswamy et al.), associating this improvement to visualizable blood-flow changes has not yet been successfully attempted.

Memory impairment in SAD has not been systematically evaluated, but small studies have shown similar findings as in clinical depression of comparable severity (see e.g. Sullivan & Payne, 2007). Most studies have not employed cognitive tests that allow detailed analyses of cognitive impairment. Contrary, self-reported cognitive difficulty seems to be the most common cognitive evaluation in SAD research. O'Brien, Sahakian, & Checkley (1993), however, showed impairments on spatial memory (computerized presentation of several white squares, followed by forced choice recognition) and response times. Upon improvement of depressive symptoms, remaining latency to respond in spatial memory tests was likely attributable to residual depression. Since only eleven SAD patients, and ten control subjects were assessed, differences in performance between groups needed to be clinically significant in order to reach statistical significance (performance differences in tests of spatial recognition, with SAD patients showing half the scores of control subjects, were statistically significant; performance differences in tests of pattern recognition, with SAD patients showing 75% of normal scores, were not statistically significant). Drake and associates (1996) failed to replicate the findings of O'Brien and associates in a similar sample of ten SAD patients and nine healthy controls. An interesting aspect of the Drake et al. study was that comparisons were also made between winter and summertime for both controls and SAD patients. A large seasonal effect was present both in SAD patients and in healthy controls, with both patients and controls performing at a more than 100% better level in summer than in winter on both pattern recognition tests and on the Stroop color word test of attentional interference[2]. Michalon et al. (1997) systematically evaluated 15 SAD patients receiving bright light therapy, 15 SAD patients receiving dim light therapy, and 29 matched controls not fulfilling SAD diagnostic requirements. Patients and controls were subjected to tests of cognitive functioning including general cognitive ability, attention, verbal memory, visual memory, visual construction and perception, language, and motor abilities. Differences between the performance of SAD patients (30) and controls (29) at baseline were significant only for the cognitive failures questionnaire (CFQ; testing autobiographical memory of adverse events involving reduced memeory performance), both tests of visual memory (recognition memory for faces and Rey complex figure delayed recall), and the visual perception test Rey complex figure copy. Both visual memory tests showed significantly increased performance after light therapy, whereas neither subjective memory difficulties, measured by the CFQ, nor visual perception improved.

Since correct interpretation of neuroimaging data requires first several studies establishing regions of interest, and later studies of these regions in more detail, neuroimaging results of SAD are at this time not conclusive.

Conclusion

SAD is a subtype of depression characterized by seasonal variation. The most likely cause of SAD symptoms is a combination of genetic susceptibility and dim light conditions in winter.

[2] Summer testing was always preceded by winter testing, so a large part of the summertime improvement is likely related to training effects.

In contrast to clinical depression in general, cognitive deficits in SAD have been insufficiently studied. Studies of larger patient samples are needed, as well as studies employing more high resolution cognitive tests. There is also a relative lack of neuroimaging studies compared to clinical depression without seasonal variation. For furthering the understanding of the relation between SAD and cognitive ability, and thus a greater understanding of the potentially different biological basis of clinical depression and SAD, larger and more well designed studies are important.

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季节性情感障碍存在记忆损伤吗？

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摘 要 季节性情感障碍(Seasonal Affective Disorder, SAD)与轻度到中度的临床抑郁有类似的症状，它通常发生于季节性日照不足的地区。造成该障碍的一个可能原因是褪黑素分泌不足。与非季节性抑郁相比，季节性抑郁的记忆损伤尚未得到充分研究。以往的研究也发现了一些类似于非季节性抑郁的记忆损伤，但通常很少达到统计的显著性，且其采用的测验任务也缺乏分辨力，未能对损伤进行足够的细节描述。这里对有关文献做一个综述。

关键词 季节性情感障碍；临床抑郁；记忆损伤；褪黑素分泌

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