

Platelet serotonergic functions and light therapy in seasonal affective disorder

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Abstract

We investigated platelet ^{14}C -serotonin uptake and platelet [^3H]LSD and [^3H]paroxetine binding in 11 patients with seasonal affective disorder (SAD). Patients were reinvestigated after light therapy, applied at 07.00–09.00 h for 10 consecutive days. The degree of depression was rated before and after light therapy using the Comprehensive Psychopathological Rating Scale (CPRS). Baseline data in patients were compared with data from a control group consisting of 11 age- and sex-matched healthy volunteers. Seven patients responded to light therapy with a > 50% reduction in CPRS scores. In non-responders, the reduction in CPRS was $24.7 \pm 5.5\%$. There was a significant inverse correlation ($P = 0.014$) between K_m for platelet ^{14}C -serotonin uptake and CPRS scores. Patients had significantly higher B_{\max} for platelet [^3H]LSD binding ($P = 0.04$) and significantly lower B_{\max} for platelet [^3H]paroxetine binding ($P = 0.016$). There was a strong, multiple correlation between B_{\max} for [^3H]LSD, as the dependent variable, and K_m , V_{\max} and B_{\max} for [^3H]paroxetine binding in patients ($P < 0.0001$) but not in controls. Responders to light therapy had significantly higher K_m ($P = 0.023$) and significantly lower B_{\max} for [^3H]paroxetine binding ($P = 0.028$) than non-responders. B_{\max} for [^3H]paroxetine binding increased significantly to normal levels after light therapy. The results indicate that SAD is associated with aberrations in the serotonin uptake mechanism. The enhanced 5-HT₂-receptor density may reflect a consequential up-regulation. © 1998 Elsevier Science Ireland Ltd.

Keywords: SAD; Platelets; Serotonin uptake; Serotonin transporters; 5-HT₂ receptors; Light therapy

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1. Introduction

Seasonal affective disorder (SAD) as defined by Rosenthal et al. (1984) is characterized by an annually recurring major depression presenting in the late fall and winter with complete remission in the late spring and summer. The disorder displays a latitude dependence and most reports describe an increase of symptoms with distance from the equator and in climatic conditions of low light (Lingjaerde et al., 1986; Potkin et al., 1986). Patients with SAD fulfil the DSM-IV criteria for major depression or bipolar disorder with the DSM-IV specified seasonal pattern.

In accordance with the serotonin hypothesis of depression (Risch and Nemeroff, 1992) it seems reasonable to assume that SAD is associated with disturbances in the brain serotonin system. There is extensive evidence of seasonal variations in the serotonergic functions in man (Lacoste and Wirz-Justice, 1989). The serotonin agonist *d*-fenfluramine has been found effective in SAD (O'Rourke et al., 1989). Symptoms atypical in major depression, such as overeating, oversleeping and carbohydrate craving and weight gain, indeed suggest a serotonergic dysfunction. Carbohydrate-rich meals, which increase brain serotonin (Fernstrom, 1988), energize patients with SAD, but sedate healthy individuals (Rosenthal et al., 1989). The assumption is further supported by the finding that euthymic, drug-free patients with SAD transiently relapse with depressive symptoms after tryptophan depletion (Neumeister et al., 1997).

Following the case report of the antidepressant effect of bright artificial light in a bipolar SAD patient (Lewy et al., 1982), several procedural frameworks of light treatment have been developed (Rosenthal et al., 1984, 1985; Kjellman et al., 1993). A survey of a large number of light therapy studies has indicated a clear treatment effect of early morning bright light and the highest remission rates for mildly depressed patients (Terman et al., 1989).

One common and fruitful approach in neurobiological studies of depression is to use platelets as peripheral models for serotonergic nerve endings in the brain. A large literature has demonstrated

aberrations in platelet serotonin uptake and 5-HT₂-receptor functions in patients with major depression (Tuomisto and Tukiainen, 1976; Rausch et al., 1986; D'haenen et al., 1988; Malmgren et al., 1989; Biegon et al., 1990; Lawrence et al., 1993; D'Hondt et al., 1994; McBride et al., 1994; Nankai et al., 1994; Hrdina et al., 1997; Pandey et al., 1995; Sheline et al., 1995). Still, there are few reports concerning platelet serotonergic functions in SAD and the effect of light treatment on these functions. The platelet serotonin transporter has been studied with [³H]imipramine in two studies. Szádóczy et al. (1989) found that SAD patients had a reduced B_{\max} that increased after light treatment in parallel with clinical improvement. Ruhrman et al. (1991), however, failed to find any effect of light treatment in their study. Imipramine has been replaced by [³H]paroxetine as the label of choice for the serotonin transporter (Mellerup and Plenge, 1986). Mellerup et al. (1993) found that platelet [³H]paroxetine binding decreased in patients who responded to light treatment, while non-responsive patients had a relatively low number of [³H]paroxetine binding sites, compared to responders, prior to treatment. On the other hand, Ozaki et al. (1994), who investigated platelet [³H]paroxetine binding and 5-HT₂ receptor stimulated Ca²⁺ response in SAD, found no abnormalities or any effect of light treatment on any of these parameters.

The psychiatric clinic at St Görän's Hospital in Stockholm has several years of experience in treating SAD patients with light therapy. The aims of the present study were (i) to compare platelet serotonin uptake and [³H]paroxetine and [³H]LSD binding to platelet membranes in SAD patients and healthy individuals; and (ii) to study the effect of light treatment on these variables in patients with SAD.

2. Materials and methods

Eleven patients (nine women and two men) were investigated and included in the study. Mean age was 45.4 ± 11.0 years, the age range was 27–69 years. All the patients met the DSM-IV criteria for major depression with seasonal pat-

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