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# Electroretinography in patients with winter seasonal affective disorder

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**Abstract**

A retinal sensitivity abnormality has been hypothesized in seasonal affective disorder (SAD). To explore this hypothesis, the electroretinogram (ERG) was used to assess retinal sensitivity at the level of the rod photoreceptor system. We examined 27 depressed patients who met DSM-III-R criteria for major depression, recurrent, with a seasonal (winter) pattern and 23 normal control subjects who were age-paired and sex-matched as much as possible with the SAD patients. ERG testing was performed in dark-adapted, dilated eyes in winter between 10:00 and 15:00 h. Retinal sensitivity was based on the light stimulus intensity necessary to reach a 50-μV amplitude threshold. We found that retinal sensitivity was significantly lower (0.21 log units) in SAD patients compared with normal control subjects and that 55% of the patients had a retinal sensitivity value one standard deviation lower than the mean value of the control subjects. These results are consistent with a retinal hyposensitivity hypothesis for SAD, but the explanation for lower rod photoreceptor sensitivity in SAD is not known. We hypothesize that brain neurotransmitter dysregulation may be at the origin of both the mood disorder and retinal sensitivity change.


*Keywords:* Electroretinography; Seasonal affective disorder; Retina; Light; Dopamine; Serotonin

## 1. Introduction

Winter seasonal affective disorder (SAD) is a subtype of depressive disorder characterized by recurrent major depressive episodes that occur in autumn/winter, with full remission of symptoms in spring/summer (Rosenthal et al., 1984). The pathophysiology of winter SAD is unknown, but ocular light sensitivity hypotheses have been the focus of several investigations in seasonal affective disorder (SAD) with mixed results. The link between SAD and the retina arose from the fact that the effect of light therapy appears to be mediated through the eyes (Wehr et al., 1987). In 1990, two contrasting hypotheses were proposed

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to account for the role of the retina in SAD (Beersma, 1990; Remé et al., 1990). Beersma (1990) proposed SAD patients have retinal *hyper*-sensitivity to light. This would lead to perception of evening room light as an extension of the photoperiod yielding a depressogenic phase delay of circadian rhythms sometimes reported in SAD (Lewy et al., 1987). Therefore, the efficacy of morning light therapy results from a corrective realignment of circadian rhythms through resynchronisation of the biological clock with the natural light/dark cycle. In contrast, Remé and colleagues (1990) proposed that SAD patients have retinal *hypo*sensitivity to light. This hypothesis is based on the proposition that in the normal population, the wintertime decrease of natural light exposure may lead to a compensatory mechanism of increased retinal light sensitivity, an ocular physiological adaptation termed *photostasis* that has been observed in some animal studies (Penn and Williams, 1986; Parker and Williams, 1995; Schremser and Williams, 1995a,b). They argued that if this process were absent or weakened in patients with SAD, they would be hyposensitive to light compared with normal subjects. Consequently, they would not be able to absorb enough light to maintain a euthymic state, explaining the need for light therapy.

There is support for both retinal hypersensitivity and hyposensitivity hypotheses, but the supporting data are highly dependent on the techniques used to measure light sensitivity. Studies using the dark adaptation threshold test (DAT) found no difference in the rod photoreceptor threshold obtained in patients with SAD and normal controls, either in summer or winter (Oren et al., 1993; Terman and Terman, 1999), but cone photoreceptor sensitivity was higher in both winter and summer in SAD patients than in controls (Terman and Terman, 1999). The latter result was interpreted as supportive of the hypersensitivity hypothesis in SAD, but for the cone photoreceptors only.

In contrast, using the electrooculogram (EOG) technique, EOG ratios have been found to be low in SAD patients relative to controls in winter (Lam et al., 1991; Ozaki et al., 1993), supporting the hyposensitivity hypothesis. Normal subjects were found to have increased EOG ratios in winter compared with summer, whereas no changes were observed in SAD patients (Ozaki et al., 1995). Interestingly, no change in the EOG ratio was observed after 1 week of light therapy even when light therapy was clinically effective. Also, supporting the hyposensitivity hypothesis were findings with the full flash electroretinogram (ERG) technique. Women with SAD compared with matched controls, but not men, had lower b-wave amplitudes (Lam et al., 1992). Because the light stimulus used in that study triggered a mixed rod-cone response, it was not possible to clearly specify the origin of the change. However, a small-sample, mixed-sex study using the pattern ERG (PERG), which elicits an electrical response from the retina (mostly the macular region), did not find any differences between SAD patients and controls (Oren et al., 1993). Recently, a more specific ERG technique in which various dim blue-green light intensities generate a detailed scotopic luminance response function (Hébert et al., 1996) was used to investigate seasonal change in rod sensitivity in subsyndromal affective disorder (S-SAD), that is, people who experience a non-clinical, milder form of winter depression (Kasper et al., 1989). S-SAD subjects showed a wintertime decrease in rod sensitivity, but normal subjects had no seasonal change (Hébert et al., 2002).

In the present study, we used flash ERG to assess retinal sensitivity in winter in a large group of well-diagnosed SAD patients and normal control subjects. In this study, patients and controls were tested in winter, and a short version of the rod luminance-response function was obtained with only four intensities. Retinal sensitivity was defined as the intensity necessary to reach a fixed b-wave amplitude criterion of 50 μV. We hypothesized that if the SAD patients were indeed significantly less sensitive to light than the controls, the intensity of light needed to reach the criterion during a depressive episode would be higher than in the control subjects.

## 2. Methods

### 2.1. Subjects

Twenty-seven depressed SAD patients who had been psychotropic drug-free for at least 5 weeks