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Brief report

The association of nocturnal serum melatonin levels with major depression in patients with acute multiple sclerosis

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Abstract

The association of nocturnal serum melatonin levels was investigated in acute multiple sclerosis (MS) patients with major depression (MD). The sample comprised 13 patients with MD and 12 with no psychiatric disorders admitted to our clinic due to acute MS attacks. Psychiatric evaluation was performed with the Structured Clinical Interview for DSM-IV (SCD-I). The level of depressive symptoms was assessed with the Beck Depression Scale (BDS). Blood samples were taken from the patients to determine melatonin level at 03.30h and 10.00h before steroid treatment started. Melatonin levels were determined using the ELISA test. Nocturnal serum melatonin levels (21.2±17.1 pg/ml) of the patients with MD were significantly lower than those (51.5±18.3 pg/ml) of the patients without MD. A significant negative correlation was found between BDS scores and nocturnal serum melatonin levels. These findings suggest that a melatonin deficiency may be among the factors involved in the occurence of depression in MS patients.

Keywords: Multiple sclerosis; Demyelinating diseases; Melatonin; Depression; Circadian rhythms

1. Introduction

Multiple sclerosis (MS), a chronic disease that leads to motor, sensorial, affective and cognitive deficits, usually has its onset young adulthood. It is a disease characterized by inflammation, demyelination and glial scarring in the pathological examination of central nervous system tissues (Sandyk and Awerbuch, 1993a; Miller, 2000).

The causal relationships between MS and affective disorders have yet to be determined, although mood disorders in MS were first described by Jean Marie Charcot in 1877 (Sandyk and Awerbuch, 1993b). In MS the rate of depression is higher than in other chronic neurological diseases. The concomitant occurrence of depression and abnormal levels of melatonin has also been reported (Miles and Philbrick, 1988).

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Melatonin is synthesized by the pineal gland (Arendt, 1995). L-tryptophan is converted into 5-hydroxy-tryptophan in pinealocytes by tryptophan hydroxylase (Chokroverty, 2000). Serotonin is produced via decarboxylation. Serotonin is converted by sequential activities of two enzymes, serotonin-*N*-acetyl transferase and hydroxyindole-*O*-methyl transferase (Claustrat et al., 2005). Melatonin is metabolized in liver and its principal metabolite is 6-hydroxy-melatonin (Miles and Philbrick, 1988; Sandyk and Awerbuch, 1993b; Chokroverty, 2000).

The biosynthesis and secretion of melatonin is controlled to a large extent by a nonadrenergic system (Lewy et al., 1981; Rabe-Jablonska and Szymanska, 2001). The suprachiasmatic nucleus of the hypothalamus causes inhibition of melatonin secretion, leading to the gamma-aminobutyric acid. Therefore, decreased melatonin levels may reflect hypothalamic dysfunction in the regulation of oscillatory melatonin secretion. Hypothalamic and periventricular lesions are often encountered in MS. At the same time, decreased melatonin levels may also reveal serotonin function disorders, as serotonin is the precursor of melatonin (Sandyk and Awerbuch, 1993b).

Melatonin is secreted nocturnally, and the nocturnal serum melatonin level is 25–85 pg/ml in adults (Sandyk and Awerbuch, 1993a,b). The melatonin level reaches its peak between 04.00h and 06.00h, and levels decline between 07.00h and 09.00h. Although melatonin levels show a constant rhythmic amplitude in each individual, there are large differences among individuals (Arendt, 1988).

Since the nocturnal melatonin secretion may be reduced in patients with depression, it is likely that decreased melatonin secretion is also associated with the depressive symptoms of MS. Lower levels of production may contribute to depression due to evidence of pineal gland calcification and hypothalamic dysfunction commonly seen in MS (Sandyk and Awerbuch, 1993b).

The aim of the present study was to investigate the association of nocturnal serum melatonin levels in acute MS patients with concomitant MD.

2. Methods

2.1. Subjects

The sample consisted of 25 patients (9 male, 16 female) previously diagnosed with MS according to McDonald criteria (Polman et al., 2005). Because of acute MS attacks, the patients were hospitalized at the Neurology Clinic of Meram Medical School of Selcuk University. None of the patients had any autoimmune disease.

Mean disease duration (±S.D.) was 7.2±7.7 years. Thirteen patients (52%) had MD, and 12 patients (48%) had no psychiatric disorders. Mean age was 40.0±10.7 (22–63) years for women and 33.0±10.4 (22–54) years for men. All were evaluated with the Structured Clinical Interview for DSM-IV (SCID-I). MS patients with psychiatric disorders other than MD were not included in the study. Patients had not received any antidepressant, steroids, beta-blockers or hormonal therapy during the month before their hospitalization.

2.2. Procedures

The Expanded Disability Status Scale (EDSS) was administered (Kurtzke, 1983). Levels of depressive symptoms were evaluated with the Beck Depression Scale.

All patients fell asleep between 23.30h and midnight on the first night of hospitalization before steroid treatment began. Blood samples (5 ml) were drawn at 03.30h and 10.00h. The blood samples were centrifuged, and their sera were separated in 30 min. Sera were kept at −80 °C. Serum melatonin levels were tested with an ELISA kit (cat. no. RE54021) from IBL-Hamburg (Hamburg, Germany; sensitivity, 1.6 pg/ml; intraassay CV, 3.0–11.4%; interassay CV, 6.4–19.3%).

All statistical analyses were performed using SPSS 13.0 Package for Windows. Chi-square tests were performed for categorical variables. Two-way analysis of variance (ANOVA) with independent groups and repeated measures for time (night, morning) were also carried out. Since an interaction between independent variables (group and time) was found, the results of two-way ANOVA were not used. Univariate analysis of covariance was performed, and the Mann–Whitney *U* test was used to compare groups. Pearson's correlation test was used to analyze the relationship between BDS scores and melatonin levels. Significance was defined as $P<0.05$ in all tests.

Table 1
Physical characteristics of the patients with multiple sclerosis

	With major depression	Without major depression
N	13	12
Gender (m/f)	4/9	5/7
Age (years)	38.5±11.2	36.3±11.4
Disease duration (years)	7.4±7.3	7.0±8.5
Number of attacks	3.8±1.8	4.2±2.7
EDSS	2.3±1.7	1.7±1.4