Actigraphy in Patients with Seasonal Affective Disorder and Healthy Control Subjects Treated with Light Therapy

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Background: *Abnormalities of the circadian rest-activity cycle are hypothesized to accompany the clinical picture of seasonal affective disorder (SAD). The purpose of this study was to investigate if bright light therapy (BLT) is able to reverse these disturbances.*
Methods: *Seventeen SAD outpatients and 17 sex- and age-matched healthy control subjects were treated with BLT administered in the morning for 4 weeks. Activity levels were measured with wrist actigraphy.*
Results: *SAD patients had 33% lower total (p = .031) and 43% lower daylight activity (p = .006) in week 1 compared with control subjects. The relative amplitude of the sleep-wake cycle was attenuated by 6% in patients (p = .025); they were phase delayed by 55 minutes (p = .023) and had significantly lower sleep efficiency (p = .030). Total (p = .002) and daylight activity (p = .001) increased after 4 weeks of treatment in SAD patients. Moreover, BLT led to increase of relative amplitude (p = .005), advance of delayed rhythms (p = .036), and improved sleep efficiency (p = .011) in patients. Intradaily stability, measuring the strength of coupling of the rhythm to external zeitgebers, increased by 9% both in patients and healthy control subjects (p = .032).*
Conclusions: *Treatment with BLT normalizes disturbed activity patterns and restores circadian rhythms in SAD patients. BLT might also stabilize the circadian rhythm in nondepressed individuals during the fall-winter season.*

Key Words: Depression, seasonal affective disorder, light therapy, activity, actigraphy, circadian rhythms

Seasonal affective disorder (SAD) is a subtype of major depressive or bipolar disorder with recurrent affective episodes at the same time of the year. Most frequently, patients experience depressive episodes during the fall-winter season (fall-winter depression), which are occasionally followed by hypomanic (or more seldom manic) episodes during the successive spring-summer period (Rosenthal et al 1984; American Psychiatric Association 2000). The prevalence of the disorder has been estimated between 1% and 10% in the general population, depending on the diagnostic criteria and the latitude where the measurements are taken (Kasper et al 1989b; Blazer et al 1998; Mersch et al 1999; Magnusson 2000). The burden of SAD is high for the individual, and the socioeconomic impact of the disorder is significant. Bright light therapy (BLT) administered in the morning has been proposed as an effective treatment in this condition (Eastman et al 1998; Lewy et al 1998; Terman et al 1998). Moreover, BLT is highly accepted among patients, poses low costs for the health system, and lacks major side effects (Wirz-Justice 1998).

Actigraphy, which is a method for objectively measuring subjects' circadian sleep and activity patterns with high-resolution time series, has been used both in research and clinical settings for many years (Tryon 1991). Further technological advances have made the construction of miniaturized wrist-worn devices with sufficient memory for longer recording periods possible. Actigraphy has been successfully employed in research of psychiatric disorders, e.g. sleep disturbances (Blood et al 1997; Krahn et al 1997), mood disorders (Kripke et al 1978; Lemke et al 1999), dementia (Ancoli-Israel et al 2003b), attention-deficit/hyperactivity disorder (Inoue et al 1998), and different psychopharmacological studies (Stanley 2003). In contrast to electrophysiological techniques, wrist actigraphy allows ambulatory measurements in patients' natural environment with minimal interference to the subjects' lifestyle (Ancoli-Israel et al 2003a).

Teicher et al (1997) have reported on rest-activity disturbances in SAD, but to our knowledge, there exists no published study measuring the effects of BLT in SAD with actigraphy. The aim of the present research project was to examine chronobiological disturbances in a cohort of patients suffering from SAD, to assess the effects of BLT on these parameters in a naturalistic setting over 1 month, and to compare these results with a matched control group likewise treated with BLT. Based on previous research (Raoux et al 1994; Teicher et al 1997; Lemke et al 1999), we formulated the a priori hypothesis of reduced activity levels; blunted, delayed, and disrupted circadian rhythms; and disturbed sleep in patients compared with control subjects. Furthermore we hypothesized improvement of these parameters during BLT.

Methods and Materials

Subjects

Seventeen patients (13 female patients and 4 male patients) with the fall-winter type of SAD and 17 sex- and age-matched healthy subjects were recruited for this research project during fall and winter at the outpatient clinic for SAD of the Department of General Psychiatry (Medical University of Vienna) by means of self-referrals and advertisements. Patients had to fulfill the Rosenthal and DSM-IV-TR criteria (Rosenthal et al 1984; American Psychiatric Association 2000) for SAD. A Global Seasonality Score (GSS) of 10 or higher on the German version of the Seasonal Pattern Assessment Questionnaire (SPAQ-D) (Kasper 1991) and a total score of 20 or higher as measured by the Structured Interview Guide for the Hamilton Depression Rating Scale, SAD

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version (SIGH-SAD, 29 items) (Williams et al 1992) was required; patients with subsyndromal SAD (s-SAD) (Kasper et al 1989a) or with axis-I comorbidity were excluded from the study. Control subjects were screened with the Structured Clinical Interview for the DSM-IV (SCID) (First et al 1996) and denied any evidence of present or past psychiatric disorders. Furthermore, control subjects with a GSS of higher than 6 were excluded by the protocol. Patients and control subjects had to be in good overall health; subjects with somatic illnesses influencing activity levels or circadian rhythms were not included. The use of any psychopharmaceutical medication was disallowed throughout the entire study period; psychotropic drugs had to be discontinued 2 weeks before study entry (5 weeks for fluoxetine). None of our patients had ever been treated with antipsychotic depot medication. Three subjects received stable doses of atorvastatin 10 mg for hypercholesterinemia; two female control subjects were taking birth control pills. The Ethics Committee of the Medical University of Vienna gave approval to this research protocol; all subjects provided written informed consent prior to any study procedures.

Light Therapy and Activity Monitoring

Patients and control subjects were equally assigned to 4 weeks of treatment with BLT during the fall-winter season (from October to February) of 2 consecutive years. Subjects were advised to perform BLT every day in the morning between 7:00 AM and 9:00 AM for half an hour at home. Portable light boxes emitting full-spectrum visible light with a brightness of 10,000 lux measured at a distance of 60 cm were used. Furthermore, study participants were instructed to wear activity monitors (Actiwatch Plus by Cambridge Neurotechnology Ltd., Cambridgeshire, United Kingdom) on their nondominant wrist. Subjects removed the actigraphs only when showering or bathing during the study period. The device contains a piezoelectric accelerometer that records the intensity and duration of all movements over .05*g*. Recording epoch was adjusted to 1 minute. After 4 weeks of daily BLT and continuous actigraphic measurements, all study subjects had a second clinical evaluation, and therapy outcome was evaluated using SIGH-SAD.

Data Collection and Statistical Analysis

Data were downloaded to a computer and processed subject by subject with the Actiwatch software (Actiwatch Sleep Analysis 2001 software, Version 1.19; Cambridge Neurotechnology Ltd., Cambridgeshire, United Kingdom). Data were carefully reviewed and checked for missing values and outliers. Total, daylight, and dark activity, derived from the actual sunrise and sunset times in Vienna (16° 20' eastern longitude and 48° 13' northern latitude) at the time of the measurements, were calculated. Furthermore, a nonparametric circadian rhythm analysis (Van Someren et al 1999) of the data and cosinor analysis (assuming that a sinusoidal curve can be fitted to the 24-hour activity rhythm) were performed (Nelson et al 1979). A sleep analysis was conducted with the sensitivity of the algorithm set to "medium" to estimate actigraphic sleep parameters. Resulting data were further analyzed with SPSS for Windows (SPSS for Windows, Release 8.0; SPSS Inc., Chicago, Illinois) for differences between patients and control subjects in weeks 1 and 4 utilizing Student *t* test. We carried out a Levene test for equal variances before computation of the *t* tests and applied a correction whenever the assumption was not met. Furthermore, we used a two-way, mixed design analysis of variance (ANOVA) model with Pillai's trace as a multivariate test, which is not influenced by violations of the sphericity assumption. We performed separate ANOVAs for each outcome measure with time (week 1, week 2, week 3, week 4) as a within-subjects factor and group (patients or control subjects) as a between-subjects factor to assess treatment effects. A preplanned contrast of the interaction (Rosnow and Rosenthal 1989) between patients versus control subjects and week 1 versus week 4 was calculated. When the interaction was significant, we examined simple main effects with one-way repeated measures ANOVA. Furthermore, we performed post hoc tests employing a Bonferroni correction when there was a significant effect of time. The $p \leq .05$ level of significance was adopted. All statistical comparisons were two-tailed.

Results

Mean age in our sample was 36.9 ± 13.5 years (arithmetic mean ± SD) and was not statistically different between patients and control subjects [$t(32) = .233$, $p = .817$]. Body weight [$t(32) = .377$, $p = .709$] and height [$t(32) = .177$, $p = .861$] did also not differ between patients and control subjects. The mean time between sunrise and sunset at the time of the measurements (09:19 ± 00:46) was not different between SAD patients and healthy subjects [$t(32) = 1.689$, $p = .101$]. The mean week of the year, when study subjects entered the study, was also not statistically different between patients and control subjects [$t(28.836) = -.163$, $p = .872$]. Mean GSS for patients was 16.0 ± 2.8, and they obtained a total SIGH-SAD score of 29.5 ± 4.7 when entering the study. In accordance with other published SAD material from Middle Europe (Winkler et al 2002), our SAD patients showed a high degree of atypical depressive symptoms with a mean atypical SIGH-SAD subscore of 13.8 ± 3.4. Patients showed good overall clinical response to BLT: after 4 weeks of treatment the mean total SIGH-SAD score dropped to 5.3 ± 2.3 [$t(16) = 22.000$, $p < .001$]. The SIGH-SAD scores were consistently low in the control group in week 1 (1.4 ± 1.5) and week 4 (1.5 ± 1.2) and did not change significantly during treatment [$t(16) = -.566$, $p = .579$]. No severe adverse events leading to cessation of treatment were observed during this study.

Activity Levels

Total activity as measured by wrist actigraphy was reduced by 32.6% in SAD patients compared with healthy control subjects in week 1 [$t(32) = 2.260$, $p = .031$] (Figure 1A). Two-way ANOVA showed a significant main effect of time [$F(3,30) = 6.150$, $p = .002$]. As the interaction contrast between patients/control subjects and week1/week4 was significant [$F(1,32) = 8.448$, $p = .007$], we performed separate one-way repeated measures ANOVAs for patients and control subjects: there was a highly significant increase in total activity in patients [$F(3,14) = 8.447$, $p = .002$] starting from week 2 ($p = .001$) as confirmed by post hoc tests. However, we failed to observe a change during treatment in healthy individuals [$F(3,14) = .432$, $p = .734$]. After 4 weeks of treatment, there was no statistically significant difference in total activity between SAD patients and control subjects [$t(32) = .869$, $p = .391$] (Figure 1B).

Daylight activity (i.e., activity between sunrise and sunset) was likewise lower in patients by 43.1% in week 1 [$t(19.860) = 3.067$, $p = .006$]. Two-way ANOVA resulted in a highly significant effect of the within factor [$F(3,30) = 10.312$, $p < .0001$] and the interaction contrast [$F(1,32) = 13.699$, $p = .001$]. Further analysis showed an increase in daylight activity in patients [$F(3,14) = 11.264$, $p = .001$] from week 2 on ($p = .0004$) and no significant change in control subjects [$F(3,14) = .701$, $p = .567$] (Figure 2A). In week 4, group differences in daylight activity were statistically