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Short communication

The relation between chronotype and treatment outcome with light therapy on a fixed time schedule

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ABSTRACT

Background: Seasonal affective disorder (SAD) is characterized by recurrent episodes of major depression in a seasonal pattern. The therapy of choice is light therapy (LT). It is suggested that LT should be administered relative to the chronotype of the patient, with the optimal timing earlier for morning than for evening types. This study aims to retrospectively investigate the relation between chronotype and the effect of LT on a fixed time in the morning in a population of SAD patients.
Methods: Data from four different studies conducted at the University Center of Psychiatry in Groningen, the Netherlands was used. Data from 132 patients was used (103 women). Depression score was determined by a structured interview (SIGH-SAD) prior to LT and after LT. Prior to LT morningness/eveningness preference of the patient was determined by the 'Morningness/Eveningness Questionnaire' (MEQ). All patients received LT at 8:00 AM at the clinic, independent of chronotype.
Results: Patients had an average MEQ score of 51.5 ± 8.2. There was no significant relationship between MEQ score and therapy success as measured with the SIGH-SAD ($F_{2,129}=0.05$, ns). When patients were divided by chronotype (ranging from definite morning to moderate evening) no significant relation between MEQ score and therapy success was found ($F_{2,129}=0.02$, ns).
Limitations: Retrospective design.
Conclusions: The lack of a significant relationship between chronotype, as measured with the MEQ, and therapy success with LT at a fixed timepoint may indicate that the anti-depressive effect of morning light in SAD patients is not explained by a phase shift of the biological clock.

1. Introduction

Seasonal affective disorder (SAD) is a mood disorder characterized by recurrent episodes of major depression with a seasonal pattern (Rosenthal et al., 1984). For winter type SAD, light therapy (LT) is the treatment of choice in the Netherlands (Spijker et al., 2013). Although the effectiveness of LT is well established and the response rates are high the mechanism underlying the effect is still unclear. Since the introduction of SAD and the positive effects of LT in 1984 by Rosenthal and colleagues, various theories have been discussed. One of the most prominent hypotheses explaining the success of light therapy is the phase advancing effect of properly timed morning light (Lewy et al., 1988). SAD patients are suggested to have a delayed circadian phase underlying depressive mood. Morning light is thought to be therapeutic as it causes a corrective phase advance. This hypothesis is later specified to the "phase angle difference" hypothesis, where it is not just the phase delay in SAD patients, but the internal phase delay compared to the mid-point of sleep that is the crucial factor for the therapeutic response (Lewy et al., 2006).

In 2001, Terman et al. showed a correlation between the magnitude of the phase advance with morning light exposure and therapy success in SAD patients (Terman et al., 2001). Based on this study an optimal timing of light therapy was defined according to an individual's circadian phase (Terman and Terman, 2005). This optimum is found to be 8.5 h after dim light melatonin onset (DLMO), a circadian phase marker. Although DLMO is a good phase marker, it is hard to obtain in the clinical practice, as the determination is both time consuming and expensive. Instead of measuring DLMO, a reasonable approximation of the timing of DLMO can be obtained with collecting a morning-evening score with the morningness-eveningness questionnaire (MEQ)

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developed by Horne and Östberg (Horne and Ostberg, 1976). The rating of this questionnaire is strongly correlated to circadian phase in SAD (Terman and Terman, 2001). By making use of an individual's MEQ score, a reasonable estimation of the optimal timing of light can be made.

2. Aims of the study

At the University Medical Center Groningen (UMCG), light therapy for SAD patients is scheduled at a fixed clock time; all patients receive light at 8AM. In the current study we aimed to see whether the therapy response at this fixed time point is different for early and late chronotypes. To our knowledge, this is the first study to link chronotype with therapy success on a fixed LT time. We hypothesize that patients with a lower MEQ score, more evening type, show a better therapy outcome than morning types, as LT on 8AM would be more optimal for late types.

3. Methods

3.1. Study design and participants

For the analysis, data from four different studies conducted between 2005 and 2011 (Bosker et al., 2015; Gordijn et al., 2012; Meesters and Duijzer, 2011; Meesters et al., 2011) are used. The studies have all been performed in the SAD outpatient clinic of the UMCG, the Netherlands. For specifications of the different light treatments see Table 1. All studies were approved by the Medical Ethical Committee of the University Medical Center Groningen.

A total number of 132 patients have been retrospectively selected based on the following criteria: all subjects met the criteria of major depressive disorder with a seasonal (winter) pattern according to the DSM-IV-TR and did not suffer from other DSM-IV classified psychiatric disorders as assessed by the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998). The group consisted of 29 men and 103 women, mean age ± SD 37.4y ± 11.9 (Table 1).

3.2. Procedures

The Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorder 24 item version (SIGH-SAD) was used to assess severity of depression (Williams et al., 1988). Prior to LT the morningness-eveningness questionnaire by Horne and Östberg was used to assess morningness-eveningness preference (Horne and Ostberg, 1976).

SIGH-SAD ratings were assessed before LT and one week after the end of LT. In the three studies which compared different methods of light therapy no significant differences between light conditions were observed: study 1, main effect "condition" $F(2,49)=0.73$, ns; study 2, main effect "condition" $F(1,20)=0.012$, ns; study 3, 67% recovery for standard treatment and 63% recovery for experimental treatment, ns. The fourth study did not use an experimental light therapy, as this study looked at gene expression in SAD patients (Bosker et al., 2015). In study 1 and 2, patients received 2 weeks of LT, while in study 3 and 4 patients received 1 week of LT. No significant effect of treatment duration was found (Knapen et al., 2014). For the current analysis we pooled the data of all studies and all different light conditions.

All patients received light therapy at 8 A.M. at the clinic, independent of their chronotype.

3.3. Statistical analysis

Therapy outcome is defined as the percentage decrease in SIGH-SAD score comparing the rating 1 week after LT with the rating just prior to LT. Responders were calculated as patients with a decrease of at least 50% in their depression score.

Under the hypothesis that there is an optimum in the therapeutic response to light for a certain chronotype, a quadratic curve fitting was used to correlate MEQ score with therapy outcome. In addition, based on the MEQ score the patients have been separated into 5 chronotype groups (1=definitely evening, 2=moderately evening, 3=intermediate, 4=moderately morning, 5=definite morning). Another quadratic curve fit is done, correlating chronotype group and therapy outcome.

4. Results

Patients had an average MEQ score of 51.5 ± 8.2 (range 32–70). There were no definite evening chronotypes, moderate evening: 12, intermediate: 95, moderate morning: 23, definite morning: 2. Patients had an average proportional change in depression score of 68% ± 29 (range −36% to 100%, a positive change resembles a reduction in depression score). The percentage responders (decrease in depression score of equal or more than 50%) amounts to 76% (n=100).

The individual therapy outcome data show a large variation. Most of the patients show a response to the therapy, having a therapy outcome between 40–100%. There are 3 patients who do not respond to the therapy (therapy success $<10\%$) and two patients show a worse depression score after light therapy (therapy success $<-10\%$). No significant quadratic correlation between MEQ score and therapy outcome was found ($F_{2,129}=0.05$, ns) (Fig. 1).

When patients were binned by chronotype score, no significant relation between chronotype group and therapy outcome was found either ($F_{2,129}=0.02$, ns). The definite morning group shows

Table 1
Characteristics of subjects, light treatment and results.

		Study			
		Study 1	Study 2	Study 3	Study 4
Participants (n)		54	42	17	19
Age mean in years (± SD)		38.2 (± 11.7)	37.1 (± 13.1)	39.2 (± 12.3)	33.9 (± 8.7)
Baseline SIGH-SAD score (mean ± SD)		26.3 (± 5.8)	24.9 (± 5.1)	24.7 (± 7.1)	30.3 (± 6.3)
Proportional reduction SIGH-SAD score in % (mean ± SD)		66.2 (± 34.2)	71.2 (± 23.8)	64.3 (± 26.2)	67.2 (± 27.4)
MEQ (mean ± SD)		51.9 (± 10.7)	50.7 (± 2.8)	52.3 (± 7.1)	51.3 (± 9.4)
Light specification[a]	Standard	5000 K (10,000 lx)	5000 K (10,000 lx)	5000 K (10,000 lx)	5000 K (10,000 lx)
	Experimental	17,000 K (10,000 lx)	17,000 K (750 lx)	LED Blue light 470 nm (100 lx)	n/a
Years of study		2005/2006	2008/2009	2010/2011	2007/2008

[a] All light conditions except the LED Blue light condition: full spectrum light, without UV.