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The effects of low-intensity narrow-band blue-light treatment compared to bright white-light treatment in seasonal affective disorder

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ABSTRACT

Background: Ever since a new photoreceptor was discovered with a highest sensitivity to 470–490 nm blue light, it has been speculated that blue light has some advantages in the treatment of Seasonal Affective Disorder (SAD) over more traditional treatments. In this study we compared the effects of exposure to narrow-band blue light (BLUE) to those of broad-wavelength white light (BLT) in the treatment of SAD.

Methods: In a 15-day design, 45 patients suffering from SAD completed 30-min sessions of light treatment on 5 consecutive days.

21 subjects received white-light treatment (BLT, broad-wavelength without UV, 10 000 lx, irradiance 31.7 W/m^2), 24 subjects received narrow-band blue light (BLUE, 100 lx, irradiance 1.0 W/m^2). All participants completed weekly questionnaires concerning mood and energy levels, and were also assessed by means of the SIGH-SAD, which is the primary outcome measure.

Results: On day 15, SIGH-SAD ratings were significantly lower than on day 1 (BLT 73.2%, effect size 3.37; BLUE 67%, effect size 2.63), which outcomes were not statistically significant different between both conditions.

Limitations: Small sample size.

Conclusions: Light treatment is an effective treatment for SAD. The use of narrow-band blue light is equally effective as a treatment using bright white-light.

Seasonal Affective Disorder (SAD), winter type, is characterized by recurring episodes of major depression with a seasonal pattern (Rosenthal et al., 1984; APA, 1994). Light therapy is a well-established, effective treatment with high response rates and minor adverse effects (Wirz-Justice et al., 2013; Meesters and Gordijn, 2016). The interest in treating SAD sufferers with blue light has grown since non-image-forming photoreceptors were discovered in the retinal ganglia cells and their influence on the biological clock and other brain regions was examined (Provencio et al., 2000; Berson et al., 2002; Hattar et al., 2002). The effects of blue-enriched light were found to be superior to placebo consisting of a deactivated ion-generator in treating SAD (Desan et al., 2007). However, these effects were not superior to those of exposure to standard bright-white light (Meesters et al., 2011; Gordijn et al., 2012). In studies comparing the effects of blue light with those of red light, the blue light was shown to be superior (Glickman et al., 2006; Strong et al., 2009).

In this study, the effects of narrow-band blue light (BLUE) are compared to those of bright white-light treatment (BLT) in the treatment of SAD.

This research protocol was approved by the Medical Ethical Committee of the University Medical Center Groningen. This study has been registered in the Netherlands Trial Register (TC = 4342).

1. Methods

Subjects were recruited from the SAD outpatient clinic of the University Center for Psychiatry in the winter of 2010/2011 (between October 1 and February 10). They were provided with written information and an invitation for a screening visit at the clinic. After assessments by means of a standardised structured interview (the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998)), subjects meeting the criteria of a major depressive disorder with seasonal pattern according to the DSM-IV-TR (APA, 1994) were included for further screening.

The severity of the symptoms was assessed by means of the Structured Interview Guide for the Hamilton Depression Rating Scale – Seasonal Affective Disorder version (SIGH-SAD; Williams et al., 2002) and the Seasonal Pattern Assessment Questionnaire (SPAQ, Rosenthal

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et al., 1987). Inclusion criteria were a SIGH-SAD score of ≥18 a Global Seasonality Score of the SPAQ ≥ 11 (Kasper et al., 1989) and at least a moderate degree of suffering from seasonal complaints.

The 15-day study protocol started at no more than 7 days after the screening visit. Participants were offered 30-min light therapy sessions at the clinic on 5 consecutive working days (days 4–8, 5 sessions with light exposure), between 7.30 and 8.30 a.m. and were followed for another week. Weekly assessments of mood and fatigue were performed during visits to the clinic on days 1, 8, and 15.

1.1. Light treatment

Subjects were randomly assigned (controlled for age and gender) to one of the treatment modalities.

BLT was delivered by means of a white fluorescent lighting device (EnergyLight HF3319, Philips Drachten, The Netherlands), correlated color temperature 5000 K, vertical photopic illuminance at 20 cm usage distance = 10 000 lx, irradiance 31.7 W/m2; equivalent melanopic illuminance of 8620 m-lux).

BLUE (goLITE HF3320, Philips Drachten, The Netherlands) characteristics were: peak LED wavelength 470 nm (full-width half-maximum 25 nm), usage distance 50 cm positioned on a table top at 45 degrees sideways, vertical photopic illuminance at eye position = 100 lx, irradiance 1.0 W/m2, equivalent melanopic illuminance 770 m-lux. The spectral distribution of these two treatment modalities can be found in our study on the effects of exposure to these fixtures in sufferers from sub-syndromal SAD (Meesters et al., 2016).

Both fixtures were used in a normally-lit room, with a single device and a single subject in the room. Taking this into account, the BLUE condition actually was blue-enriched white light. Assuming a 3000 K TL spectrum, and 250 lx as average background illumination, the effective equivalent melanopic illuminance in both cases increased by 115 m-lux, rendering the BLT condition one order of magnitude higher on melanopic illuminance.

1.2. Assessment and procedure

Both conditions started on day 1 (Friday) with a baseline measurement consisting of a SIGH-SAD interview (with the interviewers blind to the light condition), the Beck Depression Inventory, second version (BDI-II-NL, Beck et al., 2002) and a fatigue self-rating questionnaire (Short Fatigue Questionnaire, SFQ; Alberts et al., 1997). Subjects' expectations of the effects of light therapy were evaluated by means of a 6-item questionnaire consisting of 5-point scale (1 − 5) ratings on the subjects' expected benefits from each light therapy (white and blue), whether they thought either was a logical treatment and whether they would recommend either or both to a friend. They filled out this questionnaire before having seen the light fixtures. Subjects were then randomly assigned to either condition, with gender and age distributed evenly over the two groups.

The SIGH-SAD, the BDI-II-NL and SFQ were repeated on day 8 (immediately following the 5th light session), and again on day 15.

1.3. Statistical analysis

Prior to the design a power analysis was conducted based on the principles of an inferiority study and a desired power of 0.9, $p < 0.05$. The minimal the sample size was found to be 34 (2 × 17).

Baseline differences between the two conditions for the scores on the SIGH-SAD, the BDI-II, and the SFQ were tested by means of *t*-tests (continuous outcomes) and chi-square tests (dichotomous outcomes).

Effect sizes (Cohen, 1988) were calculated for each condition and reflect the differences between baseline (day 1) and day 15. Results were based on weekly assessments of the two conditions and were compared by means of repeated measures ANOVA. A responder was defined as a subject who improved by at least 50%.

In a secondary analysis, the potential impact of gender and age on outcome was examined. To this end, the interaction time*-condition*gender and time*condition*age were added to the models.

Analyses were carried out using SPSS 20. A two-tailed alpha level of 0.05 was used to determine statistical significance.

2. Results

Originally 62 participants were invited for a selection interview. Seventeen of these were excluded due to unclear diagnoses, symptoms that were too mild or factors affecting mood. Hence, 46 participants were included in the design. In the course of the study one participant was excluded because of a somatic illness.

Ultimately, 21 participants (16 women, mean age 35.56 ± 13.15, range 20–63 yr.; 5 men, mean age 39.8 ± 11.41, range 26–51 yr.) received BLT and 24 participants (18 women, mean age 37.06 ± 13.36, range 22–59 yr. and 6 men, mean age 46.67 ± 14.46, range 25–62 yr. received BLUE. The Global Seasonality Scores of the SPAQ were as follows: 15.05 ± 2.44, range 12–21 (BLT) and 14.92 ± 3.02, range 11–22 (BLUE).

Both therapies were found to be highly effective in reducing SIGH-SAD scores and improving energy levels as measured by the atypical symptom section of the SIGH-SAD.

When taking the scores of the SIGH-SAD and using Terman's criteria of remission (at least a 50% improvement and a score of < 8 on day 15; Terman et al., 1989), 15 participants in the BLT condition and (71.4%) and 14 (58.3%) for participants in the BLUE condition showed improvement. The difference in proportions meeting these specific criteria was not statistically significant.

No significant differences were found between the effects of the light conditions on any of the outcome measures (Table 1). This also holds when the results are controlled for gender, age, severity of complaints (as measured with the SIGH-SAD, HRSD, the Atypical Symptoms, or with the BDI-II, or SFQ), and expectations as measured with a self-rating questionnaire on day 1.

In both conditions the complaints assessed with the different instruments decreased during the 15-day period (Table 1): SIGH-SAD 24 items, main effect 'time' $F(2, 42) = 148.3$, $p < 0.001$), with no statistically significant differences between conditions (main effect "condition" $F(1, 43) = 0.904$, ns) nor between conditions over time (interaction effect "time*condition" $F(2, 42) = 2.82$, ns). When the SIGH-SAD was subdivided into "typical symptoms" (17-item Hamilton rating, Table 1) the following were found: a main effect "time" $F(2,42) = 62.63$, ns; main effect "condition" $F(1,43) = 0.05$, ns; main effect "time*condition" $F(2,42) = 1,56$, ns) and "atypical symptoms" (7 atypical items, Table 1), a main effect "time" $F(2,42) = 121,14$, $p = < 0.001$; main effect "condition" $F(1,43) = 2.33$, ns; main effect "time*condition" $F(2,42) = 1.43$, ns). On the basis of the weekly-assessed self-rating instruments results for the BDI-II were a main effect "time" $F(2,41) = 53,04$, $p < 0.001$; main effect "condition" $F(1,42) = 2.21$, ns; main effect "time*condition" $F(2,41) = 3.18$, ns. For the SFQ a main effect "time" $F(2,38) = 37.44$, $p < 0.001$; main effect "condition" $F(1,39) = 1.58$, ns; main effect "time*condition" $F(2,38) = 2196$, ns were found respectively.

3. Discussion

Both treatment conditions were highly effective in treating SAD. No differences in therapeutic outcome were found between exposure to BLUE and BLT. These findings are in line with the results of (Andersen et al. 2009) in an SAD population and the results from a study in sufferers of sub-syndromal SAD (winter blues; Meesters et al., 2016).

If the blue part of the light spectrum is essential for the effects of SAD treatment, it will not come as a surprise that we failed to find a difference in treatment outcome. The blue part of the BLT light spectrum has higher irradiance than BLUE. This study does, therefore, not

Table 1
Weekly average scores (± SD).

Instrument *(range)*	Condition	N	Day 1 (± SD)	Day 8 (± SD)	Day 15 (± SD)	Effect Size d	% Response	Responder N (in %)
SIGH-SAD *(0–75)*	BLT	21	25.95 (± 4.95)	13.71 (± 7.23)	6.96 (± 6.23)	3.37	73.2	18 (85.7)
	BLUE	24	23.71 (± 4.84)	10.96 (± 6.20)	7.83 (± 7.05)	2.63	67.0	16 (66.7)
HRSD *(0–52)*	BLT	21	13.48 (± 4.14)	7.81 (± 4.62	3.71 (± 3.73)	2.48	72.5	17 (81.0)
	BLUE	24	12.71 (± 3.78)	6.79 (± 4.61)	4.79 (± 5.48)	1.68	62.3	16 (66.7)
ATYP *(0–23)*	BLT	21	12.48 (± 3.66)	5.90 (± 4.07)	3.24 (± 3.11)	2.72	74	17 (81.0)
	BLUE	24	11.00 (± 3.56)	4.17 (± 2.60)	3.04 (± 2.46)	2.60	72.4	21 (87.5)
BDI-II *(0–63)*	BLT	21	25.67 (± 7.32)	13.29 (± 9.03)	6.75 (± 6.46)	2.74	73.7	17 (81.0)
	BLUE	24	24.77 (± 6.60)	15.75 (± 9.97)	13.17 (± 11.65)	1.17	46.8	13 (54.2)
SFQ *(4–28)*	BLT	21	23.76 (± 3.91)	17.40 (± 7.35)	11.8 (± 6.53)	2.22	60.5	12 (57.1)
	BLUE	24	23.57 (± 3.98)	17.79 (± 7.05)	16.22 (± 7.12)	1.27	37.6	11 (45.8)
PEQ *(6–30)*	BLT	21	22.32 (± 4.95)					
	BLUE	24	23.05 (± 4.14)					

Cohen's d effect size and response percentage from day 1 to day 15, ± SD rated by the Hamilton Rating Scale for Depression (HRSD, 17 items), the scale that has been adapted for seasonal symptoms SIGH-SAD (24 items), and the atypical symptoms separately (ATYP, 7 items), the score on the Beck Depression Inventory-II (BDI-II) and the Short Fatigue Questionnaire (SFQ) for each condition. BLT = bright white-light treatment; BLUE = narrow-band blue-light treatment. Responder = subject with an improvement of at least 50%. PEQ = Patients Expectations Questionnaire.

make it clear if the effects of light treatment are only due to the blue part of the light spectrum. Low-intensity blue light yields the same effects as light exposure to full-spectrum light. It has been suggested that SAD patients have a decreased retinal sensitivity in the non-image forming light-input pathway (Roecklein et al., 2013) and that this lowered sensitivity can cause complaints related to differences in neurobiological and behavioural responses (e.g. alertness, circadian photo entrainment).

Since irradiance of the blue part of BLT is a little larger than that in BLUE, this may explain the slightly, though not significantly, higher responses after BLT. A higher irradiance of the blue light in both conditions may, however, also lead to better results, although blue-enriched light has been shown not to be superior to full-spectrum light in treating SAD (Gordijn et al., 2012).

This does not mean that the other light wavelengths are superfluous in the treatment of SAD. The results of this study can also lead to the assumption that blue light only has a minor role in the treatment of SAD. A recent study has shown no differences in effects after exposure to blue vs. “blue-free” light in treating SAD, but the results of that study may have been influenced by the relatively late enrollment of the subjects (Anderson et al., 2016).

While creating a methodologically valid placebo condition for light treatment is impossible, the effects seen in this study may still be due to placebo. Subjects had to come to the clinic every morning, which in itself may have strong placebo effects (may be having to come to the clinic early in the morning is motivating and energizing in a direct physiological way). The response rates in this study are 73.2% and 67% respectively, which is relatively high compared to placebo responses from placebo-controlled studies. This makes it unlikely that the effects found here are exclusively due to placebo. In earlier studies on the clinical treatment of SAD, where the effects of extra ocular light were compared to a placebo condition (in the clinic), response rates for the placebo condition were 36% (Koorengevel et al., 2001). In an other study, the effects of light treatment at home compared to those of that of a de-activated ion generator, the response of the placebo condition was 11.1% (Desan et al., 2007), which is much lower.

As the sample size in this study was small, replication is necessary and conclusions can only be preliminary.

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Authors’ contributions

The original version of the experimental protocol was written by YM and VH. YM served as principal investigator. WBD participated in the clinical conduct of the trial and was research coordinator. The final manuscript was written by YM, with comments of all co-authors, all of whom read and approved the final manuscript.

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