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Published in:
Journal of Affective Disorders

DOI:
10.1016/j.jad.2011.08.016

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2012

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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The effects of blue-enriched light treatment compared to standard light treatment in seasonal affective disorder

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Article Info

Article history:
Received 16 June 2010
Received in revised form 14 August 2011
Accepted 16 August 2011
Available online 10 September 2011

Keywords:
Seasonal affective disorder
Light treatment
Blue-enriched light
Circadian system

Abstract

Background: One of the most frequently investigated hypotheses of the pathophysiology underlying Seasonal Affective Disorder (SAD) is a disturbance of circadian rhythms. Since the circadian system as well as other non-visual effects is especially sensitive to blue light, a new light therapy device with blue enriched polychromatic light was tested for its efficacy to treat SAD.

Methods: Within one winter 52 patients were treated in one of three conditions: 30 min full spectrum light (9000 lx, 5000 K), 30 min blue-enriched light (9000 lx, 17,000 K), or 20 min blue-enriched light. The study lasted 22 days with 10 days of morning-light treatment on weekdays during the first 2 weeks.

Results: Depressive symptoms (SIGH SAD) diminished over the 3-week period in all conditions, with no significant differences between conditions. The percentage responders were high, differing from 75%, 59% and 71% for the standard-LT, 30 min blue-enriched-LT, and 20 min blue-enriched-LT, respectively.

Conclusion: The lack of superiority of high intensity blue-enriched light over standard bright light treatment does not clearly support nor rule out the possibility of an important role for the circadian system or the blue sensitive non-image forming system in general, in the pathophysiology of SAD. The lack of a difference between conditions may also be the result of a saturated response to the high light intensities used. Recent data indeed suggest that low intensity blue-enriched light may be as effective as standard bright light treatment. The possibility of improving light therapy for SAD patients by applying light of shorter duration or at lower light intensities is highly relevant for optimizing treatment and will help to clarify the role of the circadian system and/or the non-image forming photoreceptors in SAD pathophysiology.


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1. Introduction

Seasonal Affective Disorder (SAD), wintertype, and successful exposure to bright artificial light treatment were for the first time described in a classic paper by Rosenthal et al. (1984). More studies of successful light treatment in SAD followed (Golden et al., 2005; Meesters et al., 1995; Terman et al., 1989; Terman and Terman, 2005; Thompson, 2001). Full-spectrum, white fluorescent light was first used as light source mimicking the distribution and range of visible and ultraviolet light in the sky (Partonen, 2001).

So far, the pathophysiology of SAD and the working mechanism of light in treating SAD have remained unclear. One of the most frequently investigated hypotheses is based on a disturbance of the circadian system. It was hypothesized that SAD sufferers in their depressed state had a delay in
melatonin secretion when compared to healthy controls, reflecting a late phase of the endogenous circadian oscillator (Lewy et al., 1987, 1988). In several studies it was argued that light administered at certain times of day corrected this disturbed phase and thereby improved mood (Lewy et al., 1988; Terman et al., 2001). Whether this is in fact the mechanism behind light treatment in SAD remains unclear (Koorengevel et al., 2003; Meesters, et al., 1993; Wirz-Justice et al., 1993), although the success of morning light treatment in particular is beyond doubt (Leyk et al., 1998; Terman et al., 2001).

Discussing the possible mechanisms underlying the positive effect of light therapy in sleep and mood disorders is important, not only to improve therapeutic strategies and to gain insight in the etiology of the disorders, but also to increase our knowledge of the functional role of the biological clock and the non-image forming system in general in everyday life. The purpose of the present study is to test a new therapeutic light source for the treatment of SAD, whose development is based on our current knowledge on the spectral sensitivity of the non-visual image forming photosensory system.

The discovery of a new photoreceptor besides the hitherto well-known rods and cones in the retina of mammalian eyes (Berson et al., 2002; Hattar et al., 2002) is an important step forward in our understanding of the non-image forming effects of light. These light sensitive retinal ganglion cells play a major role in the transport of light information to the biological clock and other brain areas (Berson et al., 2002; Dacey et al., 2005; Drouyer et al., 2007). Melanopsin is the photosensitive pigment in the retinal ganglion cells with a peak sensitivity of approximately 480 nm (blue light). It was proved to be present in both animal (Hattar et al., 2002; Provencio et al., 1998) and human retinas (Dacey et al., 2005; Dkhissi-Benyahya et al., 2006; Provencio et al., 2000) and it serves a function as non-image forming photic pigment.

Several studies showed that the human circadian system is particularly sensitive to the short wavelength portion of the light spectrum. Brainard et al. (2001) and Thapan et al. (2001) showed that melatonin suppression is largest during exposure to a narrow band light stimulus between 460–480 nm. Exposure to 6.5 h of monochromatic light of 460 nm induced a circadian phase delay twice as large as exposure to monochromatic light of 555 nm with equal photon density (Lockley et al., 2003). The authors of this study conclude that the peak sensitivity of the human circadian pacemaker is shifted more to the blue part of the spectrum relative to the peak sensitivity of the three-cone visual photopic system, which peaks around 555 nm.

Wright and Lack (2001) and Wright et al. (2004) compared the effects of red light (660 nm), amber light (595 nm), green light (525 nm), blue/green light (497 nm) and blue light (470 nm) on their capacity to phase shift the salivary melatonin rhythm. Light with shorter wavelengths turned out to be more effective than light with longer wavelengths in suppressing nocturnal melatonin concentration and phase-delaying/advancing the melatonin rhythm. The two longer wavelengths did not produce any significant phase advances, the shorter wavelength showed melatonin onset advances ranging from 40–65 min. Warman et al. (2003) compared the phase advancing properties of a full-spectrum light pulse with a light pulse without long wavelengths. The white light pulse contained 185-fold more photons than the short wavelengths light. Exposure to the filtered morning light pulse, containing mainly short wavelengths, induced larger phase advances of the offset of the melatonin rhythm.

From these studies using narrow bandwidth or filtered light pulses, it is clear that the human circadian system is more sensitive to light with short wavelengths than to light with longer wavelengths. Also other non-image forming responses to light, such as an increased alertness, thermoregulation and heart rate, show a high sensitivity to short-wavelength light (Cajochen et al., 2005) and recently it was shown that emotional processes in the brain are modulated by exposure to blue light (Vandewalle et al., 2010). Although the discovery of the retinal ganglion cells containing melanopsin has been a great impulse for new studies on the effects of narrow band short wavelength light (blue light), the classical visual photoreceptors should not be neglected as far as their influence on the circadian system are concerned (Brainard and Hanifin, 2005; Drouyer et al., 2007; Hanifin et al., 2006). In two studies it was postulated that melanopsin itself has dual photosensory mechanisms and that long wavelengths may restore melanopsin photosensitivity (Melyan et al., 2005; Mure et al., 2007). In a recent study, Gooley et al. (2010) showed that the classical photoreceptor system clearly plays a role in non-image forming responses especially at the beginning of the light pulse.

So far, only a few studies using blue light in the treatment of SAD sufferers are known. These types of studies will increase our knowledge on the pathology and may improve our therapeutic tools to treat depression. In one study, a portable LED device was used. The spectral composition of this lamp shows peaks at 464 nm and 564 nm. Within the range of 400–700 nm about 48% of the energy is emitted in the range of 420 nm–508 nm, and 37% in the range of 512 nm–616 nm. In a relatively small controlled trial the effects of exposure to this light source were compared to those of an inactivated ion generator (placebo). The effects in the light condition turned out to be superior to those in the placebo condition (Desan et al., 2007), but it is unclear to what extent the spectral characteristics of the light in this study are responsible for the improvements observed, since no light was given in the control condition. In another study, the effects of exposure to the light of narrow-band light-emitting diodes (LED’s) were investigated. Blue light (468 nm) was superior in treating SAD sufferers when compared to dim red light (654 nm) (Glickman et al., 2006). Although the short wavelength light was superior to the longer wavelength in this study, SAD sufferers still showed some improvement after they had been exposed to the red light. No comparison was made with standard light treatment (full spectrum white light without UV). This last comparison was recently made in a study of Anderson et al. (2009). They found that blue monochromatic light in a lower photopic intensity than white light, but with the same amount of blue light, is similarly effective in treatment of SAD.

A new development in the field of light sources based on the current scientific knowledge is to produce broad spectrum white light sources obtaining more photons in the short wavelength region. In chronobiological terms this light is hypothesized to be more potent in inducing non-visual effects. Recently our group published a small study to test the hypothesis that a low intensity of blue enriched
light (30-min, 750 lx) is as effective as standard LT (30 min, 10,000 lx; Meesters et al., 2011) and concluded that both are effective treatments.

In the present study the same fluorescent tubes that emit a high portion of short wavelength light on top of the normal wavelengths were tested for their superiority in treating SAD in three relatively large groups. In a carefully controlled single blind setup, blue-enriched light (color temperature 17,000 K) was compared to standard light treatment (5000 K) in SAD patients. We hypothesized that blue-enriched light improves the therapeutic effects of light treatment leading to a higher response or the same response in a shorter time compared to standard light treatment.

2. Methods

2.1. Subjects

In the winter of 2005/2006 (between October 1st, and February 10th) all patients who entered the SAD outpatient clinic of the University Medical Center Groningen, The Netherlands, to receive light therapy were asked to participate. Approximately 200 patients known for winter depression are followed each year during autumn and winter and are completing the Beck Depression Inventory for Depression (BDI-II-NL, Beck et al., 2002) weekly, starting in the first week of September. As soon as the score is equal or higher than 15 the patient is invited to visit the clinic for light therapy. All patients that reached this score were asked to participate in the research project. If they considered participation they received written information, and were invited for an intake interview. New patients referred to the outpatient clinic were diagnosed by an experienced clinical psychologist and if suffering from winter depression they were informed about the research project. After they signed the informed consent they were scheduled for the intake interview; 52 subjects (40f, 12 m; 38.8y, sd 11.6) were included in the study, of whom 28 patients had received light therapy in previous years (“known” subjects) and 24 patients received light therapy for the first time (“new subjects”). Age was not significantly different between the two groups (“known” subjects: age 40.0y ± sem 2.2, range 22.2–61.4y; new subjects: age 37.3 ± sem 2.3, range: 20.2–55.9y, F(1,50) = 0.75, ns).

The intake interview consisted of two semi-structured standardized interviews, the Mini-International Neuropsychiatric Interview (M.I.N.I., Sheehan et al., 1998) and the Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal affective disorder 24 items version. (SIGH-SAD, Williams et al., 1994). If patients met the criteria of a major depressive disorder with a seasonal pattern, wintertype, according to the DSM-IV-TR (APA, 1994), and scored on the 24 items SIGH-SAD at least 18 they were included and assigned to one of the three conditions. No atypical score threshold was used in selection of the subjects. Researchers and interviewers were completely blind for the condition during the study period of 5.5 months. Also patients were not informed on their assignment, although subjects who received 20 min of treatment could know in what condition they were in.

The protocol was approved by the Medical Ethical Committee of the University Medical Center Groningen.

2.2. Light therapy

Light treatment consisted of 2 weeks standard light therapy (Standard-LT, 5000 K) with the Energy Light® (Philips Consumer Lifestyle, Drachten, The Netherlands) or 2 weeks high color light therapy with a specially modified Energy-Light®, equipped with blue-enriched white lamps of 17,000 K that emit a higher proportion of short wavelengths (Blue-enriched-LT, 17,000 K). Fig. 1 shows the comparison of the spectral power distributions of the standard and blue-enriched lamps. Subjects came to the department on 10 workdays (days 4–8 and days 11–15 in the protocol) and obtained either 30 min Standard-LT, 30 min Blue-enriched-LT or 20 min Blue-enriched-LT between 7:45 and 8:45 a.m. Intensity of the light measured at eye level in the direction of gaze was between 9000 and 10,000 lx for both conditions (Standard-LT: 3070 μW/cm², 8.4 * 10¹⁵ photons; Blue-enriched-LT: 3810 μW/cm², 10.4 * 10¹⁵ photons).

2.3. Assessment

If the patients met the inclusion criteria, they were asked to complete the BDI-II-NL, (Beck et al., 2002), and a specific expectation questionnaire aimed to evaluate the expectation of the effects of light therapy. This last questionnaire rated on a 5 point scale for both the Standard-LT and the Blue-enriched-LT whether subjects expected to benefit from the therapy, whether they thought it was a logical treatment, and whether they thought they would recommend this therapy to a friend.

Each condition started at day 1 (Friday) with a baseline measurement, conducting a SIGH SAD interview in addition to the self rating questionnaire BDI-II-NL. Subjects who did not meet the criterion for depression (SIGH-SAD ≥ 18) at day 1 were excluded. The SIGH-SAD and the BDI-II-NL were repeated on day 8 (shortly after the 5th light session), on day 15 (shortly after the 10th light session) and on day 22 (1 week after ending the light treatment). On day 22 an evaluation questionnaire was added to check the outcome of the expectations. Starting at day 1, subjects rated their mood on a daily schedule in the morning at least 30 min after waking up, preferably at 8.00 a.m., using the Adjective Mood Scale.
items, main effect “time” F(3,47) = 66.6, p < 0.001), with no significant differences between conditions (main effect “condition” F(2,49) = 0.73, ns) nor over time between conditions (interaction effect “time * condition” F(6,96) = 0.56, ns). The same pattern was found if the SIGH SAD was separated in “typical symptoms” (17 item Hamilton rating, Table 1, main effect “time” F(3,47) = 45.1, p < 0.001; main effect “condition” F(2,49) = 0.96, ns; interaction effect “time * condition” F(6,96) = 0.3, ns) and “atypical symptoms” (7 atypical items, Table 1, main effect “time” F(3,47) = 41.2, p < 0.001; main effect “condition” F(2,49) = 0.30, ns; interaction effect “time * condition” F(6,96) = 0.67, ns). Post-hoc analysis for all three outcome variables (SIGH SAD24, HAM17 and atypical symptoms7) revealed that a significant improvement was observed after the first week (day 8) compared to baseline (day 1) for all three treatments (post hoc p < 0.05). An even further significant improvement (post hoc p < 0.05) after the second week of treatment (day 15) compared to after the first week (day 8) was found for all treatments in all variables, except for the HAM17 in the Standard-LT condition (p = 0.13). No significant changes in severity of symptoms were observed 1 week after the last day of light treatment (day 22) for all variables in all conditions compared to the day immediately after light therapy (day 15), although the continuing reduction in depression scores in the 20 min Blue-enriched-LT condition almost reached significance (SIGH SAD F(1,16) = 3.9 p = 0.06; HAM17 F(1,16) = 4.3, p = 0.06).

The percentage response at day 22 (defined as the percentage change in SIGH SAD (24 items) rating relative to day 1) is not significantly different between conditions (Table 1); on

### Table 1

Average depression scores (± SD) during each 3-week period; Cohens d effect size and percentage response from day 1 to day 15 (immediately after light therapy) and from day 1 to day 22 (1 week after last light treatment), as rated by the Hamilton rating scale for Depression (HRSD, 17 items) and the scale adapted for seasonal symptoms SIGH SAD (24 items), and the atypical symptoms separately (7 items), including the score on the Beck Depression Inventory-II for each condition. Within subjects Contrast: * = p ≤ 0.001; † = p ≤ 0.01 compared to day 1.

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<th>Day 15 (SD)</th>
<th>Day 22 (SD)</th>
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average the percentage response at day 22 differs from 58.8% in the 30 min Blue-enriched-LT up to 71.0% in the 20 min Blue-enriched-LT condition and 74.7% in the standard-LT condition (F(2.49) = 1.2, ns). The average response at day 15, the last day of the light therapy, is lower but also not significantly different between conditions; it differs from 58.0% in both Blue-enriched-LT conditions up to 66.0% in the standard-LT condition (F(2.49) = 0.3, ns). Although not statistically significant from the other treatments, the most striking difference is the relatively low response at day 22 to the 30 min Blue-enriched-LT (58.8% compared to 71.0% and 74.7% in the 20 min Blue-enriched-LT and standard-LT condition respectively).

The percentage responders at day 22 (defined as a reduction in symptoms of ≥50%) to the different treatments, was higher than 70% in all conditions, with no significant differences between conditions (76%, 72% and 71% for standard-LT, blue-enriched-LT 30 and blue-enriched-LT 20 respectively, X^2 = 0.19, ns). The fraction of patients who recovered, (reduction in symptoms of ≥50% and ≤8 on day 22), slightly differed from 50% in Blue-enriched-LT 30 to 65% in Blue-enriched-LT 20 and 76% in Standard-LT, but also this difference was not significant (X^2 = 5.35, ns).

Part of the subjects included were already known for winter depression and received successful light therapy in previous winters (n = 28), others were diagnosed during the current year and received light therapy for the first time (n = 24). Obviously a difference in response percentage may be expected between these groups, because the “known” patients responded favorably to light therapy already in previous years, and it may be expected that a certain percentage of the “new” patients will be non-responders.

A statistical test with as an additional “between” factor – patient characteristic – (“known” or “new”), revealed that there is a significant interaction effect between the course of the SIGH SAD rating over time and the factor patient characteristic (F(3.44) = 3.9, p < 0.05). This means that the pattern of the SIGH SAD ratings over time between “known” and “new” subjects differed significantly. No interaction effect with treatment condition was found (F(6.90) = 0.7, ns), meaning that this difference in response between “known” and “new” subjects was not related to the type of the light treatment. Fig. 3 shows the course of SIGH SAD in the two groups, with treatment conditions combined. At day 15, no significant difference exists between “known” and “new” patients. The average reduction in depressive symptoms at day 15 is 55.7% (sem 6.2) in “known” and 66.4% (sem 6.5) in “new” patients (t-test, n.s.). One week after the light treatment the “new” subjects on average became a little bit worse (−8.6% sem 6.8), while the “known” subjects continued to show a slight improvement (21.0% sem 5.2) compared to day 15 (t-test, p ≤ 0.001).

As a consequence, the average response in SIGH SAD rating from day 1 to day 22 indeed shows a significant difference between “known” patients treated before, and “new” patients treated for the first time: “known” patients show a reduction in depressive symptoms of 76.7% ± 4.6, “new” patients a reduction of on average 57.8% ± 7.4 (F(1.50) = 5.0, p < 0.05). From the “known” patients 82% are defined as responders, 79% as recovered, according to the criteria defined before. In the “new” patient group these values are 63% and 46% respectively. Since the two groups did not differ according to age this cannot be the explanation for the observed differences.

Unfortunately, due to randomization, the “known” and “new” subjects were not evenly distributed over the different treatment conditions. The ratio of “known”/“new” patients for the different treatment conditions is: Standard-LT 12/5; Blue-enriched-LT 30 6/12; Blue-enriched-LT 20 10/7 (X^2 = 5.13, p = 0.08). Obviously especially in the Blue-enriched-LT 30 condition, the “new” subjects were overrepresented. This may explain the somewhat lower, although not significantly so, response rates and higher SIGH SAD scores on day 22 in the Blue-enriched-LT 30 condition (see Table 1 and Fig. 2).

3.2. Daily mood ratings, speed of the therapeutic effect

It could be hypothesized that the final result of the different treatments is similar, but that the speed with which this effect is reached differs between conditions. To test this
hypothesis, the subjects completed rating scales on mood, in the morning during all 22 days. In two subjects daily ratings were missing for one week (once in Standard-LT and once in the Blue-enriched-LT condition). These subjects were excluded for the present analysis. Fig. 4 shows the course of depressive mood (AMS) in the responders to the three different light treatment conditions (12 in each in condition). The severity of depressive mood significantly reduces over time ($F(21,13) = 5.2$, $p < 0.005$), with no significant overall differences between conditions ($F(42,28) = 0.93$, ns). To analyze the speed of the response, the moment at which an individual’s smoothed curve (3 days running average) crossed the midpoint value of the three highest and the three lowest AMS scores of that individual was calculated (arrows in Fig. 4). In the Standard-LT condition this point was reached on average at day 9.3 (sem 1.1), in the Blue-enriched-LT30 at day 9.2 (sem 1.0), and in the Blue-enriched-LT20 condition at day 11.0 (sem 0.9). Anova revealed no significant differences between conditions in the speed of the effect in responders ($F(2,33) = 0.96$, ns).

3.3. Expectations

On average there were no significant differences in expectations between groups to 4 out of the 6 different questions (ANOVA): 1) do you think you would benefit from standard-LT ($F(2,47) = 0.64$, ns), 2) do you think standard-LT is a logical treatment choice ($F(2,47) = 0.98$, ns), 3) would you advise standard-LT to a friend ($F(2,47) = 1.34$, ns), 4) do you think Blue-enriched-LT is a logical treatment choice ($F(2,47) = 1.61$, ns). The only significant differences were a somewhat more negative expectation of the Blue-enriched-LT20 group to both the question whether they thought they would benefit from the treatment with more blue light (2.6±0.2) compared to the Standard-LT group (3.3±0.2, $p = 0.01$; Post Hoc ANOVA) and the Blue-enriched-LT30 (3.1±0.1, $p < 0.05$) and whether they would advise it to a friend (2.5±0.2 in Blue-enriched-LT20) compared to both Standard-LT (3.2±0.2, $p = 0.01$) and Blue-enriched-LT30 (3.4±0.1, $p < 0.001$).

3.4. Age

To test whether the response to the different treatments related to age, the subjects were split in three equally large percentiles. Cut-off points for age were set at lower than or equal to 29.8y (17 subjects), between 29.8y and 45.3y (18 subjects), and higher than 45.3y (17 subjects). Overall there was a significant effect in response of age according to the SIGH SAD ($F(2,49) = 4.00$, $p = 0.05$). Post hoc analysis revealed that the youngest group had on average a worse response (52%±10) than the middle group (80%±5, $p < 0.01$). Both groups showed no significant difference from the oldest group (71%±6, ns). No significant interaction effect was found between age and condition ($F(4,43) = 0.18$, ns). Response percentage in young, middle and oldest group to the different light conditions were respectively Standard-LT: 60%, 83%, 82%, Blue-enriched-LT30: 41%, 78%, 82%, and Blue-enriched-LT20: 55%, 80%, 74%.

4. Discussion

The therapeutic responses after exposure to blue enriched light in SAD patients were not higher compared to exposure to standard light treatment, but treatment effect was high in all three cases. The effect of blue enriched light during sessions with a duration of 20 min did not differ from sessions with a duration of 30 min exposure to either standard light treatment or blue enriched light treatment, neither in final success nor in speed of the effect. The conclusion is based on the effects measured on day 22, one week after the last treatment day as performed in our previous studies, although the same pattern is observed on day 15 immediately after treatment. Success percentages are however higher one week after ending of the treatment compared to immediately after the last light session. Assessing the treatment effect one week later excludes the possibility that the effect is due to an acute effect of light. Meesters (1995) previously discussed that improvement ratings depend on the timing of assessment, showing that effects 10 days after ending of the treatment seemed more pronounced compared to immediately

![Fig. 4. A) Course of average daily mood ratings (depressive mood with Adjective Mood Scale of Von Zerssen). Arrows indicate the day at which depressive mood is crossing the average mood rating over the whole period for each condition as an indication of response speed. Gray bars indicate the 2 times 5 days timing of light treatment. B) Average mood rating (depressive mood with Adjective Mood Scale of Von Zerssen) over 22 days ± SD.](image-url)
after treatment. The fact that treatment effects of imaginary light observed immediately after therapy were gone 10 days after the end of the treatment while the effects of morning light became even more pronounced (Richter et al., 1992) supports the idea that assessment of the effect a few days after the last light session is better to compare the effectiveness of different therapy strategies.

Monochromatic blue light was previously found to be superior compared to monochromatic red light in the treatment of SAD sufferers (Glickman et al., 2006; Strong et al., 2009). We used polychromatic light with all wavelengths of the visible light spectrum available and with the blue part extended compared to the standard light treatment. The enrichment of the blue part of the spectrum did not lead to a higher response. It is remarkable that the short sessions of 20 min blue-enriched light exposure have the same effect as the longer sessions. An explanation might be that the maximal response to light treatment is already reached very quickly and that saturation played a role in the present study. Support for the finding that the blue part of the spectrum is important for the therapeutic effect comes from a study by Anderson et al. (2009). They reported that blue monochromatic light in a lower photopic intensity than white light, but with the same amount of blue light, is similarly effective in treatment of SAD. Much lower intensities of either blue light alone, a combination of green light and blue light (Gooley et al., 2010) or blue-enriched light could therefore be as effective as the high intensities used in the standard bright light treatment devices. If using (more) blue light in treatment devices, the potential risks of retinal damage due to blue light hazard should not be forgotten. Although the devices used in the current study emit blue light intensities far below the international standards for blue light hazard (CIE, 2002), such risks are relatively high compared to those placebo responses to be interpreted as placebo effects alone, although we cannot rule out this possibility. Walsh et al. (2002) also show an increasing trend in placebo responses over time in drug-studies and this may be the case for possible placebo effects of light treatment as well.

Due to aging there is a clear reduction of blue light transmission through the lens (Charman, 2003; Giménez et al., 2010; Van de Kraats and Van Norren, 2007). This might have consequences for the non-visual effects of short-wavelength light (Herljivic et al., 2005; Sletten et al., 2009). In the last two studies, reduced effects of blue light on melatonin suppression and alertness in elderly people compared to young people were observed. In the present study the response percentage in the “middle age” group was highest and better compared to the young group, with no significant differences between the young group and the oldest group. No differences between the three treatments were found between the age groups, which may again be explained by either a saturation effect, or the fact that blue light in particular does not play a huge role in the light treatment effect of seasonal affective disorder.

It is known that expectations can play a major role in the treatment of SAD (Levitt and Levitan, 2003). We showed that expectations for the three different light treatments were not significantly different, and experience with light treatment in earlier winter seasons did not play a role in the treatment effect in the three conditions.

Light is able to induce phase shifts of the biological clock and it imposes acute effects on melatonin concentration, body temperature and alertness both during the day and during the night (Cajochen, 2007; Rüger et al., 2003, 2006). Since it seems to be especially the short wavelengths that are responsible for the non-visual effects (Cajochen et al., 2009).
2005), it was clearly expected that the non-visual effects of blue-enriched light on the biological clock and on alertness would be larger compared to standard white light. Strong support for an increased response of the biological clock to blue enriched light is lacking however. A recent study concluded that bright blue-enriched polychromatic light is not more effective than standard bright light therapy for phase advancing or phase delaying circadian rhythms at light levels about half the intensities we used in the present study (Smith et al., 2009; Smith and Eastman, 2009). However, in a working place environment blue-enriched light (17,000 K) increased levels of alertness and performance when applied during daytime compared to a standard white-light condition (4000 K) (Viola et al., 2008). Although it is difficult to estimate the amount of light reaching the retina under normal working conditions, the intensities in the blue spectrum seem to be pretty similar to the intensities used in Anderson et al. (2009) and Meesters et al. (2011), and thus much lower then used in the present study. It is concluded that tests for the superiority of blue enriched light for treating circadian rhythm sleep disorders or season- al affective disorder should use low intensities, which if consistently proven to be effective could be an improvement of the current light therapies in terms of potentially shorter therapy time, more comfortable light intensities, and lower energy demands. From the present studies in our group we conclude that bright and low blue-enriched light is not better for treating Seasonal Affective Disorder then standard bright white light treatment. On the other hand shorter (20 min) daily light exposure and lower intensities (750 lx) of blue enriched light are as effective as standard full spectrum light therapy (30 min 10,000 lx), which is an improvement of the current treatment paradigms. The lack of a difference between standard full spectrum light and blue-enriched light does not really favor but definitely not rule out the hypothesis of the biological clock and/or the melanopsin photoreceptors being involved in the etiology of SAD or in the treatment effects of light.

Role of funding source Funding for this study was provided by an unrestricted research grant of Koninklijke Philips Electronics N.V., The Netherlands. The sponsor had no role in the collection, analysis, and interpretation of the data and in the writing of the report. Approval to submit the paper was given. Dr. Gordijn’s work is currently supported by the 6th European IP: EUCLOCK (No. 018741). The European committee had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Conflict of interest During the collection of data, Koninklijke Philips Electronics N.V., The Netherlands paid for the study, including the salaries of authors MCM Gordijn and D ’t Mannetje via an unrestricted grant to the University of Groningen, The Netherlands. MCM Gordijn obtained one other unrestricted grant of Philips Consumer Lifestyle B.V., Drachten, The Netherlands, in the following year, Author Y Meesters declares that he has no conflict of interest in the period 2005 (start of the work) – 2008.

Acknowledgements The authors thank the participants for their efforts to take part in the study. The help of Joep Vries en Else de Boer in randomizing the subjects and supervising the subjects during their treatment is greatly acknowled- edged. The work was financially supported by an unrestricted research grant of Koninklijke Philips Electronics N.V., The Netherlands. Dr. Gordijn’s work is currently supported by the 6th European IP: EUCLOCK (No. 018741).


