

Lux vs. wavelength in light treatment of Seasonal Affective Disorder

Anderson JL, Glod CA, Dai J, Cao Y, Lockley SW. Lux vs. wavelength in light treatment of seasonal affective disorder.

Objective: Published dosing guidelines for treatment of Seasonal Affective Disorder (SAD) refer to photopic lux, which is not appropriate for short-wavelength light. Short wavelengths are most potent for many non-visual responses to light. If SAD therapy were similarly mediated, standards utilizing lux risk overestimating necessary dose. We investigated antidepressant responses to light using two light-emitting diode (LED) sources, each emitting substantial short-wavelength light, but < 2500 lux.

Method: A randomized, double-blind trial investigated 3-week 45 min/day out-patient treatment with blue-appearing (goLITE®) or blue-enriched white-appearing light in 18 moderately-depressed adults (12F, 49.1 ± 9.5 years). Equivalent numbers of photons within the short-wavelength range were emitted, but the white source emitted twice as many photons overall and seven-fold more lux.

Results: Depression ratings (SIGH-ADS; <http://www.cet.org>) decrease averaged 82% (SD = 17%) from baseline ($P < 0.0001$) in both white- and blue-light groups. Both sources were well tolerated.

Conclusion: Short-wavelength LED light sources may be effective in SAD treatment at fewer lux than traditional fluorescent sources.

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Key words: Seasonal Affective Disorder; phototherapy; melanopsin

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Accepted for publication December 29, 2008

Significant outcomes

- Contrary to recommendations of 3000–5000 lux-h/day for light treatment in the Seasonal Affective Disorder clinical literature (including 10 000 lux × 30 min), adult patients treated 45-min/day using light-emitting diode (LED) light sources that yielded only 98–700 lux (but emitted equivalent numbers of photons within the short-wavelength range) demonstrated high rates of remission across 3 weeks of treatment.
- Decreased symptoms with 98-lux blue-appearing light or 700-lux white-appearing light were evident within a week. Patients did not increase their complaints over the 3-week trial.
- Illuminance measurement in lux may be inadequate as a standard for dose; further data are required that specify wavelength as well as duration and irradiance.

Limitations

- Overall difference in depression change between treatment groups had an effect size of -0.66 . Therefore, 40 subjects per group would be required to attain 80% power to test this difference with $\alpha = 0.05$.
- In the absence of a no-treatment group, the role of factors other than light exposure in the improvement of these subjects cannot be quantified.
- This study did not compare the LED treatments to standard bright white fluorescent sources.

Introduction

Seasonal Affective Disorder (SAD) afflicts an estimated 0.4–9.9% of the general population in

the Northern Hemisphere (1–3). Meta-analyses and reviews of over 60 placebo-controlled trials document the therapeutic benefits of light for SAD (4–6) for patients with recurrent Major Depressive

Disorder, as well as less severe disorders (Minor Depressive Disorder, winter blues), and with annual exacerbation of a year-round mood disorder (7, 8).

As the underlying science has evolved, light-treatment recommendations have been refined. Initial studies utilized fluorescent light termed 'full spectrum' because it contained a wide range of visible and near-visible wavelengths including ultraviolet (9–12). Concerns regarding safety of the ultraviolet wavelengths led to testing cool-white fluorescent tubes, which became the standard therapeutic source (reviewed in 5). Moreover, compliance is enhanced with briefer daily sessions, and duration was reduced from 6 h/day of 2500 lux in the 1970s based on a photoperiod hypothesis (9, 10), to 1–2 h/day of 1500–2500 lux in the 1980s based on phase-shift hypotheses (11, 12). Studies in the 1990s (13, 14), by increasing the stimulus strength up to 10 000 lux, became the basis for a widely cited benchmark duration of 0.5 h/day.

Recently, a short-wavelength sensitive photoreceptor system has been discovered in the mammalian eye and is primarily responsible for 'non-visual' light responses, such as resetting the timing of the circadian pacemaker, suppressing pineal melatonin production, improving alertness and performance, and elevating brain activation as assessed from electroencephalogram-derived correlates of arousal (15–24). A short-wavelength sensitive opsin located in intrinsically-photosensitive retinal ganglion cells (ipRGCs), melanopsin ($\lambda_{\max} \sim 480$ nm), is the photopigment primarily mediating these responses (25, 26).

These new physiologic findings necessitate a reconceptualization of dose, because the lux unit, in which 'strength' (illuminance) of light traditionally has been expressed in the SAD literature, is not wavelength neutral. Thoroughly reviewed by Bierman et al. (27), the basic science can be summarized briefly here. The physiologic potency of a light stimulus depends upon the particular photopigments in the retina that absorb the light and transduce it into neural signals. Photopigments in retinal cone cells are collectively most sensitive to light around 550 nm and it is this response of the three-cone system (termed 'photopic' as it dominates in daytime vision) that the lux measurement attempts to mimic. The analytic action spectra for circadian and neuroendocrine effects of light in mammals, including humans, and the absorption spectrum of melanopsin in ipRGCs, do not match those of the classical photoreceptor systems or the spectral sensitivity of the three-cone photopic system ($\lambda_{\max} \sim 555$ nm) which is assumed by the standard lux measurement for illuminance.

Consequently, a light source that emits most of its light in the short-wavelength visible range will not be an efficient stimulator of the photopic system and will fail to achieve a high lux. It will, however, be a relatively better stimulator of melanopsin-containing ipRGCs and the behaviours mediated via this photoreceptor system.

The discovery of this physiological substrate for circadian, neuroendocrine and neurobehavioural effects of light raises the possibility that antidepressant light therapy for SAD, also considered a 'non-visual' light response, shares the same photoreceptor pathway. Indeed, Glickman et al. (28) recently reported that 45 min morning exposure (6:00–8:00 h) to a short-wavelength light-emitting diode (LED) (468 nm at $607 \mu\text{W}/\text{cm}^2$; 1.43×10^{15} photons/ cm^2/s ; $n = 12$) for 3 weeks produced significantly better antidepressant effects in 12 SAD patients (54.5% remission) than did exposure to dimmer red light (654 nm at $34 \mu\text{W}/\text{cm}^2$; 1.13×10^{14} photons/ cm^2/s ; $n = 12$; 30.8% remission) housed in identical devices. If SAD light therapy is mediated by the melanopsin system, the relative potency of light sources for SAD treatment would be influenced by the amount of short-wavelength light they emit and using lux to measure illuminance at the eye will fail to convey adequately the relative potency of light devices. This is of potential importance clinically because by selecting the appropriate wavelengths of light, it may be possible to reduce the intensity and/or duration of light exposure while maintaining at least an equivalent therapeutic effect, possibly increasing the therapeutic window.

Aims of the study

We conducted a between-subjects double-blind trial of out-patient treatment using narrowband blue light-emitting diode (LED) (goLITE®; Apollo Health, American Fork, UT, USA) or broadband blue-enriched white LED light housed in identical devices. This two-site 3-week clinical trial in adults with SAD systematically measured symptoms of major depression and also 16 categories of potential adverse effects.

Material and methods

Subjects

For inclusion, adults aged 18–64 years met criteria for recurrent major depressive episodes with winter-type seasonal pattern by Diagnostic and Statistical Manual of the American Psychiatric Association, 4th edn. (DSM-IV) criteria (29). All

subjects were free of medical illness and not pregnant as determined by detailed history and physical examination including blood and urine chemistries and thyroid function tests. At baseline, SAD subjects had depression ratings of at least 20 on the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS) (30).

Exclusions were photosensitizing medications (such as amiodarone, benoxaprofen, chlorpromazine, demeclocycline, fleroxacin, nalidixic acid, ofloxacin, piroxicam, porfimer, psoralens, quinidine, temoporfin) or herbal remedies (St. John's wort or melatonin supplements). Other exclusion criteria included: history of concurrent psychiatric illness interfering with protocol compliance; active suicidal or homicidal ideation or plan; rapid cycling or severe premenstrual syndrome; history of substance abuse/dependence with ≤ 1 year remission; Global Assessment of Functioning (GAF) < 50 ; light treatment in the previous month; night-work or other habitual alteration of sleep/wake cycle; macular degeneration, colour blindness [Ishihara < 10 (31)] or cataract. Subject characteristics are shown in Table 1.

Study protocol

Subjects were screened at the Clinical Trials Center at Brigham and Women's Hospital (BWH), and seen at the Department of Psychiatry BWH out-patient offices or the Developmental Studies Program at McLean Hospital depending on convenience to the subject. Human Subjects review

committees at each site approved the study and each subject gave written informed consents for screening and for study.

Screening. Subjects were recruited by public service announcements and advertisement in newspapers appearing between August and October, 2005. After a research coordinator assessed eligibility using a telephone screening script [including the Personal Inventory for Depression and SAD (32)], the site PI (JLA, CAG) reviewed consent, answered questions, and then interviewed each subject using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (33).

Measures. Trained clinicians blind to treatment condition, unaware of the study hypothesis or what devices were being compared, rated depression symptoms on SIGH-ADS, and current mania/hypomania symptoms on the Hypomania Interview Guide for Seasonal Affective Disorder (HIGH-SAD-C) (34). To probe systematically for other potential adverse effects, the rater inquired about 16 current discomforts (listed in Fig. 4 legend). Subjects rated each as None, Mild, Moderate, or Severe (later coded on an ordinal scale for analysis).

Visit 1. Raters assessed baseline symptoms using the SIGH-ADS, HIGH-C, and Current Discomforts between September, 2005 and February, 2006. The site-PI provided each subject with a light-treatment device and instructions. Consecutively-enrolled subjects were randomized using sequences produced in advance by a research coordinator from a random number table to generate up to six subjects per condition at each site [sample size based on effect size reported in (28)]. Each site-PI had a different treatment assignment sequence. Subjects were informed that different wavelengths of light were being compared but were not given information about the wavelengths emitted by their device. Instructions were identical for both devices. After viewing the device and reviewing instructions, patients made treatment expectation ratings on a 100 mm visual analogue scale (not significantly different).

The PI instructed and demonstrated placement of the device at 50 cm from the bridge of the nose, and instructed the subject to measure from the face to the light source. Subjects were told not to stare directly at the light, but to position it to provide illumination to the area of the eyes. Subjects were instructed about potential side effects, asked to keep a regular sleep/wake schedule, and reminded to refrain from forcing themselves to awaken

Table 1. Characteristics of the sample

	Blue Narrow-Band	White Broad-Band	<i>P</i> -value*
	(<i>n</i> = 9)	(<i>n</i> = 9)	
	Freq (%)	Freq (%)	
Gender			
Female	6 (66.7%)	6 (66.7%)	ns†
Male	3 (33.3%)	3 (33.3%)	
Age: years mean (SD)	49.4 (6.5)	48.7 (12.2)	ns
Race/ethnicity			
Caucasian	6 (66.7%)	7 (78%)	ns
Caucasian Hispanic	1 (11.1%)	1 (11.1%)	
Asian	0 (0.0%)	1 (11.1%)	
African American	2 (22.2%)	0 (0.0%)	
Primary diagnosis			
Major depression	9 (100.0%)	6 (66.7%)	0.0824
Bipolar II	0 (0.0%)	3 (33.3%)	
Current psychiatric medications	2 (22.2%)	3 (33.3%)	ns
No prior light treatment	8 (88.9%)	9 (100.0%)	ns
SIGH-ADS ₂₉ at baseline	28.9 (5.6)	33.7 (4.4)	0.0611

**P*-values from Fisher's exact test.

†ns, not significant and $P \geq 0.15$.

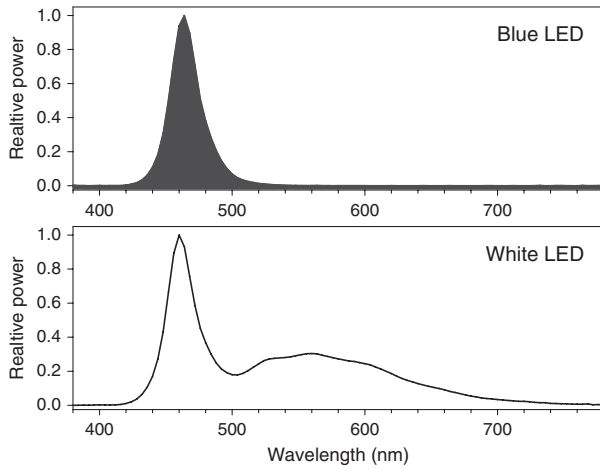


Fig. 1. Spectral power distributions for the blue and white LED goLITE devices plotted relative to their spectral peak (blue LED λ_{\max} = 464 nm; white LED λ_{\max} = 460 nm).

extremely early to use the light device. Each subject signed a written agreement to return the device at the end of the project. Subjects began daily 45-min sessions of light exposure at a consistent time each morning shortly after they normally awakened (between 6 and 9 AM).

Visits 2, 3, 4. Every week each subject completed the SIGH-ADS, HIGH-SAD-C and Current Discomforts assessment with symptom rater, and was instructed each time not to discuss any information about the treatment. After the rating, subject met with the site-PI to review the log of use of the device, sleep/wake times, and response. Based on the response, the duration of daily light could be adjusted; at the final visit subjects were given the option of continuing with the light, switching to the alternative device, or referral for other treatment.

Light treatment devices

Both conditions utilized goLITE[®] light therapy devices. The 15 cm \times 15 cm devices contain 66 LEDs mounted \sim 1 cm apart in an 11 \times 6 array,

embedded behind a plastic diffuser \sim 11 cm wide by 6 cm high. The device output can be adjusted manually from 10 to 100% and subjects were provided with a device set to the 50% level. Fig. 1 shows the power spectra of the devices measured directly at a distance of 50 cm. The narrowband (\pm 27 nm half-peak bandwidth) blue LED device emits light with a single peak (λ_{\max}) of 464 nm (Fig. 1, top panel). The broadband white-appearing LED emits light across the full visible range (400–700 nm) but is enriched in the short-wavelength range (Fig. 1, lower panel). As shown in Table 2, the white-appearing LED device emits approximately twice the total number of photons as the blue, but approximately the same number across the spectral range of the short-wavelength source (Table 2). Given the difference in the spectra, the illuminance (lux) of the blue is approximately seven times lower than the comparison device (Table 2).

Safety. At irradiance levels of commonly utilized light therapy devices, dermatologic safety concerns are minimal. Similarly, thermal damage to cornea, lens or retina requires milliwatt-to-watt exposure, far in excess of that emitted by these devices.

Potential photochemical ocular damage is an important concern, however, that must be addressed for each light device for SAD treatment. Ocular safety for 10 000 lux white fluorescent sources has been assessed and comprehensive ophthalmologic examinations of individuals with healthy eyes who used white-fluorescent light daily during fall/winter months for up to 5 years did not reveal adverse effects (35). Shorter wavelengths of light are of greater concern due to photokeratitis of the cornea and cataract from 180–400 nm ultraviolet light, and photochemical injury to the retina at 310–550 nm with a peak near 440 nm. Glickman et al. (28) carefully evaluated ocular safety using 468 nm at 607 $\mu\text{W}/\text{cm}^2$ (1.43×10^{15} photons/ cm^2/s) and reported no adverse effects in their short-term trial. Both the blue- and white-LED

Table 2. Radiometric and photometric comparison of the blue and white LED goLITE devices. Light sources were measured at the 50% setting at a distance of 50 cm perpendicular to the light source using a PR-650 SpectraScan Colorimeter with a CR-650 cosine receptor (Photo Research Inc., Chatsworth, CA). The measured irradiance, illuminance and total photon density (380–780 nm) values for two randomly selected devices used in the study are shown, in addition to the calculated photon density over the range of the blue LED device (424–532 nm) for both the blue and white LED devices

Device	Spectral characteristics	Irradiance ($\mu\text{W}/\text{cm}^2$)	Illuminance (Lux)	Photon density (photons/ cm^2/s) 380–780 nm	Photon density (photons/ cm^2/s) 424–532 nm
Blue goLITE	Narrow bandwidth λ_{\max} = 464 nm	144	98	3.38×10^{14}	3.35×10^{14}
White goLITE	Broad bandwidth λ_{\max} = 460 nm	262	711	7.00×10^{14}	3.46×10^{14}

goLITE[®] devices were subjected to an optical radiation hazard analysis by a medical physicist and determined to have an averaged radiance well below the 10-mW/cm²/sr safety limit for continuous viewing at a distance of 50 cm set forth in safety regulations by the American Conference of Governmental Industrial Hygienists and the International Commission on Non-ionizing Radiation Protection (36, 37).

Statistical analysis

An intent-to-treat approach was used; data analyses included all subjects and employed Hierarchical Linear Modeling version 6.0 (HLM6) and SAS version 8 (38–40). Pearson Chi-square tests were used to test the baseline differences between two light therapy groups for categorical variables; *t*-tests or analysis of variance (ANOVA) were used for continuous variables. Repeated measures ANOVA, with baseline score as a covariate, was initially used to assess the total SIGH-ADS29 scores across all treatment weeks. Analyses of component subscales of SIGH-ADS including the 17-item Hamilton Depression Rating Scale and 8-item Atypical Symptoms yielded comparable results to the total SIGH-ADS29.

A linear mixed model approach explored therapeutic effect (reducing SIGH-ADS29 score) during treatment. Random effects that describe the individual differences are included in the model as latent variables and clearly estimated. Estimates of fixed effects, which are conditional on the random effects, portray the average status of subjects.

To determine a proper specification of the individual growth equation and baseline statistics for evaluating subsequent level-2 model, we first fit an unconditional random-coefficient regression model without person-level predictors. Subsequent analyses introduced treatment and other covariates (e.g. research site, gender, race/ethnicity, age, major psychiatric diagnosis and current psychiatric medications) into the models. In view of the sample size, not more than two covariates were entered into the model simultaneously with the primary independent variable. To capture an acceleration of change in SIGH-ADS29 score at the early follow-ups, the original score was transformed to the square root and values of the square of SIGH-ADS29 score were used in all linear mixed effects regression model analyses. The best-fit person-level model, indicated by a higher log-likelihood, chosen as the final model, is as follows:

Level-1 Model

$$Y_{ti}(\text{square root of SIGH – ADS29 score}) \\ = \pi_{0i} + \pi_{1i}(\text{Week}) + e_{ti}$$

Level-2 Model

$$\pi_{0i} = \beta_{00} + \beta_{01} \times (\text{light treatment group}) + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \beta_{11} \times (\text{light treatment group}) \\ + \beta_{12} \times (\text{Age}) + r_{1i}$$

Mixed-effect regression models were estimated by means of restricted maximum likelihood estimation. An α -level of 0.05 was used to test for significance; trends <0.10 were kept in the final model and are discussed when appropriate.

Results

A total of 33 volunteers were assessed for eligibility, of which 13 were excluded due to failure to meet eligibility criteria, declining to participate or logistic difficulty with study procedures. Of 20 subjects randomized to treatment, one assigned to white light withdrew prior to week 1 due to difficulty scheduling treatment sessions and one was unable to follow treatment schedule due to a change in residence. Data are reported for the 18 remaining subjects, nine in each treatment group. Sixteen completed the full 3-week course of treatment, whereas two in the white-light group discontinued treatment after 2 weeks because of inadequate benefit. One in the blue group missed the visit 3 assessment and his visit 4 ratings were conducted by telephone.

Treatment response

As shown in Table 1, the severity of depression at baseline was moderate (SIGH-ADS29 mean \pm SD, range = 31.28 \pm 5.46, 21–42) and the pretreatment mean of the blue light group was relatively lower than that of the white light group (see Table 1). Depression severity scores decreased in both groups as shown in SIGH-ADS total symptom ratings (see Fig. 2).

Repeated-measures ANOVA including baseline score as a covariate, summarized in Table 3, revealed the group \times time interaction was non-significant ($F = 0.89$, d.f. = 3, 45, $P = 0.45$) (see Table 3).

Response to remission was defined as a pre- to post-treatment reduction in SIGH-ADS29 score to ≤ 8 (41). Given the minimum entry score of 20, all responders thus showed $\geq 60\%$ improvement. As

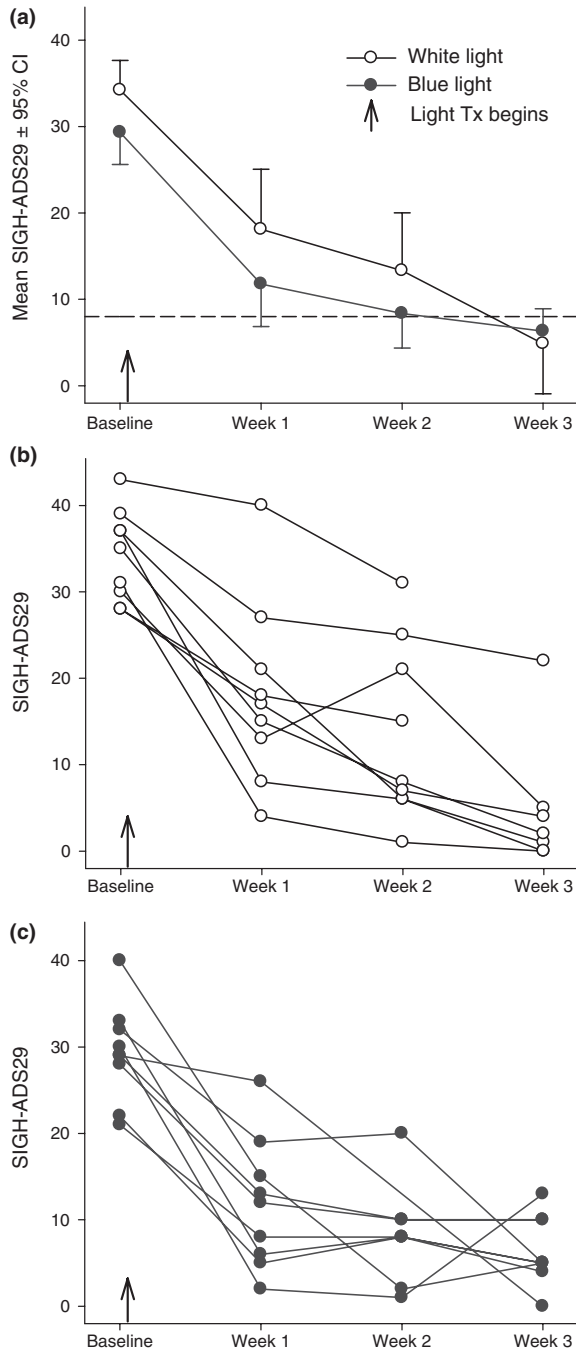


Fig. 2. Change in depression across three weeks of light treatment (a) mean ± 95% confidence interval for 29-item total on Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS29) blue light group vs. white light group ($n = 9$); (b) SIGH-ADS29 individual subjects receiving white light, and (c) individual subjects receiving blue light. Arrow indicates treatment began after visit 1. Dotted line at SIGH-ADS = 8 indicates criterion for recovery. Repeated-measures ANOVA including baseline score as a covariate revealed the time effects were significant ($P < 0.0001$), group × time interaction was non-significant ($F = 0.89$, d.f. = 3, 45, $P = 0.45$).

Table 3. Baseline and follow-up measures of SIGH-ADS29. Mean SD for 29-item total on Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS29) for blue light group ($n = 9$) and white light group ($n = 9$) at baseline and across three weeks of treatment. Depression decreased across time in both groups ($P < 0.0001$). Response to remission was defined as a pre- to post-treatment reduction in SIGH-ADS29 score to ≤ 8 (given the minimum entry score of 20, all responders showed $\geq 60\%$ improvement). Remission rates did not differ significantly between treatment groups

	Blue ($n = 9$) Mean (SD)	White ($n = 9$) Mean (SD)	<i>P</i> -values
SIGH-ADS29			
Baseline	28.9 (5.6)	33.7 (4.4)	Baseline: ns
Week 1	11.8 (7.2)	18.1 (10.6)	Group × Time: ns
Week 2	8.3 (5.3)	13.6 (10.2)	Time: $P < 0.001$
Week 3	4.9 (3.6)	4.9 (7.3)	Time effect within each group: <0.0001
Remission rate			
Week 1	3 of 9 (33.3%)	1 of 9 (11.1%)	ns
Week 2	5 of 8 (62.5%)	5 of 9 (55.6%)	ns
Week 3	7 of 9 (77.8%)	6 of 7 (85.7%)	ns

Table 4. Mixed effect regression analysis for SIGH-ADS29† (final model)

Parameters	Estimates				
	Coefficient	Standard error	<i>t</i> Ratio	d.f.	<i>P</i> -value
Fixed effect					
Model for initial status					
Patient mean score	5.24	0.18	29.83	16	<0.001
Treatment (blue vs. white)	-0.36	0.18	-2.026	16	0.059
Growth rate Model					
Mean growth rate	-2.10	0.54	-3.91	15	0.002
Treatment (blue vs. white)	0.06	0.11	0.58	15	0.569
Age	0.02	0.01	1.91	15	0.074
Random effects					
Initial status	0.27	0.07		16	13.40
Growth rate	0.26	0.07		15	18.08
Level-1 Error	0.83	0.68			

†Outcome variable = SIGH-ADS29^{1/2}.

shown in Table 3, remission rate at each follow-up was not significantly different between the two treatment groups (see Table 3).

Rates of improvement

As shown in Figure 3, rates of improvement were comparable for the two light sources (see Fig. 3). Table 4 presents results of unconditional random-coefficient regression modelling, which indicated

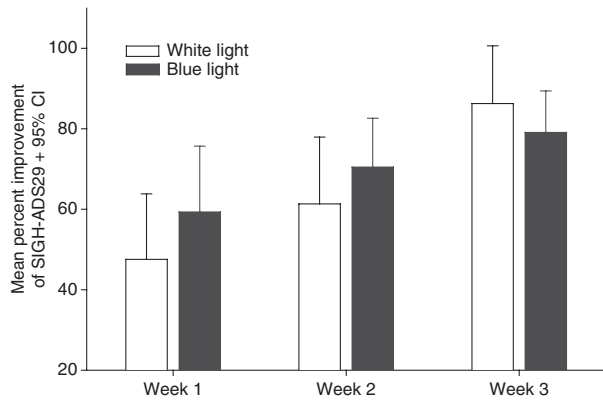


Fig. 3. Relative improvement in depression across three weeks of light treatment as percent of baseline 29-item total on Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS29) \pm 95% confidence interval for blue light group vs. white light group ($n = 9$).

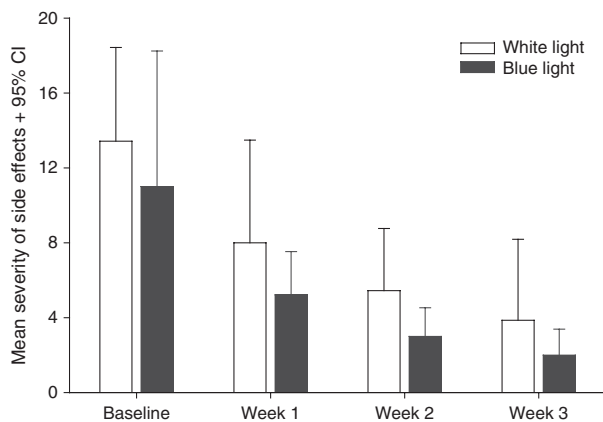


Fig. 4. Change in aggregate number \times severity (0 = none, 1 = mild, 2 = moderate, 3 = severe) mean 95% confidence interval of 16 Current Discomforts (headache, eye irritation, vision problems, increased appetite, decreased appetite, abdominal discomfort, tight chest, sleep problem, thought concentration memory, drowsiness, fatigue, dizziness, anxiety, irritability, and depression/down) reported from baseline through three weeks of light treatment for blue light group vs. white light group ($n = 9$). The overall severity of current discomforts gradually and significantly decreased over the course of the light treatments (F value = 22.33; d.f. = 3; $P < 0.0001$).

that the estimated mean SIGH-ADS29 score at baseline was 27.5 (5.24^2) and depression decreased on average by 4.4 (2.10^2) per week during the light treatment (see Table 4). Estimates for the variances of individual growth parameters for initial mean SIGH-ADS29 score (0.12) and mean growth rate (0.06) *n.s.*, indicate that patients did not vary significantly in SIGH-ADS29 total at entry and the change in SIGH-ADS29 over treatment did not vary significantly.

The estimated correlation between true change of the SIGH-ADS29 score and true baseline

SIGH-ADS29 score was 0.985. Thus, patients who had higher scores at baseline tended to decrease at a higher rate during light therapy. A set of mixed-effect regression models was fitted to estimate the effects of the two light sources and of time in treatment, controlling for potential confounding effects of study site, age, race, primary diagnosis and current psychiatric drug use. Interactions indicated only treatment type marginally related to the baseline SIGH-ADS29 score (t ratios = -2.026 , $P = 0.059$). The type of light did not predict different individual change in SIGH-ADS29 score over treatment. Overall, results show the two light sources present beneficial treatment effects in reducing SIGH-ADS29 score. Only patient's age marginally related to the change; younger patients tend to decrease more in SIGH-ADS29 score with treatment.

Adverse effects

No subjects reported mania or hypomania on HIGH-SAD. Two subjects reported some over-activation and were instructed to reduce light stimulus (blue: one patient to 30 min at 30% intensity after visit 2; white: one patient to 45 min at 40% intensity after visit 2).

At baseline the most frequently reported Current Discomforts were fatigue ($n = 10$, 56%), irritation ($n = 10$, 56%) and depression/down ($n = 10$, 56%). Others included anxiety ($n = 8$, 44%), sleep disorder ($n = 7$, 39%), increased appetite ($n = 6$, 33%) and thought concentration memory ($n = 6$, 33%). The severity of current discomforts gradually and significantly decreased over the course of light treatments (overall severity of current discomforts: $F = 22.33$; d.f. = 3; $P < 0.0001$; Fig. 4). The number of current discomforts showed a similar pattern ($F = 15.38$; d.f. = 3; $P < 0.0001$; data not shown).

Strong correlations were found between number of current discomforts and overall severity of current discomforts at all time points (Pearson Correlation Coefficients > 0.90). No difference was found between the treatments in reducing the number and severity of current discomforts (number of current discomforts: $F = 0.31$; d.f. = 3; $P = ns$; overall severity of current discomforts: $F = 0.08$; d.f. = 3; $P = ns$) (Fig. 4). After the 3-week trial, most frequently reported Current Discomforts were fatigue ($n = 4$, 22%), headache ($n = 3$, 17%), eye irritation ($n = 3$, 17%), increased appetite ($n = 3$, 17%), sleep disorder ($n = 3$, 17%), drowsiness ($n = 3$, 17%), anxiety ($n = 3$, 17%) and irritability ($n = 3$, 17%). The number and severity of current discomforts

reported were strongly correlated with the overall SIGH-ADS29 score at follow-up (Pearson Correlation Coefficients range from 0.56 to 0.76).

Discussion

This double-blinded evaluation of 3-week outpatient treatment using narrow bandwidth 464 nm blue-appearing or a broader 400–700 nm white-appearing light for SAD, yielded recovery rates of 77.8% and 85.7%, which are comparable to those reported for other active treatments (41–45). Patients knew that they were receiving light exposure, but neither patients nor symptom raters had any information regarding the wavelengths of light emitted by either device, they did not view the device for the alternate condition, and they had no way to determine the degree to which their treatment involved the ‘active’ component. The primary information patients had regarding the hypotheses and devices was that there was no placebo condition in this study.

The results are noteworthy since the illuminance from the devices was much lower than required by standard treatment recommendations based on white fluorescent light. If, as current guidelines suggest, emissions in lux are crucial and a threshold of 3000–5000 lux-h/day is required (4, 46) then neither treatment should have produced greater than the 40% maximum recovery rates seen with inactive placebos (28, 41, 42, 44, 45).

Our data suggest that current dosing guidelines are insufficient for informing clinical practice and risk overestimating the necessary dose. If SAD light treatment is mediated by the same short-wavelength-sensitive photoreceptor system as other non-visual light responses, the optimal wavelength response will be blue-shifted and therefore illuminance measurement in lux, which assumes photopic spectral sensitivity, will be inadequate as a standard for dose. Consequently, large clinical trials of short-wavelength light should not be restricted to treatment of > 2500 lux. Minimizing light exposure is clinically important since it may entail less risk of adverse effects. Adverse effects of light therapy have been reported in the literature and overdosing of light can lead to agitation (47, 48). In this study, light exposure was decreased in two subjects to resolve complaints of mild over-activation.

There were no statistically or clinically significant differences between conditions. Whether by linear mixed model analysis or categorical assessment of percent of subjects reaching remission, our results indicate depression in both groups decreased significantly over time. Response to either light was generally rapid (occurred by

week 1) and accompanied by decreases in other complaints.

These results extend the one published study to date, which found blue light (398 lux) more effective than a plausible placebo source using red light (28). Together, they support the possibility that lux is not an optimal measure of stimulus strength. If photon emissions in the short-wavelength range are central to treatment efficacy, then our narrow-bandwidth source could be equally effective as the higher-lux stimulus because both emitted $\sim 3.4 \times 10^{14}$ photons/cm²/s within the short-wavelength range (424–532 nm). By comparison, $\sim 10\,000$ lux traditional cool-white fluorescent sources (4100 K) emit $\sim 1.5 \times 10^{15}$ photons/cm²/s within this range and the ~ 2500 lux boxes emit $\sim 4.1 \times 10^{14}$ photons/cm²/s.

Our results suggest that it is premature to conclude 3500–5000 lux-h/day is required for an adequate trial of light for SAD, particularly in the absence of a proven mechanism of action. In addition to relying on an outdated physiologic model of photoreception, these guidelines assume that light therapy for SAD obeys the reciprocity law for light exposure (exposure = time \times intensity), such that short-duration high intensity light is equivalent to longer-duration lower intensity light. This has given rise to the concept of ‘lux-hours’ in calculating dose for SAD treatment (4, 46). Given the non-linear relationship between light intensity and duration on circadian responses (49–52) the assumption of reciprocity may not be correct.

Although relative effectiveness of cool-white fluorescent sources has supported the current dosing guidelines, alternative strategies should be explored until the mechanism of action of light treatment is established. Previous studies have shown favourable outcomes with lower intensity light in dawn simulator paradigms (42, 45), and equivalent effects of higher- vs. lower-lux light visors in large multi-centre trials (reviewed in 5). Our data indicate that further research is warranted to assess thoroughly the effects of a broader range of devices and dosing strategies that incorporate wavelength as well as duration and irradiance of therapeutic light exposure and assess long-term safety. Narrow-bandwidth light devices require further evaluation. Understanding the spectral sensitivity of therapeutic effects of light is required before light dosing for clinical applications can be quantified definitively.

Acknowledgements

The authors thank the staff of Center for Clinical Investigation and Clinical Trials Center of the Brigham & Women’s Hospital,

Drs Annaswamy Raji and David J. Wolfe, and Melissa Hines, M.S.W., L.C.S.W., for assessment of subjects; Y. Lavrova, Emily Reid, and Jason Sullivan for logistical support; and David H. Sliney, Ph.D. for safety analysis of the light sources. This study was supported by an investigator-initiated grant from Apollo Health, Inc., which provided light treatment devices but had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. NCT00114322, 2005-P-000160: Light-Emitting Diode (LED) Light for Seasonal Affective Disorder (SAD) Treatment <http://www.clinicaltrials.gov/>. Lockley was supported in-part by the National Space Biomedical Research Institute through NASA NCC 9-58.

Declaration of interests

Dr Anderson, Dr Glod, Ms. Dai and Ms. Cao report no financial interests. Dr Lockley is a co-inventor on a patent in the field of sleep/circadian rhythms specifically concerning using different wavelengths of light to reset the human circadian pacemaker. All such patents are assigned to the Brigham and Women's Hospital per institutional policy.

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