An Examination of the Acute Effects of Bright Light Therapy in a Non-Clinical Sample

By

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Abstract

The integral role of light in physiological and psychological well-being is illustrated by the application of phototherapy, or bright light therapy (BLT), in treating mood disorders such as seasonal affective disorder and non-seasonal depression. More recently, BLT has been applied in treating jet lag due to transmeridian travel, complications from shift work, and disorders of sleeping and waking. Despite the numerous potential applications of BLT, deleterious side effects have not been fully explored in a non-clinical population. Thus, I examined the acute side effects (nausea, headache, blurred vision, eye strain) of a single 30-minute exposure of bright white light (10,000 lux) therapy and a comparison dim red light (<500 lux) in non-depressed sample of young adults, with a focus on the potential moderating role of depressive symptoms. Linear regressions revealed no significant main effects for light. However, self-reported nausea and total side effect intensity significantly decreased in response to white light, but not red light, for those with greater depressive symptomatology. In addition, a repeated-measures analysis of variance revealed a significant group-by-time interaction for sad mood, which decreased at a higher rate in the white light condition compared to the red light condition. Also, a post-hoc analysis revealed a significant increase in eye strain for both conditions, with no significant difference between them. These results suggest that the high prevalence of acute adverse side effects in the extant BLT literature may not fully apply to non-clinical populations.

Keywords: Phototherapy, Illumination, Side Effects (Treatment), Safety

An Examination of the Acute Effects of Bright Light Therapy in a Non-Clinical Sample

The United States Department of Health and Human Services (2000) reported that unhealthy lifestyles are responsible for most of the top ten cases of mortality and morbidity in the country. Accordingly, lifestyle-based interventions carry considerable potential to prevent and ameliorate numerous forms of physical and mental illness (for review, see Walsh, 2011). One such interventional strategy – the use of artificial bright light exposure to supplement the body's reliance on sunlight for physiological and psychological well-being – has come into increasingly widespread use in recent decades (reviewed in Terman & Terman, 2005) based on its ability to influence circadian rhythms and neural signaling.

Plants and animals entrain circadian rhythms through *zeitgebers*, the environmental cues that assist in regulation of an organism's biological clock. In animals, circadian rhythms assist the body in cyclical regulation of biochemical, physiological, and behavioral processes. Light, the strongest zeitgeber for mammals, is processed through retinal ganglion cells of the eye containing specialized photoreceptors, which signal to the suprachiasmatic nucleus (SCN) in the brain's anterior hypothalamus (Moore & Eichler, 1972; Stephan & Zucker, 1972) through photopigments such as melanopsin (for a review, see Rollag, Berson, & Provencio, 2003). This pathway, designated the retinohypothalamic tract, wherein the SCN generates circadian rhythms, aids the body in directing the circadian clock and, in turn, assists the body in hormonal release, particularly melatonin (N-acetyl-5 methoxytryptamine) regulation (Berson, Dunn, & Takao, 2002; Gooley, Lu, Chou, & Scammell, 2001; Hannibal, Hindersson, Knudson, George, & Fahrenkryg, 2002; Hattar, Liao, Takao, Berson, & Yau, 2002).

Melatonin, synthesized from tryptophan and secreted by the pineal gland, assists in transmission of daily and seasonal circadian messages emanating from the SCN, while

simultaneously contributing to numerous other physiological processes (for a review, see Goldman, 1999; Reiter, 1993; Simonneaux & Ribelayga, 2003). Highlighting the reciprocal relationship with the SCN, melatonin production surges at night in response to diminished light. Similarly, as the SCN drives arousal and waking with the presence of light, its effects are counteracted by melatonin receptors in the SCN, triggering induction of sleep as light decreases (Challet, 2007). Melatonin production and the retinohypothalamic tract illustrate the brain's sensitivity to light, which derives from a hypothesized evolutionary mechanism designed to anticipate predictable cycling of physiology and behavior in response to environmental changes. Consequently, the chief cues for entrainment of the human circadian system, as a byproduct of evolutionary phylogenetic selection pressures, are sunrise and sunset.

Animal models highlight the importance of light for healthy biological functioning. For instance, rats kept in complete darkness develop neuronal damage and express depressive behaviors (Gonzalez, & Aston-Jones, 2008). Similar biological evidence is found in human genetic research. For example, individuals with major depression with seasonal onset pattern, commonly known as *seasonal affective disorder* (SAD), a disorder characterized by increase in depressive symptoms in the winter months when daylight hours are most limited, were recently found to be at least five times more likely to have a mutation in the gene responsible for melanopsin expression (Roecklein et al., 2009). These findings illustrate the closely knit relationship between light and healthy physiological and psychological functioning. The disturbance of normal biological rhythms, caused by disruption in light entrainment due to dysregulated sunlight exposure, has instigated further examination into the putative function of light as a treatment option for a range of lifestyle-linked maladies.

Prescribed to treat a host of conditions, bright light therapy (BLT), or *phototherapy*, consists of exposure to daylight or artificial bright light for a determined period of time at a specific time of day. Application of BLT has been examined in circadian phase sleep disorders, such as jet lag (Boulos et al., 1995) and shift work problems (Eastman et al., 1995), and disorders of sleeping and waking (Terman et al., 1995). Simultaneously, research on BLT has yielded particularly encouraging results in the treatment of SAD (for a review, see Terman & Terman, 2005). BLT has potential applications for treating other mood disorders, including major depressive disorder (MDD, [reviewed in Prasko, 2008]), bipolar disorder (Sit, Wisner, Hanusa, Stull, & Terman, 2007), antepartum and postpartum depression (Oren et al., 2002), and premenstrual dysphoric disorder (Krasnik, Montori, Guyatt, Heels-Ansdell, & Busse, 2005). Future potential applications have also been examined in treating behavioral disturbance and insomnia in dementia (Ancoli-Israel, Martin, Kripke, Marler, & Klauber, 2002), primary and secondary features of Parkinson's disease (Willis & Turner, 2007), attention deficit hyperactivity disorder (Rybak, McNeely, Mackenzie, Jain & Levitan, 2006), seasonal variations in eating disturbances associated with bulimia nervosa (Lam, Goldener, Solyom, & Remick, 1994), and general symptom elevations found in chronic anorectic women (Daansen & Haffmans, 2010). Despite the potential for a wide array of application, the side effects and tolerability of BLT has not been extensively examined.

The therapeutic effects of light have long been documented, with the medical use of sunlight tracing back to antiquity (Kellogg, 1910, 2003; Wehr & Rosenthal, 1989). However, it gained popularity in the late 19th century with Dr. J.H. Kellogg's promotion of light treatment for an array of illnesses, including melancholia (Kellogg, 1910, 2003). Light treatment also garnered a 1903 Nobel Prize for N.R. Finsen for his research on the treatment of lupus vulgaris.

Other skin-related problems treated by light therapy include acne vulgaris (Riddle, Terrell, Menser, Aires, & Schweiger, 2009), psoriasis (Walters, Burack, Coven, Gilleaudeau, & Krueger, 1999), and eczema (Polderman, Wintzen, le Cessie, & Pavel, 2005). However, light treatments for mental illness fell out of favor after the early part of the 20th century due to a paucity of supporting empirical evidence.

A resurgence of interest in the relationship between mental health and light developed with the work of Wetteberg (1978) and Lewy and colleagues (1980), who examined the effect of light on melatonin production. Early intervention research targeted SAD with the first published study by Rosenthal and colleagues (1984). In the interim, numerous published trials have refined and extended the treatment protocol. Most such studies (e.g., Avery, Khan, Dager, & Dunner, 1990; Lewy, Sack, Miller, & Hoban, 1987; Prasko et al., 2002; Sack et al., 1990; Terman et al, 1990) show morning light to be superior to evening light, which reflects the natural diurnal variation in retinal photoreceptor sensitivity (Remé, Wirz-Justice, & Terman, 1991). Based on these findings, phase-shifting of the brain's circadian clock has been targeted as the hypothetical mechanism of light's therapeutic effect. Specifically, the putative biological mechanism for BLT to treat depressive symptoms is through the suppression of melatonin production in the brain, which may induce a therapeutic alteration of dysregulated circadian rhythms (Lewy, Wehr, Goodwin, Newsome, & Markey, 1980).

Altering neurotransmitters circuitry may provide an alternative mechanism underlying the therapeutic effect of bright light exposure. Sunlight directly influences serotonin turnover in the brain, with the lowest rate of turnover in the winter, and more rapid turnover with increased luminosity (Lambert, Reid, Kaye, Jennings, & Esler, 2002). Similarly, BLT increases serotonin-based central nervous system activity in depressed individuals (Rao et al., 1992). Furthermore,

individuals with bipolar disorder who are homozygotic for the long variant of the serotonin transporter-linked polymorphic region (5-HTTLPR), speculated to be involved in stress sensitivity (Caspi, Hariri, Holmes, Uher, & Moffitt, 2010), show longer-lasting mood elevation after a combination of BLT and sleep deprivation, in comparison with heterozygotes and homozygotes for the short variant (Bendetti et al., 2003). Studies with BLT have also indicated some dopamenergic effects in the brain (Neumeister et al., 2001; Oren, 1991).

BLT has likewise proven beneficial in the treatment of sleep disorders. In advanced sleep phase syndrome (ASPS), individuals experience early waking and difficulty remaining awake in the evening. Conversely, in delayed sleep phase syndrome (DSPS), individuals experience sleep onset insomnia, or difficulty initiating sleep, and problematic morning awakening. Such sleep disorders maintain a misalignment of sleeping and waking compared to the individual's circadian clock. Selective application of bright light in the morning (to correct DSPS) or in the evening (to correct ASPS) has been effective in instituting normal sleep-wake cycles (for a review, see Gooley, 2008), as appropriately-timed exposure to bright light can shift the sleep-wake cycle to earlier or later times in order to align a disruption between the circadian system and desired sleep-wake schedule. Application of this methodology has been applied to other circadian disorders, including non-24-hour sleep-wake disorder, where the sleep-wake cycle is free-running, and shift work sleep disorder, where insomnia occurs during the day and fatigue during nighttime for individuals who must remain awake at night (for a review, see Gooley, 2008). Similarly, Jet Lag Disorder (JLD), a circadian rhythm sleep disorder characterized by insomnia or excessive daytime sleepiness in response to transmeridian jet travel that alters typical rhythm, has been treated successfully with BLT (Boulos et al., 1995). Overall,

the treatment of circadian rhythm sleep disorders with BLT has been successful due to the brain and body's acute sensitivity to light.

Researchers (e.g., Wirz-Justice, Benedetti, & Terman, 2009) now generally recommend that BLT be administered via a light box protocol tested successfully in peer-reviewed clinical trials. The optimal length and luminance of light exposure is 10,000 lux (a unit of illumination equal to a luminous flux of 1 lumen per square meter) at a comfortable sitting distance, usually 12-14 inches from the participant's eyes, for a period of 30 minutes (Terman et al. 1990; Terman, Terman, & Ross, 1998). However, lower light intensities can be effective if applied for longer durations (Eastman, Young, Fogg, Liu, & Meaden, 1998; Lewy et al., 1998), as researchers have observed an inverse relationship between length of light presentation and strength of light when reviewing treatment efficacy. Light boxes should utilize fluorescent bulbs and a screen that filters out ultraviolet (UV) rays, which are harmful to the eyes and skin. The lamps should emit white light rather than colored light because, so far, colored light lamps have not been unequivocally shown to provide a therapeutic advantage (for a review, see Anderson, Glod, Dai, Cao, & Lockley, 2009) and may have possible deleterious side effects (Bynoe, Del Priore, & Hornbeck, 1998; Ham, Mueller, & Sliney, 1976; Remé, Williams & Rol, 1998; Wu, Seregard, & Algvere, 2006). The projection of light should be maintained downward toward the eyes at an angle to minimize aversive visual glare and to provide maximal therapeutic effect (Glickman et al., 2003). The timing of BLT throughout the course of the day differs depending on the targeted malady. For example, to avoid triggering a manic episode, individuals with bipolar disorder are advised to apply BLT in the afternoon rather than the morning (Leibenluft et al., 1995; Sit et al., 2007). Generally, BLT for MDD or SAD is applied in the morning, unless individuals experience difficulty with sleep onset. Similarly, application of BLT for JLD, shift work

problems, and disorders of sleeping and waking, will differ contingent on a need for either forward or backward circadian realignment.

Within five years of Rosenthal and colleagues' (1984) work on treating depressive symptoms with BLT, 25 published studies already attested to the potential efficacy of light therapy for SAD (Terman et al., 1989), and a subsequent meta-analysis of randomized, controlled trials of BLT for the American Psychiatric Association Committee on Research in Psychiatric (Golden et al., 2005), using strict criteria for only the most methodologically sound trials, concluded that BLT is superior to placebo in reducing symptoms of SAD, with an effect size of 0.84. In fact, remission rates were found to be nearly three times higher (Odds Ratio of 2.9) among BLT patients in comparison with those receiving placebo. Similarly, a meta-analysis (Even, Schröder, Friedman, & Rouillon, 2007) found the response to BLT was significantly better than control treatment among high-quality, methodologically sound studies and in those studies that applied morning light treatment to non-seasonal depression. Likewise, when limiting their evaluation to the most methodologically sound studies, Golden et al. (2005) found that BLT was an effective stand-alone treatment for non-seasonal depression, with an effect size of 0.53. Furthermore, Golden and colleagues noted that this observed effect size is similar to that of most antidepressant medication trials. In summary, there is considerable published evidence that retinal exposure to light of sufficient intensity and duration, at an appropriate time of day, can have marked effects on the affective and physiological symptoms of seasonal-onset depressive illness, with a likely therapeutic benefit for non-seasonal depression as well.

However, despite promising findings of the effectiveness of BLT in treating depressive illness, psychotropic medication is currently the most commonly prescribed treatment for depression (Sleath & Shih, 1998), with about 164 million antidepressant prescriptions written in

the United States to 27 million individuals (Olfson & Marcus, 2009). Selective serotonin reuptake inhibitors (SSRIs), the newest and most popular type of antidepressant medication, and serotonin and norepinephrine reuptake inhibitors (SNRIs), which are similar to SSRIs, induce side effects that include headache, gastrointestinal effects, akathisia or restlessness, agitation, hypomania and, possibly, sexual dysfunction (Schatzberg, Cole, & DeBattista, 1997). SSRIs and SNRIs constitute a second generation of antidepressants that do not provide a therapeutic advantage over first generation antidepressants but are considered more tolerable (Anderson, 2008). Side effect rates differ between medications; however, estimates show that as many as 86% of those taking antidepressant medications will experience at least one side effect (Hu et al., 2004). Antidepressants can also cause, though rarely, potentially life-threatening cases of seizures and agranulocytosis (for a review, see Mago, Mahajan, & Thase, 2008). Another potentially life-threatening side effect of SSRIs is serotonin syndrome, a condition caused by elevated serotonin in the body (Boyer & Shannon, 2005).

Antidepressants have also been scrutinized due to their potential deleterious side effects on adolescents and young adults. The Food and Drug Administration (FDA, [Lenzer, 2006]) conducted a review of published and unpublished controlled clinical trials of antidepressants and revealed that 4% of those taking antidepressants thought about or attempted suicide compared to 2% of those receiving a placebo. These findings have prompted the FDA to mandate that antidepressants carry a “black box” label warning of their potential to increase suicidality in children and adolescents (Friedman & Leon, 2007) and a proposal was made to extend the warning to include young adults up through age 24 (Stone et al., 2009). Such recorded unpleasant side effects can interfere with treatment and rates of discontinuation of treatment vary from 5-39% due to adverse effects from SSRIs (Ruhé, Huyser, Swinkels, & Schene, 2006).

The findings of intolerability and discontinuation of treatment due to adverse effects of medication, combined with the use of BLT to treat both affective and non-mental health ailments, warrants further research to help clarify the tolerability and prevalence of side effects of BLT. Despite the numerous potential applications of BLT, deleterious side effects have not been fully explored. Although Gallin and colleagues (1995) have provided evidence for the ophthalmologic safety of bright light in both long term and short term application, and no difference has been found in cone and rod functioning with BLT compared to typical indoor light (Gagné, Gagné, & Hébert, 2007), sparse evidence has been collected on incidence and tolerability of undesired side effects.

The most extensive examination of the adverse effects of BLT using the currently prescribed dosage and length of exposure, 10,000 lux for 30 minutes, was conducted by Kogan and Guilford (1998). Researchers controlled for symptoms present before the study and using a self-report of symptoms from a checklist found that 32 out of 67 participants undergoing an average of 6.8 sessions reported side effects, with nine individuals reporting two or more. About 20% of participants reported either headaches or eye/vision difficulties. This finding supports those of Oren and colleagues (1991) and Labbate and colleagues (1994), who concluded that headache and eye/vision difficulties, while occurring at only slightly higher rates, were the most common side effects. Terman and Terman (1999) also found headaches and eye/vision vision difficulties as prominent concerns, with an addition of nausea as another potential chief side effect. Avery and colleagues (2001) found headache as the most common side effect, one reported by 10 % of their sample. Unfortunately, each of the aforementioned studies lacked a control group, thereby limiting the interpretability of their findings.

Volz, Mackert, and Stieglitz (1991) conducted the only placebo-controlled study that directly addressed the issue of adverse effects with BLT. Employing a control group of 50 lux red light compared to 2500 lux white light for two hours a day over seven consecutive days, the study found no significant differences in any reported side effects between groups; notably, however, the dosage of light and length of presentation employed in this study vary from the current most widely prescribed dosage and length (i.e., 10,000 lux for 30 minutes).

The most severe adverse effects have been identified in individuals with bipolar disorder, and studies (e.g., Leibenluft et al., 1995; Sit et al., 2007) have identified a potential increased risk of triggering hypomania with morning exposure. Rare cases of mania and hypomania have also been noted in individuals treated for non-seasonal depression (Bauer, Kurtz, Rubin, & Marcus, 1994; Kripke, 1991; Schwitzer, Neudorfer, Blecha, & Fleischhacker, 1990).

BLT has also been employed as a non-pharmacological adjunct to antidepressant medication (e.g. Kripke, Mullaney, Savides, & Giltin, 1989; Levitt, Joffe, & Kennedy, 1991). To examine the side effects of such adjuvant BLT usage, Muller and colleagues (1997) studied 28 non-seasonally depressed participants assigned to four weeks of pharmacotherapy (Trimipramine) or pharmacotherapy and BLT, with the bright light treatment group receiving 5000 lux exposure for two hours per day. No significant differences in overall side effect prevalence were observed between groups, but investigators found a dissimilar side effect profile in each group. Specifically, both groups showed differential ameliorating and aggravating somatic complaints that were impossible to disentangle from depressive symptoms, a finding which highlights the difficulty of assessing adverse treatment effects from a clinical population.

Individuals with MDD often (75%) report somatic complaints (Vaccarino, Sills, Evans & Kalali, 2009), and MDD is the most frequent comorbid diagnosis of patients with somatization

syndromes (Katon, 1984; Katon, et. al., 1991; Rief, Schaefer, Hiller & Fichter, 1992). For example, Terman and Terman (1999) reported an array of undesired physiological symptoms in individuals with SAD present before application of BLT, many of which remitted during treatment. In other words, these investigators observed among seasonally depressed patients *a BLT-induced reduction in some depression-linked physical complaints that are often otherwise measured as potential "side effects" of bright light exposure*. Thus, utilizing clinical samples to examine adverse effects of BLT may yield results that do not readily generalize to non-clinical populations.

Few studies have examined the effect of BLT on non-clinical populations, and none have reported directly on the potential adverse effects that may occur in these populations. However, as previously reviewed, we know in general that exposure to bright light is associated with physiological changes, such as direct serotonin turnover in the brain, melatonin reduction, and muscular eye movement. Depressed individuals may experience an amplified perception of these physiological changes, or may be more prone to interpret these changes as adverse or undesired physical symptoms stemming from greater vigilance regarding negative information (Erickson et al., 2005). Similarly, individuals with depressive symptomatology may be more likely to interpret physiological changes as aversive. For example, compared to controls individuals with MDD are hypersensitive to heat stimuli in sensory and the affective dimensions, a bias particularly apparent in the innocuous heat range (Strigo, Simmons, Matthews, Craig & Paulus, 2008a). Also, increased emotional reactivity of anticipatory pain may lead to impaired ability to modulate pain experience in MDD, as been shown with heat stimuli (Strigo, Simmons, Matthews, Craig & Paulus, 2008b). Recent research (Lozano et al., 2008) has also indicated a potential role of the anterior cingulate cortex in depression leading to an inability to cognitively

contain negative stimuli. Converging lines of evidence point to an increased affective and neurological bias for non-noxious stimuli in depressed populations, which may be paralleled in over-reporting of adverse effects in interventions such as BLT. Thus, further investigation is necessary to elucidate the potential effect of depressive symptomatology on the report of side effects after bright light exposure.

Across relevant published reports of BLT side effects, the most commonly reported problems were considered mild and transient, and did not interfere with treatment indicating an acceptable tolerability of side effects. Furthermore, reports of side effects were also reduced with repeated exposures. For example, Kogan and Guilford (1998) reported that on the first day of BLT, 24 participants (34.3%) reported side effects, which decreased to 17 (24.3%) by the second day. By day three only 12 individuals (17.9%) reported side effects, and by days four and five, fewer than 10% of the participants reported side effects. Headaches, with one exception, ceased after the third day and few eye/vision problems occurred after the second day.

The purpose of the present investigation is to evaluate the side effect profile of one-session BLT compared to a dim red light, while accounting for the potential moderating effect of depressive symptomatology. An extensive literature search did not reveal any placebo-controlled studies utilizing the currently prescribed dosage and duration (10,000 lux for 30 minutes) of BLT. Similarly, no research has evaluated the potential moderating effect of depressive symptomatology on the report of side effects, or utilized a non-clinical sample to examine side effect, or examined the acute side effects of a single session exposure of bright light. Sampling from a non-clinical population allows for greater safeguards against the somatization effect often observed in clinical samples. With increased use of BLT in non-clinical samples it becomes more important to understand the effect of depressive

symptomatology on the report of side effects. Since previous research has shown that most side effects emerge during or immediately after the initial session, and diminish with repeated exposures, the present study evaluated the side effects associated with only one session at the currently prescribed dose and luminance (10,000 lux for 30 minutes). Since it is hypothesized that depressive symptomatology has a moderating effect on reporting of side effects, positive and negative affect were also measured in order to permit an ancillary examination of BLT's acute effects on mood.

The chief objective of this study was to examine the tolerability and side effects of a single session of bright light exposure. Primarily, this experiment investigated how applying 30 minutes of 10,000 lux white light affects somatic domains relevant to normal daily functioning. My principal study hypothesis was that depressive symptomatology moderates the experience of side effects with BLT, with an increased perception of side effects associated with increased depressive symptomatology in the bright light, but not the control, condition. Since previous findings have demonstrated BLT's salubrious mood effects even among healthy individuals (e.g. Partonen & Lönnqvist, 2000), BLT was also expected to decrease negative affect at a greater rate from pre-treatment to post-treatment compared to red light.

Method

Participants

Participants were recruited from the University of Kansas participant pool as a course requirement. All participants were students in an introductory psychology class; however, introductory psychology serves as an option for students to complete a General Education requirement allowing students from various majors to enroll. All participants provided written informed consent and the study was approved by the Institutional Review Board. The exclusion

criteria were a history of depressive disorders, bipolar disorder, or retinal light sensitivity. Participants were excluded from the final analyses if they reported consuming more than five alcoholic beverages over the previous 24 hours and if they endorsed all of the symptoms on a side effects questionnaire prior to treatment.

Materials

Artificial bright light was emitted by a Sunlight Jr. (The Sunbox Company, Gaithersburg, MD) light box. The Sunlight Jr. is a triangular shaped light box (14.5" Tall x 7" Wide (Face) x 6" Sides) that emits a full spectrum of light and employs a spectrally transparent prismatic diffuser to block UV rays. At a distance of 14 inches the light box emits a luminance of 10,000 lux. A red filter was positioned over the prismatic diffuser to filter all but red light and reduce the luminance to less than 500 lux at a distance of 14 inches.

Procedures

After the consent process, participants were excluded if they endorsed eye sensitivity to light or a history of depressive disorder or bipolar disorder. Participants completed an assessment battery and then randomly assigned either to the bright light condition (10,000 lux) or the low-level red light condition (less than 500 lux) after meeting study criteria. Participants were informed that the goal of the study was to examine the effect of different types of light on their responses to the questionnaires. To receive light exposure, individuals were seated alone in a room at a table with a light box positioned 14 inches from their eyes, above their head, and facing them at a 45 degree angle. All sessions occurred between 8 and 11 AM in a room unexposed to natural light. Additionally, the experiment room's fluorescent overhead lighting was dimmed to approximately 50 lux. During the 30-minutes exposure, the participants were instructed to read popular culture and/or current events magazines provided by the experimenters

and to always maintain their gaze forward. An experimenter assessed adherence to instructions throughout the session but did not interact with the participants in any other capacity. After the 30-minute exposure, participants completed another assessment battery. Data collection began in November, 2010 and spanned through the end of May, 2011.

Measurements

The Quick Inventory of Depressive Symptomatology – Self Report (QIDS) is a 16 item, self-report questionnaire designed to assess the severity of depressive symptoms (Rush et al. 2003). The QIDS assesses all the criterion symptom domains designated by the *Diagnostic and Statistical Manual of Mental Disorders - 4th edition* (DSM-IV [APA, 1994]) to diagnose a major depressive episode. Each item is scaled 0–3, with 0 as the *least severe* and 3 as the *most severe*. QIDS spans a 7-day period prior to assessment as the time span for assessing symptom severity. Total scores range from 0-27 with scores indicating mild (6-10), moderate (11-15), severe (16-21), and very severe (21-27) depression. Content validity derives from QIDS items that rate the nine symptom domains used to define a major depressive episode (APA, 1994). The QIDS has been shown concurrent validity with the Hamilton Rating Scale for Depression and to have high internal consistency (Lamoureux et al., 2010; Rush et al. 2003). The QIDs was utilized because it is the most recently validated tool for depression that has been used with regionally and ethnically diverse samples (Trivedi et al., 2004),

The Toronto Side Effect Scale (TSES) is a 32-item clinician-rated instrument that measures adverse events (Voanderkooy, Kennedy, & Bagby, 2002) measuring frequency (never – everyday) and severity (no trouble – extreme trouble) on a 5-point scale. The product of the severity and frequency scale produce an “intensity” score. The TSES has been modified for the present study due to a dearth of rating scales for side effects (Wisniewski, Rush, Balasubramani,

Trivedi, & Nierenberg, 2006) and the propensity for the TSES to be modified to suit a study's goals (e.g. Thomas et al., 2008; Zimmerman et al., 2010). The modified TSES is 19-item self-report measure of presently perceptible physiological symptoms excluding those items originally intended to measure side effects that are not applicable to BLT (e.g. sexual dysfunction, weight loss/gain) with an addition of symptoms relevant to light therapy (e.g. irritability, eye strain). Each symptom has been modified to a binary choice assessing the presence or absence of a symptom while the severity scale has been preserved. A total side effect intensity score is produced with the sum total of severity endorsements.

The Profile of Mood States (POMS) is a validated self administered measure of mood disturbance within six domains, including, fatigue-inertia, vigor-activity, tension-anxiety, depression-dejection, anger-hostility, and confusion-bewilderment (McNair, Lorr, & Droppelman, 1971). The scale ranges from 0 to 4 for each item, with 0 indicating that the item was not at all accurate in describing how the participant felt, and 4 indicating that the item was extremely accurate in describing how an individual is feeling. The POMS was modified to a 28-item checklist of adjectives and negative affect was measured based on two categories: anxiety (including on edge, nervous, and tense) and sad mood (including unhappy and sad). Positive affect was measured using three categories: vigor (including full of pep, energetic, and lively), well being (including happy and cheerful), and calm (including calm and relaxed). Concurrent validity of the POMS has been shown with the Visual Analog Mood Scale and concurrent validity of subscales on the POMS with the Beck Depression Inventory, State-Trait Anxiety Inventory, and the Geriatric Depression Scale (Nyenhuis, Yamamoto, Luchetta, Terrien & Parmentier, 1999). Internal Consistency Reliability for the full-length POMS has ranged from 0.74 to 0.91 (Shacham, 1983), and shortened versions of the POMS similar to the version used in

the current study have been found to have similar internal consistency (Bourgeois, LeUnes, & Meyers, 2010).

Statsitical Analyses

All analyses were conducted using PASW Statistics 18, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago,IL, www.spss.com). First, the presence of potentially confounding between-group differences on demographic (gender, age) and clinical characteristics (depressive symptoms, sleep quality, physiological symptoms present prior to light exposure, and mood prior to light exposure) were tested by means of univariate analyses of variance.

To investigate moderation of the associations between light condition and side effects by depressive symptoms, multiple regression analyses were performed. In such analyses, computed pre-post change scores in total side effect intensity and severity of the four most commonly reported side effects of light therapy - headache, eye strain, blurred vision, and nausea – were used as dependent variables. Each score was calculated as the difference of the post-treatment and pre-treatment scores on the TSES. Condition (bright light, red light), centered QIDS scores, and a condition-by-QIDS interaction term served as independent variables of interest. Depressive symptomatology was measured using the QIDS and centered for the analyses to increase interpretability of interactions (Aiken & West, 1991). An interaction term was created as the product of the centered continuous predictor (QIDS) and the categorical predictor (condition). Each regression analysis consisted of two steps. In the first step, condition and the centered QIDS was regressed on the dependent variable. In the second step, the interaction term was added to the model. A moderating effect was considered present when the interaction term was statistically significant within a statistically significant model. An alpha level of .05 was utilized in all regression analyses.

A within-subjects, repeated measures, 2x2 factorial design using time (pre, post) by condition (bright light, red light) was used to analyze mood-related effects. Specifically, main effects of time (pre-post) and condition, as well as a time-by-condition interaction effect, were analyzed using a repeated measures analysis of variance (ANOVA) for negative affect, positive affect, sad mood, and anxiety. An alpha level of .05 was utilized in all analyses.

Finally, simple between-group differences in specific side effects were analyzed by means of paired sample t-tests with a Bonferroni correction, and a within-subjects, repeated measures, 2x2 factorial design – time (pre, post) by condition (bright light, red light) – was used to analyze changes in total side effect intensity and nausea severity.

Results

One hundred and forty-eight undergraduate students (53% female, mean age = 19.51) met criteria for the study and were included in the final analyses. Seventy-seven (52%) participants were randomized into the control, red light group. Means, range, and standard deviations for other variables of interest are provided in Table 1. Univariate analyses of variance revealed no significant preexisting differences in baseline characteristics between participants in the two experimental conditions. Table 2 presents the prevalence of reported side effects at pre-treatment and post-treatment within each condition.

Five separate multiple regression models were evaluated to determine the effects of experimental condition and depressive symptomatology on reported side effects; standardized betas, unstandardized betas, and the standard error for unstandardized betas are provided in Table 3. The regression model with condition, QIDS score (depressive symptoms), and the condition-by-QIDS interaction term significantly predicted change in severity of nausea and change in total side effect intensity. The condition-by-QIDS interaction term was statistically

significant in the prediction of total side effect intensity; likewise, the interaction had a significant effect for nausea severity. Adjusted R-squared for the change in nausea severity was .044; in other words, about 4.4 % of the variability in nausea severity change score was accounted for by the model. Adjusted R-squared for the change in total side effect intensity was .089; thus, about 8.9 % of the variability in the difference in the total intensity of side effects was accounted for by the model. No significant main or interaction effects emerged for headache, blurred vision, or eye strain.

Figure 1 presents a plot of the moderation effect between low QIDS scores (1 *SD* below the mean) and high QIDS scores (1 *SD* above the mean) for total side effect intensity and Figure 2 presents a plot for the moderation effect in severity of nausea. For both interactions, the effect of light condition depends on the participant's level of depressive symptomatology. To further examine the nature of these interactions, separate subgroup analyses were conducted to evaluate the relationship between the QIDS and side effects. In these analyses, the QIDS-side effect intensity association was significant for the bright white light group ($\beta = -.436$, $p < .001$) but not for dim red light group ($\beta = .02$, $p > .85$). Similarly, the QIDS-nausea severity relationship was significant for the bright white light group ($\beta = -.406$, $p < .001$) but not for dim red light group ($\beta = .1$, $p > .39$). The results indicate that as QIDS scores increase, bright white light decreases nausea severity and total side effect intensity, while dim red light does not. A post hoc analysis was also conducted to compare overall changes in total side effect intensity and nausea severity across time (pre-treatment to post-treatment) by light condition. A within-subjects, repeated measures, 2x2 factorial design revealed no significant main effects or time-by-condition interaction on total side effect intensity. Means and standard deviations for side effect intensity

are provided in Table 4. Similarly, no significant main effects or interaction effect were observed for nausea.

Table 5 presents the results of the two-way (time x light condition) ANOVAs utilizing mood state as the dependent variable. Examination of the effect of light on negative affect (the composite of anxiety and sad mood) yielded a significant main effect of time, such that the average post-treatment score (M = 0.54, SD = 1.32) was significantly lower than at pre-treatment (M = 1.01, SD = 2.05). Similarly, a main effect of time emerged for positive affect, wherein average post-treatment scores (M = 7.47, SD = 4.94) were lower than pre-treatment (M = 8.52, SD = 4.89), and anxiety (pre-treatment: M = 0.47, SD = 1.37; post-treatment: M = 0.19, SD = 0.72). Main effects of condition and interaction effects were non-significant for these dependent variables. A main effect of time also emerged for sad mood, such that the average post-treatment score (M = 0.37, SD = 0.85) was significantly smaller than pre-treatment (M = 0.55, SD = 1.06). Furthermore, the time-by-condition interaction effect (Figure 3) was also significant for sad mood, indicating that sad mood decreases at a greater rate post-treatment in the bright white light group (M = 0.35, SD = 0.79) compared to the dim red light group (M = .39, SD = .91).

Finally, following an inspection of prevalence rates for each side effect, post hoc analyses were conducted to test for a significant increase in the most common side effects in the study sample – eye strain, blurred vision, or headache – from pre-treatment to post-treatment. To prevent inflation of Type I error rate a Bonferroni adjustment for level of significance, .017 (.05/3), was applied. There was a significant effect of time for eye strain, $t(147) = -4.907$, $p < .001$, such that the average post-treatment eye strain intensity (M = .921, SD = .076) was greater than at pre-treatment (M = .523, SD = .043). There was no significant effect for blurred vision ($t(147) = -1.589$, $p > .49$) or headache ($t(147) = -.675$, $p > .11$).

Discussion

The present investigation represents the first placebo-controlled study of bright light therapy (BLT) side effects at the most widely recommended and utilized dosage and duration (10,000 lux for 30 minutes). Similarly, this study is the first to evaluate a potential moderating effect of depressive symptomatology on the report of side effects, the first to examine side effects of BLT in a non-clinical sample, and also the first to examine the acute side effects of a single session exposure of bright light. The potential usefulness of addressing such questions is highlighted by the increasingly widespread use of BLT with non-clinical populations for short periods of time (e.g., Boulos et al., 2002).

There was no main effect of condition on report of side effects. However, as hypothesized, exposure to bright white light – but not dim red light – had a differential effect on perceived side effect intensity when moderating for depressive symptomatology. Contrary to expectations, however, bright white light actually induced a pre-post *reduction* in reported side effects among individuals with higher baseline depressive symptomatology. In other words, among participants in the bright light condition, those who had elevated depressive symptoms tended to report significantly lower overall side effect severity *after* light exposure than they did at the baseline assessment prior to exposure; this pattern was not observed in the red light condition. Based on mean QIDS score the sample likely contains a subset of individuals who experienced clinically significant depressive symptoms and those suffering from dysphoria. In more detailed analyses of pre-post changes among the most commonly reported phototherapy side effects – nausea, headache, blurred vision, and eye strain – the aforementioned light condition-by-depression interaction was only significant with respect to nausea. That is,

participants with higher depressive scores tended to report reduced nausea after exposure to white light.

While not expected in the present investigation, the potential ameliorating effect of BLT has been previously reported in the literature. Specifically, Terman and Terman (1999) concluded that within their sample of seasonally depressed patients, treated for 10-14 days with BLT, side effect remission rates (from pre-treatment to post-treatment) generally equaled or exceeded the rate of side effect emergence. Although they did not explicitly examine the side effects of BLT, the findings of other previous investigations using clinical samples may also be relevant. For example, there appears to be an increase in general physical and psychological well being in women with anorexia nervosa (most of whom also had elevated depressive symptoms) after BLT (Daansen & Haffmans, 2010). Potentially, an effect similar to the one seen in this study – an interaction between high depressive symptomatology and BLT - led to a reduction in undesirable physical symptoms and, thus, improvement in physical well-being. A similar mechanism may also help explain the reported reduction in agitation and dyskinaesia due to BLT in individuals with Parkinson's disease (Willis & Turner, 2007).

Many principal side effects of interest – eye strain, blurred vision, and headache – were not differentially altered in response to light condition. Likewise, there was no significant pre-post increase in the study's aggregate (composite) side effects measure as a function of bright light exposure. Although such findings run counter to those of many previous reports (e.g., Kogan & Guilford, 1998; Labbate et al., 1994; Oren et al., 1991), the present results replicate those of the only other placebo-controlled study that primarily examined adverse effects of BLT. Volz and colleagues (1991), found no difference in side effects between a bright light and a dim red light condition. However, the current findings are the first to replicate those of Volz and

colleagues using the currently prescribed dosage and length and the first to use a non-clinical sample. Across both groups, only eye strain severity was significantly exacerbated from pre-treatment to post-treatment, which is consistent with previous research indicating that eye strain is a potential concern of BLT. However, this study demonstrated that eye strain is not a consequence of the luminosity or color of light.

Although previous studies (e.g., Kogan & Guilford, 1998; Labbate et al., 1994; Oren et al., 1991) have reported blurred vision as a likely side effect of BLT, the contradictory current findings may stem from this study's categorical division of blurred vision and eye strain as distinct side effects, as opposed to previous studies that conflated eye and vision problems in a single item. The current findings establish a potential delineation in eye-related side effects that future studies should continue to examine. Interestingly, only eye strain was significantly exacerbated from pre- to post-treatment in the present study, but the increase was equivalent across the red and white light groups. Previous uncontrolled studies could not provide specificity regarding the cause of increased eye strain, which this study provided. Specifically, the current results suggest that 30 minutes of exposure to an artificial light source - no matter the strength of luminance and either red or white coloration – will increase eye strain, but not blurred vision.

The current finding of a decrease in nausea severity in those with high depressive symptomatology differs somewhat from that of Terman and Terman (1999), who found that in most study patients the emergence of nausea was more frequent than its remittance among individuals with SAD. The investigators also found that non-responders to BLT were equally likely to report the emergence or remission of nausea, but that those receiving evening light were much more likely to report the emergence of nausea than those receiving morning exposure. It is

possible that Terman and Terman would have observed higher remission rates for nausea among the subset of study non-responders who received morning BLT exposure, but they reported no analyses germane to this possibility. Alternatively, the present study's finding of an anti-nausea effect of BLT might be attributable to the use of a young, non-clinical participant sample, or perhaps to the use of a single session of BLT exposure rather than daily exposure over the course of several days.

As hypothesized, BLT was also observed to have a mood-restorative effect, such that sad mood showed a significantly greater pre-post reduction among those in the white light condition than those exposed to the control red light. This result is consistent with previous findings (e.g., Partonen & Lönnqvist, 2000) of a decrease in depressive symptoms with BLT in a non-clinical sample. However, this is the first study with a non-clinical sample and a light-placebo control to show an effect immediately after a single session of BLT. The present finding provides further support not only for the clinical use of BLT, but also for its use in non-clinical populations – an important consideration, inasmuch as up to 10% of young adults report consistently low mood in the winter, but only a small subset meet the full diagnostic criteria for SAD or other mood disorders (Wicki et al., 1992). The acute improvement of sad mood via BLT may have a beneficial effect in everyday life and, thus, potential implications for preventing depressive illness (Bar, 2009). Accordingly, the present findings, if replicated, might point to a distinct new application of BLT – the reduction of dysphoria among otherwise healthy individuals.

The rapidly observed mood-restorative effect of bright light exposure in this study is not likely attributable to BLT's circadian phase shifting effect, which would not generally be evident until the surge of melatonin release in the evening. Rather, the present results are consistent with an acute biological-change theory. As previously shown, sunlight exposure directly enhances

serotonin turnover in the brain (Lambert et al., 2002), and BLT likewise increases serotonergic activity in depressed individuals (Rao et al., 1992). Thus, the acute mood-restorative effects of BLT may also derive from increased serotenorgic activity. In fact, similar acute effects of BLT have been reported in other studies (Kripke, Risch, & Janowsky, 1983; Sher et al., 2001). Intriguingly, BLT has also been shown to prevent the lowering in mood typically observed following acute tryptophan depletion (aan get Rot, Benekelfat, Boivin, & Young, 2008) – a procedure which reduces central serotonergic activity. Notably, however, not all relevant investigations have reported mood-restorative effects with BLT among depressed (Bauer et al., 1994) and non-depressed (Rosenthal, Rotter, Jacobsen, & Skwerer, 1987; Kasper, Rogers, Madden, Joseph-Vanderpool, & Rosenthal, 1990) samples. Such effects may be more difficult to assess in depressed individuals due to the very high intensity of sad mood at baseline, which could require repeated exposures of BLT to show a significant detectable effect. Moreover, prior studies often used lower intensity light exposure for longer duration, as opposed to the currently prescribed dosage.

The study's finding of an anti-emetic effect – i.e., a reduction in nausea – with bright light among more depressed participants is somewhat surprising, especially since serotonin *antagonists* are used to treat nausea, and BLT serves as a serotonergic *agonist*. However, similar anti-nausea effects have previously been reported with BLT. For instance, participants undergoing acute tryptophan depletion in a dim light control condition reported nausea from the procedure, and yet those who were exposed to bright light did not (aan get Rot et al., 2008). Since the potential serotonergic effects of BLT are not mediated via the intestinal serotonin receptors – but, rather, those of the central nervous system – bright light may affect nausea through the mechanism of altered mood, which can in turn impact the report of symptom severity

(Salovey, Rothman, Detweiler, & Steward, 2000). In other words, sad mood may potentially color individuals' sensitivity to physiological cues, and the amelioration of such sad mood through BLT could readily account for the finding of a decrease in reported physiological symptoms (side effects) among participants who entered the study with elevated depressive symptoms. Certainly, future studies should further examine this possibility.

The present study has numerous limitations. First, while a single-session light exposure allows for a high degree of experimental control, it does not reflect the common usage of BLT, which is often applied on numerous consecutive days for a span of several weeks at a time. While previous findings suggest the report of side effects tends to diminish with repeated exposure (Kogan & Guilford, 1998), the full array of potential side effects for each participant may not have been triggered by a single session's exposure in the present investigation. Further, the study sample was relatively young, with low mean baseline levels of undesired physical symptoms (as assessed by the study's side effects measure), sad mood, and depressive symptomatology. It would be desirable in any attempted replication, therefore, to include participants with a broader range of ages, including older individuals who may express greater variability in undesired physical symptoms.

This study also appears to be somewhat limited from the standpoint of its practical significance. Although the observed reductions in sad mood and nausea severity were statistically significant, they may be too small to be of practical utility. The average difference in the reduction of sad mood between the BLT group and the control group was only 0.40 on an 8-point scale. Such a change may be too minimal to be perceived by an individual as beneficial. Similarly, there was a low baseline prevalence of nausea in the study, with only three individuals in each light condition endorsing nausea at pre-treatment. Thus, the study's result of a potential

anti-nausea effect of BLT among dysphoric participants requires replication with a sample characterized by a higher prevalence of nausea. Likewise, it would be valuable to see an attempted replication among individuals with higher baseline levels of sad mood.

The strengths of this study lie in its use of a placebo group and the relatively large sample size for a placebo-control examination of BLT-related effects. Also, this study controls for physical symptoms present before light exposure, thereby permitting an examination of the directionality of side effect severity. Commonly, studies of side effects only examine prevalence rates *after* intervention – i.e., only the emergence or remission of symptoms rather than their increase or decrease in severity, as this study did. Furthermore, this study examined the side effect profile associated with the currently accepted dosage of BLT (10,000 lux) in a non-clinical sample, thereby addressing a significant research question which up to this point had not been examined.

The present findings demonstrate the importance of understanding the full extent of potential adverse effects of BLT, a significant area of investigation given the increasing frequency with which BLT is being used in both clinical and non-clinical settings. These results also indicate that the reported prevalence of acute adverse side effects in the extant clinical literature may not apply fully to non-clinical populations. After one exposure of BLT, change in total symptom intensity and nausea severity was ameliorated for those with higher scores on depressive symptomatology. Furthermore, no increase in headache or blurred vision emerged in the present investigation. Only eye strain showed a significant exacerbation from pre-treatment to post-treatment, but it occurred in both the bright white light and the control groups. These findings suggest that BLT may be more tolerable, with fewer side effects, when employed with non-clinical, as opposed to clinical, populations. While these findings provide support for the

high tolerability of BLT, further research is needed to determine the extent to which the results may extend beyond young, non-clinical samples.

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Table 1

Baseline characteristics of participants in red light and white light conditions

	Condition	Min	Max	Mean	SD	*t*
Red	Age	18	31	19.45	1.80	-
(*n*=77)	Hours of Sleep	3	13	6.84	1.48	-
	ISI	0	17	6.35	4.11	-
	QUIDS	0	21	5.25	4.30	-
	Nausea intensity	0	3	0.09	0.46	-
	Headache intensity	0	4	0.38	0.95	-
	Blurred vision intensity	0	4	0.17	0.64	-
	Eye Strain intensity	0	5	0.13	0.62	-
	Total side effect intensity	0	30	3.94	5.82	-
	Anxiety	0	4	0.36	0.94	-
	Sad Mood	0	4	0.42	0.85	-
	Positive Affect	0	19	8.50	5.04	-
	Negative Affect	0	6	0.78	1.54	-
White	Age	18	29	19.56	1.97	-
(*n*=71)	Hours of Sleep	3	12	6.85	1.62	-
	ISI	0	20	5.93	4.47	-
	QUIDS	0	20	6.35	4.89	-
	Nausea intensity	0	3	0.07	0.39	-
	Headache intensity	0	4	0.45	0.91	-
	Blurred vision intensity	0	1	0.04	0.20	-
	Eye Strain intensity	0	3	0.08	0.41	-
	Total side effect intensity	0	25	4.73	5.33	-
	Anxiety	0	12	0.58	1.72	-
	Sad Mood	0	5	0.69	1.24	-
	Positive Affect	0	20	8.55	4.77	-
	Negative Affect	0	13	1.27	2.47	-
Total	Age	18	31	19.51	1.88	-0.351
(N=148)	Hours of Sleep	3	13	6.84	1.55	-0.043
	ISI	0	20	6.15	4.28	0.597
	QUIDS	0	21	5.78	4.61	-1.463
	Nausea intensity	0	3	0.07	0.39	0.289
	Headache intensity	0	4	0.45	0.91	-0.485
	Blurred vision intensity	0	1	0.04	0.20	1.602
	Eye Strain intensity	0	3	0.08	0.41	0.525
	Total side effect intensity	0	25	4.73	5.33	-0.867
	Anxiety	0	12	0.58	1.72	0.947
	Sad Mood	0	5	0.69	1.24	-1.585
	Positive Affect	0	20	8.55	4.77	-0.061
	Negative Affect	0	13	1.27	2.47	-1.456

Table 2

Prevalence of side effects for each condition pre-treatment and post-treatment

	Pre-Treatment		Post-Treatment	
	Red	White	Red	White
Nervousness	27 (35%)	24 (34%)	8 (10%)	11 (16%)
Agitation	5 (7%)	12 (17%)	8 (10%)	11 (16%)
Tremor or shakiness	4 (5%)	4 (6%)	4 (5%)	4 (6%)
Muscle twitching	10 (13%)	6 (9%)	4 (5%)	3 (4%)
Abdominal pain	8 (10%)	4 (6%)	5 (7%)	2 (3%)
Upset stomach	9 (12%)	12 (17%)	7 (9%)	8 (11%)
Nausea	3 (4%)	3 (4%)	5 (7%)	0
Weakness or fatigue	22 (29%)	21 (30%)	26 (33%)	21 (30%)
General dizziness	4 (5%)	6 (9%)	10 (13%)	6 (9%)
Daytime drowsiness	23 (30%)	30 (42%)	32 (42%)	33 (47%)
Sweating	8 (10%)	7 (10%)	2 (3%)	2 (3%)
Flushing	1 (1%)	1 (1%)	1 (1%)	0
Headache	12 (16%)	18 (25%)	22 (29%)	22 (31%)
Blurred vision	7 (9%)	3 (4%)	8 (10%)	9 (13%)
Eye strain	6 (8%)	4 (6%)	20 (26%)	17 (24%)
Dry mouth	8 (10%)	10 (14%)	10 (13%)	10 (14%)
Irritability	9 (12%)	10 (14%)	7 (9%)	5 (7%)
Restless energy	8 (10%)	10 (14%)	13 (17%)	11 (16%)
Average number of side effects	2.26	2.49	2.61	2.46

Table 3

Results of regression analyses

			b	SE *b*	*β*
Regression 1 (total severity)					
	*Step 1	Constant	.255	.528	
		Condition	-.674	.765	-.072
		QIDS	-.228	.083	-.222**
	***Step 2	Constant	.389	.518	
		Condition	-.687	.747	-.073
		QIDS	.023	.120	.022
		Condition*QIDS	-.461	.163	-.330**
Regression 2 (nausea)					
	Step 1	Constant	.007	.056	
		Condition	-.071	.082	-.072
		QIDS	-.012	.009	-.107
	*Step 2	Constant	.020	.055	
		Condition	-.072	.080	-.073
		QIDS	.013	.013	.124
		Condition*QIDS	-.046	.017	-.313*
Regression 3 (headache)					
	Step 1	Constant	.013	.097	
		Condition	.070	.141	.041
		QIDS	-.023	.015	-.127
	Step 2	Constant	.010	.098	
		Condition	.071	.141	.042
		QIDS	-.030	.023	-.160
		Condition*QIDS	.011	.031	.044
Regression 4 (blurred vision)					
	Step 1	Constant	.016	.059	
		Condition	.107	.086	.103
		QIDS	.006	.009	.057
	Step 2	Constant	.005	.059	
		Condition	.108	.085	.105
		QIDS	-.014	.014	-.128
		Condition*QIDS	.038	.018	.250
Regression 5 (eye strain)					
	Step 1	Constant	.348	.069	
		Condition	-.021	.139	-.013
		QIDS	.020	.015	.107
	Step 2	Constant	.350	.097	
		Condition	-.021	.139	-.013
		QIDS	.024	.022	.131
		Condition*QIDS	-.008	.030	-.032

Note: * $p < .05$. ** $p < .01$. *** $p = .001$

Table 4

Means and standard deviations for average side effect intensity

	Red		White		Total	
	M	SD	M	SD	M	SD
Pre	3.94	5.82	4.73	5.33	4.32	5.59
Post	4.31	6.03	4.18	4.52	4.25	5.34

Note: Pre = pre-treatment. Post = post-treatment

Table 5

Results of 2x2 repeated measures ANOVA including main effects for time (pre, post), main effects for condition (red, white), and the interaction effects of time-by-condition

Variable	Time	Condition	Interaction
Negative affect	14.973***	2.411	1.980
Positive affect	11.344**	0.653	0.694
Anxiety	10.381**	2.372	0.091
Sad mood	6.318*	0.643	4.624*

Note: F values provided. * $p < .05$. ** $p < .01$. *** $p = .001$.

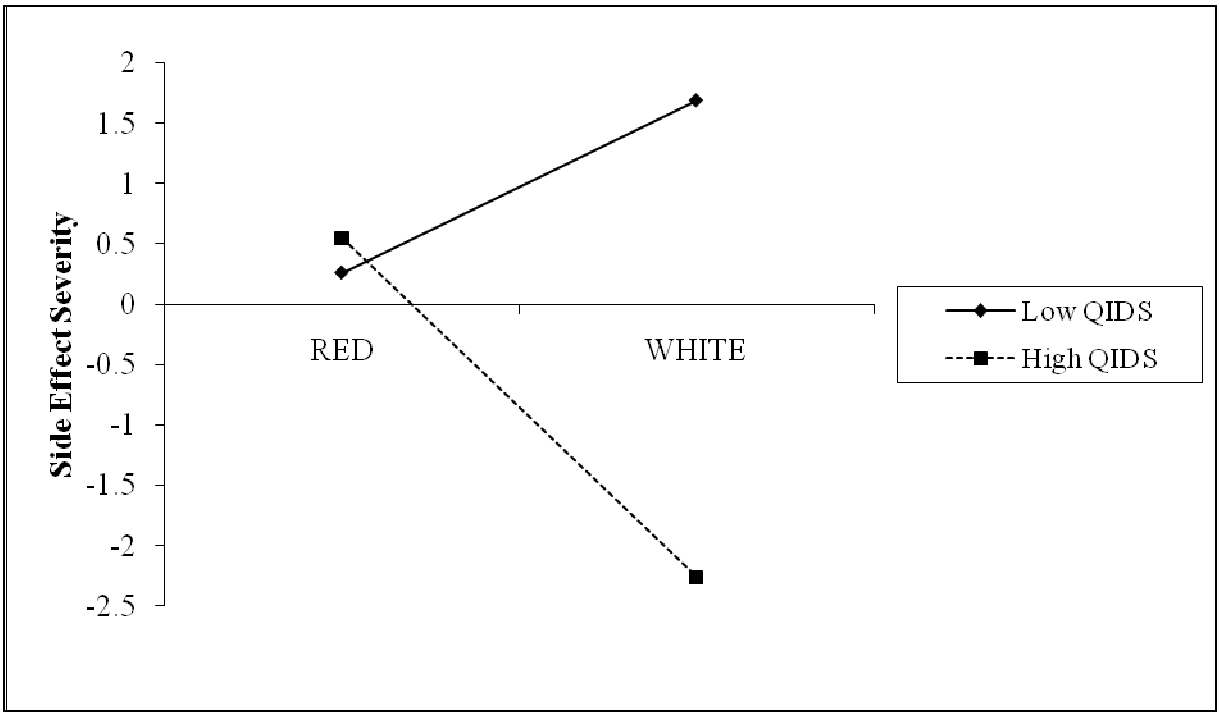

Figure 1. Relationship between total side effect severity from bright white light versus dim red light across individuals with low and high levels of QIDS. For those with high QIDS scores, bright white light decreases intensity of side effects, while dim red light does not.

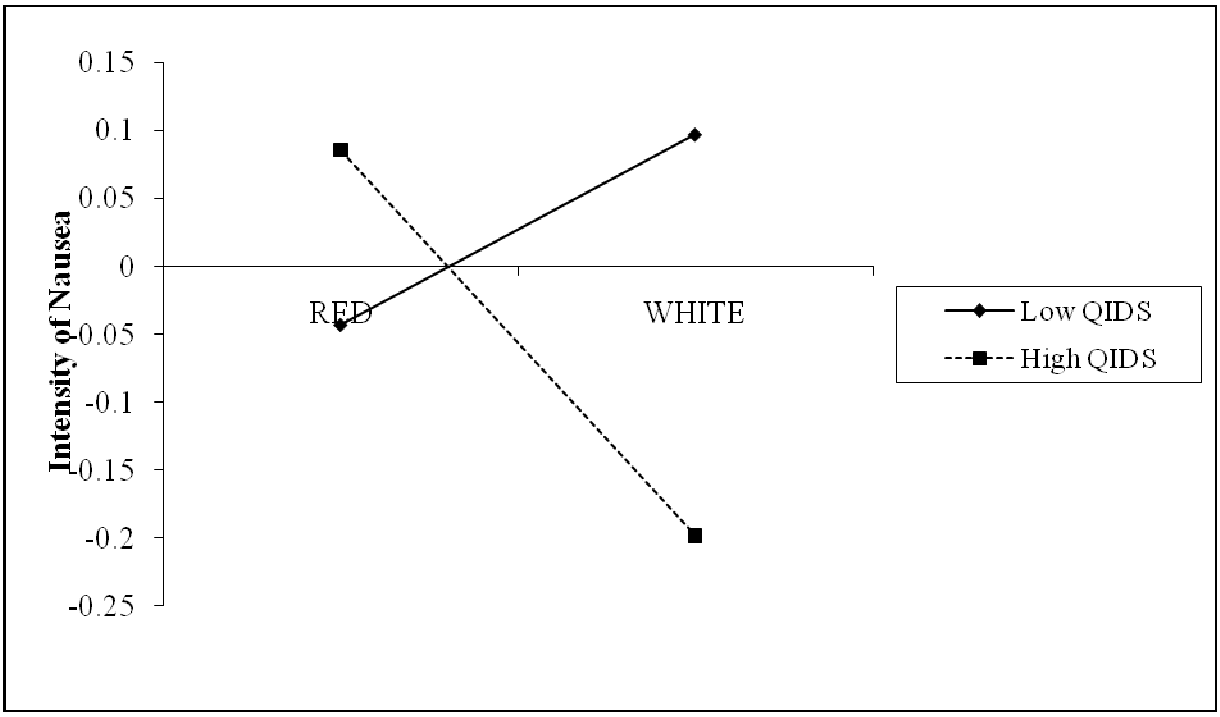

Figure 2. Relationship between nausea intensity from bright white light versus dim red light across individuals with low and high levels of QIDS. For those with high QIDS scores, bright white light decreases nausea severity, while dim red light does not.

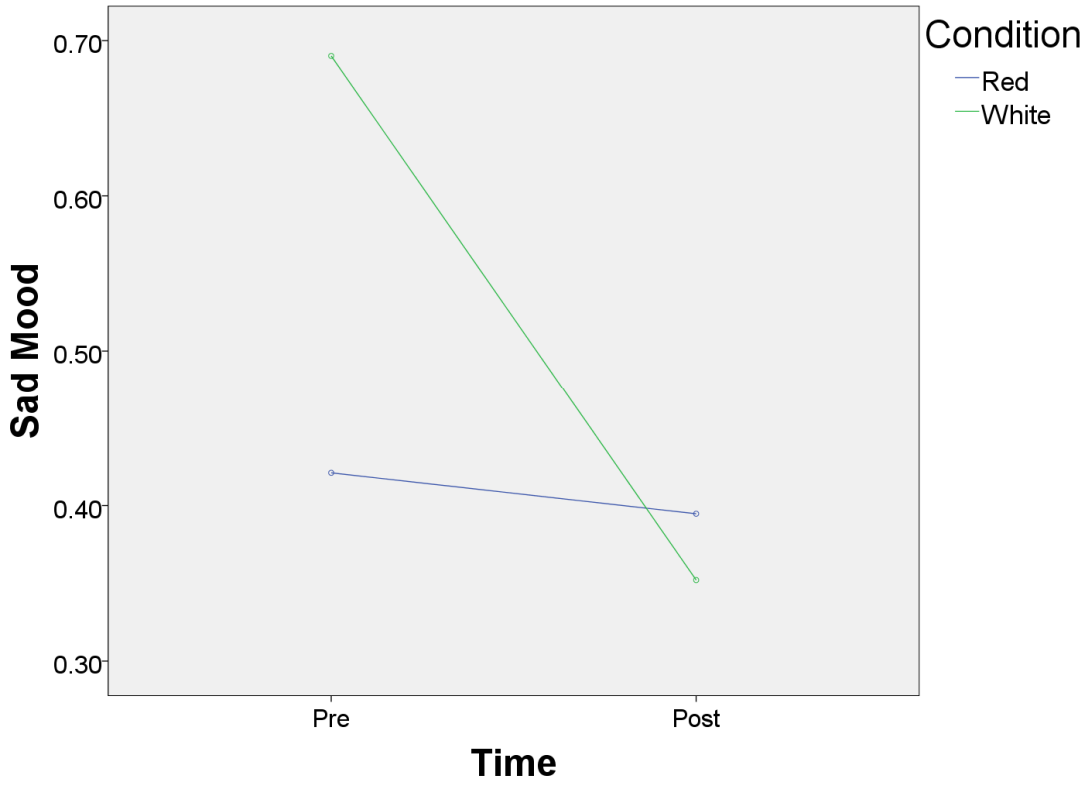

Figure 3. Decrease in sad mood over time in response to bright white light versus dim red light. Sad mood decreases at a greater rate in the bright white light group than the dim red light group.