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Research paper

A systematic review of light therapy on mood scores in major depressive disorder: light specification, dose, timing and delivery

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Abstract

Background: Depression is associated with prolonged disability, mortality, and morbidity. Ninety percent of patients with Major depressive disorder (MDD) have sleep problems. Light therapy has been shown to be effective in treating sleep disorders and MDD. This review aims to assess the characteristics (colour, intensity), exposure dose (duration and timing) and the mode of delivery (light boxes, visor etc) of light in reducing depression, measured by mood scores, in MDD.
Method: a systematic literature search was performed on 6 major databases. The Physiotherapy Evidence Database (PEDro) Scale was applied to assess study quality.
Result: Twenty-four articles satisfied the inclusion criteria. Effective light intensities varied from 176 -10,000 lux. Effective modes of delivery included light box, table lamp, visor and light emitting diode (LED) glasses. Effective light colours included white, green, and blue with the white colour being the most commonly used. The duration of light treatment ranged from 30 min to 2 h, and evening light generally improved mood.
Conclusion: Light therapy, with exposure durations in the range of 30 min to 2 h per day, intensity range of 176 to 10,000 lux, in any of blue, green, or white light colour and exposure during morning mostly demonstrated a positive change in mood effects. Factors other than the light properties, such as anti-depressant medication use, depression episodes and severity, natural light exposure and sleep deprivation may confound the effects of light therapy.

Keywords: *Bright Light; Depression; Natural Light; Non-Seasonal Affective Disorder; Phototherapy.*

1. Introduction

Depression, described as an experience of low self-esteem, lack of interest, fatigue, suicidal thoughts, parasomnia and lack of appetite [1], is often associated with prolong disability, mortality, morbidity with numerous health issues and economic impact [2]. Major depressive disorder (MDD) is by far the most prevalent of all mood disorder diagnoses [3]. Depression, a topical issue, requires timely re-evaluation to report the degree of prevalence [4]. In 2005, depression was found to be the fourth most prevalent disorder managed by Australian general practitioners (GPs) [5]. In 2007, a survey conducted by the Australian Bureau of Statistics found that the prevalence of mental illness (including depression) in young adults was 26%, which was one third higher than the overall adult population [6]. In 2010, depression remained the most prevalent disorder seen by the GPs [7]. Sleep disturbance is a key etiological factor of depression and has been found to be prevalent in 90% of the patients plagued with a major depression [8]. Troubled sleep and feelings of exhaustion and tiredness are commonly encountered during depression episodes [9-11]. Several sleep related issues faced by these patients are: not being able to sleep (initial insomnia), not sleeping as much as they normally do (mid insomnia), getting up several times at night and getting up earlier than normal in the morning (terminal insomnia), and finally not being able to go back to sleep once awake [12]. These observations suggest sleep disturbances in circadian timing, and thus interventions to deal with the likely disturbances should consider the individual's circadian cycle [13].

Among methods used in treating sleep problems in depressive illness are psychotherapy or a combination of antidepressant medicines and psychotherapy [14]. However, these therapies do not completely target the link between depression and phase shifts in circadian sleep-wake cycles. Moreover, there are several side-effects of antidepressant medications with greater rates of relapse [10]. Hence, sleep disturbances can be addressed through wake therapy (sleep deprivation) and light therapy [15]. Treatments for patients facing the most severe form of depression included a combination of wake therapy, light therapy and drug therapy [15]. The results were superior to that achieved by antidepressant drugs alone. The combined treatment showed an improvement of 27% in a single week, whereas, antidepressant medications reported an improvement of only 8-11% [15]. From among these therapies, light therapy offers several advantages, such as fast response and low degree of risk to patients [16]. Furthermore, combination of light treatment with drug and wake therapy have achieved faster results with higher success rates than antidepressants alone. Thus light therapy has been considered a better and more successful remedy for depressive disorders [17].

Treatment using light involves exposing patients to light at regular intervals for a certain time period. The devices used include light boxes that filter out ultraviolet waves, light emitting diodes (LED)

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technology that is smaller in size, fluorescent lamps that produce visible light (390-780 nm) and other devices to create bright light. Light therapy is particularly appropriate for patients who are resistant to and cannot tolerate medications. Given that the treatment is non-pharmacological and non-invasive, patients approve of it readily and at times, prefer it as well [18]. Light therapy has also been successfully used to treat seasonal affective disorder (SAD). SAD is a disorder that occurs when people experience depression intermittently in response to seasonal changes, most frequently during the fall and winter seasons due to short daylight. The photoperiod can be increased by five to six hours to reverse the seasonal changes using bright (2500 lux), full-spectrum light in the hours of morning, evening and at night [19]. Patients with Non-seasonal Affective disorder (NSAD) or MDD can also benefit from light treatments [20-24]. In fact bright-light therapy for MDD patients was 12-35% more beneficial than dim-light placebos or anti-depressants [25].

The effectiveness of light therapy for NSAD has been evaluated in three meta-analyses [26-28]. The reviews by [27], [28] concluded that light therapy was efficacious for NSAD, and bright light as an adjunct to antidepressant pharmacotherapy is effective for seasonal affective disorder and nonseasonal depression. The comprehensive analysis also suggests that light therapy can improve melatonin amplitude and cyclical sleep patterns along with improvement in depression score [29].

There are currently no guidelines to determine which patients will benefit from light therapy, as a few studies have demonstrated no impact of light therapy on patients with NSAD [20, 21, 30-32]. Furthermore, there has been no systematic evaluation and synthesis of the published literature regarding characteristics (colour, intensity), exposure dose (duration and timing) and the mode of delivery (light boxes, visor etc) of light for use as a treatment for NSAD patients. The purpose of this review is to identify the elements that contributed to successful light therapy, as measured by the mood score, and identify any contravening factors and provide informed guidelines for future light therapy research for the treatment of depression.

2. Method

2.1. Search strategy

Database searches were performed in MEDLINE (via OvidSP, 1946 - April 10, 2015), PSYCHINFO (via OvidSP, 1806 - April 10, 2015), CINAHL (via Ebsco, 1982 - April 10, 2015), EMBASE (1980 - April 10, 2015), PubMed (1966 - April 10, 2015) and Cochrane Collaboration Library (1993 - April 10, 2015). The search terms included (depression or “major depressive disorder" or “non-seasonal affective disorder”) and (light or “light therapy” or “bright light” or phototherapy). The search was limited to English language articles with subjects aged 18 and above. Articles that used light intervention on MDD were included. Articles that employed light intervention on seasonal affective disorder, on mental disorders (e.g., Alzheimer, dementia) other than MDD, on other diseases such as cancer, or on children, were excluded.

2.2. Study selection/ quality assessments

The Physiotherapy Evidence Database [33] for measuring study quality was used for the assessment of methodological quality in those articles.

2.3. Data extraction

The variables extracted were number of patients, sex, type of depression and diagnostic questionnaires used, mode of light delivery, light specifications (colour and intensity) for both intervention and placebo groups, timing and duration of treatment, mood outcomes from the light therapy and whether the participants were on antidepressant medications or not.

3. Results

The initial search identified 1662 articles after removal of duplicates. Following reviewing their titles, abstracts and/or full text, 24 articles were selected and further assessed using the PEDro scale. The excluded articles were either irrelevant to this review, or met the exclusion criteria. Five articles that examined the effect of sleep deprivation on depression as the main outcome were also excluded (Fig. 1).

3.1. Demographic data and questionnaires used to assess mood

Table 1 presents the extracted data listing demographic data, depression type, and the depression diagnostic tools employed by the respective studies. The total number of participants across the studies was 1024 (310 male, 626 female and 88 unreported sex). The age ranged from 35 to 70 years old. Diagnostic and Statistical Manual of Mental Disorders –III Revision and –IV (DSM-III-R and -IV) were prevalent diagnostic questionnaires in selected articles. Twenty-one studies used Hamilton Depression Rating Scale (HDRS) for scoring mood states [9], [11], [15], [16], [20-23], [30], [32], [34-44]. The other studies used scales such Geriatric Depression Scale, Major Depression Inventory and The International Classification of Diseases. Only a few studies identified patients’ sleep related issues including hypersomnia and early or delayed sleep phases [10], [11], [30], [32].

3.2. PEDro scale quality assessment

Table 1 shows the results of quality assessment of the articles using the PEDro scale. According to the PEDro scale, the qualities of selected studies were generally high ranging from 7/11 to 11/11.

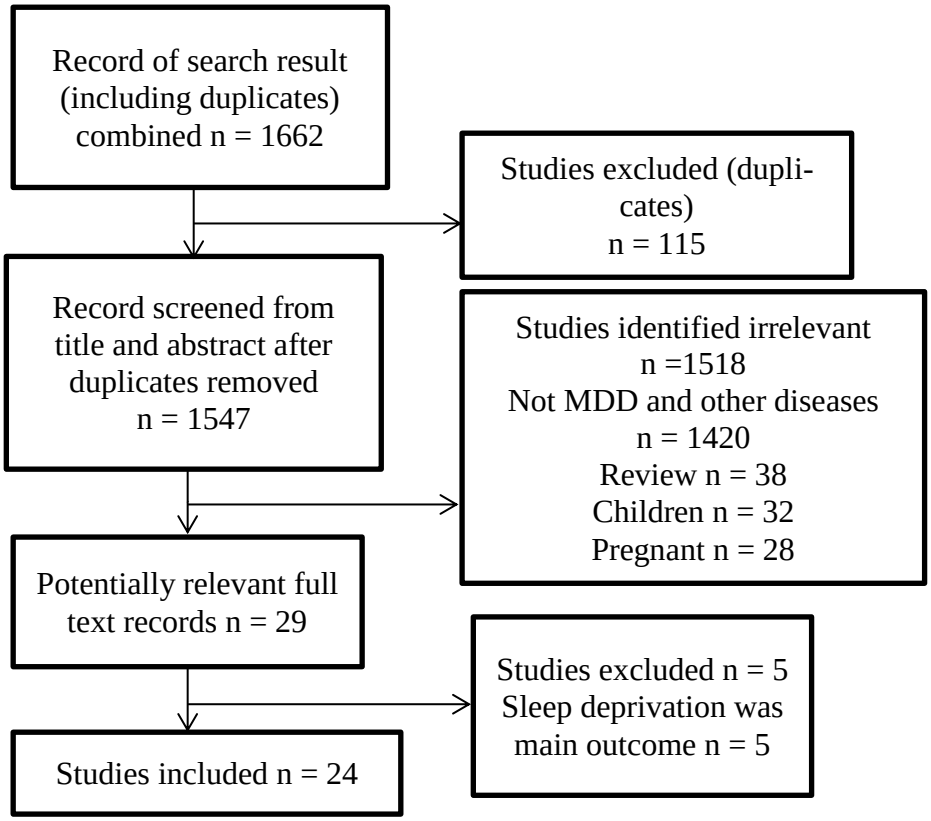


Fig. 1: Flow Chart of the Number of Articles Identified from the Search, Excluded and Included in the Review.

Table 1: Quality Assessment Results of Included Studies with Details of Subjects and Depression

Author (year)	Sex	Mean ± SD age	Type of depression	Diagnostic Questionnaire	PEDro Score Total
Baumgartner et al.,[38]	7M/27F	BL: 52.2 ± 13.2 C: 56.3 ± 1.2	MDD	DSM-III-R	11
Beauchemin & Hays[24]	8M/11F	39.0 ± 11.5	MDD-single episode, MDD-recurrent, BD	DSM-IV	7
Benedetti et al.,[41]	6M/24F	BL: 53.0 ± 10.0 C: 56.2 ± 12.3	MDD, BD	DSM-IV	10
Deltito et al.,[16]	1M/16F	36 ± NR	MDD, BD, UBD	DSM-III-R	10
Fritzsche et al.,[37]	14M/26F	47.0 ± 11.0	MDD, SAD	DSM-IV	10
Goel et al., [40]	8M/24F	43.1 ± 12.0	MDD	DSM-IV	9
Holsboer-Trachsler et al.,[42]	22M/22F	52.0 ± 9.0	MDD, BD, UBD, DD	DSM-III-R	10
Kripke et al., [9]	11M/1F	Mean age not reported	MDD, BD	RDC	9
Kripke et al., [22]	50M/1F	48.0 ± NR	MDD, BD	DSM-III	9
Lieverse et al., [39]	31M/58F	BL: 69.7 ± 8.1 C: 69.0 ± 6.1	MDD	DSM-IV	11
Loving et al., [15]	2M/11F	44.0 ± NR	MDD	DSM-IV	9
Loving et al., [30]	34M/47F	67.1 ± 5.5	MDD	GDS, DSM-IV	9
Mackert et al., [21]	8M/34F	54.0 ± 13.0	MDD, BD	DSM-III-R,CGI	11
Martiny et al., [44]	32M/70F	BL: 43.0 ± 15.1 C: 45.1 ± 16.0	MDD	MDI, PGWB, and SCL-90R	11
Martiny et al., [35]	29M/63F	BL: 44.6 ± 15.6 C: 46.3 ± 15.2	MDD	DSM-IV	11
McEnany & Lee [10]	29F	Pre.M: 37.5 ± NR Post.M: 55.9 ± NR	MDD	BDI, SCL-90R	11
Prasko et al., [36]	12M/22F	42.1 ± 10.0	MDD	DSM-III-R	11
Rao et al., [31]	53*	BL: 53.1 ± 1.0 C: 52.1 ± 1.0	MDD	DSM-III-R, RDC and ICD9	11
Stewart et al., [43]	7M/23F	NSAD-AD: 40.0 ± 12.0 SAD: 52.1 ± 1.0	NSAD-AD, SAD	DSM-III	11
Strong et al., [34]	9M/26F	44.3 ± 12.6	NSAD, SAD	DSM-IV,HAMD17,CGI	11
Thalen et al., [11]	12M/51F	Female: 49.1 ± 1.0 Male: 49.0 ± 3.0	MDD, SAD	DSM-III-R	7
Volz et al., [20]	5M/25F	52.2 ± 12.3	MDD	RDC, ICD-9	10
Yamada et al., [23]	35*	47.6 ± 2.2	MDD	DSM-III-R	11
Yerevanian et al., [32]	2M/15F	41.5±13.5	MDD, SAD	DSM-III-R,BDI,GAS	7

BD: Bipolar depression; UBD: Unipolar depression; DD: Dysthymic Disorder; DSM: Diagnostic and Statistical Manual of Mental Disorders; GDS: Geriatric Depression Scale; HDRS: Hamilton Depression Rating Scale; ICD-9: The International Classification of Diseases; MDI: Major Depression Inventory; MDD: Major depressive disorder; NSAD: Non-seasonal affective disorder; PGWB: the Psychological General Well-Being Scale; RDC: Research Diagnostic Criteria; SAD: Seasonal affective disorder; SCID: Structured Clinical Interview for DSM-IV Axis I Disorders; SCL-90R: Symptom Check L; BL: Bright Light Group, C: Control Group; CGI: Clinical Global Impressions; Pre.M: Pre-Menopausal; Post.M: Post-Menopausal; NSAD-AD: Non-seasonal Affective Disorder-Atypical Depression; HAMD-17: Hamilton Depression Rating Scale-17; GAS: Global Assessment Scale; NR: Not reported. *number in each sex not reported.

3.3. Mode of delivery and light specification (colour and intensity)

Out of the 24 pertinent articles, only 5 reported a no effect while all other studies reported positive effects. Sixteen reported use of a light box, three employed a table lamp, one used a visor, three used a ceiling light, and one used a LED light for the light therapy (Table 2). Regardless of the mode of delivery, all modes showed positive mood effects.

Light sources of different colours showed positive effects on mood. Of the 24 studies, 21 used white light (16 had positive effects), two used blue light (both positive effects) and one green light (positive effect) (Table 2). Light intensities used were 176 lux for LED glasses, 1,000-3,000 lux for ceiling lights, 10,000 lux for visors, and 400-2,500 lux for table lamps and 2,500-10,000 lux for light boxes. Positive effects on mood were found across most intensities. Positive effects were observed using intensities ranging from 400 lux to 10,000 lux, although four of the five studies that found no mood effects used an intensity range between 2500-8,500 lux with one study indicating an intensity of ≥ 2,000 lux. Some of the patients were already on anti-depressants.

Table 2 Effect of light source and its intensity, duration, and timing on mood changes, treatment duration and whether anti-depressive medication was used during the trial. Light sources included light box, light box/lamp, visor, ceiling lamp and LED light.

Study	Mode of Delivery	Light Colour	Intensity (lux)	Placebo group	Duration	Timing	Treatment Duration	On Anti-depressant Medication	Mood effects	HDRS Scores	
										Baseline	Post-treatment
Baumgartner et al.,[38]	Light box	white	2500	red 50 lux	2 h	a.m.	1 week	No	Positive	BL:19.2 ± 4.3 C:19.9 ± 4.0	BL:15.0 ± 4.8 C:17.0 ± 4.9
Beauchemin & Hays[24]	Light box	white	10000	white 2500 lux	30 min	a.m.	6 days	Yes	Positive	NR	NR
Benedetti et al.,[41]	Table lamp	green	400	other [b]	30 min	a.m.	4 weeks	Yes	Positive	BL:23.7 ± 6.9 C:22.6 ± 4.9	BL:7.4 ± 07.7 C:13.1 ± 8.3
Deltito et al.,[16]	Light box	white*	2500	white* 400 lux	2 h	a.m.	1 week	No	Positive	BL:31.0 ± NR C:26.0 ± NR	BL:6.0 ± NR C:19.0 ± NR
Fritzsche et al.,[37]	Light box	white	2500	red 50 lux	2 h	a.m.	2 week	Yes	Positive	TSD-R BL:17.1 ± 6.0 C:15.0 ± 3.0 TSD-NR BL:16.1 ± 4.0 C:15.0 ± 4.1	TSD-R BL:7.1 ± 7.0 C:6.1 ± 2.1 TSD-NR BL: 11.1 ± 3.1 C:12.0 ± 5.1
Goel et al., [40]	Light box	white	10,000	other [b]	1 h	a.m.	5 weeks	No	Positive	BL:15.1 ± 3.0 HDNAI: 17.1 ± 3.1 LDNAI: 17.0 ± 2.1	BL:7.1 ± 6.1 HDNAI: 8.0 ± 6.1 LDNAI: 13.0 ± 6.0
Holsboer-Trachsler et al.,[42]	Light box	white	5000	normal treatment	2 h	p.m.	6 weeks	Yes	Positive	BL:22.7 ± 5.3	BL:14.1 ± 5.8
Kripke et al., [9]	Ceiling light	white	1000-2000	red 25 lux	1 h	a.m.	1 day	No	Positive	BL:10.0 ± 7.0 C:12.1 ± 6.1	NR
Kripke et al., [22]	Ceiling light	white	2000-3000	red 50 lux	2 h	p.m.	1 week	No	Positive	BL:100 % ± 5 % C:100 % ± 5 %	BL:86 % ± 5 % C:90 % ± 5 %
Lieverse et al., [39]	Light box	pale blue	7500	red 50 lux	1 h	a.m.	3 week	No	Positive	BL:18.1 ± 5.1 C:16.0 ± 4.1	BL:8.1 ± 6.1 C:10.1 ± 6.1
Loving et al., [15]	Light box	white	10000	red 100 lux	30 min	a.m.	1 week	Yes	Positive	BL:24.0 ± 9.8 C:18.8 ± 7.2	BL:17.4 ± 11.4 C:15.0 ± 8.1
Loving et al., [30]	Light box	white	8500	red <10 lux	1 h	a.m./mid /p.m.	4 weeks	Yes	No effect	BL:16.9 ± 07.2 C:17.6 ± 05.4	BL:11.1 ± 07.1 C:11.3 ± 06.0
Mackert et al., [21]	Light box	white	2500	red 50 lux	2 h	a.m.	1 week	No	No effect	BL:19.1 ± 4.0 C:19.0 ± 4.0	BL:15.0 ± 5.0 C:17.0 ± 6.0
Martiny et al., [44]	Light box	white	10000	red 50 lux	1 h	a.m.	5 weeks	Yes	Positive	BL:31.0 ± 7.1 C:31.0 ± 7.1	BL:12.08 ± 8.08 C:15.03 ± 9.0
Martiny et al., [35]	Light box	white	10000	red 100 lux	1 h	a.m.	5 weeks	Yes	Positive	BL:10.0 ± 5.1	BL:8.0 ± 6.0

Study	Mode of Delivery	Light Colour	Intensity (lux)	Placebo group	Duration	Timing	Treatment Duration	On Anti-depressant Medication	Mood effects	HDRS Scores	
										Baseline	Post-treatment
McEnany & Lee [10]	Visor	white	10000	circadian adaptation glasses	1 h	a.m.	26 days	No	Positive	C:12.0 ± 5.0 NR	C:08.1 ± 5.0 NR
Prasko et al., [36]	Light box	white	5000	red 500 lux	2 h	a.m.	3 weeks	Yes	Positive	BL&M: 23.0 ± 6.0 BL&MP: 23.0 ± 3.1 DL&M: 24.1 ± 3.1	BL&M: 17.0 ± 11.0 BL&MP: 8.1 ± 5.1 DL&M: 13.0 ± 7.1
Rao et al., [31]	Table lamp	white	2500	red 50 lux	2 h	a.m.	1 week	No	No effect	NR	NR
Stewart et al., [43]	Light box	white	2500	other*	2 h	a.m. & p.m.	2 week	No	Positive	NSAD-AD: 16.0 ± 03.1 SAD:16.0 ± 4.1	NSAD-AD: 3.0 ± 0.1 SAD:3.0 ± 0.1
Strong et al., [34]	LED glasses	blue 470nm	176	red 21 lux	2 h	a.m.	3 weeks	No	Positive	BL:20.0 ± 3.1 C:19.1 ± 5.0	BL:10.0 ± 5.0 C:6.0 ± 3.1
Thalen et al., [11]	Ceiling light	white	1500	other [c]	2 h	a.m./ p.m.	10 days	Yes	Positive	a.m.:15.6 ± 1.3 p.m.:17.4 ± 1.6	a.m.:13.0 ± 1.7 p.m.:14.4 ± 2.2
Volz et al., [20]	Light box	white	2500	50 lux	2 h	a.m.	1 week	No	No effect	BL:20.0 C:19.05	BL:15.0 C:18.0
Yamada et al., [23]	Light box	white	2500	yellow 500 lux	2 h	a.m./ p.m.	1week	No	Positive	15.5 ± 4.2	9.6 ± 5.3
Yerevanian et al., [32]	Table lamp	white	≥ 2000	other [c]	2 h	a.m./ p.m.	1 week	Yes	No effect	23.0 ± 9.0	24.0 ± 3.0

*Light colour not reported - white colour is assumed. Other: Studies compared to either medication[a], low or high density negative air ions[b], or Seasonal Affective disorder[c]. TSD-R: Total sleep deprivation responders. TSD-NR: Total sleep deprivation nonresponders. HDNAI: High density negative air ions LDNAI: Low density negative air ions; BL: Bright Light, C: Control, BL&M: Bright light and medication; BL&MP: Bright light and medication-like Placebo; DL&M: Dim light and medication; NSAD-AD: Non Seasonal Affective Disorder-Atypical Depression; NR: Not Reported.

3.4. Duration and timing of the light therapy

The duration of light therapy employed ranged from 30 min to 2 h per day, and was generally effective on mood. However, four studies with 2 h light exposure and a study with 1 h light exposure showed no improvements on mood. The treatment period ranged from 1-4 weeks. Most of the studies (n=17) delivered the treatment in the morning only, one study delivered the treatment in the morning and evening, three studies delivered the treatment in the morning or evening 2 studies delivered the treatment in the evening only and one study delivered the treatment in the morning or midday or in the evening. One of 1 study that delivered the therapy in the morning or midday or evening, 1 study of 3 that delivered the therapy in the morning or evening and 3 of 17 that delivered the therapy in the morning only failed to show efficacy.

3.5. Taking anti-depressant medication during light therapy

In 11 of the 24 studies, participants were on the anti-depressant medication during the light therapy. These studies showed positive effects of the therapy, except two studies [30, 32]. Of the 13 studies where participants did not use anti-depressants, 10 showed positive effects.

4. Discussion

This paper assessed the properties of light, its timing, duration and intensity, and the mode of delivery that are therapeutic determinants in reducing depression in MDD, with a focus on mood state as the outcome measure. 79.2% (n=19) of studies found that light therapy was effective in lifting mood state, consistent with the findings of previous reviews [27, 28]. Despite the positive findings, it is challenging to clearly define the elements that contribute to the efficacy of light therapy. Factors other than the light properties, such as anti-depressant medication use, depression episodes and severity, natural light exposure, treatment compliance and sleep deprivation were discussed to establish their impact on light therapy.

4.1. Light characteristics

The findings revealed that light intensities ranging from 176 to 10,000 lux showed positive effects on depression. However, previous studies demonstrated that an intensity of at least 2,000 lux was required to produce positive effects on depression [45], [46]. Remarkably, studies that used low intensity light (176, 400, 1,000 and 1,500 lux) also showed improvements in depression scores [9], [11], [34], [41] suggesting that even low intensity light was effective on mood alleviation.

All colours of light (blue, green and white) were effective in improving mood. White light is the most widely used source in 21/24 studies. Its effectiveness may be due to the presence of blue and green colours as components of white light [47]. Indeed, the supra-chiasmatic nucleus (SCN) is sensitive to changes in bright light of white, blue and green and change of seasons [12], [23], [34], [39], [41]. The SCN controls circadian rhythms, which dictates the timing of physical, behavioural and mental patterns [9]. The output of SCN is modulated by light and darkness within an individual's surrounding on physiological rhythms [48]. Thus appropriate timing of light exposure can re-align altered sleep-wake patterns [9].

Lewy et al. [13] suggested that evening light is more effective to correct sleep phase advance whereas morning lights has a therapeutic effect for phase delay. Unlike SAD, non-seasonal patients are more likely to have heterogeneous chronobiological patterns and could have either sleep phase advance or phase delay [28]. Of the 24 studies reviewed, one study demonstrated effective sleep phase delay by morning light timing and improved sleep length by aligning the timing of melatonin secretion [24] as well as enhancing mood [11], [24]. Given the scarce literature on light timing and mood, it is

too soon to rule out the timing of light exposure (AM or PM) as insignificant in light treatment.
The optimal duration of light exposure needed for effective mood alleviation is also controversial. Wirz-Justice et al. [46] suggested that 2 h light exposure is more effective than 30 min. However, the duration of light therapy that ranged from 30 min to 2 h showed positive effects on mood. Nevertheless, four studies that used 2 h light exposure failed to show efficacy. Importantly, if an exposure of as little as 30 min [15], [24], [41] can be demonstrated reproducibly to be efficacious for depression, other parameters defined, then a breakthrough in treatment can be claimed.

4.2. Antidepressant medication – resistance to medication

Light therapy alone resulted in similar clinical effects as the use of anti-depressants alone [9], [10], [16], [22], [23], [34], [38-40], [43]. However, studies that combined antidepressant therapy with light therapy found greater improvement than with light therapy alone [11], [15], [24], [35-37], [41], [42], [44] suggestive of synergistic effects. On the other hand, the use of antidepressant medication with light therapy also showed no mood effects [30, 32]. Such discrepancy in findings may be that the use of different study methodology made comparisons difficult. Discrepancy may also be explained by patients who may have demonstrated resistance to pharmacotherapy [49]. The interaction of the antidepressant effect of medication limits the understanding of the efficacy of light therapy. In addition, non-responders to therapies are common [50]. Therefore, it is necessary to identify patients groups who are homogenous, for example, those who are antidepressant medication-resistant prior to the commencement of light therapy, or patients either currently in or not currently in a depression episode.

4.3. Depression episodes and severity

Of the 24 studies, twenty-one studies indicated that the patients were studied during a depression episode. Patients continued to experience mild depression at the end of their treatment. This observation was despite the patients of these studies were on antidepressant medication [11], [15], [34], [36], [38], [44]. Lifestyle stressors and medical morbidity may influence mood. Of the 21 studies employing the HDRS scale, 5 studies showed no significant changes in the mood state following the light therapy [20], [21], [30-32]. Interestingly, these studies that showed no improvements reported high baseline HDRS scores (range 16.85 to 23.4, n=4). Whilst light exposure can lift mood, persistent stressors such as unresolved personal, psycho-social or economic factors, in those with high baseline scores may mask the effects of the light therapy. None of the 4 studies monitored these stressors.

4.4. Natural light exposure

Natural light and its daily exposure may have a direct impact on the mood state of patients undergoing light therapy. Indeed it represents a major confounding factor in these studies and could be the reason behind the results that showed minimal effects. Although two studies monitored the patients' natural light exposure using the Actillume (Ambulatory Monitoring INC., Ardsley, NY) [30] and an Actigraph (Philips Resprionics)[39] with a light sensor to monitor the sunlight exposure and adherence, neither studies reported the amount of light received nor discussed its confounding effects. Some authors advised patients to wear a dark cover that wrapped around the glasses if they were outdoor in order to not get much of the sunlight [10]. These findings suggest that, ideally, natural light exposure should be monitored during the treatment period, for example, with the Actiwatch2 (Philips Respironics) that is equipped with a light sensor, in future studies, would help unmask the true efficacy of light therapy.

4.5. Treatment compliance

Treatment compliance can directly impact on study outcomes. All 24 studies, including the 5 that did not show significant mood changes showed 100% study compliance with light exposure. At least in the current review study compliance does not appear to be a factor affecting the light therapy

4.6. Sleep deprivation

It has been well documented that sleep deprivation alleviates depression [51]. Loving et al. [15] found that patients with MDD who were treated with a combination of bright light, sleep deprivation, and medication improved 27% and a rapid response within 1 week. They noted that this response was superior when compared with the use of antidepressant drugs alone, which produced only a relative benefit of 8-11%. Subsequently, Fritzsche et al. [37] showed that people who responded to sleep deprivation also responded to light therapy (regardless of intensity and colour) whereas, those who did not respond to sleep deprivation also did not respond to light therapy. This linked response is of interest. Should the finding prove to be reproducible, it would be feasible to conduct a sleep deprivation study to establish suitability for light therapy. It remains intriguing but unclear as to the mechanism that underlies the effectiveness of sleep deprivation and light therapy, and whether both treatments share a common path.

5. Summary and conclusions

Light therapy worked in 19/24 studies but there were no clear-cut mechanisms identified that would explain these results. Remarkably, light therapy, with light duration of a range of 30 min to 2 h per day, intensity ranging from176 to 10,000 lux, colour (blue, green, or white), or its timing (AM or PM) mostly demonstrated a positive change in mood effects. However, it remains challenging to provide informed guidelines for light therapy as there may be numerous factors that could confound the study effects. The current data also do not permit determination of which patients will benefit from light therapy. Importantly, there is a need to understand the unique effect of light therapy without the imposing effect of antidepressants or natural light. There is also a need to establish that the paralleled mood enhancement effect seen with sleep deprivation and light therapy is a real phenomenon that can be reproduced. These foundation studies need to precede with well-designed clinical trials of light and depression, which control for patients factors such as responsiveness to sleep deprivation, the severity of depression, life stressors, natural light exposure, depressant medications and drug resistance.

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