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ORIGINAL RESEARCH

Comparison of effects of bright light therapy alone or combined with fluoxetine on severity of depression, circadian rhythms, mood disturbance, and sleep quality, in patients with non-seasonal depression

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Purpose: To compare effects of bright light therapy (BLT) alone or combined with the selective serotonin reuptake inhibitor (SSRI) fluoxetine, on severity of depression, circadian rhythms, mood disturbance, and sleep quality, in patients with non-seasonal depression.

Patients and methods: Drug-free patients who were administered 10,000 lux of BLT for 30 minutes for 7 days comprised the BLT group (n = 7), while patients who started fluoxetine as an add-on treatment day comprised the SSRI + BLT group (n = 8). The primary outcomes were severity of depression, measured using the Hamilton Depression Rating Scale (HAM-D) and the Beck Depression Inventory (BDI); chronotype, measured using the Morningness Eveningness Questionnaire (MEQ); mood disturbance, measured using the Profile of Mood States (POMS) survey; and sleep quality, measured using the Pittsburgh Sleep Quality Index (PSQI), before and after treatment in both groups.

Results: All patients completed the study, and none reported obvious side effects. The mean onset age of depression was 26.1 years ± 5.3 years in the BLT group and 27 years ± 9.5 years in the SSRI + BLT group ($P = 0.425$). The number of past depressive episodes was 1.29 ± 0.76 in the BLT group, and 1.5 ± 0.8 in the SSRI + BLT group ($P = 0.427$). The difference between pre- and posttreatment scores revealed no significant difference between groups for the HAM-D scale, BDI, MEQ, POMS survey, and the PSQI.

Conclusion: This study suggests that BLT is effective with respect to the severity of depression, circadian rhythms, mood disturbance, and sleep quality, in non-seasonal depression. However, there was no evidence in favor of adjunctive fluoxetine with BLT in the treatment of non-seasonal depression, for any of the rating scales used in our study.

Keywords: bright light therapy, mood states, nonseasonal depression, sleep disorders, sleep quality

Introduction

The beneficial effect of bright light therapy (BLT) in seasonal affective disorder (SAD) either alone or as an add-on therapy to antidepressant drugs is well accepted, with early onset of action and mild adverse-effect profiles.[1] However, the effect of BLT in non-seasonal depression has been controversial. While some controlled studies reported significant improvements,[2] others failed to do so.[3] Even if the improvement may be less than those seen in SAD, it can be assumed that at least some patients with

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non-seasonal depression respond to BLT.[4] Recent research also suggested that the use of BLT might be useful as an adjunctive treatment to antidepressants in non-seasonal depression, both in terms of results from clinician-rated depression scales and results from patient-reported symptom and well-being scales.[5]

Sleep disturbances are common among depressive patients, and abnormalities of sleep architecture constitute the most robust psychobiological correlates of major depression. From a clinical perspective, there is an association between sleep problems and depression.[6] The relationship between sleep-related breathing disorders and depressive symptoms was shown in a population of school-aged children, by Carotenuto et al.[7] Also, sleep disturbance in adolescence has been associated with adult mental health problems, such as depression and substance abuse.[8] Disturbed sleep (insomnia and/or hypersomnia) has been included as one of the nine diagnostic criteria for major depressive episodes in the DSM-III, DSM-III-R, and DSM-IV. Sleep fragmentation, decreased quantity and altered distribution of delta sleep, reduced duration of the first non–rapid eye movement (REM) period (ie, REM latency), redistribution of REM sleep into the first half of the night, and increased number of REMs per minute of REM sleep were also shown by clinical study.[9] These symptoms have been related to impaired functioning of the suprachiasmatic nucleus (SCN). Activation of the SCN has been hypothesized as one of the mechanisms of BLT action on mood, sleep, circadian rhythms, and hypothalamic–pituitary axis activity.[10] Light induces specialized light-sensitive retinal ganglion cells to release glutamate in the SCN, through a monosynaptic pathway called the retinohypothalamic tract.[11] BLT also targets depression-associated neurotransmitter systems (serotonin, noradrenalin, and dopamine) and targets the same brain structures as antidepressant drug treatments.[12]

The aim of the present study was to compare effects of BLT alone or combined with a selective serotonin reuptake inhibitor (SSRI) on the severity of depression, circadian rhythms, mood disturbance, and sleep quality, in patients with non-seasonal depression.

Patients and methods

Study population and design

The study was approved by the clinical research ethics board at the research center, Üsküdar University, Istanbul, Turkey and executed in accordance with the Helsinki Declaration. Subjects were assured that patient anonymity should be strictly preserved. After giving written, informed consent, eligible subjects entered a 1-week baseline phase without treatment to regularize their sleep–wake schedule (patients were instructed to sleep only between the hours of 10:00 pm and 8:00 am).

Drug-free patients who were administered 10,000 lux of BLT for 30 minutes for 7 days comprised the BLT group. Patients who were started on fluoxetine 20 mg/day and 10,000 lux of BLT for 30 minutes for 7 days as an add-on treatment comprised the SSRI + BLT group. The patients were randomly allocated into the two groups by means of a computer-generated random number list.

The inclusion criteria for the study were age between 18–65 years of age and major depressive episodes with a nonseasonal pattern. Depression was diagnosed using the Structured Clinical Interview for DSM-IV Axis I Disorders, Turkish clinical version.[13] The severity of depression was rated using the Structured Interview Guide for the Hamilton Scale for Depression (HAM-D).[14] Subjects were required to have an initial assessment score of 14 or higher on the 17-item HAM-D Scale, Turkish version, which indicates moderate to severe depression.

Subjects were excluded from the study if they: (1) were pregnant or lactating (or were sexually active women of childbearing potential not using a medically accepted means of contraception); (2) were at serious suicidal risk in the judgment of the investigator; (3) met the DSM-IV criteria for organic mental disorders or other major psychiatric disorder; (4) had a serious unstable medical illness; (5) had retinal disease or a family history that precluded the use of bright light; (6) had a history of severe allergies or multiple drug adverse reactions; (7) were currently using other psychotropic drugs, including lithium, L-tryptophan, or melatonin; (8) were currently using beta blocking drugs; (9) were previously treated with light therapy; or if (10) they performed shift work or traveled south during the protocol.

Bright light therapy administration

The active light treatment consisted of daily exposure to a white fluorescent light box (SADelite Daylight 10000; Northern Light Technologies, Montreal, QC, Canada) fitted with an ultraviolet filter and rated at 10,000 lux at a distance of 60–80 cm from screen to cornea, for 30 minutes as soon as possible after awakening and between 7:00 am and 8:00 am. The patients were advised not to stare directly into the light source and that the light should meet the eye at an angle of 30°–60°. The duration of therapy was 7 days for all participants. Patients were given verbal instructions on the

use of the light box, and health care personnel attended all sessions.

Outcome parameters

Assessments were performed at the following two time points: just before the start of light treatment, and immediately on completion of the 1-week treatment interval. The primary outcome measures were as follows:

- 17-item Hamilton Depression Rating Scale (HAM-D): The HAM-D is a worldwide used clinician-administered rating scale for the evaluation of depression severity.[14] Though it exists in different versions with up to 36 items, the 17-item version is the most frequently used and meets established criteria for reliability and validity. The present study used the more structured 17-item version.[15] The scores on the first 14 items are based on a semistructured interview of the patient, interrogating their experiences over the previous week. The scores on the last three items (Insight, Psychomotor Retardation, and Psychomotor Agitation) are based on observations of the patient's behavior during the interview session.
- Beck Depression Inventory Scale (BDI): The BDI is a commonly used 21-item measure of depression.[16] Each item consists of four statements describing increasing intensities of symptoms of depression. Items are rated on a scale from 0–3, reflecting how participants have felt over the past week. Possible scores range from 0–48; higher scores reflect more severe depressive symptoms.
- Morningness Eveningness Questionnaire (MEQ): The MEQ measures chronotype (or circadian rhythms) by self-rated preference for the morning versus the evening hours.[17] In studies of clinically depressed men and women, depressed patients had lower MEQ scores (greater "eveningness") than nondepressed controls.[18]
- Profile of Mood States Survey (POMS): The POMS is an easily completed 5-point mood adjective checklist. It is specifically intended for use as a research instrument for assessing changes in affective states across events or interventions in psychologically healthy adults.[19] The 65 items form six subscales, five negative mood states, and a single positive mood dimension. It is also possible to calculate a total score of mood disturbance, known as the POMS total, by summing the scores of the five subscales for the negative mood states and subtracting from this the score for the positive subscale. The five negative mood state subscales are tension-anxiety, depression-dejection, anger-hostility, fatigue-inertia, and confusion-bewilderment. The single positive mood state subscale is vigor-activity.
- Pittsburgh Sleep Quality Index (PSQI): PSQI is a self-rated questionnaire designed specifically to measure sleep quality in clinical populations; it yields seven component scores and a global score.[20] The seven components are subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. As the questions in PSQI are related to usual sleep habits during the previous month, we modified the time interval from "last month" to "last week."

Additionally, at baseline and at the end of the study, patients were systematically interviewed about possible adverse effects.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 19.0 for Windows (IBM, Armonk, NY, USA). A normal distribution of the quantitative data was checked using the Kolmogorov–Smirnov test. Parametric tests were applied to data of normal distribution and nonparametric tests were applied to data of questionably normal distribution. The independent samples *t*-test was used to compare independent groups. The data were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Statistical significance was assumed for $P < 0.05$.

Results

Seven drug-free patients (one male, six females; mean age 28.4 ± 5.2 years) comprised the BLT group, while eight patients (two males, six females; mean age 28.9 ± 11.2 years) who were started on fluoxetine comprised the SSRI + BLT group. All patients completed the study. None reported obvious side effects, and none dropped out of the treatment protocol. BLT and fluoxetine were well tolerated. There were no hospitalizations or suicides during the study period. The mean onset age of depression was 26.1 ± 5.3 years in the BLT group and 27 ± 9.5 years in the SSRI + BLT group. The number of past depressive episodes was 1.3 ± 0.8 in the BLT group and 1.5 ± 0.8 in the SSRI + BLT group. No significant difference was observed in terms of the mean onset of depression and number of past depressive episodes between the groups ($P = 0.425$ and $P = 0.427$, respectively).

There was no evidence in favor of adjunctive fluoxetine with BLT in the treatment of non-seasonal depression, for

Table 1 Pretreatment scores, posttreatment scores, and the difference of pre- and posttreatment scores for both groups in the 17-item Hamilton Depression Rating Scale, Beck Depression Inventory Scale, and the Morningness Eveningness Questionnaire

	Pretreatment (mean ± SD)	Posttreatment (mean ± SD)	Difference (mean ± SD)	*P*-value
HAM-D				
BLT group (n = 7)	21.57 ± 11.99	6.43 ± 9.66	−15.14 ± 14.50	0.267
SSRI + BLT group (n = 8)	17.25 ± 6.14	8.75 ± 6.45	−8.50 ± 6.87	
BDI				
BLT group (n = 7)	22.43 ± 9.93	16 ± 15.79	−6.43 ± 8.24	0.594
SSRI + BLT group (n = 8)	19 ± 7.91	14.63 ± 8.16	−4.38 ± 6.28	
MEQ				
BLT group (n = 7)	46.57 ± 8.06	48.14 ± 5.76	1.57 ± 3.78	0.094
SSRI + BLT group (n = 8)	48.5 ± 12.41	45.63 ± 10.59	−2.88 ± 5.46	

Abbreviations: HAM-D, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory; MEQ, Morningness Eveningness Questionnaire; BLT, bright light therapy; SSRI, selective serotonin reuptake inhibitor; SD, standard deviations.

any of the rating scales used in our study. Table 1 shows the 17-item HAM-D, BDI, and MEQ scores in the BLT and SSRI + BLT groups before and after treatment. The analysis of the difference between the pre- and posttreatment scores revealed no significant difference between groups. Table 2 shows POMS scores in the BLT and SSRI + BLT groups before and after treatment. The analysis of the difference between these pre- and posttreatment scores revealed no significant difference between groups in any of the subgroups of the POMS scores. Table 3 shows PSQI scores in the BLT and SSRI + BLT groups before and after the treatment. The analysis of the difference between pre- and posttreatment scores revealed no significant difference between groups in any subgroup of PSQI scores.

Discussion

To our knowledge, this is the first study that examines the effect of BLT on sleep quality as well as on mood, in non-seasonal depression. Our study results revealed that there was no evidence in favor of adjunctive fluoxetine with BLT for the treatment of non-seasonal depression, for any of the rating scales used. For the BLT group, the results showed

Table 2 Pretreatment scores, posttreatment scores, and the difference of pre- and posttreatment scores for both groups in the Profile of Mood States Survey

	Pretreatment (mean ± SD)	Posttreatment (mean ± SD)	Difference (mean ± SD)	*P*-value
Tension				
BLT group (n = 7)	23.57 ± 7.16	18.43 ± 8.22	−5.14 ± 6.52	0.122
SSRI + BLT group (n = 8)	20.5 ± 6.66	19.88 ± 6.33	−0.63 ± 2.07	
Depression				
BLT group (n = 7)	29.57 ± 18.09	19 ± 17.35	−10.57 ± 12.73	0.199
SSRI + BLT group (n = 8)	22.25 ± 10.55	18.71 ± 10.14	−3.50 ± 3.59	
Anger				
BLT group (n = 7)	22.71 ± 11.66	15 ± 13.09	−7.71 ± 10.95	0.166
SSRI + BLT group (n = 8)	19 ± 11.03	18.13 ± 13.35	−0.88 ± 4.91	
Vigor				
BLT group (n = 7)	15 ± 5.29	14.86 ± 3.80	−0.14 ± 3.80	0.400
SSRI + BLT group (n = 8)	12.63 ± 2.97	13.88 ± 4.02	1.25 ± 2.31	
Fatigue				
BLT group (n = 7)	14.43 ± 6.48	10.57 ± 7.35	−3.86 ± 6.49	0.685
SSRI + BLT group (n = 8)	13.875 ± 5.62	11.13 ± 6.27	−2.75 ± 2.66	
Confusion				
BLT group (n = 7)	13.29 ± 5.59	9.57 ± 7.11	−3.71 ± 4.86	0.429
SSRI + BLT group (n = 8)	12 ± 4.11	10 ± 4.72	−2.00 ± 2.73	
Total				
BLT group (n = 7)	88.57 ± 44.98	57.71 ± 53.68	−30.86 ± 38.78	0.235
SSRI + BLT group (n = 8)	75 ± 37.02	64 ± 39.74	−11.00 ± 12.24	

Abbreviations: BLT, bright light therapy; SSRI, selective serotonin reuptake inhibitor; SD, standard deviations.

Table 3 Pretreatment scores, posttreatment scores and the difference of pre- and posttreatment scores for both groups in Pittsburgh Sleep Quality Index

	Pretreatment (mean ± SD)	Posttreatment (mean ± SD)	Difference (mean ± SD)	*P*-value
Subjective sleep quality				
BLT group (n = 7)	1.86 ± 0.69	1.43 ± 0.98	–0.43 ± 0.79	0.211
SSRI + BLT group (n = 8)	1.5 ± 0.76	1.63 ± 0.52	0.13 ± 0.83	
Sleep latency				
BLT group (n = 7)	3 ± 1.63	3 ± 1.53	0.00 ± 0.58	0.194
SSRI + BLT group (n = 8)	3.25 ± 2.43	2.5 ± 1.85	–0.75 ± 1.39	
Sleep duration				
BLT group (n = 7)	1.29 ± 1.11	1.14 ± 1.21	–0.14 ± 1.35	0.321
SSRI + BLT group (n = 8)	0.88 ± 1.36	1.38 ± 1.51	0.50 ± 1.07	
Sleep efficiency				
BLT group (n = 7)	1.43 ± 1.39	1 ± 1.29	–0.43 ± 1.62	0.401
SSRI + BLT group (n = 8)	0.38 ± 1.06	0.75 ± 1.39	0.38 ± 1.92	
Sleep disturbance				
BLT group (n = 7)	2.29 ± 0.76	1.71 ± 0.76	–0.57 ± 0.53	0.089
SSRI + BLT group (n = 8)	1.5 ± 0.76	1.38 ± 0.74	–0.13 ± 0.35	
Use of sleep medication				
BLT group (n = 7)	0.14 ± 0.38	0 ± 0	–0.14 ± 0.38	0.244
SSRI + BLT group (n = 8)	0 ± 0	0.38 ± 1.06	0.38 ± 1.06	
Daytime dysfunction				
BLT group (n = 7)	3 ± 1	2 ± 1.53	–1.00 ± 1.53	0.678
SSRI + BLT group (n = 8)	2.63 ± 1.41	2 ± 1.41	–0.63 ± 1.85	
Global				
BLT group (n = 7)	13 ± 4.28	10.29 ± 6.26	–2.71 ± 3.86	0.270
SSRI + BLT group (n = 8)	10.13 ± 6.03	10.13 ± 5.33	0.00 ± 5.07	

Abbreviations: BLT, bright light therapy; SSRI, selective serotonin reuptake inhibitor; SD, standard deviations.

that depressive symptom severity decreased after BLT, in all the HAM-D, BDI, MEQ scales, while the POMS total mood disturbance score showed a positive effect, and sleep quality increased in the PSQI scales. For the SSRI + BLT group, the depressive symptom scores measured in the HAM-D and BDI decreased, but the MEQ revealed worsened (although not significantly) results. Also, the POMS subscale scores of vigor and the PSQI component scores for subjective sleep quality, sleep duration, sleep efficiency, and use of sleep medication were worsened, but this difference was not significant. None of our patients experienced any obvious side effects.

A core biological clock mechanism, residing in the SCN within the anterior hypothalamus, regulates circadian rhythms in the brain and body of mammals. The periodicity of these endogenous rhythms is continuously synchronized or entrained by environmental signals, primarily the light–dark cycle. Desynchronization of the normal circadian rhythms, including the sleep-wake rhythm, is common in major depressive disorder.[21] Manipulation of circadian rhythms either using BLT or behavioral therapy has shown promise in improving symptoms.

BLT represents a potent, nonpharmacological treatment modality whose efficacy and tolerability have been a matter of extensive research. Studies in the 1990s became the basis of a widely cited benchmark for BLT with light intensities of up to 10,000 lux and duration of 30 min/day.[22] Evidence[23] suggests that the melatonergic (MT[1] and MT[2]) and the 5-Hydroxytryptamine (5HT2C) serotonergic receptor subtypes are important modulators of circadian rhythmicity. Melanopsin, a short-wavelength, light-sensitive G-protein-coupled receptor located in human retinal ganglion cells, is known to transduce short-wavelength light signals into neural signals.[24] Since melanopsin is primarily responsible for resetting the timing of the SCN, suppressing pineal melatonin secretion, and for improving alertness and the electroencephalogram-derived correlates of arousal, it has been hypothesized that short-wavelength light with a low light intensity might be a stimulator for melanopsin-containing retinal ganglion cells and the behaviors mediated via this photoreceptor system.[25] A meta-analysis on the efficacy of BLT was published by Golden et al in 2005 and systematically gathered efficacy data following the principles of evidence-based medicine.[26] The authors initiated a systematic review of all existing data from

trials using BLT in seasonal and non-seasonal depression, from trials using dawn simulation for SAD, and from trials using BLT as adjunctive therapy to psychopharmacological treatment in non-seasonal depression. Of 173 studies, 23 qualified for inclusion into the meta-analysis. The results showed effects were impressive, equivalent or superior to most psychopharmacological trials. With regard to sleep quality, the present study showed (although not significantly) that BLT was effective in improving sleep quality, in accordance with mood changes. The suppression of melatonin secretion by BLT in the early morning hours may result in an improvement in mood states, including depression. On the other hand, BLT also causes a phase advance in circadian rhythms and an improvement in sleep quality.

Terman and Terman found that 2500-lux light exposure for at least 2 hours/day for 1 week resulted in significantly higher remission when administered in the early morning compared with administration in the evening or at midday.[27] Three studies were able to conclusively demonstrate that early morning administration of BLT was associated with higher remission rates than was evening administration.[26–30] In the present study, BLT was administered for 30 minutes as soon as possible after awakening, between 7:00 am and 8:00 am.

With regard to BLT for non-seasonal depression, there is no consensus with respect to optimal timing, dosage, and treatment duration. We chose 1 week of daily light exposure like other studies that used short-term treatment of up to 1 week to report their findings.[31,32] Furthermore, a Cochrane review of studies of BLT in non-seasonal affective disorder concluded that BLT may be effective in as little as 1 week.[33]

Generally, BLT is well tolerated and well accepted by patients.[3,4] Side effects are rare and tend to remit spontaneously or after dose reduction. The most common side effects are headache, eyestrain, nausea, and agitation. Evening administration of BLT can increase the incidence of sleep disturbances.[34] Suicidality may sporadically occur early in the treatment course, and menstrual irregularities have also been reported.[35] In the present study, none of the patients reported obvious side effects, and none dropped out of the treatment protocol. There were no hospitalizations or suicides during the study period. Although there is some evidence for retinal degeneration after prolonged exposure to intensive visible light in rodents, this was not confirmed in humans.[35] Nevertheless, patients with a family history of retinal damage or patients needing photosensitizing medication are advised to consult their ophthalmologist before initiating treatment. We excluded patients who had retinal disease or a family history that precluded the use of bright light from the study group.

Some caveats and limitations in our study should be noted. First, we limited our focus to an open study rather than a placebo-controlled study. Second, a placebo effect cannot be excluded since there was no control group in this trial (in trials of BLT, it is difficult to design a control group that is blind to both researchers and patients). Thus, the raters were also not blind to the conditions. Third, although the therapeutic drug regimen in the SSRI + BLT group was standardized, the duration of the treatment was not similar in each patient. Finally, our study includes a relatively small sample size, and generalization of the findings is relatively difficult.

As a conclusion, this study suggests that BLT was effective with respect to the severity of depression, circadian rhythms, mood disturbance, and sleep quality in non-seasonal depression. However, there was no evidence in favor of the use of adjunctive fluoxetine with BLT in the treatment of non-seasonal depression, for any of the rating scales used in our study. Future research is needed to examine objective sleep electroencephalogram (EEG) variables in patients with non-seasonal depression.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Lewy A, Bauer V, Cutler N. Bright morning light reduces depressive symptoms in seasonal affective disorder. *West J Med*. 1999;171(5–6):316.
2. Beauchemin KM, Hays P. Phototherapy is a useful adjunct in the treatment of depressed in-patients. *Acta Psychiatr Scand*. 1997;95(5):424–427.
3. Hill H, Batt C, Maier S, Weisbrod M, Kick H. Light-therapy of affective disorders with and without seasonality: biological markers. *German Journal of Psychiatry*. 1998;1:41–52.
4. Kripke DF. Light treatment for nonseasonal depression: speed, efficacy, and combined treatment. *J Affect Disord*. 1998;49(2):109–117.
5. Martiny K, Lunde M, Undén M, Dam H, Bech P. Adjunctive bright light in non-seasonal major depression: results from patient-reported symptom and well-being scales. *Acta Psychiatr Scand*. 2005;111(6):453–459.
6. Franzen PL, Buysse DJ. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. *Dialogues Clin Neurosci*. 2008;10(4):473–481.
7. Carotenuto M, Esposito M, Parisi L, et al. Depressive symptoms and childhood sleep apnea syndrome. *Neuropsychiatr Dis Treat*. 2012;8:369–373.
8. Roane BM, Taylor DJ. Adolescent insomnia as a risk factor for early adult depression and substance abuse. *Sleep*. 2008;31(10):1351–1356.
9. Nutt D, Wilson S, Paterson L. Sleep disorders as core symptoms of depression. *Dialogues Clin Neurosci*. 2008;10(3):329–336.
10. Riemersma-van der Lek RF, Swaab DF, Twisk J, Hol EM, Hoogendijk WJ, Van Someren EJ. Effect of bright light and melatonin on cognitive and noncognitive function in elderly residents of group care facilities: a randomized controlled trial. *JAMA*. 2008;299(22):2642–2655.

11. Hattar S, Liao HW, Takao M, Berson DM, Yau KW. Melanopsin-containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. *Science*. 2002;295(5557):1065–1070.
12. Wirz-Justice A. From the basic neuroscience of circadian clock function to light therapy for depression: on the emergence of chronotherapeutics. *J Affect Disord*. 2009;116(3):159–160.
13. Çorapçıoğlu A, Aydemir Ö, Yıldız M, et al. DSM-*IV Eksen I Bozuklukları İçin Yapılandırılmış Klinik Görüşme SCID-I Klinik Versiyon* [Structured Clinical Interview for DSM-IV Axis I Disorders]. Ankara, Hekimler Yayın Birliği;1999. Turkish.
14. Akdemir A, Örsel S, Dağ İ, İşcan N, Özbay H. Hamilton depresyon derecelendirme ölçeğinin geçerliliği, güvenilirliği ve klinikte kullanımı. [Reliability, validity and clinical use of the Turkish version of the Hamilton Depression Rating Scale] *3P Dergisi*. 1996;4:251–259. Turkish.
15. Whisman MA, Strosah K, Fruzzetti AE, Schmaling KB, Jabobson NS, Miller DM. A structured interview version of the Hamilton Rating Scale for Depression: Reliability and validity. *Psychol Assess*. 1989;1: 238–241.
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561–571.
17. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *Int J Chronobiol*. 1976;4(2):97–110.
18. Gaspar-Barba E, Calati R, Cruz-Fuentes CS, et al. Depressive symptomatology is influenced by chronotypes. *J Affect Disord*. 2009;119(1–3): 100–106.
19. McNair DM, Lorr M, Droppleman LF. *Manual for the Profile of Mood States*. San Diego, CA: Educational and Industrial Testing Service; 1971.
20. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193–213.
21. Lam RW. High-quality remission: potential benefits of the melatonergic approach for patients with major depressive disorder. *Int Clin Psychopharmacol*. 2007;(22)Suppl 2:S21–25.
22. Partonen T. Effects of morning light treatment on subjective sleepiness and mood in winter depression. *J Affect Disord*. 1994;30(2):99–108.
23. Lam RW. Addressing circadian rhythm disturbances in depressed patients. *J Psychopharmacol*. 2008;(7):13–18.
24. Berson DM, Dunn FA, Takao M. Phototransduction by retinal ganglion cells that set the circadian clock. *Science*. 2002;295(5557):1070–1073.
25. Peirson S, Foster RG. Melanopsin: another way of signaling light. *Neuron*. 2006;49(3):331–339.
26. Golden RN, Gaynes BN, Ekstrom RD, et al. The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence. *Am J Psychiatry*. 2005;162(4):656–662.
27. Terman M, Terman JS. Light therapy for seasonal and nonseasonal depression: efficacy, protocol, safety, and side effects. *CNS Spectr*. 2005;10(8):647–663.
28. Eastman CI, Young MA, Fogg LF, Liu L, Meaden PM. Bright light treatment of winter depression: a placebo-controlled trial. *Arch Gen Psychiatry*. 1998;55(10):883–889.
29. Terman M, Terman JS, Ross DC. A controlled trial of timed bright light and negative air ionization for treatment of winter depression. *Arch Gen Psychiatry*. 1998;55(10):875–882.
30. Lewy AJ, Bauer VK, Cutler NL, et al. Morning vs evening light treatment of patients with winter depression. *Arch Gen Psychiatry*. 1998;55(10):890–896.
31. Sumaya IC, Rienzi BM, Deegan JF 2nd, Moss DE. Bright light treatment decreases depression in institutionalized older adults: a placebo-controlled crossover study. *J Gerontol A Biol Sci Med Sci*. 2001;56(6): M356–M360.
32. Loving RT, Kripke DF, Shuchter SR. Bright light augments antidepressant effects of medication and wake therapy. *Depress Anxiety*. 2002;16(1):1–3.
33. Tuunainen A, Kripke DF, Endo T. Light therapy for non-seasonal depression. *Cochrane Database Syst Rev*. 2004;(2):CD004050.
34. Swiecicki L. Phototherapy for winter depression: report of three cases. *Psychiatr Pol*. 1993;27(6):667–672. Polish.
35. Pjrek E, Winkler D, Willeit M, Konstantinidis A, Thierry N, Kasper S. Menstrual disturbances a rare side-effect of bright-light therapy. *Int J Neuropsychopharmacol*. 2004;7(2):239–240.