



Effects of daylight on sleep and circadian rhythms in patients with depression

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ABSTRACT

Current research has shown depressive symptoms are associated with sleep disturbances and misalignment of circadian rhythms. A chronobiological intervention combined with the usual antidepressant treatment may improve depressive symptoms along with sleep quality and circadian rhythms in patients with depression. This feasibility study was carried out with 38 participants: 21 outpatients suffering from non-seasonal major depressive disorder (MDD) and 17 healthy volunteers (general population). Patients were randomly assigned to two groups: 11 patients received a chronobiological intervention which consisted of regular specified daylight exposure for 14 days in conjunction with pharmacological treatment (LIGHT group), while 10 patients received only treatment-a-usual (TAU group). Depressive severity at inclusion was assessed with the Montgomery-Asberg Depression Scale and the International Neuropsychiatric Interview was used to exclude comorbid psychiatric disorders. The evolution of depressive symptoms was assessed using the Quick Inventory of Depressive Symptomatology-Self Report. Patients' chronotype was evaluated with the Munich Chronotype Questionnaire and sleep with Pittsburgh Sleep Quality Index and a sleep agenda. In addition, circadian parameters (motor activity, skin temperature and light exposure) were assessed using the Kronowise® device and target sleep quality indices were calculated. Depressive patients undergoing psychopharmacological treatment, who received a specific instruction to increase their exposure to daylight improved their depressive symptoms, sleep quality, motor activity and peripheral temperature rhythms more than the TAU group.

1. Introduction

Major depressive disorder (MDD) is characterized by a persistent low or depressed mood, anhedonia or decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts, that cause social or occupational impairment [1]. MDD affects approximately 5 % of the Spanish adult population annually [2,3]. In addition, in a Mallorca primary care setting, between 25 % and 35 % of adult patients have mental disorders (29 % with a depressive disorder) [4]. Depression is responsible for

significant economic expenditure on health treatments. It has been estimated that the total annual social cost of depressive disorders in the Spanish adult population was €6,145 million in 2017 [2]. Even though antidepressant drugs (AD) are widely used for the treatment of MDD, approximately 50 % of patients do not experience an adequate response to these therapies [5].

Daylight via the eye exerts different functions through different physiological mechanisms on the brain and body. A critical discovery revealed that there is a non-visual pathway via photoreceptors in the retinal ganglion cells that directly access the circadian clock through a retinal-hypothalamic tract. These intrinsically photosensitive retinal

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ganglion cells contain a photopigment (melanopsin) with highest sensitivity to short-wavelength, blue light. This is the major neural pathway by which light modulates the circadian system [6]. Additionally, daylight is the most powerful synchronizer (“zeitgeber”) adjusting circadian rhythms. Daylight, as already well documented for artificial bright light, is antidepressant [7]. Increased exposure to daylight in the hospital environment shortens time to remission leading to an earlier discharge [8–10].

Bright light therapy (BLT) has been classically used for the treatment of Seasonal Affective Disorder [11,12]. The combination of BLT with antidepressants accelerates and potentiates the clinical response in nonseasonal depressive episodes, also in bipolar patients [13–16]. A meta-analysis concluded that BLT produces faster antidepressant benefits than AD alone and is clearly superior [14]. However, despite the available scientific evidence, chronotherapeutic methods are poorly understood and scarcely applied in health systems, as well as in therapeutic regimens for depression. For this reason, it is important to focus on the circadian system as a crucial therapeutic approach to treating depression [17].

The research we present posits that exposure to daylight in the morning will speed up the remission of depressive symptoms and improve the synchronization of circadian rhythms in depressive patients. Therefore, a scheduled chronobiological intervention of exposure to daylight in the morning in conjunction with antidepressant treatment in outpatients with non-seasonal major depression: a) will be more effective than pharmacological treatment alone in the reduction of depressive symptoms, and b) improve the quality of sleep and the adjustment of circadian rhythms.

The objectives of this study are: 1) To analyse the degree of acceptance and adherence to daylight therapy, as well as recruitment and adherence to the study, 2) To quantify light exposure with a device (KW6) in patients receiving a chronotherapeutic intervention (LIGHT group) versus patients who do not receive it (TAU group), 3) To assess changes in depressive symptoms after 14, 21 and 28 days of follow-up, and 4) To evaluate the subjective and objective sleep quality of patients of both groups.

2. Materials and methods

2.1. Participants

Twenty-one patients attending a Mental Health Unit in Palma de Mallorca (Balearic Islands) presenting a non-seasonal major depressive episode, who started with a new antidepressant treatment or changed from the previous antidepressant treatment due to lack of efficacy; most patients with depression were on sick leave. And 17 healthy volunteers recruited from the general population.

The criteria for the selection of patients were: A) Inclusion criteria: 1) Aged between 18 and 65 years of both genders, 2) Diagnosis of non-seasonal major depressive disorder (MDD) according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders [1], 3) Had to obtain a score ≥ 24 in the Spanish version [18] of the Montgomery-Asberg Depression Scale [22], and 4) Had to understand the research objectives, that their participation was voluntary, and sign informed consent. B) Exclusion criteria: 1) Substance abuse (> 24 g/day of alcohol in women, 40 g/day in men, use of cocaine, heroin, and other drugs of abuse), 2) Had another psychiatric or neurological disorder, 3) Had comprehension difficulties or low educational level, 4) Had skin problems and eye sensitivity and/or photophobia, and 5) Performed shift work.

2.2. Study design

This was a feasibility study with a double branch, randomized experimental design. Sampling was probability sampling with simple randomization. Patients were divided into two groups: LIGHT and

treatment-as-usual (TAU). All patients received the same written explanation about the aim of the study and procedure (included in the informed consent form). The only difference was that LIGHT group received specific instructions to expose themselves to daylight in the morning along with the pharmacological antidepressant treatment prescribed by their psychiatrist.

The healthy control participants (HCtrl) were recruited from the general population, matched by age and gender to the patients, to verify KW6 data between depressive and non-depressive population. Healthy controls reported no affective, or emotional problem, did not take any psychotropic drugs, and continued with their usual routine of activities. All participants were located on the island of Mallorca (latitude: $\sim 40^\circ$ N) with a mean of 82 % sunny days, 5°C (night) and 22°C (day) and ~ 12 h of daylight.

The recruitment was done in two periods: 1 $^\circ$) March to October 2021, and 2 $^\circ$) January-May 2023: we had to stop due to the COVID-19 pandemic and then, structural problems obliged closing the Mental Health Unit for several months.

Interventions:

– Patients in the LIGHT group were given specific written instructions to expose themselves to daylight for 14 days. The specific instruction was: ‘You must be outside, at least one hour daily in the morning before 11:00 a.m. You can take a walk or just sit to expose yourself to daylight. You should not wear sunglasses. If direct sun exposure bothers you, you can wear a hat or stay in the shade. During this time, you cannot do a specific exercise (such as running or cycling) or other activities.

They received, in addition, general recommendations for healthy habits in writing, as the TAU group, except recommendation 1.

– Patients in the TAU group were given written general recommendations for healthy habits considered as placebo [19]: 1) Exposure to sunlight at your convenience, 2) Physical exercise appropriate to your needs, 3) Sleep the amount of time you need, 4) Stay in or get out of bed at your convenience, and 5) Eat a healthy and balanced diet.

2.3. Questionnaires and scales

The following scales and questionnaires were used in this study: 1) The International Neuropsychiatric Interview (MINI) [20,21] to exclude other comorbid psychiatric disorders; 2) Montgomery-Asberg Depression Scale (MADRS) [22]. Clinician performed scale validated for the Spanish population [18] to assess depression, uncontaminated by anxiety items; 3) Sleep Quality Index (PSQI) [23,24]. Self-applied scale that collects information related to sleep in the last month in adults; 4) Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR16) [25]. It is a validated questionnaire for the Spanish population [26] of depressive symptomatology of the last week, self-applied; and 5) Sleep and activity agenda: this is a self-registration form on paper to record the time and frequency of sleep periods during the day and night.

2.4. Light, peripheral temperature and motor activity Recording

The ambulatory circadian monitoring device KW6 (Kronowise®; Kronohealth S.L., University of Murcia, Spain), is a multi-sensor device worn on the non-dominant wrist [27]. It records motor activity (MA), peripheral skin temperature (PT), and light intensity (LI). Using from the MA data (the ‘time in movement’ variable) during the assumed sleep period (23:00 to 07:50), the Actiwatch Activity and Sleep Analysis© 2001 Software (Actiwatch 2001, V1.16 Cambridge Neurotechnology) was employed to obtain the objective sleep quality parameters: 1) Efficiency, 2) Latency, 3) Percentage of immobility, 4) Percentage of mobility, and 5) Fragmentation. Therefore, sleep variables were analysed using both subjective instruments (agenda and PSQI) and objective instruments (KW6).

2.5. Procedure

After the initial assessment conducted by the psychiatrist, eligible patients were invited to.

participate in the study. Following an explanation of the protocol, participants were asked to read a participant information sheet (PIS). If they agreed, they signed the Informed Consent (IC) form before being directed to the researchers (a biologist and a psychology master student) for randomization and study protocol procedures. Each clinical evaluation session lasted approximately 50 min. The assessment and intervention protocol were as follows for the different groups:

During visit 1 (day 1), inclusion and exclusion criteria were reviewed, the clinical interview was conducted using the MINI neuro-psychiatric interview (for exclusion of patients with comorbid psychiatric disorders) together with assessments including the PSQI and QIDS-SR16. Additionally, participants were equipped with the KW6 device to record physiological parameters and light exposure and were instructed to complete a sleep and activity agenda. They were randomized and received specific instructions based on their randomization. During visit 2 (day 14), the QIDS-SR16 was given to patients to fill it up, and data from the KW6 device were downloaded, followed by collection of the agenda. On visit 3 (day 23), another QIDS-SR16 assessment was performed, and the KW6 device reattached. Finally, during visit 4 (week 4, day 28), the agenda was collected, the KW6 device was removed for data retrieval, and the PSQI and QIDS-SR16 were re-administered. The mean comparison of the KW6 data (circadian parameters PT and MA) was performed with the data collected during visits 2 and 4.

HCtrl participants attended twice. In the first, inclusion and exclusion criteria were revised, and demographic data collected. They received the sleep and activity agenda and the KW6. The agenda and the KW6 were collected in a second visit after 5–7 days.

2.6. Data analysis

Statistical analyses were conducted using IBM SPSS Statistics 29.0 software. Descriptive statistics were computed for various sociodemographic and clinical variables of the depression (LIGHT and TAU) and HCtrl group.

Parametric inferential statistics were employed with ANOVA with the register's exposure light for 24 h, and a *t*-test to contrast the average day-night light scores between the LIGHT, TAU and HCtrl groups. In addition, effect sizes [28].

Non-parametric inferential statistics were employed to average contrast using the Mann-Whitney *U* test (*U*) for independent samples (comparing averages between the LIGHT, TAU, LIGHT-HCtrl, and TAU-HCtrl groups). The Wilcoxon test was used for paired samples, such as pre-post-intervention comparisons within the LIGHT and TAU groups, and for independent samples, comparing post-intervention outcomes between the LIGHT and TAU groups. Additionally, effect sizes for different variables in the LIGHT and TAU groups were calculated.

Data collection and analysis were conducted using the Circadianware program specifically tailored to the Kronowise® device. Data points deviating more than 3 times the standard deviation of the average were also removed [29].

The KW6 software performed parametric and non-parametric analyses of the variables Peripheral Temperature (PT), as a variable representative of autonomic balance at the skin vessel level), motor activity (MA), and 'time in movement': is the total duration of physical activity recorded by the device over a specific period of time (23:00 to 7:50), which is typically nocturnal. The following indices were obtained to describe the circadian system [29]: 1) Midline Estimating Statistic of Rhythm (MESOR), 2) Inter-day stability index (IS), 3) Intra-day variability index (IV), 4) Relative amplitude (RA), and 5) Circadian Function Index (CFI). These variables are the parameters of the marker rhythms (MA and PT) of the sleep-wake rhythm for the study of the circadian system. The MA data recorded with the KW6 device were processed

using the Actiwatch Activity and Sleep Analysis© 2001 Software.

2.7. Ethical Aspects and data Security

This study was conducted in compliance with the principles of the Declaration of Helsinki [30], Organic Law 3/2018, on the 5 December, on the protection of personal data and guarantee of digital rights, and this study was approved by the Research Committee of the Son Espases University Hospital (HUSE, CI-481–20, 14th January 2021) and the Research Ethics Committee of the Balearic Islands (CEI-IB, IB 4429/21 PI, 24th February 2021). All participants signed the informed consent.

3. Results

3.1. Socio-Demographic data

Table 1 presents the sociodemographic data of the total sample. A higher participation of women was observed in all groups. There were no significant differences in relation to age. There were significant differences in years of education between depression groups (LIGHT, TAU) and HCtrl group. There were no differences between the two branches in MADRS at inclusion: the average scores and standard deviations of the MADRS for the LIGHT group were 26.36 (5.41) and MADRS for the TAU group were 26.90 (5.68).

3.2. Exposure to LIGHT

Fig. 1 shows the Light intensity (lux) exposed during 24 h for the LIGHT, TAU and HCtrl groups (see supplement 1, Broad explanation of data analysis and applied statistics in Fig. 1. Fig. 1b shows the light intensity day-night contrast (lux) for the LIGHT, TAU, and Control groups (see supplement 2).

The average scores and standard deviations of the light intensity were higher over 24 h of 6001,070 lux for the LIGHT group than for the TAU group of 326 (394) lux, and HCtrl group of 232 (186) lux.

3.3. Effect of daylight on mood

Fig. 2 shows the evolution QIDS-SR16 scores for the LIGHT and TAU patients during four visits (weeks). Table 2 shows the individual direct scores and averages (standard deviations) of QIDS-SR16 of the participants for the LIGHT and TAU groups (see supplement 3).

3.4. Munich chronotype questionnaire (MCTQ)

The chronotype analysis showed a great variability in the chronotypes and there were no significant differences between the LIGHT and TAU groups. The LIGHT group: 18.18 % belonged to the "extreme evening" category, 18.18 % to the "evening" category, 45.45 % to "indefinite", 18.18 % to "morning". The TAU group: 10 % belonged to the "extreme evening" category, 10 % to "evening", 70 % to "indefinite", and 10 % to "morning".

3.5. Effect of daylight on sleep quality

3.5.1. Subjective measures of sleep

The results showed for the LIGHT and the TAU groups respectively, both groups with a cut-off score that indicated poor sleep quality, both pre-treatment and post-intervention (see table 3; supplement 4).

3.5.2. Objective measures of sleep

Table 4 shows the average scores (standard deviations) of the circadian parameters (MESOR, IS, IV, RA, and CFI) for peripheral temperature and motor activity circadian obtained with the KW6 for participants in the LIGHT, TAU and HCtrl groups pre-postintervention.

Table 5 shows the average scores (standard deviations), and

percentages (%) of the variables: efficiency, latency, percentage of immobility, percentage of mobility and fragmentation of sleep.

4. Discussion

The main objective of this study was to examine the feasibility and the impact of a chronobiological intervention on the progression of depressive symptoms in outpatients undergoing pharmacological treatment for a non-seasonal major depressive episode. The sample exhibited a higher percentage of female participants, consistent with the prevailing trends in depression prevalence and incidence rates [3] while age distribution was similar across both groups.

Results confirmed the research hypothesis despite the relatively low number of participants:

patients who increased exposure to daylight (LIGHT group) in addition to the usual antidepressant treatment, showed significant differences in the pre-–post-intervention in global QIDS-SR16 scores, and for the components ‘depressed mood’ and ‘changes in weight’ ($p < 0.05$) in the QIDS-SR16 test.

The LIGHT group also improved their subjective sleep quality. Regarding objective sleep measures, we failed to find statistical differences between the two groups in the pre-post-intervention average of different variables measured with KW6.

4.1. Daylight

Daylight is a primary regulator of circadian rhythms [31,32] influencing mood disorders either directly through its effects on brain regions involved in mood regulation or indirectly by impacting sleep and the circadian system [33]. Insufficient exposure to daylight has been associated with various health risks, including depression, anxiety as well as sleep disturbances and obesity [34]. However, there is no consensus on the optimal intensity, duration, timing, or spectrum of light exposure necessary for maintaining good health [35].

To examine the impact of daylight, participants in the experimental group (LIGHT) were instructed to increase their exposure over a 14-day period, spending at least one hour outdoors in the morning before 11:00 a.m., without exercise. The morning period for daylight exposure was selected due to the effective suppression of melatonin production in the pineal gland during early morning hours [36]. Precisely, directly the zeitgeber effect of morning light to resynchronise the circadian system [37] resulting in increased circulating serotonin levels throughout the day [38].

The analysis of light intensity data (from KW6) revealed higher levels in the LIGHT group during the designated treatment period. This indicates good adherence to the regimen and underscores the feasibility of incorporating this approach as an adjunct to conventional antidepressant drug therapy.

4.2. Mood

The QIDS-SR16 facilitated the evaluation of various domains of depression symptoms based on DSM-5® criteria and disease severity.

Significant reductions in QIDS-SR16 scores were observed in the LIGHT group, whereas such reductions were not statistically significant in the TAU group. These findings suggest that daylight therapy was more effective to alleviate depressive symptoms in patients undergoing pharmacological treatment for depression. Improvements in the LIGHT group were particularly prominent in pre- and post-intervention global QIDS-SR16 scores, as well as in subcategories 2 (mood) and 3 (changes in weight and appetite), which were not observed in the TAU group.

These results are consistent with findings from previous studies [17,39] which have indicated that exposure to daylight may contribute to the reduction of depressive symptoms. Furthermore, also align with those obtained in other studies involving patients with depression (hospitalized and outpatients) that demonstrated positive effect of a

greater exposure to both daylight and artificial light [9,10,40].

Daylight, Sleep, and Depression

The LIGHT group exhibited significantly higher light levels of daytime light exposures, while showing considerably lower nighttime light intensity compared to the other groups. The observed disparity in daylight exposure between the LIGHT and the HCtrl group may be attributed to most patients with depression being on sick leave, whereas healthy participants were working and may not experience direct light exposure at work. In addition of receiving higher light intensity during the day, the LIGHT group also demonstrated significantly lower nighttime light intensity compared to the other groups. These results align with prior investigations on light exposure and mental health [41], which identified a correlation between increased nocturnal light exposure and depressive symptoms in older individuals, highlighting the pivotal role of light in mental well-being. The lower levels of light intensity received by the LIGHT group and the higher day-night contrast may have contributed to the enhancement of mood. This finding underscores the importance of maintaining a robust light day-night contrast, which has been shown to be crucial for regulating biological rhythms [42]. We hypothesize that patients in the LIGHT group have lower exposure to light at night because they sleep better.

4.4. Subjective sleep quality

The PSQI questionnaire [23,24] is the most widely used for the assessment of sleep quality [43]. We know that there is a clear relationship between sleep disorders and depression [44]. However, it is challenging to elucidate whether sleep problems worsen mood or whether depression causes a disturbance in sleep quality. This is likely a bidirectional relationship mediated by chronodisruption [45]. Most patients with depression had sleep disturbances (increased sleep latency, difficulties staying asleep, early morning awakenings). The results of this study showed that participants in the LIGHT and the TAU groups had high scores in the PSQI both pre-treatment (> 14) and postintervention (> 11) as was also shown in previous studies [46–48]. After chronobiological intervention, scores obtained for the participants of the LIGHT group showed improvements in almost all components of sleep quality with significant differences for the daytime dysfunction component. Additionally, they increase their sleep duration (from 6 to 7 h to > 7) and efficiency (from 65–74 % to 75–84 %). These results are consistent with the Münch study, because they found that light therapy can have a beneficial impact on sleep, improving sleep quality and duration. TAU group showed a trend toward significant differences observed for sleep disturbances, although the magnitude of improvement was smaller compared to the LIGHT group.

Addressing sleep disturbances is crucial in the treatment of depression as they represent modifiable risk factors in the development, persistence, and recurrence of depressive episodes. Additionally, recent reviews have supported the notion that sleep problems in older adults predispose them to depressive states. Furthermore, studies have highlighted specific sleep durations (less than 7 h or greater than 8–9 h) as risk factors for depression [49,50] correlating with poorer quality of life [51].

4.5. Objective sleep quality

The parameters TP, MA, and daylight exposure define the sleep-wake rhythm [52,53]. TP, related to sleepiness, is as valid as polysomnography [54,55]. MA has been clinically validated to assess sleep disorders [56,57]. Light acts as a key “zeitgeber” [7,37].

In the LIGHT group, parameters reflecting improved stability and adjustment (PT, IS, RA, and CFI) increased, while IV decreased, indicating lower circadian variability. Similar changes were observed in MA, although without significant differences. In the TAU group, the improvement in rhythm was less evident and, in some cases, opposite (higher IV). These results are relevant, since greater instability is

associated with more symptoms of anxiety and depression [58,59].

A rigorous methodology was used with multisensory recordings obtained using Kronowise® and analyzed with Actiwatch Activity and Sleep Analysis® 2001 Software. This allowed for the assessment of objective components of sleep such as efficiency, latency, immobility, mobility, and fragmentation. The objective assessment was consistent with the subjective assessment using the PSQI [23,24], providing comprehensive and reliable information on sleep variables.

4.6. Limitations and future directions

This study presented some limitations: 1) The sample size is small. Nevertheless, this study proves the feasibility of a chronobiological intervention in depressive patients in regular clinical practice, 2) There is no basal record of light exposure of the patients pre-intervention, 3) Controlling for covariates such as gender and education, 4) The HCtrl group was evaluated only with KW6 pre-treatment, and 5) We studied only the short-term effect of daylight exposure.

Future research: 1) Enlarging the sample size to conduct an extensive study would yield more robust and consistent findings regarding the effects of daylight, 2) Heightening awareness among healthcare professionals about the beneficial impacts of daylight exposure could significantly enhance the remission of depressive symptoms in depressive patients and improve the quality of their sleep, 3) Exploring the potential integration of chronobiological interventions, such as exposure to daylight, either as standalone therapy or as adjunctive treatment, into clinical practice guidelines for depression treatment and prevention in at-risk population, and 4) We believe that the involvement of nurses in this chronobiological intervention can make an important contribution to treatment and reduce the pressure of care.

5. Conclusions

The results obtained were supported by previous scientific literature on the positive effect of daylight on people with depression. In sum, this study provides: 1) Patients in the LIGHT group were exposed to significantly higher light intensity (amount) in the early hours of the morning than the TAU and the Control groups. The light day-night contrast was significantly higher in patients in LIGHT group than in the TAU and the Control groups; 2) Depression symptoms measured with the QIDS-SR16 improved significantly in patients in the LIGHT group compared to the TAU group; 3) Subjective sleep quality measured with PSQI showed a non-significant trend towards improvement in the LIGHT group after intervention, and this was not the same for the TAU group; and 4) Objective sleep and circadian parameters showed a non-significant trend towards improvement in the LIGHT group after the intervention. Finally, this methodology could be part of a chronobiological protocol to complement the treatment of people with depression within the multidisciplinary team in mental health units in nonhospitalized patients.

CRedit authorship contribution statement

José Ángel Rubiño-Díaz: . **M. Cristina Nicolau:** . **Anna Riera:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Aida Martín:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Formal analysis, Data curation. **Francesca Cañellas:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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