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ORIGINAL ARTICLE

Bright light therapy with a head-mounted device for anxiety, depression, sleepiness and fatigue in patients with Parkinson's disease

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Abstract

The beneficial effects of bright light therapy (BLT) on the disabling non-motor symptoms of Parkinson's disease (PD) remain uncertain. The objective of this study was to investigate if daily BLT, with a head-mounted device (Luminette®), has a beneficial effect on depression, anxiety, daytime sleepiness and fatigue in patients with PD. In this double-blind, placebo-controlled study, 16 patients with PD were randomized to receive either 1 month of BLT or 1 month of placebo therapy, separated by a 2-week washout period, in a crossover fashion. Patients completed questionnaires for the Hospital Anxiety and Depression Scale (HADS), the Epworth Sleepiness Scale (ESS) and the Fatigue Impact Scale (FIS) before and after each treatment period. The primary outcome measures were changed from baseline in scores between treatment groups. No significant changes were observed in the HADS anxiety scores and FIS scores after BLT and after placebo. The ESS scores decreased non-significantly only after BLT. A post hoc analysis of patients who had baseline ESS scores > 11 revealed a significantly greater decrease in ESS scores after BLT than after placebo. Future studies investigating the effect of BLT on sleepiness could focus specifically on patients with high ESS scores.

Keywords Parkinson's disease · Sleepiness · Phototherapy · Depression · Anxiety

Introduction

Parkinson's disease (PD) affects more than 6 million people worldwide [1]. Although the disease is primarily defined by its motor symptoms, patients with PD often present non-motor manifestations including depression, anxiety, excessive sleepiness and fatigue, which have been associated with poor quality of life [2–4]. A study in 2008 reported an average prevalence of major depressive disorders and minor depression in patients with PD of 17% and 22%, respectively [5]. Anxiety disorders are more common in patients with PD than in the general population with reported prevalence varying from 5 to 11% [6, 7]. Excessive daytime sleepiness is also a frequent complaint in patients with PD, even before introducing levodopa and dopamine agonists which are known to induce sleepiness [8–11]. In one study, self-reported sleepiness was found in 46% and objective sleepiness in 13.4% of patients with PD [12]. Nocturnal sleep disturbances and excessive daytime sleepiness have been shown to be common in patients with PD, possibly related to diminished amplitude and amount of melatonin secretion [13, 14].

Bright light therapy (BLT) has been used successfully to treat a variety of conditions, including seasonal and non-seasonal depression, sleep disorders, mood disorders, and cognitive functions [15–18]. BLT was shown to be particularly well tolerated in healthy populations [19]. Furthermore, BLT using a head-mounted device has been shown to be effective and well tolerated for improving well-being and vigilance in the workplace [20, 21] and in treating adolescents with a delayed sleep phase syndrome [22].

Few studies have investigated the use of BLT in PD and results on its beneficial effects on the non-motor symptoms

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of PD vary between the studies [23–27]. In some studies, BLT has been reported to improve psychological parameters [26], depression [23] and sleepiness [25], and in other studies BLT was not associated with significant changes in anxiety, depression [25, 27] or sleepiness [23]. In light of these conflicting data, further studies seem warranted.

In this randomized, double-blind, placebo-controlled, crossover, study, we investigated if daily BLT with a head-mounted device would have a beneficial effect on depression, anxiety, daytime sleepiness and fatigue in patients with PD.

Methods

Population of patients

Study participants were recruited by their neurologists at clinical outpatient visits from January to March 2018. Participants received an information letter and met with one of the two assessors (students of the Faculty of Motor Sciences, Université Catholique de Louvain) who explained the study. Patients previously diagnosed with PD, able to attend clinical outpatient visits and capable of using study material at home, were eligible for the study. Patients participating in other studies were not eligible. Sixteen patients agreed to participate in the study.

Study design

The study took place from March to May 2018. The principal investigators used a web-based randomization tool [28] to randomize patients into two treatment groups in a crossover fashion (Fig. 1). Neither the assessors nor the participants were aware of the randomization process nor the group to which participants had been assigned. In the first group (AB; $n=8$), patients initially received 1 month of active BLT and then 1 month of placebo therapy. In the second group (BA; $n=8$), patients initially received 1 month of placebo therapy and then 1 month of active BLT. The treatment periods A and B were separated by a washout period of 2 weeks. Patients were asked to answer evaluation questionnaires before and after each treatment period (ET_0, ET_1, ET_2, ET_3).

Materials and methods

A portable head-mounted device (Luminette®, Lucimed SA, Villers-le-Bouillet, Belgium) was used for both active BLT and placebo therapy. Both devices have the same external

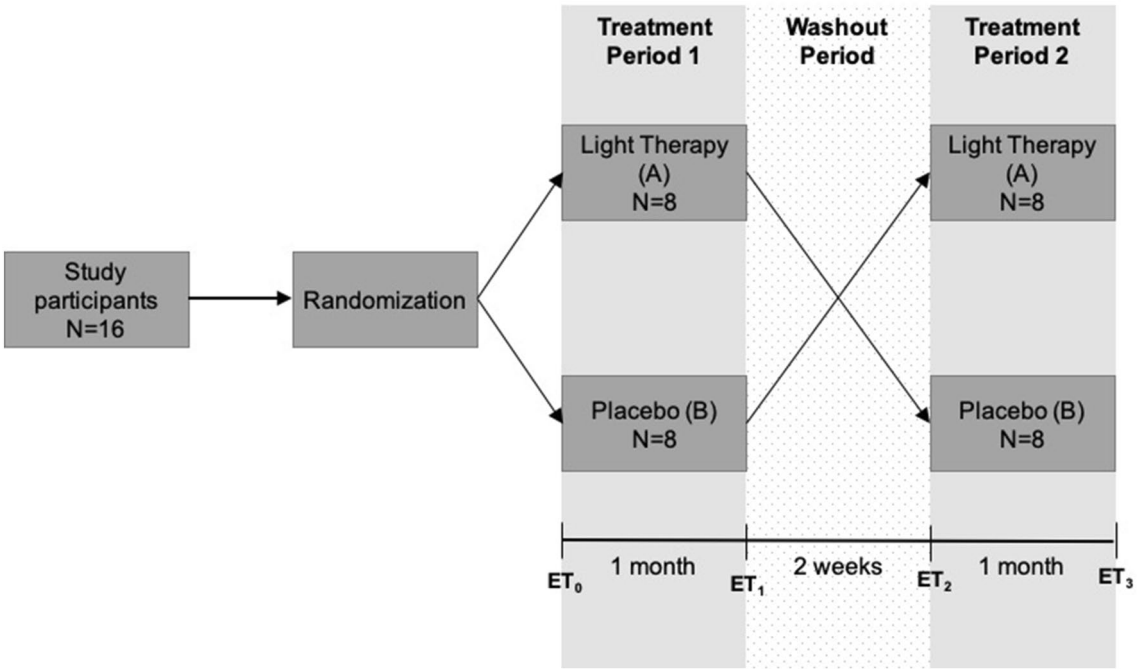

Fig. 1 Study design of the randomized, double-blind, placebo-controlled crossover study. Each of the 16 patients was randomly assigned to one of the two possible treatment sequences (A then B, group AB or B then A, group BA, separated by a washout period). Evaluation questionnaires were completed before and after each treatment sequence. ET_0 evaluation questionnaires before treatment period 1, ET_1 evaluation questionnaires after treatment period 1, ET_2 evaluation questionnaires before treatment period 2, ET_3 evaluation questionnaires after treatment period 2

appearance; however, the active device emits blue enriched light (maximum wavelength 468 nm) and the placebo device emits orange enriched light (maximum wavelength 660 nm). The light emitted is, therefore, perceived differently. The active device can operate with three intensities and patients were instructed to use the lowest intensity (average 472.7 lx). The placebo device only operates with one intensity (average 175 lx). To assure blinding, both patients and assessors were unaware of which device emitted active or placebo light. Participants were aware of the brand name of the devices. Patients were instructed to wear the device every morning for 1 month, if possible at the same time daily, for 45 min. Patients were allowed to read or to perform simple daily tasks while wearing the device. A calendar was provided for patients to record their daily use of the device.

Patients were asked to answer three questionnaires before and after each treatment: the Hospital Anxiety and Depression Scale (HADS) [29], the Epworth Sleepiness Scale (ESS) [30] and the Fatigue Impact Scale (FIS) [31]. The HADS measures anxiety and depression separately on 7 items on a scale of 0–3 for each. Normal is defined from 0 to 7, borderline abnormal from 8 to 10 and abnormal from 11 to 21 [29]. The ESS quantifies daytime sleepiness in different daily situations through eight questions on a scale of 0–3 for each. The ESS is interpreted as follows: 0–5 lower normal daytime sleepiness, 6–10 higher normal daytime sleepiness, 11–12 mild excessive daytime sleepiness, 13–15 moderate excessive daytime sleepiness, 16–24 severe excessive daytime sleepiness [30, 32, 33]. The FIS evaluates the perceived functional limitations caused by fatigue during the previous month with 40 questions. Each question is rated from 0 (no problem) to 4 (extreme problem) [31].

Statistical methods

Data are expressed as mean and SD unless otherwise indicated. Statistical analyses were performed with Excel® (Microsoft corp.) and SigmaStat® (Systat Software Inc.) software. Unpaired *t* tests were used to compare parameters between groups. Pearson's Chi Square tests were used to compare categorical variables. A two-way repeated measures ANOVA was used to compare variables. Patients were considered as dependent variables and treatments (BLT and placebo) and pre- and post-treatment evaluations as independent variables. Bonferroni *t* test was used to assess the all pairwise multiple comparison procedures. A p value < 0.05 was considered as significant.

Endpoints

The primary endpoint of this study was the change in scores for anxiety, depression, sleepiness and fatigue before and after active BLT compared with placebo treatment.

Results

Sixteen patients were enrolled and randomly divided into two equal groups who received treatment in a crossover design (AB or BA) (Fig. 1). No significant differences were shown in mean age, sex ratio, baseline HADS depression scores and FIS scores of these two groups (Table 1). The mean baseline HADS anxiety scores were higher, but non-significantly, in the AB group [9.25 (SD 3.54)] compared with BA group [5.75 (SD 3.45)] ($p = 0.06$). The mean baseline ESS scores were significantly higher ($p = 0.01$) in the AB group [12.75 (SD 6.3)] compared with the BA group [5.5 (SD 3.25)]. The mean duration of PD since diagnosis was similar in both groups. The medications patients were taking for PD were unchanged for the duration of the study. The number of patients taking dopamine agonists, levodopa or rasagiline before and during the study is shown in Table 1.

No significant difference was seen in the mean HADS anxiety scores (from 7.75 to 7.5; $p = 0.66$) or depression scores (from 5.31 to 5.19; $p = 0.77$) after active BLT and after placebo treatment (from 7.13 to 7.06; $p = 0.91$ and from 5.81 to 5.63; $p = 0.85$, respectively) (Fig. 2). The mean HADS anxiety scores were between the predefined ranges of normal (0–7) and borderline abnormal (8–10) values. The mean HADS depression scores were all in the normal range. The mean baseline ESS scores were in the normal range for both groups and no significant effect was seen after active BLT or placebo (from 9.06 to 8.62; $p = 0.59$ and from 9.06 to 9.50; $p = 0.59$, respectively) (Fig. 2).

One patient from the AB group failed to complete all the FIS questionnaires and was removed from the FIS score analysis. The mean FIS scores decreased non-significantly after both active BLT (from 67.80 to 61.53; $p = 0.14$) and after placebo treatment (from 66.73 to 60.87; $p = 0.17$) (Fig. 2), but the ANOVA analysis showed a significant effect between the pre- and post-intervention time points (from 67.27 to 61.2, $p = 0.02$).

As the HADS and ESS scores are not linear, patients were grouped into the different score categories according to their HADS (Fig. 3) and ESS scores. Patients were then further categorized as being in the normal or abnormal range according to their scores and changes between the normal and abnormal categories before and after BLT or placebo were evaluated and found to be non-significant ($0.29 < p < 0.71$).

Table 1 Demographic and clinical characteristics, baseline scores on questionnaires and total light exposure for participants in groups AB and BA

	AB group	BA group	*p* value
Demographic and clinical characteristics			
Women, *n* (%)	4 (50%)	2 (25%)	0.30
Age, years	66.50 (6.30)	68.88 (5.89)	0.45
Duration of PD since diagnosis, months	33.25 (31.71)	35.50 (20.0)	0.99
Dopamine agonist treatment, *n* (%)	8 (100%)	5 (62.5%)	0.05
Levodopa treatment, *n* (%)	1 (12.5%)	3 (37.5%)	0.25
Rasagiline treatment, *n* (%)	4 (50%)	5 (62.5%)	0.82
Baseline scores on questionnaires (ET_0)			
HADS anxiety score	9.25 (3.54)	5.75 (3.45)	0.06
HADS depression score	5.88 (2.42)	5.88 (3.18)	1.00
Epworth Sleepiness Scale score	12.75 (6.3)	5.50 (3.25)	0.01
Fatigue Impact Scale score	83.71 (30.54)	59.75 (36.88)	0.20
Light exposure			
Total bright light exposure, minutes (percentage of total instructed exposure time)	1194.55 (98.32%)	1197.69 (98.58%)	0.64
Total placebo light exposure, minutes (percentage of total instructed exposure time)	1186.36 (97.64%)	1187.31 (97.72%)	0.10

AB group, received bright light therapy then placebo; BA group received placebo then bright light therapy

Values are expressed as mean (standard deviation) unless otherwise specified

ET_0 evaluation questionnaire at baseline, before treatment period 1, *HADS* Hospital Anxiety and Depression Scale, *PD* Parkinson's disease

Discussion

In this randomized, double-blind, placebo-controlled, crossover study, we investigated the effect of daily BLT with a head-mounted device on depression, anxiety, daytime sleepiness and fatigue in patients with PD and found no significant beneficial effect of BLT compared with placebo light therapy. Compliance was excellent. We consider the device to be safe as no notable adverse events were recorded and the device was generally considered easy to use by patients.

Few studies have investigated the effect of BLT in patients with PD and have shown diverging results.

We did not show significant decreases in HADS depression and anxiety scores with BLT. In a recent randomized controlled study, Rutten and colleagues found that BLT was not more effective than control light therapy for reducing depressive symptoms in 83 patients with PD [27]. Similarly, Videnovic and colleagues recently reported that BLT was not associated with significant changes in anxiety, depression or quality of life [25]. Conversely, Willis and colleagues reported that BLT was effective in improving psychological parameters [26] and Paus and colleagues reported in 2007 that BLT led to significant improvement in depression scores and more so in patients with higher baseline scores [23]. It should be noted that in the present study the mean baseline HADS depression score was in the normal range and that only a few patients (3/16) had abnormal scores despite their initial subjective complaints. In our study, we observed a non-specific decrease of FIS scores after both BLT and placebo which could be explained by a placebo effect or by the natural increase of light from March to May.

Paus and colleagues reported a reduction in ESS for both BLT and placebo and concluded that BLT had no significant effect on sleepiness [23]. In a placebo-controlled randomized study involving 31 patients with PD and an ESS score of 12 or greater, Videnovic and colleagues reported a significant improvement in daytime sleepiness with BLT [25]. Two other recent studies also reported improvement in sleep-related parameters, ESS, or subjective sleep quality with BLT [26, 27]. In our study, the overall mean ESS score was not significantly influenced by BLT. However, baseline ESS scores were found to be low (< 12), indicating that on average, patients did not have excessive sleepiness at the beginning of the study. This may be due to the short duration of PD (Table 1) or low-dose medication regimens in our patient cohort. Unlike Videnovic et al. in our study patients were selected based solely on their subjective complaints of sleepiness or fatigue rather than on their ESS scores. Interestingly, a subgroup analysis of the six patients with an ESS score of 12 or greater in our study (most of whom were in the AB group) showed a greater decrease in mean ESS scores after BLT (from 15.50 to 13.17; $p = 0.14$) than after placebo treatment (16.00 to 15.50; $p = 0.36$). This represents a significant difference between active BLT and placebo at the post-intervention time point ($p = 0.035$) (Fig. 2).

In previous studies, the timing and duration of BLT vary considerably (twice daily, morning only, evening only).

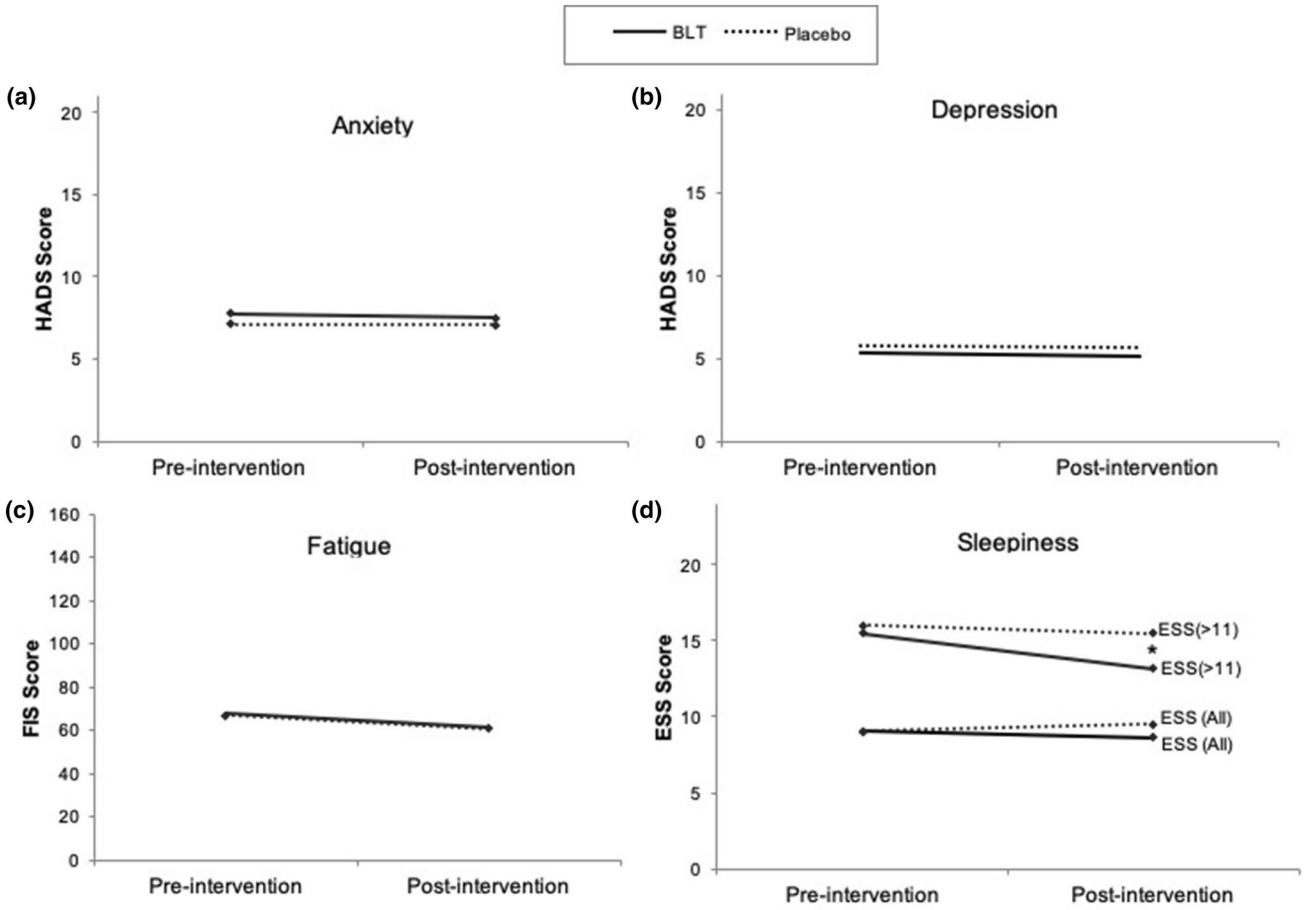

Fig. 2 Pre- and Post-intervention changes of the mean scores evaluated on questionnaires before and one month after active BLT or placebo therapy for **a** anxiety, **b** depression, **c** fatigue and **d** sleepiness in all patients and sleepiness for the subgroup analysis of the patients with a baseline ESS score > 11. *BLT* bright light therapy, *HADS* Hospital Anxiety and Depression Scale, *ESS* Epworth Sleepiness Scale, *ESS (> 11)* baseline ESS > 11, *ESS (All)* All patients, *FIS* Fatigue Impact Scale

In the present study, patients were exposed for 45 min every morning for 1 month to the lowest light intensity of the device. The effect on mood and sleep may have been greater if daily exposure had been longer, if higher intensity of light had been used or if treatment periods had been longer.

Our study is the first study in which a head-mounted device (Luminette®) was used to evaluate BLT in patients with PD. In other studies to date, light boxes were used for this purpose [23, 25–27]. With the use of a head-mounted device, compliance may be improved because patients can remain mobile during light exposure and continue performing tasks such as eating, reading and walking.

Increased natural seasonal light during our study period (March to May) could be a confounding factor that may have influenced seasonal mood disorders and that is difficult to evaluate.

Despite the similarity in appearance between the placebo and active BLT devices, blinding may have been compromised if patients researched information about light emitting equipment.

Patient medication may be another confounding factor influencing sleepiness in particular. Dopamine agonists (DA) are known to increase daytime sleepiness in patients with PD [9]. However, patients maintained initial treatment throughout the study and there seemed to be no significant difference in the pre- and post-intervention scores for the few patients on DA compared with other patients.

To our knowledge, other studies did not use a crossover design. In addition to reducing sample size, such a design could be an advantage for examining symptoms of depression, anxiety and sleepiness which may be influenced by confounding factors such as medication, lifestyle, severity of PD and co-morbidities.

Despite the use of a crossover design, the small number of patients is a limitation of the present study and may explain the absence of significant effects. Therefore, increasing population size is strongly suggested to adequately power future

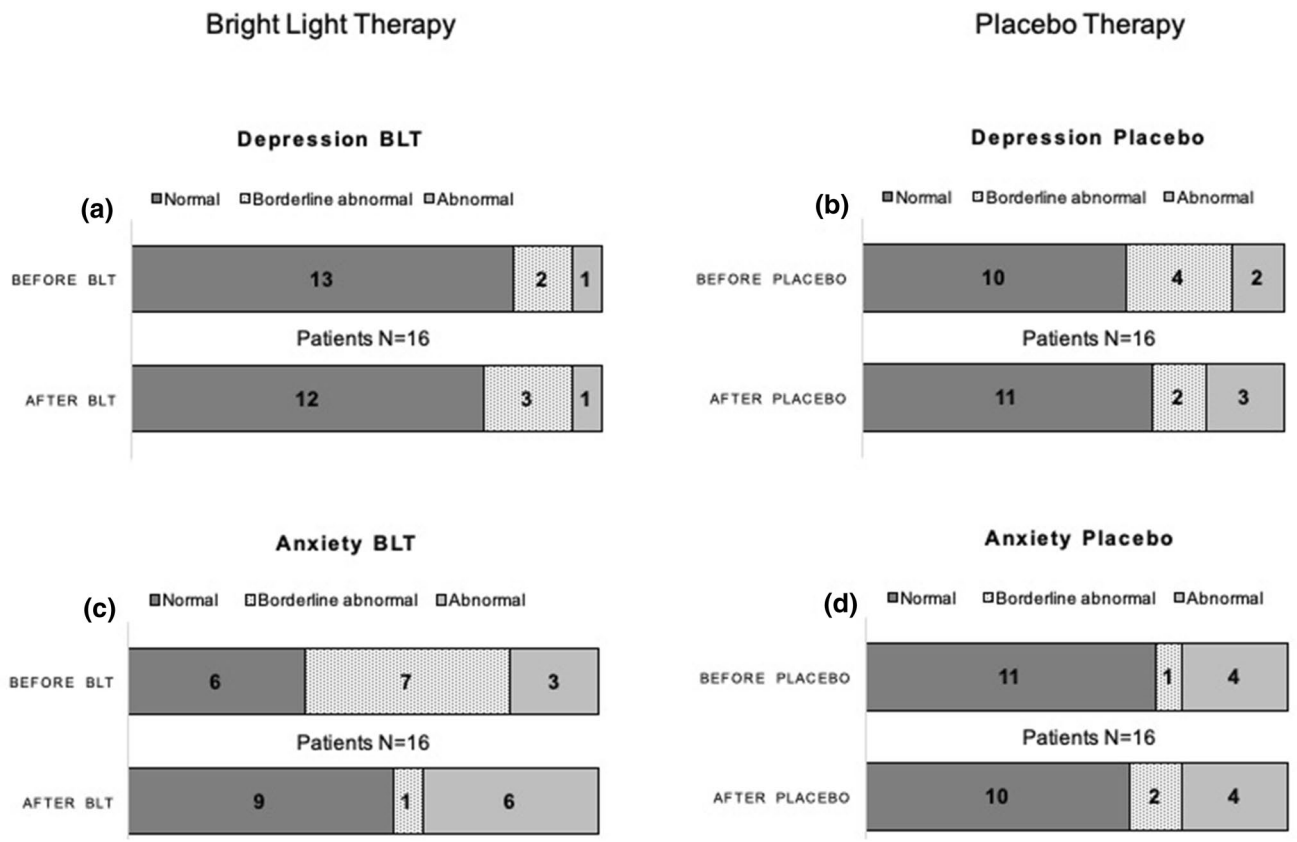

Fig. 3 Number of patients in each score category for depression (**a**, **b**) and anxiety (**c**, **d**), respectively, before and after bright light therapy (BLT) and placebo light therapy. Depression and anxiety were evaluated using the Hospital Anxiety and Depression Scale. Scores from 0 to 7 are considered normal, 8–10 borderline abnormal and 11–21 abnormal

studies. Furthermore, patients were selected based on their subjective complaints, but most patients did not have abnormal baseline HADS and ESS scores. It has been suggested that the beneficial effect of BLT is greater when baseline scores are higher and our subgroup analysis suggests that patients with an ESS score > 12 could benefit more from BLT. It may, therefore, be interesting to focus future studies on patients with high ESS and HADS scores.

Conclusion

Bright light therapy was well tolerated and compliance was excellent in patients with PD. No significant beneficial effect of BLT with a head-mounted device (Luminette®) on depression, anxiety, daytime sleepiness and fatigue in patients with PD was found compared with placebo light therapy. However, BLT led to a small improvement in daytime sleepiness compared with placebo and more so in patients with higher ESS scores.

Future studies investigating the effect of BLT on non-motor symptoms in PD should focus specifically on patients with high ESS scores and should also investigate whether longer periods of BLT exposure, higher light intensities, longer treatment periods and exposure at different times of year could be more beneficial.

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Funding No funding was received for this study.

Compliance with ethical standards

Conflict of interest Lucimed SA, Villers-le-Bouillet, Belgium provided the active and placebo light therapy devices (Luminette®) but did not fund the study nor were they involved in any aspect of the study management (design, collection of data, data analysis or preparation of the manuscript). There were no conflicts of interest with this donation. Neither the authors nor the institution conducting the study have a conflict of interest with Lucimed. Patients were aware of the brand name on the product.

Ethical approval The study protocol, questionnaires and consent forms were approved by the institutional ethics committee of Clinique Saint Pierre, Ottignies, Belgium and the study was performed in accordance with the ethical standards of this committee and those of the 1964 Declaration of Helsinki [34] and its amendments.

Informed consent All participants gave written informed consent prior to study start.

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