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Bright Light Therapy in Parkinson's Disease: A Pilot Study

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Abstract: **Several observations suggest a beneficial effect of melatonin antagonism for Parkinson's disease (PD). Although bright light therapy (BLT) suppresses melatonin release and is an established treatment for depression and sleep disturbances, it has not been evaluated in PD. We examined effects of BLT on motor symptoms, depression, and sleep in PD in a randomized placebo-controlled double-blind study in 36 PD patients, using Parkinson's Disease Rating Scale (UPDRS) I–IV, Beck's Depression Inventory, and Epworth Sleepiness Scale. All patients received BLT for 15 days in the morning, 30 min daily. Illuminance was 7.500 lux in the active treatment group and 950 lux in the placebo group. Although group differences were small, BLT led to significant improvement of tremor, UPDRS I, II, and IV, and depression in the active treatment group but not in the placebo group. It was very well tolerated. Follow up studies in more advanced patient populations employing longer treatment durations are warranted.** © 2007 Movement Disorder Society

Key words: bright light therapy; Parkinson's Disease; depression; melatonin; tremor

Bright light therapy (BLT) has been proposed as the treatment of choice for seasonal affective disorder,[1] and was also shown to be effective in nonseasonal depression, circadian sleep phase disorders, and sleep disturbances in dementia. It is supposed to stabilize circadian melatonin secretion and improve monoaminergic function in the central nervous system. Release of melatonin is inhibited by retinal exposure to light and stimulated in darkness. Thus, melatonin is a chronological pacemaker, signaling the environmental light/dark cycle to the organism.

Melatonin has antioxidant properties, and its age-related decline has been suggested as an important factor for the development of different neurodegenerative disorders.[2] However, a number of observations indicate that melatonin might be unfavorable in Parkinson's disease (PD): Melatonin suppresses dopamine release in the central nervous system with antidopaminergic effects in the striatum,[3] and melatonin antagonism by pinealectomy or constant light leads to amelioration of PD symptoms in rats treated with MPTP- or 6-OHDA.[4] Furthermore, experiments using the (putative) melatonin receptor antagonists ML-23 and S-20928 showed improvement of motor symptoms.[5] In PD patients, F-Dopa PET suggested pineal dysfunction and melatonin secretion patterns were disturbed.[6] These observations correlated with disease severity. In addition, higher levels of melatonin were found in PD compared to healthy controls, and they returned to normal by stimulation of the internal globus pallidus.[7]

Despite these reports on a potentially beneficial effect of melatonin antagonism in PD, surprisingly little information on effects of BLT in PD patients is available. This is even more unusual, as depression and sleep

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disturbances are frequent non-motor-symptoms of PD with a considerable negative impact on quality of life.[8] For both symptoms, BLT is effective, though not specifically in PD.

We conducted a randomized placebo-controlled double-blind study of BLT in PD, focusing on changes in motor performance, depression, and daytime sleepiness.

METHODS

Patients

Thirty six consecutive patients with idiopathic PD were recruited from our outpatient movement disorders unit. Patients were excluded from the study, if they (1) took potentially photosensitizing medication, especially imipramine, hypericum, phenothiazine, lithium, chloroquine, hydrochlorothiazide, or tetracycline, (2) had changes of any medication during the last two weeks, (3) were at suicidal risk in the judgment of the investigators, or (4) had signs of dementia as measured by Mini Mental State Examination (MMSE; score $\leq$23). Beside MMSE, clinical examination included Hoehn & Yahr Staging (H&Y), and the Unified Parkinson's Disease Rating Scale (UPDRS) I–IV. Depression was measured by Beck's Depression Inventory (BDI) and daytime sleepiness by the Epworth Sleepiness Scale (ESS). Prior to begin of BLT, all patients underwent examination by an ophthalmologist (AV), and no contraindications were found.

Patients were matched according to gender, age, duration of disease, severity of disease (H&Y), and depression (BDI), and randomized to active treatment and placebo groups by an unblinded investigator (MA), who was not involved in the treatment of patients.

Bright Light Therapy

We used commercially available white fluorescent light boxes by Philips, model *Bright Light Energy*, product number HF3304 (costing about 130 Euro in Germany), which were provided by the manufacturer for purposes of the study only. For therapy of seasonal affective disorder, illuminance of 10.000 lux for 30 min daily had been proven to be most effective, while illuminance of less than 2.500 lux is thought to be ineffective.[9] Following these observations, patients were instructed to use the light box every morning for 30 min, 1 hour after awakening (however not later than 9 am), with head-to-light distance of 20 cm in the active treatment, and 100 cm in the placebo group. Illuminance was measured with a luminance meter (Lunasix F, Gossen, Germany) and was 7.500 lux in the active treatment and 950 lux in the placebo group. A shorter distance to increase illuminance in the active treatment group was not practicable. Tutorials were given by the unblinded investigator, and a measurement tape was handed out to ensure proper positioning. Although compliance of head-to-light distances was emphasized, patients were left unaware of correlation between distance and illuminance, and the manufacturer's instruction manual was removed.

TABLE 1. *Patient samples and matching criteria*

	Active treatment (n = 18)	Placebo (n = 18)
Sex (male/female)	12/6	11/7
Age (years)	63.6 ± 9.8	63.4 ± 9.7
Disease duration (years)	7.4 ± 4.3	7.9 ± 4.7
Hoehn & Yahr Staging	2.7 ± 0.6	2.5 ± 0.4
BDI	9.9 ± 6.1	8.7 ± 6.1
MMSE	29.1 ± 1.3	28.9 ± 1.6

BDI, Beck's depression inventory; MMSE, mini mental state examination.

Study Protocol

BLT was conducted in February, March, and April 2006. Clinical examinations took place on Day 0 and 15 at the same time of day between 9 am and 1 pm. All were conducted by an experienced movement disorders specialist (TSH or SP) unaware of the patient's allocation to active treatment or placebo group. No changes of any medication were allowed two weeks prior and during the study. Patients were instructed to maintain timing of medication and breakfast, and their usual amount of exposure to daylight.

Statistical Analysis

Patient characteristics and inclusion criteria were compared using student's *t*-test. The paired *t*-test was performed to compare measurements before and after BLT. Because of the exploratory character of our study, results from statistical analyses were not corrected for multiple testing to avoid inflation of Type II errors.

Ethics

The study was approved by the Ethics Committee of the University Clinic of Bonn.

RESULTS

Patient Characteristics (Table 1)

There was no significant difference in sex, age, disease duration, H&Y staging, BDI, and MMSE between active treatment and placebo groups at the first examination. All

TABLE 2. *Effects of BLT on UPDRS, depression, and daytime sleepiness*

	Active treatment (n = 18)			Placebo (n = 18)		
	Before BLT	After BLT	*P*	Before BLT	After BLT	*P*
UPDRS I	2.6 ± 1.6	1.6 ± 1.4	<0.01	1.6 ± 1.9	1.3 ± 1.5	n. s.
UPDRS II	12.6 ± 6.8	11 ± 7.7	<0.01	9.2 ± 4.6	8.8 ± 5	n. s.
UPDRS III total	24.8 ± 10.1	24.6 ± 10.8	n. s.	19.3 ± 11.5	18.4 ± 10.9	n. s.
tremor	4 ± 2.5	3.3 ± 2.5	<0.05	2.5 ± 2.5	2.2 ± 2.6	n. s.
bradykinesia	9.4 ± 3.9	10 ± 4.3	n. s.	8.2 ± 5	8.4 ± 5	n. s.
rigidity	6.7 ± 5	6.2 ± 4.6	n. s.	4.3 ± 3.9	3.8 ± 2.5	n. s.
UPDRS IV	1.8 ± 1.9	1.1 ± 1.7	<0.05	2.3 ± 2.3	2.1 ± 2.3	n. s.
BDI	9.9 ± 6.1	7.7 ± 5.1	<0.05	8.7 ± 6.1	6.5 ± 1.5	n. s.
BDI > 10[a]	16.3 ± 5.9	12 ± 5.5	<0.05	14.1 ± 5.8	12 ± 6.9	n. s.
ESS	9.2 ± 4.8	7.7 ± 4.3	<0.05	7.9 ± 4.8	6.5 ± 4.4	<0.05
ESS > 10[b]	13.9 ± 3.4	11 ± 3.9	<0.05	15.3 ± 3.9	11 ± 3.7	<0.05

[a]BDI > 10: active treatment n = 6, placebo n = 7; ESS, Epworth sleepiness scale.
[b]ESS > 10: active treatment n = 7, placebo n = 4.
p: paired t-test; BLT, bright light therapy; n. s., not significant; UPDRS, Unified Parkinson's Disease Rating Scale (I mentation, mood, behavior; II activities of daily living; III motor examination; IV complications of therapy); BDI, Beck's depression inventory.

patients completed BLT according to the study protocol. Four patients in the active treatment (22%) and none in the placebo group reported minor and transitory side effects, being eyestrain, and feeling of general malaise (two patients each, respectively).

UPDRS (Table 2)

BLT led to a significant improvement in UPDRS I (mentation, mood, behavior; $P < 0.01$), II (activities of daily living; $P < 0.01$), and IV (complications of therapy; $P < 0.01$). UPDRS III was not changed significantly. However, analysis of major motor symptoms (tremor; bradykinesia; rigidity) revealed a slight improvement of tremor ($P < 0.05$). No significant changes in any score were observed in the placebo group.

Depression and Daytime Sleepiness (Table 2)

BLT lowered BDI score with an average improvement of 2.2 points ($P < 0.05$). In PD patients having at least a mild disturbance of mood (BDI > 10), an even clearer improvement of 4.3 points was noted ($P < 0.05$). BDI was not significantly improved in the placebo group. No correlation between improvement of BDI and UPDRS I or II score was found. ESS score was reduced in both active treatment and placebo group ($P < 0.05$).

DISCUSSION

UPDRS

Enhancement of UPDRS I and II did not correlate with BDI scores suggesting an effect of BLT on mentation/behavior, and activities of daily living, independent from depression. On the whole, PD motor symptoms were not influenced significantly by BLT, although activities of daily living, which represent motor functions at least partially, improved. Interestingly, in a study on secretion patterns of melatonin in PD, patients with tremor predominance secreted more melatonin than patients without tremor,[10] which might explain the particular improvement of this motor feature in our patients. Despite the assumed dopaminergic effect of light induced melatonin antagonism, specific complications of therapy (UPDRS IV) were not worsened, but improved slightly.

Depression

BLT lowered BDI scores significantly. This was even more obvious in patients with BDI > 10, and comparable to treatment with serotonin reuptake inhibitors.[11] However, there is a lack of controlled studies on antidepressant therapy in PD, an important deficiency given the high frequency of depression of up to 50% in PD and the possible worsening of motor symptoms by antidepressants.[12] BLT might therefore present an important alternative or add-on treatment for depression in PD.

Daytime Sleepiness

With a prevalence of up to 45%, excessive daytime sleepiness represents an important symptom in PD.[13] ESS scores were reduced both in active treatment and placebo groups, indicating that BLT has no distinctive effect on sleepiness. This is in accordance to a recent study reporting a weak correlation between melatonin antagonism and suppression of sleepiness in response to BLT.[14] Furthermore, sleep disturbances are frequent in PD, and patients might suffer from an underlying sleep disorder (e.g. sleep apnea) that is not influenced by BLT.[15]

This is the first controlled study of BLT in PD. We conclude that it is a safe, easy to use, and inexpensive nonpharmacological treatment option, which significantly improves tremor and most noncardinal features of PD. However, our study must be regarded as exploratory, and we are aware that absolute changes were moderate, most probably due to the mild clinical symptoms of the included patients and the short treatment duration. As our results raise the possibility that—at least for depression—more severely affected patients show a greater response, future examinations of BLT in PD should focus on more advanced patient populations and treatment durations of at least four weeks.

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Alien Limb Following Posterior Cerebral Artery Stroke: Failure to Recognize Internally Generated Movements?

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Video 

Abstract: **We describe two rare cases of alien limb syndrome following right posterior cerebral artery (PCA) stroke. Both patients present with left hemianopia, visual neglect and proprioceptive loss in addition to their alien limb symptoms. Lesion subtraction from seven control PCA patients revealed that medial parietal-occipital and thalamic areas were selectively damaged in the alien limb patients. We propose that loss of the sense of motor intention and internal model of the current state of the arm, combined with deficient proprioceptive and visual feedback of the moving limb, are critical for genesis of posterior alien limb and discuss how affected regions normally function to ensure awareness of self-generated motor activity.** © 2007 Movement Disorder Society

Key words: alien hand; intention; sensory alien limb; awareness; motor preparation

This article includes supplementary video clips, available online at http://www.interscience.wiley.com/jpages/0885–3185/suppmat.

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