BLUE LIGHT THERAPY FOR SLEEP IMPAIRMENT IN PARKINSON*S DISEASE - Pilot Study -

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1. Primary Objective:The primary objective is to evaluate the efficacy of Propeaq light therapy glasses with integrated blue LED lights on sleep disorders in patients with PD using the PSQI.
2. Secondary Objectives: The secondary objective of the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON44444

Source
ToetsingOnline

Brief title
Blue light in Parkinson disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: European Academy of Neurology

Intervention

Keyword: light therapy, Parkinson's disease, sleep disorders

Outcome measures

Primary outcome

The primary outcome of this study will be the change in Pittsburgh Sleep

Quality Index score (PSQI).

Secondary outcome

The following parameter will serve as secondary outcome measures:

a. Motor Symptoms measurements:

- The MDS-Unified Parkinson*s Disease Rating scale (MDS-UPDRS) parts I-IV

b. Non- motor symptoms measurements:

- Sleep impairment: Epworth Sleepiness Scale (ESS), Global Impression of

Clinical Change (GICC), sleep diary

- Cognition: Mini-Mental State Examination (MMSE), Montreal Cognitive

Assessment (MoCA)

- Depression and Anxiety: Hamilton Depression Rating Scale (HADS)

Study description

Background summary

Parkinson*s disease (PD) is a neurodegenerative disorder characterized by the coexistence of motor and non-motor features. Sleep disturbances are among the most common (non-motor) symptoms occurring inup to 90% of PD patients and reducing quality of life and daytime functioning. Sleep impairment may refer to diurnal or nocturnal symptoms with extensive daytime sleepiness (EDS), sudden sleep attacks during daytime as well as insomnia and restless leg syndrome (RLS). Potential underlying causes of sleep disorders include motor symptoms (rigidity and bradykinesia), autonomic dysfunction (nocturia, diaphoresis),

abnormal REM sleep behaviour (RBD), sleep apnoea, medication influence, neurodegeneration itself of central sleep regulatory areas such as the hypothalamus as well as age-related sleep changes. Increasing evidence suggests that the suprachiasmatic nuclei (SCN), functioning as the circadian pacemaker and responsible for the endogenous physiologic cycles occurring on approximately a 24-hour cycle, is perturbed in PD. These circadian cycles are synchronized to the environmental light or dark and to social activity cycles by zeitgebers (cues indicating environmental time). Light represents the most effective zeitgeber of the circadian timing system and supplementary exposure to light has beneficial effects on sleep quality and daytime vigilance in healthy older people and patients suffering from dementia. In addition, dopamine neurotransmission plays an essential role in circadian rhythm regulation especially in promoting wakefulness. Dopamine is involved in retinal light adaptation, melanopsin and clock gene expression and influences circadian rhythmicity through selected central nervous system structures (raphe nuclei, locus coeruleus, hypothalamus and thalamus).
Several rodent models of PD have clearly demonstrated the pathological involvement of the SCN in PD, offering a potentially powerful and novel therapeutic target. The disturbance of circadian timing in PD also seems to have an impact on several other non-motor symptoms, including depressive symptoms and autonomic functions, as well as motor functions such as rigidity and bradykinesia. As medication prescribed for sleep disturbances often results in side effects, there is a great need to develop and evaluate nonpharmacological approaches to manage not only sleep disorders in patients, but also many other symptoms which are related to the perturbation of circadian disruption.
Bright light therapy (BLT) was introduced to improve circadian rhythmicity as well as mood and sleep disorders. Firstly, a positive effect on sleep and mood was observed in the healthy general population but also in seasonal affective disorder and depression. BLT was also found to be useful in neurodegenerative disorders like PD. In previous studies patients diagnosed with PD received BLT with a light intensity of 1000 - 6000 Lux for 30- 90 minutes in the morning or prior to bedtime. Results indicated noticeable improvement in mood, sleep and interestingly, in motor functions. Based on recommendation 10000 Lux should be used for 30 minutes and the time of administration should depend on the type of symptoms or patient*s chronotype. BLT is considered as a safe treatment option and only minor side effects have been reported such as: headache, eye or vision-related complains and nausea. The effectiveness of BLT may be attributed to its zeitgeber function, which resets circadian rhythmicity reflected in a shift in serum melatonin concentrations. Studies have shown that blue light with a wave length in the range of 460-480 nm is more effective in entraining the SCN compared to monochromatic light with a wave length around 555 nm. In addition, it has been observed that blue light around the 460 nm range is more effective in phase-shifting circadian output than exposure to white light of longer duration and higher irradiance. Blue light therapy has been, for example, studied in otherwise healthy subjects in whom it increased alertness and improved

cognitive functioning.
So far, five previous studies have used BLT (white light) in PD patients showing improvements in sleep and other non-motor symptoms after two weeks of therapy. Two studies have also shown an improvement in motor function. These studies were, however, limited by either a small number of patients, retrospective design and most have made use of unwieldy light boxes. Also the option of blue light instead of white light as a treatment option has not been explored in PD. In our study we propose a novel approach to light therapy using Propeaq light therapy glasses with integrated LED lights emitting blue light with a 468 nm wavelength more specifically targeting retinal melanopsin and the retinohypothalamic tract and thereby more likely to effectively reset the SCN in PD patients. Moreover, replacement of light boxes with glasses might positively influence the study compliance and repeatability of results as well as give further insights to underlying mechanisms of circadian disruption in PD.

Study objective

1. Primary Objective:

The primary objective is to evaluate the efficacy of Propeaq light therapy glasses with integrated blue LED lights on sleep disorders in patients with PD using the PSQI.

2. Secondary Objectives:

The secondary objective of the study is to evaluate efficacy of Propeaq light therapy glasses with integrated blue LED lights on a wide range of other domains such as motor symptoms as well as other non-motor symptoms (e.g. mood, cognition).

Study design

The study design will be a placebo controlled single-blind study. All participants will be randomly allocated to receive either blue light therapy (intervention) or red light therapy (placebo).During or prior to the pilot trial, participants will not receive any information relating to which colour of glasses concerns the intervention and which colour the placebo.

Intervention

Intervention group:
Intervention will consist of blue light therapy being administered. Participants will wear the Propeaq light therapy glasses for one hour twice daily (total two hours each day). During the first daily session the participants will wear the glasses for one hour after they wake up in the

morning and during the second session they will wear the glasses for one hour starting two hours before preferred bed time.

Control group:
Placebo will consist of red light therapy being administered using the same glasses as the blue therapy but with red coloured glass instead of blue coloured glass. The red light protocol will be identical to the blue light protocol again requiring the participants to wear the glasses twice daily for one hour (total two hours each day).

Each participant will use the blue light therapy for a total of two weeks or the red light therapy for two weeks as well.

Study burden and risks

Light therapy was well tolerated in all studies with PD patients. The rate of adverse events was around 6%. Reported side effects include mild headache, sleepiness and itchy eyes. These adverse effects all resolved spontaneously after secession of the intervention. The same amount and nature of side effects have been reported in the red light placebo therapy. In terms of benefit, based on previous studies with white light BLT, we expect that the participants receiving the blue light therapy will show significant improvements in e.g. daytime sleepiness, sleep quality and several self-reported subjective sleep metrics, such as sleep fragmentation, sleep quality ease of falling asleep. In addition we expect improvement of depressive mood and motor scores, reflected by better scores on the UPDRS scale.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female subjects diagnosed with idiopathic PD according to UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria with Hoehn & Yahr stage 2-4
- Ability to obtain written inform consent (IC) for participation in the study
- Age of > 30 years (inclusively)
- Score of 5 or more on the Pittsburgh Sleep Quality Index score (PSQI) or Excessive daytime sleepiness (EDS) defined by an Epworth Sleepiness Scale (ESS) score of 7 or more
- Anti-PD treatment (such as levodopa formulations, dopamine agonists, selective MAO-B inhibitors, anticholinergic agents or amantadine) at a stable dose in the last 30 days prior to the initial screening assessment

Exclusion criteria

- Atypical Parkinsonism (Subjects with Parkinsonian features caused by disorder such as multiple system atrophy, progressive supranuclear palsy, dementia with Lewy bodies or multiple brain infarcts)
- Severity of Parkinson*s disease defined as stage 1 or 5 according to Hoehn & Yahr stages
- Significant cognitive impairment as defined by the Mini-Mental State Examination (MMSE) score <24
- Clinically significant psychiatric illness, including psychotic attacks, major depressive disorder (HAM-D = Hamilton Depression Rating Scale >=14). Subjects with a lifetime history of suicidal attempt (including an active attempt, interrupted attempt or aborted attempt)
- Antidepressant treatment for less than 3 months prior to screening
- Participation in other, interventional, research studies
- Known conditions associated with sleep disorders other than PD or conditions inferring with the delivery of the blue light treatment:
• Obstructive sleep apnoea syndrome
• Eye-related diseases (e.g. cataract, glaucoma, blindness)

• Any other condition that in the opinion of the investigator may interfere with the interpretation of the study results or constitute a health risk for the subject if he/she takes part in the study
• Current or history of malignancy or migraine within 5 years before screening
Current use or use within three months prior the initial screening of hypnosedative or stimulant drugs such as benzodiazepines or melatonin

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-12-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Propeaq Lightglasses
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	19-10-2017
Application type:	First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL62354.091.17