SIXTY MINUTE EVENING EXPOSURE OF SPECIFIC BANDWIDTH LIGHT FOR THE TREATMENT OF IDIOPATHIC PARKINSON*S DISEASE

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The objective of the study is to determine whether exposure to the SpectraMax light therapy device, emitting light in a combined spectra of blue/green light (460 * 570 nm) with an intensity of approximately 1300 Lux, will be more effective in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41705

Source
ToetsingOnline

Brief title
Light therapy for treatment of Parkinson's disease

Condition

- Other condition
- Movement disorders (incl parkinsonism)
- Mood disorders and disturbances NEC

Synonym
Parkinson's disease / paralysis agitans

Health condition

angststoornissen

Research involving
Human

Sponsors and support

Primary sponsor: PhotoPharmics, Inc
Source(s) of monetary or material Support: Door Photopharmics Inc.

Intervention

Keyword: Light therapy, Parkinson's disease

Outcome measures

Primary outcome

The primary effectiveness endpoint is the change in the MDS-UPDRS (Movement

Disorders Society * Unified Parkinson*s Disease Rating Scale) composite score

of sections II and III at Treatment Visit 3 (after six months of treatment).

Secondary outcome

1. Change of the scores on Parts I, II, III, IV and of the total MDS UPDRS.

2. Change of the score on the Beck Depression Inventory (BDI-II)

3. Change of the score on the Beck Anxiety Inventory (BAI)

4. Change of the three sub domain and total scores on the Parkinson*s

Disease Sleep Scale-2 (PDSS 2)

5. Change of the score on the Epworth Sleepiness Scale (ESS)

6. Change of the eight sub-scales and total scores on the Parkinson's

Disease Questionnaire (PDQ-39)

7. Change of the Clinical Global Impression - Severity Index (CGI-S),

Efficacy Index (CGI-E) and final Global Improvement (CGI-I) score.

8. Change of the score on column 1, column 2 and combined total of the

Wearing-Off Questionnaire (Q10)

The following data will be collected and analyzed separately from the primary

and secondary endpoint data for exploratory research purposes and will be

reported separately from the Investigation Final Report:

9. Elbow-to-Fist (ETA) and Floor-to-Knee (FTK) Timed Motor

Tests

10. Improvement of sleep latency, total sleep time, and number

and frequency of awakenings as measured by actigraphy

Study description

Background summary

Idiopathic Parkinson*s Disease and Circadian Function:
Parkinson*s disease (PD) is traditionally described as a neurodegenerative disorder affecting the dopamine (DA) function in the nigro-striatal dopamine (NSD) system, giving rise to the characteristic motor symptoms of rigidity, bradykinesia, and tremor. The neurodegenerative process is not limited to the NSD system, but affects other systems as well [1] and many PD patients experience a range of non-motor symptoms, comprising cognitive, mood and sleep disturbances [1, 2]. The motor symptoms, as well as the non-motor symptoms, have a negative impact on quality of life and daily functioning in PD patients [3-6].
Treatment of PD is mainly based on dopamine replacement in the form of the DA precursor L-dopa or DA agonists. Unfortunately, not all symptoms respond to dopaminergic treatment, and the efficacy of these agents decreases as the disease progresses [7]. Moreover, L-dopa and DA agonists can induce side-effects, such as response fluctuations and dyskinesias [7]. Therefore, research on alternative treatment strategies for the motor and non-motor symptoms of PD is imperative.
Research on the circadian system has demonstrated that a misalignment of the circadian rhythm can induce depressive symptoms and sleep disturbances [8, 9]. In PD, there is a frequent co-occurrence of sleep disturbances and depressive symptoms [10, 11]. This points to a dysfunction of the circadian system as a common underlying factor. The center of the circadian system is the circadian *pacemaker*, which is located in the suprachiasmatic nucleus (SCN) of the hypothalamus. Its endogenous rhythm is slightly different from the 24-hour day-night cycle and has to be entrained by signals (or *zeitgebers*) such as light, activity and food [12]. Light provides the *daytime* signal, by exciting

specialized melanopsin containing ganglion cells in the retina, that project towards the SCN via the retino-hypothalamic tract [8]. The output signals of the SCN convey circadian timing information to brain areas regulating behavior, body temperature, autonomic and neuroendocrine systems, including the secretion of melatonin by the pineal gland [8]. The secretion of melatonin is inhibited by the SCN during the light cycle, but the SCN also contains melatonin receptors that inhibit SCN firing, thereby creating a negative feedback loop [13, 14].

Circadian malfunction is suggested to play an important role in the development and progression of PD [15]. The balance between melatonin and dopamine, which sit in functional opposition to regulate day/night activities, appears to have an important role in this process [16]. In an animal model of PD, motor dysfunction was exacerbated by administration of exogenous melatonin [17]. In another study, intravitreal injection of very small amounts of L-dopa or a melatonin antagonist improved motor function in rats with experimentally induced PD, suggesting involvement of the retina [18]. In PD patients treated with L-dopa, a phase-advanced circadian rhythm was observed compared to healthy controls and de novo PD patients [19-21]. The influence of circadian malfunction on the frequently occurring sleep-wake disturbances in PD has recently been studied in an experimental model of PD in non-human primates [22]. The results of this study suggest that DA depletion of the NSD system prevents the circadian system to effectively drive rhythmic locomotor rest-wake activity [22].

The circadian system appears to play a key role in PD, and might therefore provide an important starting point for an alternative treatment for this disease. Bright light therapy (BLT) acts as a strong zeitgeber and can restore circadian rhythmicity [23, 24]. BLT might therefore be able to exert positive effects on both the motor and nonmotor symptoms in PD patients.

Study Background:

This study aims at evaluating the safety and efficacy of a non-invasive BLT device to be used with ongoing dopaminergic treatment for PD.

The positive effects on BLT in PD have been studied in both preclinical and clinical research. In an experimental model of PD in rats, exposure to constant light significantly improved motor function [17]. In PD patients, the effects of BLT have been evaluated in several pilot studies and one retrospective, open label study [16, 25-27]. These studies demonstrated that BLT for PD patients might have a positive effect on motor function, sleep disorders and mood [16, 25-27]. However, a randomized, placebo-controlled trial on the effects of BLT in PD patients is still lacking.

In the past, BLT studies employed broad bandwidth, polychromatic light at high intensities (10,000 + lux). Recent research has demonstrated that exposure to narrow-band blue light is more potent in melatonin suppression than longer wavelength light [28]. In PD patients, who have a phase-advanced circadian rhythm,[19-21] blue light might be more effective in restoring circadian rhythm than polychromatic light [29]. Unpublished, pilot data from PD patients suggests that while blue light produces improvement, green light may yield

further benefits [30, 31]. The high intensity of 10,000 Lux of previously used BLT produces glare and can induce side effects such as headaches, nausea, jitteriness, or eyestrain.[32] Optimizing the bandwidth of light may not only improve the efficacy of BLT, but also allow a reduction of the intensity of the light administered, decreasing side effects [32]. Therefore, this study will investigate the effectiveness of light that produces the majority of its energy in the medium wavelength frequencies (~460 * 570 nm), at an intensity of 1300 Lux.

Study objective

The objective of the study is to determine whether exposure to the SpectraMax light therapy device, emitting light in a combined spectra of blue/green light (460 * 570 nm) with an intensity of approximately 1300 Lux, will be more effective in reducing the primary motor and non-motor symptoms of PD, than a placebo device that emits polychromatic light with an intensity of 100 Lux. This study embraces the latest development in circadian function and phototherapy in an attempt to determine the potential efficacy of light therapy in treating PD.

Study design

Dit betreft een multicenter, gerandomiseerde, placebo-gecontroleerde studie..
De studie wordt verdeeld in drie perioden: screening, behandeling en follow-up. Na de formele screening zal er een baseline-meting van twee weken zijn, die wordt gevolgd door een behandelingsperiode van zes maanden. Aan het einde van de behandelperiode wordt de lamp geretourneerd. Eén maand later zal de deelnemer terugkomen voor een follow-up meting.
De screening vindt plaats bij het eerste polikliniek bezoek. Deelnemers krijgen aansluitend een baseline-meting. Zij krijgen hierbij een slaapdagboek en actimeter voor een baseline-meting van hun slaap en activiteit gedurende twee weken. Aan het einde van deze baseline-meting zal de onderzoekscoördinator op huisbezoek gaan om de actiwatch en het slaapdagboek op te halen. Patiënt die de meting hebben volgens afspraak hebben volbracht zullen gerandomiseerd worden naar de experimentele of controlegroep. De onderzoekscoördinator zal de lichttherapie-lamp installeren en de deelnemer instrueren de lamp één maal daags in de avond gedurende een uur te gebruiken conform de verstrekte instructies.
De behandelperiode duurt 6 maanden. Meting van primaire motorische en niet-motorische symptomen vindt plaats bij de baseline-meting en op Maand 1, 3 en 6 Behandelbezoek (of eerder, bij een bezoek na vroegtijdige beëindiging van de studie), en bij het Follow-upt bezoek na zeven maanden. Het slaapdagboek en de actigrafie worden herhaald in de twee weken voor het Behandelbezoek van Maand 3 en 6.
In totaal vinden er dus vijf polikliniek-bezoeken plaats: één screenings- en baseline-meting, drie behandelmetingen en één follow-up meting (zie tabel 2 en

3 van het protocol). Voor alle metingen geldt dat patiënten gezien worden in de ochtend. Gedurende de onderzoeksperiode zal een standaard speling van +/- vijf dagen toegestaan worden voor het plannen van metingen. De onderzoekscoördinator zal twee keer per maand telefonisch contact hebben met de deelnemers tot de zesde maand. Alle afspraken zullen plaatsvinden in de ochtend. Bij afname van de UPDRS wordt rekening gehouden met het medicatieschema van de dopaminerge medicatie; niet eerder dan 1 uur na de laatste dosis, en niet later dan 1 uur vóór de volgende geplande dosis.

Intervention

The Spectramax* light therapy device is an artificial light source with a combined spectrum of blue/green light (460 * 570 nm) at an irradiance of approximately 400 µW/cm2. The control light therapy device is identical in appearance to the Spectramax* light device, but it emits a broad bandwidth polychromatic light of approximately 50 µW/cm2 (100 lux). Participants will be exposed to the light source for 1 hour daily for 6 months.

Study burden and risks

At the irradiance levels emitted by commonly utilized light therapy devices, dermatologic safety concerns are minimal. The Spectramax light therapy lamp is certified to Risk Group 0 indicating no photobiological risk as per the international standard, IEC 62471:2006. Similarly, thermal damage to cornea, lens or retina requires milliwatt-to-watt exposure, far in excess of that emitted from these therapeutic devices. While these devices emit less than 2,000 lux, ocular safety for 6,000 lux white fluorescent sources has been assessed and comprehensive optometric examinations of individuals with healthy eyes who used white-light therapy daily during fall/winter months for up to 5 years did not reveal adverse effects (Gallin et al., 1995; Gorman et al., 1993). The control and blue-green light LED sources to be utilized in the present research have been determined to have an averaged radiance well below the 10-mW/cm2*sr safety limit for continuous viewing (see Appendix for Sliney reports).
Over the last 25 years, light therapy with bright fluorescent light, and LED light therapy have been tested in many individuals and serious irreversible adverse effects have not been reported. The most common side effect of light therapy is irritability or agitation that remits after termination of the light or decrease of the daily duration of exposure. Participants will be carefully monitored for such side effects and light therapy exposure will be decreased or eliminated if these adverse effects occur.
Written instructions will be given, potential adverse effects will be discussed, and subjects will be instructed to telephone the study site with any questions or should any adverse effects occur. The Investigator shall withdraw any subject where continued involvement in the investigation may negatively affect the subject*s safety or welfare.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Males and females, with Stage II * IV, Idiopathic Parkinson*s Disease, as assessed by Hoehn-Yahr Scale
2. On optimized, stable dopamine replacement therapy for at least 1 month

Exclusion criteria

1. Subjects younger than 45 years old.
2. Participation in a study of investigational or marketed drugs or devices during the 30-day period prior to the start of the study or during the study
3. Subjects who are medically complicated, medically unstable and/or have other severe co-morbid disease states, as determined by the investigator.

4. History of concurrent psychiatric illness that would preclude compliance with the protocol and/or ability to complete the study safely
5. History or current diagnosis of major psychiatric disorder including Bipolar I Disorder that could interfere with accurate assessment and effective treatment
6. Beck Depression Inventory score of greater than or equal to 14
7. Patients on stable anti-depressant dose for less than 6 weeks
8. An anticipated need for dopamine therapy change for the duration of the trial
9. Less than one month of stopping an anti-depressant or psychoactive medication
10. History of current or recent (within previous 12 months) alcohol, narcotic or other drug abuse by DSM-5 criteria
11. Active suicidal or homicidal ideation or plan as determined by the Investigator, or a score of 2 or higher item 9 of the BDI-II.
12. Previous use of light therapy treatment
13. Females of childbearing age, e.i. capable of becoming pregnant
14. Night shift work within the past 6 months, or planned during the investigation
15. Planned travel for more than two weeks outside of two time zones from the state in which the trial is being conducted
16. Planned travel outside of two time zones from home during the last two months of the Subject*s involvement in the Investigation
17. Current use or use within the previous 1 month of photosensitizing or other medications that in the opinion of the investigator would interfere with the safety of the subject during the trial including:
a. amiodarone,
b. benoxaprofen,
c. chlorpromazine,
d. demeclocycline,
e. fleroxacin,
f. nalidixic acid,
g. ofloxacin,
h. piroxicam,
i. porfimer,
j. psoralens,
k. quinidine,
l. temoporfin tetracycline,
m. oral isoretinoin (Accutane),
n. St. John*s wort,
o. melatonin.
18. History of significant eye trauma or disease, retinopathy, and/or cataract of a level that would significantly affect transmission or processing of light through either eye
19. Other neurological disorders that in the opinion of the investigator would interfere with the conduct of the study
20. Pre-existing major joint problems that in the opinion of the investigator would interfere with subject compliance
21. History of cerebral insult or central nervous system infection that in the opinion of the Investigator would preclude successful participation in Investigation related procedures.
22. Cognitive impairment, e.g. as determined by the Montreal Cognitive Assessment, that in the opinion of the Investigator would interfere with the conduct of the Investigation.

23. Focal neurological deficits that in the opinion of the Investigator would interfere with the conduct of the Investigation.
24. High Total Drug Burden or severe dyskinesia attributable to dopamine replacement therapy that would preclude successful participation in the Investigation related procedures or interventions in the opinion of the site Investigator. Total Drug Burden is defined as the total of the L-dopa equivalents, plus peripheral decarboxylase inhibitor, of each medication in the patient*s drug therapy.
25. Subjects who refuse to sign written informed consent or give approval for notification of the subject*s personal physician of their interest to participate in the investigation.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-02-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Spectramax Light Therapy Lamp
Registration:	No

Ethics review

Approved WMO

Date:	11-07-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL46350.029.14

Study results

Date completed:	20-07-2016
Actual enrolment:	30

Summary results
Trial is onging in other countries