Neurostimulation for the treatment of mild cognitive impairment in Parkinson*s disease: an acceptability cross-over study

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

Summary

ID

NL-OMON56853

Source
ToetsingOnline

Brief title
NESCIO-PD

Condition

- Movement disorders (incl parkinsonism)
- Dementia and amnestic conditions

Synonym
cognitive impairment, thinking problems

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Mild cognitive impairment, Parkinson's disease, Repeated transcranial magnetic stimulation, Transcranial direct current stimulation

Outcome measures

Primary outcome

Acceptability of the interventions, as measured with an acceptability

questionnaire based on the Theoretical Framework of Acceptability (*TFA-PD

questionnaire*; Sekhon et al., 2017, 2022).

Secondary outcome

1) Acceptability and feasibility outcomes supporting the main study parameter,

including a) objective feasibility data on intervention compliance and

attrition indices of drop-out, b) feasibility of at-home tDCS usage measured

with the System Usability Scale (Brooke, 1996), and c) acceptability of the

interventions based on qualitative data from focus groups, co-led by the

involved end users (*patiëntonderzoekers*) from the Dutch PD Patient

Association;

2) Subjective cognitive function (PD-Cognitive Functional Rating Scale;

Cognitive Failures Questionnaire);

3) Objective cognitive function (Trail Making Test, Letter Fluency, Tower of

London, Rey Auditory Verbal Learning Test (*15 Woordentest*), Symbol Digit

Modalities Test, Wechsler Adult Intelligence Scale IV-NL - Digit Span subtest);

4) Neuropsychiatric symptom severity (depression: Beck Depression Inventory-Ib;

anxiety: Parkinson Anxiety Scale);

5) Functional mobility (Timed Get-up and Go test);

6) Structural and functional neuroimaging to enhance precision of DLPFC

targeting.

Study description

Background summary

Mild cognitive impairment (MCI) is a highly prevalent non-motor characteristic in Parkinson*s disease (PD) affecting about 40% of individuals (Baiano et al., 2020). PD-MCI is associated with limitations in daily life functioning and quality of life, and with neuropsychiatric symptoms. Importantly, it constitutes a risk factor for later development of PD-related dementia (Hoogland et al., 2017).
There are no curative treatment options for PD*or PD-MCI*yet. Symptomatic treatment of cognitive impairment in PD currently consists of optimization of dopaminergic therapy, improving cognitive inflexibility and bradyphrenia, but also exacerbating other cognitive deficits (Robbins & Cools, 2014). Despite many endeavors to pharmacologically improve PD-MCI, there is no effective medicament. Additionally, other, non-pharmacological treatment options such as cognitive training have shown moderate effect sizes, but with limited transfer to daily functioning (Gavelin et al., 2022; Orgeta et al., 2020).
Non-invasive brain stimulation (NIBS) through repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) may show promise in treating PD-MCI (Dinkelbach et al., 2017; He et al., 2022; Jiang et al., 2020; Suarez-Garcia et al., 2020). NIBS is, however, intensive and complex in use, specifically for individuals with motor and cognitive difficulties, which might limit its potential for clinical use.

Study objective

The primary objective of this study is to assess the acceptability and feasibility of four-week, high-frequency rTMS and anodal high-definition tDCS of the DLPFC as potential intervention methods for the treatment of PD-MCI.
Secondary study objectives include:
1) Explore demographic and clinical factors that impact the acceptability and feasibility of NIBS for the treatment of PD-MCI.
2) Render separate effect size estimations for the efficacy of rTMS and tDCS on cognitive function, measured with subjective cognitive function questionnaires and objective measurements (neuropsychological assessment).

3) Explore the effects of NIBS on neuropsychiatric symptoms and functional mobility.
4) Explore the use of functional and structural MRI to optimize neurostimulation targeting in PD-MCI.

Study design

This intervention study will adapt a cross-over design with three conditions: a baseline condition, rTMS, and tDCS.

Intervention

Participants will undergo four consecutive phases: 1) a no-intervention baseline condition, 2) 12 sessions of 20-minute repetitive transcranial magnetic stimulation (rTMS) (10Hz) or anodal transcranial direct current stimulation (tDCS) targeting the left dorsolateral prefrontal cortex (DLPFC), 3) a second no-intervention baseline condition, 4) the second NIBS intervention. All phases have a duration of 4 weeks and the NIBS interventions are counterbalanced between two groups.

Study burden and risks

The study consists of 1) two four-week intervention periods, with three (rTMS)/five (tDCS) 20-minute intervention sessions per week. For the rTMS intervention, stimulation will be performed at the Amsterdam UMC, location VUmc (and thus includes travel time); 2) one 120-minute assessment (baseline) that includes neuropsychological and motor assessment, and MR imaging, and four 60-minute assessments that only includes neuropsychological and motor assessment.
The risks of the intervention have been shown to be small for individuals with Parkinson*s disease, are minimized by the exclusion criteria and the intervention protocols fall within the reported safety guidelines. The research team is experienced in the use of both interventions in a variety of populations (e.g., stroke, obsessive-compulsive disorder, elderly with bipolar disorder). Moreover, the research team is experienced in the execution of clinical trials on non-pharmacological interventions for the treatment of non-motor symptoms in Parkinson*s disease (e.g., bright light therapy, cognitive training, acceptance & commitment therapy). There are no risks of the assessments.
There is a potential benefit of NIBS on cognitive function, based on small earlier studies. Additionally, NIBS targeted at the DLPFC may positively impact depressive symptoms.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Clinical diagnosis of Parkinson*s disease, diagnosed by a neurologist;
- Mild to moderate disease stage (Hoehn & Yahr disease stage < 4);
- Movement Disorders Society Level I criteria for PD-MCI;
- In case of (dopaminergic) medication use, participants are on stable medication for at least one month before participation and expect to remain on stable medication during the study.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Indication for dementia based on the SAGE (cut-off < 14; Scharre et al.,

2010);
- Severe depressive disorder (Beck Depression Inventory - Ib score > 18);
- Psychotic disorder (except for benign hallucinations with insight), screened with the Scale for Assessment of Positive Symptoms for Parkinson*s disease;
- Indication of alcohol or drug abuse;
- Contra-indication for NIBSrTMS according to Magstim Rapid2 Manual; rTMS should not be::
• used on or in the vicinity of patients or users with cardiac demand pacemakers, implanted medication pumps, cochlear devices, implanted defibrillators and/or implanted neurostimulators
• used on or in the vicinity of patients with implanted metal objects• used on patients where the skin in the area to be contacted is broken
• used on patients who suffer from multiple sclerosis
• used on those with large ischaemic scars
• used on pregnant women
• used on infants under the age of 2 years
• used on epileptic individuals
• used on those with a family history of convulsions
• used on individuals with brain lesions that could affect seizure threshold
• used on individuals suffering from multiple sclerosis
• used on individuals taking tricyclic antidepressants, neuroleptic agents or any other drug that could lower seizure threshold,
• used on individuals suffering from sleep deprivation during rTMS procedures
• used on individuals with a heavy consumption of alcohol or those using epileptogenic drugs
• used on individuals with severe heart disease or with increased intracranial pressure be used on those who have uncontrolled migraines
- Contra-indication for tDCS according to Neuroelectrics Starstim Manual; tDCS should not be used in case of:
• Patients with a history of seizures;
• Patients with unexplained episodes of loss of consciousness, since such condition could be related with brain alterations or epilepsy;
• Patients with unstable or non-controlled neuropsychiatric illness;
• Patients having implanted brain medical devices;
• Patients with implanted pacemakers;
• Patients having any electrically, magnetically or mechanically activated implant;
• Patients having cardiac, neural or medication implants;
• Patients having vascular clips or any other electrically sensitive support system in the brain;
• Patients with serious brain injury;
• Patients showing damage of skin at sites of stimulation (the device can only be used in healthy skin without wounds, otherwise the resistance to current can be altered);
• Patients suffering from skin problems, such as dermatitis, psoriasis or eczema;
• Patients suffering from severe or frequent headaches;

• Patients with any serious life-threatening disease such as congestive heart failure, pulmonary obstructive chronic disease or active neoplasia;
• Pregnant women (women of childbearing age should undertake a pregnancy test to confirm eligibility before treatment).
- Contra-indication for MR imaging:
• metal in the body (pacemaker, port-a-cath, prosthesis, (cochlear) implant) • previous brain surgery
• head trauma that resulted in unconsciousness for at least 1 hour • clips
• (old metal containing) tattoo • irremovable piercings
• irremovable metal braces • pregnancy
• claustrophobia other problems lying still for 45 minutes • metal in the teeth
• neurostimulator (including deep brain stimulation)
- Space-occupying lesion on MRI.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-08-2024
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDC
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	31-05-2024
Application type:	First submission
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	NL84843.018.23