Guiding personalized treatments for Parkinson*s tremor with individual neuroimaging * an exploratory study

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

Summary

ID

NL-OMON45367

Source
ToetsingOnline

Brief title
Tremor fingerprints in Parkinson's disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease, tremor

Research involving
Human

Sponsors and support

Primary sponsor: Neurologie
Source(s) of monetary or material Support: ZonMw (Off Road subsidie)

Intervention

Keyword: fMRI, Parkinson, tDCS, tremor

Outcome measures

Primary outcome

(1) Within-subjects reproducibility of tremor-related activity and connectivity (*tremor fingerprint*; quantified using concurrent EMG-fMRI across two different days); (2) Modulation of tremor-related activity and connectivity by TACS (comparison of the three TACS conditions); (3) Modulation of tremor by TACS (quantified using accelerometry), and its correlation with network parameters derived from the tremor circuit (i.e. thalamo-cortical connectivity).

Secondary outcome

Not applicable. See Primary outcome measure.

Study description

Background summary

Parkinson*s disease is the second most common neurodegenerative disease worldwide. Clinically, Parkinson*s disease is characterized by motor slowing (bradykinesia), stiffness (rigidity) and resting tremor. Parkinson*s tremor has a variable and inconsistent response to available medication, and only very few patients proceed to invasive treatments such as deep brain surgery. This is caused by pathophysiological heterogeneity between patients, which is currently not taken into account. Non-invasive treatments * and individual predictors of treatment success * are therefore very much needed. Using combined EMG-fMRI, we have previously shown that Parkinson*s tremor is associated with increased activity in a cerebello-thalamo-cortical tremor circuit. However, it is unclear to what extent inter-individual variability between patients in the architecture of the tremor circuit is unique and reliable (between-sessions replicability) and whether this variability can explain relevant clinical

information (such as treatment success).

Study objective

The main goal of this study is to use individual pathophysiological characteristics (pattern of activity and connectivity within a patient*s tremor network; *tremor fingerprint*) to predict the effect of a new and non-invasive anti-tremor treatment (transcranial alternating current stimulation, TACS, over the motor cortex) in individual patients. Furthermore, we aim to unravel through which mechanisms TACS over the motor cortex influences the tremor circuitry.

Study design

This is a combined observational and intervention study. First, we will localize tremor-related activity using concurrent EMG-fMRI scanning on two separate days (to determine replicability). Second, we will apply network analyses (dynamic causal modelling) on tremor-related activity in order to compute tremor network parameters for each individual patient (e.g. effective connectivity). Third, we will test for the effects of transcranial alternation current stimulation (TACS) over the motor cortex on tremor severity and on tremor-related activity and connectivity. This leads to individual tremor *fingerprints* that predict treatment effects.

Intervention

The intervention involves TACS, which is a non-invasive, non-painful way of stimulating underlying cortical brain tissue through electrodes applied to the scalp. When applied rhythmically at the frequency of cortical oscillatory activity, it can exert excitatory or inhibitory (depending on the phase) effects on brain function. In this research, we will apply TACS over the motor cortex contralateral to the tremulous hand, in the same frequency, and phase-locked to, the ongoing tremor. There are three conditions: inhibitory TACS (anti-phase), stimulating TACS (in-phase), and sham (no/fake stimulation). TACS will be applied both outside and inside the MRI scanner, to test for the effect on the tremor circuitry.

Study burden and risks

This research involves capacitated adults. This research has no direct benefit for the participants. The scientific benefit of this study is to achieve a better understanding of the pathophysiology of a severe symptom (Parkinson*s tremor). The outcomes of this study may give rise to future new treatments for Parkinson*s tremor. The burdens of this study are relatively small: there are no invasive procedures, and the time asked from each participant is two day-parts of approximately 3 hours.

Considering the exclusion criteria, the screening procedure and constant monitoring of the subjects we do not expect (S)AE side effects. MRI measurements themselves do not pose any risk, if appropriate precautions are made. However, the noise and the relative confined space of the MRI scanner may cause discomfort to some subjects. Like for MRI, risks of TACS are considered negligible. Participants may experience mild tingling, itching, or burning sensations on the skin under the electrode which usually disappear after a while. In any case, the experimenter will make sure that the stimulation is fully tolerable at the beginning as well as throughout the experiment. The most common side effects are a transient mild headache which is short lasting and responds well to light painkillers like paracetamol, as well as a mild feeling of fatigue. In rare cases, nausea and vertigo have been reported. Measurements will always be stopped whenever the participant wants to or whenever the participant does not tolerate any measurement. Finally, some patients may experience discomfort due to resurgence of the parkinsonian symptoms following withdrawal of anti-parkinsonian medication. This is, however, in no way dangerous for the patient. Patients will be asked to bring their own medication to the laboratory, so that they can take their medication immediately after the experiment.

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

- Idiopathic Parkinson*s disease according to UK brain bank criteria.
- Presence of a clear resting tremor of at least one arm (UPDRS tremor-score > 2).

Exclusion criteria

- neuropsychiatric co-morbidity
- contraindications for MRI scanning (e.g. pacemaker, implanted metal parts, deep brain stimulation, claustrophobia)
- Severe head tremor or dyskinesias.
- Cognitive impairment (MMSE < 26)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-01-2018
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	03-05-2017
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	NL60572.091.17

Study results

Date completed:	07-09-2019
Actual enrolment:	30

Summary results
Trial is onging in other countries