Functional brain network changes as indicators of deep brain stimulation-induced cognitive and psychiatric side effects in Parkinson*s disease related to electrode contact points: a proof of concept study

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a) Identification of stimulation site-specific functional and structural brain network characteristics in patients with PD and STN-DBS.b) Relating subject-specific stimulation sites and functional network changes to measures of cognitive and...

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

Summary

ID

NL-OMON46346

Source
ToetsingOnline

Brief title
MEG in Parkinson*s disease patients with DBS

Condition

- Movement disorders (incl parkinsonism)
- Nervous system, skull and spine therapeutic procedures

Synonym
idiopathic parkinsonism, paralysis agitans, Parkinson□s disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: -Deep brain stimulation (DBS), -Magneto-encephalography (MEG), -Non-motor side effects, -Parkinson□s disease

Outcome measures

Primary outcome

The main study parameters are stimulation site-specific neurophysiological

measures, as obtained by MEG recordings, and individual differences in the

exact locations and structural connections of each stimulation site, as

obtained by pre- and post-DBS brain imaging. These network parameters will be

correlated with clinical measures of cognitive and psychiatric side effects.

Secondary outcome

N.a.

Study description

Background summary

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective surgical intervention for motor symptoms in Parkinson*s disease (PD), but it can induce negative cognitive and psychiatric side effects in up to 25% of patients. Usually the electrodes targeted at the STN are implanted bilaterally. Each electrode may have four or eight contact points. Clinical improvement and side effects differ per stimulated contact point, but the cause of these effects is only partly understood. At present, it may take months to identify the optimal DBS settings via trial and error. Stimulation of white matter tracts surrounding the STN is considered important for the clinical effects of

DBS. The relationship between contact points and white matter tracts, hence the stimulation sites, can be approximated using diffusion tensor imaging (DTI). Magnetoencephalography (MEG, a recording of magnetic fields related to brain activity) can be used to characterize stimulation site dependent functional networks that can be associated with the occurrence of (side) effects. The combination of contact point-specific functional and structural brain network characteristics can help to identify stimulation sites prone to induce side effects. This could improve clinical outcome by aiding DBS electrode placement and contact point selection.

Study objective

a) Identification of stimulation site-specific functional and structural brain network characteristics in patients with PD and STN-DBS.
b) Relating subject-specific stimulation sites and functional network changes to measures of cognitive and psychiatric side effects.

Study design

This explorative study is an observational, cross-sectional study using MEG to characterize stimulation site-specific functional brain network characteristics. The functional networks will be obtained by alternatingly stimulating individual stimulation sites. This will be combined with clinical data from the Academic Medical Center (AMC) Amsterdam, where patients have undergone STN DBS. In the context of standard clinical care, pre- and post-DBS neuroimaging and evaluation of cognitive side effects will be conducted. Pre-DBS assessment of psychiatric symptoms takes place in the context of standard clinical care as well, whereas post-DBS information on psychiatric side effects will be obtained using questionnaires in anticipation of- and during the study visit for MEG recordings at VUmc.

Study burden and risks

MEG recordings are non-invasive, pain free and have negligible risks. Based on literature and our own experience in a pilot study, MEG recordings during DBS are a safe procedure. Participants will make one extra trip to the VUmc for the study visit. Changing DBS settings within the limits stated in the individual DBS passport of the participants is a risk-free procedure. As participants are in supine position on a comfortable bed during MEG recordings, we do not expect them to experience unacceptable motor symptoms. Although participants do not directly benefit from this exploratory study, results could lead to a better understanding of the underlying pathophysiology of DBS-related cognitive and psychiatric side effects in PD. The potential societal benefit is considerable, since this knowledge may lead to optimization of electrode placement and contact point selection in STN-DBS. Hence, this can considerably improve the

clinical outcome of this frequently used treatment.

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

-Having undergone STN-DBS placement for PD six months or longer before MEG registrations;
-Age * 18 years;
-Written informed consent for the study;
-Monopolar stimulation (this restriction was chosen in order to improve inter-individual comparability);
-Pre-operative DTI data available and of sufficient quality. The patient*s nose should be included in at least one pre-operative MRI to allow optimal co-registration with the MEG data;
-Post-operative NPO is available and was performed in the same DBS settings as during the MEG recordings.

Exclusion criteria

-Hoehn and Yahr stage (41) higher than 3, as determined in the DBS ON- (but medication OFF-)state during the visit to the outpatient clinic to establish the optimal DBS-settings, approximately ten days after surgery;
-Anatomical deformities that prevent the subject from undergoing an MEG registration in supine position (i.e. thoracic kyphosis);
-Continuous intrajejunal levodopa or subcutaneous apomorphine infusion in addition to DBS;
-Subjects who cannot read, speak or understand Dutch;
-Dementia according to the Movement Disorder Society criteria for PD with dementia (43). Mental competence is necessary in order to give informed consent for participation in the study and to follow instructions during MEG recordings. Minor cognitive decline post-DBS is not an exclusion criterion, since this is one of the outcome parameters of this study;
-Conditions that will cause excessive MEG artefacts (other than the DBS electrode and stimulator). A list of items that cause MEG signal perturbation is given in the participants information folder, on a poster at the entrance of the MEG system, and in this document (section 11);
-A history of stroke or major vascular lesions on brain MRI;
-A history of major traumatic brain injury;
-Peri-operative intracerebral complications (e.g. bleeding or infection) related to STN-DBS placement inflicting permanent changes;

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-09-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2018
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	NL62093.029.17