Elucidating the therapeutic mechanism of DBS by simultaneously stimulating and recording from the target brain region.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Observational non invasive

Summary

ID

NL-OMON50295

Source
ToetsingOnline

Brief title
Elucidating the mechanism of DBS

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
Obsessive-compulsive disorder; anxiety disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Hersenstichting Nederland;Medtronic (medical devices),Medtronic B.V.

Intervention

Keyword: DBS, OCD, scalp/intracranial EEG

Outcome measures

Primary outcome

1. DBS-related changes in amplitude, phase stability and frontostriatal connectivity of theta (~4 Hz), alpha (~10 Hz) and gamma (>40 Hz) EEG oscillations at electrode contacts and scalp

2. Amplitude, phase stability of theta, alpha and gamma EEG oscillations measured at the electrodes that prelude and accompany the emergence of a compulsive episode during real-life situations

3. DBS-related clinical changes on clinician-rated questionnaires:

- Yale Brown of Obsessive-Compulsive Scale (Goodman et al., 1989)

- Hamilton Scale for Depression (Hamilton, 1960)

- Hamilton Anxiety Scale (Hamilton, 1959)

- Symptom provocation during IAPS picture task (Bradley and Lang, 2007)

- Shortened 5-item obsessive-compulsive scale (VAS - visual analogue scale)

Secondary outcome

1. Characteristics of corticostriatal EEG oscillations that are associated with various cognitive and behavioral paradigms and with sleep.

2. Written dairy of OCD symptom experiences and daily activities (for 1 day)

3. Demographic information not obtainable from clinical file (e.g. handedness)

Study description

Background summary

Deep Brain Stimulation (DBS) of the ventral part of the anterior internal capsule (vALIC) is a promising option for patients with otherwise treatment-refractory obsessive-compulsive Disorder (OCD) (Denys et al 2010). However, the high variability among patients and clinical response patterns has made it difficult to gain systematic insight into the optimal neurosurgical target and stimulation settings. At present, stimulation parameters are based on clinical feedback and previous experience with other patients, which is time-consuming, inefficient and subjective. A quantitatively driven approach to tailor stimulation parameters is urgently needed for more effective and efficient clinical treatment. Preliminary work by our group indicates that neural changes in the frontostriatal network are essential for efficacy of DBS. Recently we acquired prototype bi-directional brain radio devices that not only stimulate but also record activity from the targeted brain structure. We propose to use these unique devices in select patients already implanted with or eligible for DBS electrodes, in order to develop more effective and systematic stimulation DBS parameters. Moreover, these devices will also afford us the possibility to get a greater understanding of the neural pathophysiology of OCD that can be targeted with DBS and other treatment modalities, by allowing us to monitor the brain activity of patients as they experience symptoms in daily life situations.

Study objective

Our primary objectives are to decode **signatures** of activity from the electrode that might prelude or accompany an OCD attack, by analyzing its activity in an experimental setting and in real-life situations, and to correlate symptom changes with corticostriatal response at different settings by recording local neural activity (EEG oscillatory amplitude) and network activity (EEG oscillatory phase stability and frontostriatal connectivity) at the electrodes and the scalp.

Our second objective is to investigate DBS induced changes in corticostriatal EEG oscillations that are associated with various cognitive and behavioral paradigms and with cortisol levels.

Study design

Observational cohort study in 11 OCD patients that are in need of battery replacement or are eligible for a first DBS implantation. Instead of a regular neurostimulator, these patients will receive a bi-directional brain radio device. We will use this device to record DBS-related neural changes which will

be correlated with relevant clinical changes.

Study burden and risks

The benefit for participants of this study will be indirect, as the results of this study will allow more efficient DBS for other OCD patients. Patients eligible for the study are in need of a stimulator replacement or a new DBS system. As replacement of the stimulator or new implantation of a DBS device is a surgery that will need to be performed anyhow, there is no additional surgical risk. In addition to the possibilities for recording brain activity, the experimental stimulators have exactly the same functional performance as the regular stimulators, so that there will be no loss of therapeutic effect for the patients. There are no risks associated with EEG acquisition and the burden can be considered minimal. The treatment itself is not a point of investigation in this study. We classify this study as having a low chance of possible risks and a low degree of harm, leading to a moderate risk to patients, since a DBS system is used outside of the intended use.
The main burden for the patient consists of a 15-20% shorter (1.5-2 months) shorter interval between two stimulator replacement surgeries, as the experimental stimulator has a shorter lifetime than a regular stimulator due to the recordings. Additional burden will be the periods of symptom provocation they will have to endure when the stimulators are turned off and during provocation tasks, and the time and effort they are asked to invest in the study visits and in recording their symptoms and daily activities at home, according to the study protocol.

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

Subject has provided informed consent.
Primary diagnosis of OCD with DBS-implantation performed in the AMC in the previous years.
Primary diagnosis of OCD and indicated for DBS-implantation in the AMC.
DBS-treatment responsiveness, defined as an improvement in Y-BOCS of >35% at last follow-up compared to pre-surgical baseline

Exclusion criteria

Subject is unwilling or unable to comply with all study-required follow-up evaluations.
Alcohol or substance abuse during last 6 months

Study design

Design

Study type:	Observational non invasive
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-06-2015
Enrollment:	11
Type:	Actual

Medical products/devices used

Generic name:	Activa PC + S Neurostimulator System
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	24-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2019

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	NL52782.018.15
Other	NL7486