Deep Brain Stimulation in Treatment-refractory patients with Major Depressive Disorder.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23670

Source
NTR

Brief title
DBS in TRD

Health condition

Major Depressive Disorder

Sponsors and support

Primary sponsor: Academic Medical Center (AMC) Amsterdam, NL
St Elizabeth Ziekenhuis Tilburg NL
Source(s) of monetary or material Support: Academic Medical Center (AMC) Amsterdam, NL

Intervention

Outcome measures

Primary outcome

Main study:

1. The Hamilton depression rating scale and the Montgomery Åsberg depression rating scale:

A. Improvement is defined as a drop in HDRS or MADRS of 25–49%;

B. Response is defined as ≥50% decrease from baseline in HDRS or MADRS;

C. Remission as HDRS ≤7 or MADRS ≤7.

Neuroimaging/neuropsychology study:

1. Changes in dopaminergic system;

2. Changes in activity in cortical-limbic-thalamic-striatal network;

3. Change in cognitive functioning before and after DBS.

Secondary outcome

Main study:

1. Other efficacy measures:

A. Inventory for Depressive Symptoms (IDS-SR);

B. Hamilton Anxiety Scale (HAM-A);

C. Snaith-Hamilton Pleasure Scale (SHAPS);

D. Symptom Checklist 90 (SCL-90);

E. Quality of life enjoyment and satisfaction Questionnaire and MOS SF36;

F. Sheehan Disability Scale (SDS);

G. The Clinical Global Impression (CGI).

Neuroimaging/neuropsychology study:

1. Structural differences in cortical-limbic-thalamic-striatal network.

Study description

Background summary

BACKGROUND:
Although small previous studies show efficacy of DBS in refractory MDD patients, not much is known about the efficacy or the neurobiological and neuropsychological effects and alterations of brain function during DBS in general or more specifically in MDD.

AIMS & OBJECTIVES:
We aim to investigate clinical efficacy and changes in brain function after deep brain stimulation (DBS) of the nucleus accumbens in 26 patients suffering from refractory MDD.

The main objectives of this study are (1) to assess clinical efficacy of DBS, (2) to assess the effects on D2 receptors binding using SPECT imaging, (3) to assess changes in cerebral perfusion associated with deep brain stimulation (DBS) using fMRI, and to assess changes in neuropsychological functioning over time.

MEASUREMENTS:
Apart form clinical ratings, we will perform repeated SPECT, functional MRI (fMRI) neuroimaging and neuropsychological tests over 18 months of treatment. As control groups for neuroimaging and neuropsychological measures, we will obtain fMRI in 30 healthy controls, and neuropsychological measurements in 30 healthy controls, 30 patients treated with ECT, and 30 chronically depressed patients who are receiving treatment as usual.

DESIGN:
After selection and screening, patients will be implanted bilateral electrodes in the N. Accumbens. After an optimization period of 3 months (if necessary prolonged until 6 months), a double blind cross-over on/off paradigm will be used to investigate clinical efficacy. Furthermore, patients will undergo [123I] IBZM SPECT scanning before surgery, after optimization (month 3-6) and at endpoint at month 18. Functional MRI scans will be obtained at the same timepoints. An additional fourth fMRI-scan will be made after switching the stimulation off (during 1 week after opitimization). During fMRI we will obtain a standard reward task, a face-recognition task and a resting-state scan.

During the study the design has been changed (after approval by the Medical Ethical Committee of the Academic Medical Center). The optimization period had a minimum duration of 3 months and a maximum duration of 12 months (instead of 6 months) to ensure optimal treatment. The Hamiltion Anxiety Scale (HAM-A), Snaith-Hamilton Pleasure Scale (SHAPS), Symptom Checklist 90 (SCL-90), and the additional fourth fMRI-scan 1 week after optimization after switching the stimulation off have been removed from the protocol to reduce patient burden. The protocol is closed with the last follow-up taking place on August 2, 2016.

Study objective

The primary objective of the present study is to assess efficacy of DBS in the nucleus accumbens for patients with refractory MDD. Secondary objectives are the evaluation of long term efficacy and tolerability of DBS for patients with therapy refractory MDD and its effects on neuropsychological and brain function.

For the additional neuroimaging/neuropsychology part we expect an increase in dopaminergic neurotransmission in SPECT scanning to be related to efficacy of DBS. In fMRI we expect changes in activity within the nodes of the implicated cortical-limbic-thalamic-striatal network.

Study design

All measurements are performed both before DBS and after DBS at 5 different timepoints.

Intervention

Stereotactic implantation of bilateral DBS electrodes in the nucleus accumbens in the DBS group.

After an optimization period of 3 months (if necessary prolonged until 6 months), a double blind cross-over on/off paradigm will be used to investigate clinical efficacy.

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Eligibility criteria

Inclusion criteria

1. Primary diagnosis: MDD (single episode or recurrent; 296.2 or 296.3) according to the DSM-IV criteria based on a psychiatric interview and the SCID as diagnostic instrument;

2. Illness duration > 2 years, chronic MDD;

3. HAM-D total > 18;

4. Disabling severity with substantial functional impairment according to the DSM-IV criterion C and a Global Assessment of Function (GAF) score of 45 or less;

5. The level of impairment must have been persistent for at least 2 years;

6. Age: 18-65 years old;

7. Written informed consent;

8. Able to fully understand the consequences of the procedure (IQ > 80);

9. Dutch or English speaking and able to answer the study questions;

10. Capable to make his or her own choice without coercion;

11. Treatment refractoriness defined as failure of:

A. At least 2 adequate treatments of at least two distinctly different classes of 2nd generation antidepressants (SSRI, SNRI, NaSSA) for a period of 6-8 weeks, and;

B. An adequate trial of a TCA 6-8 weeks (at therapeutic drug levels), and;

C. TCA + addition of lithium when tolerable at least 6 weeks at therapeutic drug levels (>0.6 mmol/L), and;

D. An adequate trial of a MAOI, and;

E. ≥6 sessions of ECT, for which the series of ECT was terminated either due to adverse effects or insufficient response (including at least 6 sessions of bilateral ECT).

OR:

F. Patients who are kept stable with maintenance ECT, but who relapse after discontinuation

of this maintenance ECT are also eligible, but need to fulfill the above inclusion criteria.

Exclusion criteria

1. Unstable physical condition;

2. Organic cause;

3. Parkinson’s disease, dementia, epilepsy;

4. Schizophrenia/ history of psychosis unrelated to MDD;

5. Alcohol or substance abuse (including benzodiazepines) during last 6 months;

6. Current Tic disorder;

7. Antisocial personality disorder;

8. Bipolar Disorder;

9. Pregnancy;

10. Mental retardation;

11. Participation in a SPECT study in the year prior to this study;

12. Standard MRI scan exclusion criteria (pregnancy, pacemaker and metals contraindicated for MRI except for the DBS implantation and stimulator itself);

13. The use of anticoagulants must be able to be stopped before surgery.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non-randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2010
Enrollment:	26
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	23-11-2009
Application type:	First submission

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
NTR-new	NL2001
NTR-old	NTR2118
Other	MEC AMC : 09-220
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A