Deep brain stimulation of the medial forebrain bundle for patients with treatment-resistant depression

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Establishing efficacy of MFB DBS for TRD by comparing active DBS with sham DBS. Secondary aims are establishing an adverse events profile, establishing effects on quality of life, cost-effectiveness, (neuro)psychological and neuroimaging measures.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON54601

Source
ToetsingOnline

Brief title
MFB DBS for TRD

Condition

- Mood disorders and disturbances NEC

Synonym
depression; major depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw;nr. 636310016,Boston Scientific Cooperation International,Boston Scientific;in kind: levering van 24 DBS devices

Intervention

Keyword: deep brain stimulation, efficacy, randomized controlled trial, treatment-resistant depression

Outcome measures

Primary outcome

Difference in scores between active and sham DBS on the Hamilton Depression

Rating Scale, 17 items (HAM-D-17, range 0-52 with higher scores indicating more

symptoms);

Secondary outcome

Percentage of responders after the open label phase (defined as a >=50%

reduction of the baseline HAM-D-17 score).

Change over time of HAM-D score, MADRS score, and IDS-SR score.

Adverse events.

Change of cognitive functions (measured with neuropsychological tests), quality

of life (using questionnaires), personality (using questionnaires), brain

activity (MRI scans), and physical functioning.

Acute changes before and after turning on DBS (measured with a diary).

Study description

Background summary

Multiple open-label studies have shown approximately 40% of treatment-resistant depressed patients to respond to deep brain stimulation (DBS) of the ventral striatum and surrounding capsula. Recent pilot studies show efficacy of deep brain stimulation (DBS) in patients with depression is dependent on the distance of the electrode to a specific brain bundle: the medial forebrain bundle (MFB).

Study objective

Establishing efficacy of MFB DBS for TRD by comparing active DBS with sham DBS. Secondary aims are establishing an adverse events profile, establishing effects on quality of life, cost-effectiveness, (neuro)psychological and neuroimaging measures.

Study design

24 patients are included in a longitudinal, open-label study, followed by a double blind, randomized crossover trial. All patients recieve open-label DBS for the first 6 months, during which DBS parameters are optimized. Subsequently, patiens are randomized to 1 week of active DBS, followed by 1 week of placebo DBS, or vice versa. A washout phase of 4 (+/- 1) weeks between the two phase is implemented to prevent carry-over effects. After the crossover phase, patients are followed up for one year in an open-label fashion.

24 healthy controls are tested 3 times: at baseline, after 6 and after 18 months to control for aspecific or practice effects over time.

Intervention

DBS targeted to the MFB. After the open-label phase patients are randomized to active DBS followed by sham DBS, or vice versa.

Study burden and risks

Over a period of 1.5 years, patients need to visit the hospital nine times: once for screening, and eight times for study visits. All visits take 1-4 hours, and the full protocol takes approximately 26 hours. For the treatment, the patient needs to undergo surgery, for which the patients needs to be admitted to the neurosurgery department for 3 days. For the optimization of the treamtent, the patients is admitted at the Psychiatry ward for 2-5 days, after which the patient needs to visit the outpatient clinic approximately 5-15 times. We estimate the benefits outweigh the risks of the treatment. First, patients can have a direct clinical benefit from participation. Second, risks are judged to be moderate and monitored closely by experienced teams of psychiatrists, neurosurgeons, psychologists and specialized nurses. In case of suspected risk of harm for the patient, we can admit patients to our clinic. In addition, the study in its entirety is monitored by in-house monitors, as well as a Data Safety Monitoring Board (DSMB).

Healthy controls need to visit the hospital 4 times for neuropsychological tests and MRI scans. All visits take approximately 1-4 hours, and the full protocol takes approximately 10 hours.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 5
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 5
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Primary diagnosis: Major Depressive Disorder
2) Treatment-resistance defined as inadequate response to (or intolerable side effects) of all of the following:
a. At least 2 adequately dosed treatments of at least two 2nd generation antidepressants (SSRI, SNRI, NaSSA) for a period of 6-8 weeks
b. An adequately dosed treatment with a tricyclic antidepressant (TCA) for 6-8 weeks
c. TCA + addition of lithium when tolerable at least 6 weeks at therapeutic drug levels (>0.6 mmol/L))
d. An adequately dosed treatment with a monoamine oxidase inhibitor OR >=1 session 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 patients who are kept stable with maintenance ECT, but who relapse after discontinuation of this maintenance ECT are also eligible, but need to fulfill all other inclusion criteria.

Besides the above defined treatments, we will evaluate the adequacy of all attempted antidepressant treatments, including off-label strategies such as esketamine. In case on- or off-label treatments are available to the patient, but have not been tried adequately, these options are discussed with and offered to the patient before offering deep brain stimulation.
3) HAM-D total >= 18
4) Illness duration > 2 years
5) Age: 20-75 years old

Exclusion criteria

1) Bipolar Disorder
2) Schizophrenia /history of psychosis unrelated to MDD
3) Alcohol or substance abuse (including benzodiazepines) during last 6 months, excluding nicotine use
4) Primary and severe personality disorder diagnosed independently from TRD
5) Explicit suicidal plans requiring hospitalization in a closed ward
6) Contraindications to have surgery
7) Depression as a result of acute brain damage (e.g. stroke / hemorrhage)
8) Parkinson*s disease, Tourette syndrome, dementia, epilepsy, tic disorder
9) Pregnancy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-04-2021
Enrollment:	48
Type:	Actual

Medical products/devices used

Generic name:	deep brain stimulation
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	05-06-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-05-2022
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	NL71221.018.19
Other	NL8211