The TREMBLE study: Multicentre randomized controlled trial of awake versus asleep tractography based Deep Brain Stimulation for Essential Tremor

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Primary Objective: For the primary objective, the following research question is answered: Does performing asleep thalamic DBS provide an equal reduction in tremor compared to awake thalamic DBS, measured by the Essential Tremor Rating Assessment…

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

Summary

ID

NL-OMON53748

Source
ToetsingOnline

Brief title
TREMBLE

Condition

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

Synonym
essential tremor, trembling

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Deep brain stimulation, Essential tremor, General anesthesia, Tractograhy

Outcome measures

Primary outcome

The primary outcome measure is the amount of decrease in tremor indicated by change in the Essential Tremor Rating Assessment Scale score after 6 months of thalamic DBS.

Secondary outcome

-The Amsterdam Linear Disability Score for functional health status

-Quality of Life in Essential Tremor Questionnaire

-Patient satisfaction with the treatment

-Patient evaluation of treatment burden

-Operating time

-Hospitalization time

-Change of tremor medication

-Side effects and complications

Study description

Background summary

Deep brain stimulation (DBS) of the thalamus is an effective surgical treatment for the patients with disabling essential tremor, despite optimal pharmacological treatment. Currently, the standard DBS procedure is performed

under local anesthesia (awake), which is very burdensome for patients. Due to advances in MRI tractography techniques (displaying connecting pathways between brain regions using magnetic resonance imaging) the target area for DBS can now be clearly visualized and therefore it may be possible to perform the entire procedure asleep without the need for intraoperative clinical testing. Several studies, including a recent randomized controlled DBS trial in Parkinson's disease at the Amsterdam UMC, have shown that asleep DBS is safe. This trial also showed that Parkinson*s patients experienced asleep DBS as less invasive, both psychologically and physically. Logically, asleep DBS also lowers the burden of surgery for essential tremor patients. This is expected to increase the accessibility for DBS. This would allow more people with essential tremor to be helped, as well as in an earlier stage of their disease; more patients will benefit for a longer time period from DBS. To determine whether asleep DBS for essential tremor suppresses tremor as well as awake DBS, a comparative study is warranted.

Study objective

Primary Objective: For the primary objective, the following research question is answered: Does performing asleep thalamic DBS provide an equal reduction in tremor compared to awake thalamic DBS, measured by the Essential Tremor Rating Assessment Scale after 6 months of DBS.

Secondary Objective(s): The Amsterdam Linear Disability Score for functional health status, Quality of Life in Essential Tremor Questionnaire, patient satisfaction with the treatment, patient evaluation of treatment burden, operating time, hospitalization time, change of tremor medication, side effects and complications.

Study design

This study will assess the effectiveness of asleep thalamus DBS compared to the current standard practice of awake DBS in a multicentre prospective randomized open blinded end-point (PROBE) study design. Because both patient and neurosurgeon are aware of receiving general or local anesthesia, it is not possible to blind them for treatment assignment. Patients will be instructed not to reveal the received treatment with the physician performing the 6-month assessments and neuropsychological evaluation in order to secure a blinded end-point.

Intervention

Patients are randomized for DBS under general anesthesia or DBS under local anesthesia. According to the standard DBS procedure, two brain-electrodes are connected to an implanted neurostimulator, which is placed subcutaneously in

the subclavicular area.

Study burden and risks

Awake DBS at present is very burdensome and by many patients and health care providers considered to be an overly invasive treatment for essential tremor. Through this trial, we aim to investigate whether asleep DBS in essential tremor can become the new treatment standard. This is expected to increase the accessibility for DBS. This would allow more people with essential tremor to be helped, as well as in an earlier stage of their disease than currently; more patients will benefit for a longer time period from DBS. Several studies, including a recent randomized controlled DBS trial in Parkinson's disease at the Amsterdam UMC, have shown that asleep DBS is safe and asleep DBS to have a shorter procedure length. The proposed research project involves treatment options that are standard care in daily practice. The therapies will not be combined with other research products. Both treatments have a low risk of serious complications and a higher risk of minor side effects. Regular follow up will be used. Participation in this study constitutes negligible risk according to NFU criteria for human research.

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

- Age > 18 years; - Idiopathic essential tremor - Disabling tremor despite optimal pharmacological treatment - A life expectancy of at least two years

Exclusion criteria

- Legally incompetent adults;
- Previous tremor-neurosurgery (e.g., DBS, thalamotomy);
- Contraindications for DBS surgery, such as a physical disorder making surgery hazardous;
- Psychosis;
- Current depression;
- Unable to provide written informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-02-2024

Enrollment:	110
Type:	Actual

Ethics review

Approved WMO Date:	29-06-2023
Application type:	First submission
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	NL80368.018.23