Deep brain stimulation for refractory tinnitus

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The goal is to assess the effect of MGB-DBS on tinnitus severity. Secondary objectives are:- To assess side effects of MGB-DBS on hearing and neuropsychological functioning.- To explore neurophysiological hallmarks.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Aural disorders NEC
Study type	Interventional

Summary

ID

NL-OMON52782

Source
ToetsingOnline

Brief title
DBS for tinnitus

Condition

- Aural disorders NEC

Synonym
ringing of the ears, Tinnitus

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Deep Brain Stimulation, Tinnisus

Outcome measures

Primary outcome

The main endpoint is tinnitus severity, identified by means of a questionnaire, the Tinnitus Function Index (TFI), which is validated in Dutch. The TFI will be measured on a regular basis depending on the stage the study is in.

Secondary outcome

Secondary endpoints:

- Tinnitus loudness and burden, both identified by means of Visual Analogue Scales (VAS). The VAS will be measured regularly.

- Neuropsychological outcome: cognitive functioning (test battery), quality of life (36-Item Short Form Health Survey; SF-36), depression and anxiety (Beck Depression Inventory II; BDI-II, Beck Anxiety Inventory; BAI)

- Audiological evaluation: pure-tone and speech audiometry, auditory brainstem responses (ABR).

- Electrophysiological measurements: EEG, local field potentials.

Study description

Background summary

Tinnitus is the perception of a sound in the absence of an audible source. Currently up to 15% of the general population suffers chronically from tinnitus. The most severe degree of tinnitus is experienced by 2.4% of the population and is associated with insomnia, depression, anxiety and even suicide. Up to date there is no effective standard therapy. Current therapies mostly focus on treating the distress caused by tinnitus instead of reducing

the actual phantom sound. Nevertheless, many patients do not benefit from the current approaches and become severe and chronic tinnitus sufferers. In these patients neuromodulation-based treatments can be a promising option.
Tinnitus perception is associated with many complex changes in several different brain structures. The general accepted hypothesis is that neuronal changes occur in both auditory and non-auditory brain structures, most often as a compensating mechanism on reduced input from the auditory nerve caused by cochlear hair cell damage. These central neuronal changes include an increase in spontaneous firing rate, synchronized activity, bursting activity and tonotopic reorganization.
In high-frequency deep brain stimulation (DBS) a reversible lesion-like effect is mimicked. From findings in Parkinson*s disease patients who also had tinnitus and were treated with DBS, we know that stimulation can alter or even completely diminish perception of tinnitus. It can be expected that modulation of specific structures within the complex tinnitus pathways can disrupt pathological neuronal activity and thereby alter tinnitus perception or distress caused by this phantom sensation. We found in animal studies that DBS in the central auditory pathway can indeed significantly decrease tinnitus-like behavior. In a questionnaire study we found that around one-fifth of the patients would be reasonably willing to accept invasive treatments and one-fifth would be fully willing to undergo invasive treatment like DBS.
Based on preclinical studies and human case studies, we expect that DBS of the central auditory pathway will inhibit tinnitus perception and distress caused by this phantom sensation. Based on studies performed within Maastricht University Medical Center (MUMC), we selected the medial geniculate body of the thalamus (MGB) as the most potential target to treat tinnitus with DBS.

Study objective

The goal is to assess the effect of MGB-DBS on tinnitus severity.
Secondary objectives are:
- To assess side effects of MGB-DBS on hearing and neuropsychological functioning.
- To explore neurophysiological hallmarks.

Study design

Clinical intervention study (double blind, randomized cross-over design). Two different stimulation paradigms will be investigated: ON and OFF stimulation.

Intervention

Subjects will receive bilateral DBS electrodes, radiologically and electrophysiologically guided in the MGB of the thalamus, following a standard surgical procedure.

Study burden and risks

Implantation of DBS electrodes is a routine surgical procedure at Maastricht University Medical Center (MUMC). Complications can be defined as follows:

1. The complications that can arise from the operation include small bleeding in the brain that does not cause any symptoms (chance between 1-5%), brain haemorrhages or cerebral infarctions, which may cause unilateral paralysis (chance less than 1%) or death (less chance than 0.4%) temporary headache after the operation, and seizures in 0-5% (which have no lasting consequences). As with any operation, (wound) infections can occur. Very often (approximately in 1%) the electrodes have to be removed. Also, defects can occur on the device (in 10-75%) such as a battery that has run out or a cable that is broken. This can usually be solved easily, but in a number of cases a reoperation is required to replace the defective part.

2. Side effects caused by deep brain stimulation: when electrical stimulation is given this has an effect on the brain structure in which the electrode lies, and to a lesser extent on structures surrounding it. The risks of the electrical stimulation of the MGB are expected to be small, but could mean auditory deprivation or auditory sensation. These side effects are expected to be reversible by switching off the stimulation. The stimulation parameters will be optimized during the first 6 weeks after surgery during the weekly visits. Stimulation can be turned off. In the worst case, the entire electrode can be removed without any residual damage.

3. The risk is that treatment (DBS) has little or no effect on the condition (tinnitus)

The benefit of this treatment can be a reduction in the loudness of the tinnitus sound and tinnitus with an improvement in quality of life as a result.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria, all by consideration of the multidisciplinary expert group:, • Medically refractory tinnitus. Patient does not respond to available tinnitus treatment and is thoroughly evaluated by the multidisciplinary tinnitus team in MUMC. Available tinnitus treatments are hearing aids (except if hearing is normal) and evidence-based cognitive treatment in Hoensbroek (Cima et al., 2012) or a similar version of this treatment in the MUMC
• Minimum age 18 years, maximum age 69 years.
• Experiencing tinnitus which is:
o Not pulsatile
oUnilateral or bilateral
o Severe tinnitus (based on the TQ score >= 47)
o Chronic and stable (present > 2 years and stable > 1 year).
• Bilateral hearing of high tone Fletcher Index < 60 dB
• Willingness to participate in this study (informed consent)

Exclusion criteria

• Anatomic cause of tinnitus (e.g. vestibular schwannoma, tumour, middle-ear pathology)
• DSM-V psychiatric disorders, other than depression or anxiety disorder (such as bipolar disorder, dementia, addiction, personality disorders); diagnosed by a psychiatrist
• Depression or anxiety disorder which was already present before tinnitus

• Cognitive impairment (assessed with standard *cognitive functioning battery test* questionnaires) or coping problems (CISS-21)
• Active ear diseases that needs further attention according to research team
• Pregnancy or breast-feeding
• Active suicide thoughts or attempts
• Underlying malignancies, whenever life expectancy is lower than 2 years
• Other exclusion criteria are the same as for the standard DBS operation in clinical care: significant cerebral atrophy, multiple white matter lesions or focal brain anomalies.
• Contra-indication for Magnetic Resonance Imaging (claustrophobia or implanted metal objects such as cardiac pacemakers, intracardiac lines, implanted medication pumps, implanted electrodes in the brain, other intracranial metal objects with the exception of dental fillings).
• Also general contra-indications for surgery are considered as exclusion criteria, e.g. coagulopathies, The specialist team can decide on clinical grounds that a patient does or does not qualify for MGB-DBS treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-01-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Generic name:	Deep Brain Stimulation
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	06-03-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL67027.068.18