REC2Stim as a treatment for refractory epilepsy in the sensorimotor cortex

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Seizures (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON56134

Source
ToetsingOnline

Brief title
REC2Stim

Condition

- Seizures (incl subtypes)

Synonym
epilepsy, seizures

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: het Epilepsiefonds,Medtronic B.V.

Intervention

Keyword: Central lobe, Cortical stimulation, Eloquent cortex, Epilepsy

Outcome measures

Primary outcome

Mean and maximum duration of the seizure-free interval, motor performance, and quality of life at the end of the study compared to these parameters prior to implantation.

Secondary outcome

Spectral content in a time window prior and post stimulation, number of interictal epileptiform discharges in a time window prior and post stimulation

Study description

Background summary

People with central lobe epilepsy (CLE), with seizures arising from the precentral and postcentral gyrus, typically show a high rate of convulsive seizures that do not respond to anti-epileptic drugs, with large impact on quality of life. They often seek surgical relief, but since the area contains the body*s indispensable sensorimotor representation, CLE surgery will lead to permanent functional deficits. Surgical modifications such as multiple subpial transections have rendered only 16% of the patients seizure free. Cortical stimulation case studies in CLE have shown seizure frequency reduction of more than 90%, but in our experience, stimuli in the central lobe can hardly be applied without interfering with motor function. This means that patients with CLE end up in a quandary without therapeutic solution.

Study objective

We propose cortical electrical stimulation therapy of a conceptually novel type. We systematically determine individual settings, stimulation site and seizure detection algorithm in a predictive model. In REC2Stim (Rational Extra-eloquent Closed-loop Cortical Stimulation), at the start of a seizure, a train of electric pulses is delivered to a nearby extra-eloquent area connected with the epileptogenic area within the sensorimotor cortex. Success will

constitute a therapeutic modality for pharmacoresistant patients with an epileptic focus in eloquent area.

Study design

This is a prospective study.

Intervention

Clinical intracranial EEG monitoring (normally 7-10 days) will be prolonged for two days, for systematic testing of different stimulation settings and their effect on interictal epileptiform EEG activity (as a surrogate marker for ictal epileptiform activity), from which site and final parameters for chronic stimulation will be determined. Upon removal of the clinically implanted electrodes, a neurostimulator with sensing capabilities, Activa PC+S, will be implanted and attached to two 4-lead intracranial electrode strips covering the predefined stimulation site and the eloquent epileptogenic area.
During a data collection phase, stimulation-free data will then be collected to train the seizure detection algorithm up to at least 50% sensitivity. When not enough seizure data is collected, this phase will be extended. The next phase is the REC2Stim phase, in which cortical stimulation is applied when seizure activity is detected. When cortical closed-loop stimulation results in seizure reduction in two consecutive months, a period of sham stimulation will follow. The duration of which is dependent on the patient*s individual seizure frequency. The REC2Stim phase can be extended if seizure frequency is not decreased with at least 50%, and the principal investigator expects that this seizure frequency can be reduced, and/or quality of life can be improved. In that situation, sham stimulation will be delayed as well. Study participation is one year. In case of delay of one or more phases, the participant is asked whether he or she wants to continue participation or wants to end participation. This question is repeated each year, unitl the patient decides to end participation, the prinicpal investigator decides to end participation in the study, or the Activa PC+S battery is depleted.

Study burden and risks

Participants have tried various anti-epileptic drugs and are not candidates for epilepsy surgery. Therefore, they have no real therapeutic options left. Our study is the only one focusing on these CLE patients. The study burden consists of 2 extra monitoring days with tests; at least 15 post-implantation visits: 6 visits in the data collection phase (8 hours per visit), in which ictal data is recorded, 9 visits in the REC2Stim phase in which intracranial EEG data is streamed for one hour, and seizure detection algorithm and stimulus settings may be adapted (9 x 2 hours); questionnaires to fill out before and after implantation (2 x 45 minutes); and keeping a weekly diary to track number and severity of seizures (48 x 10 minutes). Risks include disappointment or

depression when this treatment also proves ineffective; implant site infection (2.5%); and intracranial hemorrhage (2.1%). When electrodes and/or neurostimulator need to be explanted, there is the risk of the additional surgery. These risks are estimated to be similar to other deep-brain stimulations (in use for Parkinson*s disease and epilepsy). The potential benefit may be large (seizure freedom without functional deficits).

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

- at least 16 years of age
- potential central lobe epilepsy
- on average 2 or more seizures per day or ongoing EPC
- mentally and physically capable of giving informed consent

- minimally 3 anti-epileptic drugs been admitted without effect on seizure frequency (refractory epilepsy)

Exclusion criteria

- coagulopathy, including use of anticoagulant or antiplatelet agents
- known allergy to the materials of the implant
- progressive neurological or systemic disease
- contra-indications to the presence of a chronically implanted device, such as the need for repeated MRI, or concurrent infections
- any brain lesion that would place the patient at an elevated risk for bleeding
- any progressive brain disease, e.g. Rasmussen*s encephalitis or glioma
- presence of any active implanted metallic device, such as cardiac pace-maker, vagal nerve or deep brain stimulator, cochlear implants, spinal cord stimulator or metallic parts from non-medical origin
- presence of aneurysm clips
- SOZ outside eloquent cortex

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-11-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Activa PC+S and intracranial electrode strips
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	10-07-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-08-2023
Application type:	Amendment
Review commission:	METC NedMec

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
ClinicalTrials.gov	NCT04158531
CCMO	NL66795.041.18