Predicting efficacy of neuromodulation in epilepsy

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

Summary

ID

NL-OMON55238

Source
ToetsingOnline

Brief title
PREDYCT

Condition

- Seizures (incl subtypes)

Synonym
Epilepsy, medically refractory epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Spectrum Twente
Source(s) of monetary or material Support: PIHC-Voucher en nationaal epilepsie fonds (NEF)

Intervention

Keyword: Epilepsy, Neuromodulation, Ultra long-term EEG, Vagus Nerve Stimulation (VNS)

Outcome measures

Primary outcome

The primary goal of the pilot study was to test the feasibility of the subcutaneous EEG electrode. The pilot study will be interpreted as successful, when in at least 4 out of 5 patients the EEG can successfully be recorded with the subcutaneous EEG electrode during the first 4 months. Hereby, the following criteria are defined to determine whether the measurement was successful in an individual patient:

- The EEG electrode is still correctly placed after four months (two months after VNS surgery).
- Experienced pain of wearing the subcutaneous EEG electrode at a Visual Analogue Scale (VAS) lower or equal to 4 (scored at two weeks after insertion of the electrode).
- Percentage of time that the EEG recording was successfully retrieved of at least 30% (during the first four months after insertion of the electrode).
- The quality of the EEG signal is comparable to the quality of the pre-operative 64-channel EEG. This will be assessed and qualitatively described by a clinical neurophysiologist.

For results of the pilot study (phase 1) we refer to paragraph 8.2.2. of the study protocol.

Currently we are expanding the cohort to evaluate the predictive value of the pre-operative ultra long-term EEG recordings measured with the subcutaneous electrode, the pre-operative resting state 64-channel EEG and pre-operative MRI. The primary outcome measure for this prediction model is the response rate (i.e. change in seizure frequency) to VNS assessed with the subcutaneous EEG electrode.

Secondary outcome

Secondary study parameters of the feasibility study are:

- The patient satisfaction and experienced pain of placing, wearing and removal of the subcutaneous EEG electrode at three timepoints (directly after placing the electrode, at two weeks after implantation and after removal of the electrode).

Secondary study parameters of the extended study are:

- The correspondence between seizures reported by the patients (using diaries) and the seizures recorded by the subcutaneous electrode.
- Differences in network characteristics derived from 64-channel EEG, and MRI before and after VNS.
- The effect of VNS on psychological well-being including quality of life, anxiety and depression.
- The effect of VNS on sleep quality (total sleep duration, time to first REM, total time in deep sleep measured with the subcutaneous EEG recording).
- The effect of VNS measured on the Clinical Global Impression Improvement (CGI-I) questionaire.

- Smartphone usage before and after seizures is measured using the TapCounter app (including tapping speed, the number of apps used per hour and telephone use per hour) (optional).

Study description

Background summary

In patients with medically refractory epilepsy who are not eligible for surgical treatment, neuromodulation including vagus nerve stimulation (VNS) remains as a last resort. However, a good response (> 50% seizure reduction) is achieved in only approximately 50% of patients. At present, we cannot predict who will benefit from VNS. Ultra long-term EEG measurements have recently become feasible by using minimally invasive subcutaneous electrodes. We hypothesize that the combination of this technique with network analysis of resting state fMRI and 64-channel EEG can provide insight in the brain circuits involved in the disturbed brain dynamics and can result a significant improvement in response prediction of individual patients who are candidates for VNS.
Currently there is no experience with the subcutaneous EEG electrodes in epilepsy patients undergoing VNS therapy. Therefore, we will start with a pilot to evaluate the feasibility.

Study objective

We started to evaluated the feasibility of subcutaneous EEG electrodes in epilepsy patients undergoing VNS therapy in a pilot study. This part is currently finished.

Currenrly, we are extending the cohort and aim to identify biomarkers to predict success rate for VNS using pre-operative features from ultra long-term EEG recordings, resting-state 64-channel EEG, and MRI.

Study design

We propose a prospective observational cohort study.

Study burden and risks

Two months prior to implantation of the stimulator, patients will be implanted with a subcutaneous EEG electrode.This electrode is inserted under the skin above the ear under local anesthesia. This procedure takes approximately 30

minutes. The subcutaneous electrode will be explanted 13 months after VNS implantation. Brain activity will be recorded continously from 2 months pre-operatively to 13 months post-operatively). During this period, test subjects must wear the corresponding device and change this device once a day to charge. The risks of placing, wearing and explanting the electrode are minimal.

We will further record baseline (2 months pre-operative, before insertion of the subcutaneous EEG electrode) and postoperative (13 months postoperative, after explantation of the subcutaneous EEG electrode) 64-channel EEG and MRI (anatomical, DWI and fMRI). In addition, patients will be asked to keep diaries of their perceived seizures during the study period. We will also ask all patients three times to fill in a short questionnaire to evaluate patients* satisfaction with the subcutaneous electrode and the effect of their VNS and twice to fill in four questionnaires about psychological well-being.

If the location of the epileptic focus is unknown prior to the implantation of the subcutaneous electrode, an ambulatory EEG recording of 24 hours will be made to better determine on which side the subcutaneous electrode should be placed. Optionally, an app will be installed on the subjects' smartphone which will record their smartphone use.

If we can find biomarkers from ultra long-term EEG and/or networks from 64-channel EEG or MRI to predict the effect of VNS in epilepsy patients, this will lead to new clinical guidelines for personalized treatment of pharmacoresistant epilepsy patients. The number of patients who undergo an invasive operation to implant a VNS stimulator without any benefit can be reduced. Therefore, the risk and burden for the participating patients are in proportion with the potential value of the study.

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

- Adult (>=18 year) patients with medically refractory epilepsy, who are candidates for VNS implantation.
- Known with focal epilepsy with a (fronto)temporal seizure*onset zone (as corroborated by EEG or magnetic resonance imaging [MRI]) or a generalized epilepsy.
- A self*reported seizure frequency of at least one seizure per month.

Exclusion criteria

- Prior brain surgery
- Cognitive impairments that causes the patient to be unable to understand the research purpose and give informed consent.
- Exclusion criteria (for safety issues) to undergo an MRI scan
- Planned or expected MRI scan during the period where the subcutaneous electrode is implanted

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-11-2020
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Subcutaneous EEG electrode
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	05-06-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-02-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL73089.100.20