From computational models of epilepsy to clinical protocols

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

Summary

ID

NL-OMON42360

Source
ToetsingOnline

Brief title
Epilepsy Translational Model

Condition

- Seizures (incl subtypes)

Synonym
epilepsy, seizures

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW-translationeel 40-41200-98-9238

Intervention

Keyword: epilepsy, epilepsy surgery, neural mass, single pulse stimulation

Outcome measures

Primary outcome

The development of a rapid SPES protocol that produces the same information as

the classic SPES protocol.

Secondary outcome

NA

Study description

Background summary

Epilepsy is a common neurological disease with a worldwide prevalence of 0.5-0.8%. About 25% of patients with seizures do not respond to drug treatment, and the majority of these patients suffer from focal epilepsy. These patients can successfully be treated with brain surgery if the region in the brain responsible for the seizures can be identified. The epileptogenic zone is delineated by using non-invasive measurements (MRI, EEG, MEG, PET). In 8-10% of the patients, invasive measurements with seizure registration are required after placement of electrodes directly on the cortical surface. The patient is monitored for 1-2 weeks with video-EEG, waiting for spontaneous seizures to occur and when the region of seizure onset is identified, this leads to a strategy for surgical resection. At the same time, critical functional cortical areas are localized by electrocortical stimulation mapping (ESM).

Intracranial EEG monitoring is stressful and prolonged, which poses risks of infection and bleeding complications, and makes these recordings extremely time-consuming, costly and scarcely available.
Procedures that shorten monitoring can be of great value, when these are independed of the occurrence of seizures. Such methods, provided that they are efficient and easy to use, could provide opportunities in avoiding chronic registrations by intra-operative usage.

Single Pulse Electrocortical Stimulation (SPES) is such an alternative. Short electrical stimuli are given at two neighbour electrodes on the cortex and the EEG response in all the other electrodes is analyzed. These responses can be

classified by their timing and appearance as pathological (epileptiform) or normal. It has been shown that pathological responses are reproducible and are related to the seizure onset zone. Removal of the area of pathological responses predicts favorable outcome of surgery. This implies that waiting for spontaneous seizures might be unnecessary when replaced by systematically screening the cortex for SPES pathological responses.
SPES and its analysis of large areas of cortex require many hours when all electrode pairs are to be stimulated in a consecutive fashion. Therefore, intra-operative implementation, which could even render prolonged monitoring unnecessary, seems currently out of reach. Understanding of the effects of cortical stimulation, necessary for optimization of the established clinical protocol, is hampered by the limited possibilities to test all stimulus parameters and response variables in patients. A translational model is needed that allows us to investigate parameter settings, the best order of stimulation, but also the effect of anti-epileptic or anesthetic drugs that alter excitability. Traditional animal models for epilepsy are mostly based on rodents and focus on hippocampal (archicortical) or generalized epilepsy, which is hardly representative of human focal neocortical epilepsy. We feel that this gap should be filled by computational models based on anatomical and physiological knowledge.

Study objective

Our goal is to build a faster SPES algorithm for execution and analysis which produces the same information as the current, classic SPES protocol. This faster protocol is obtained by predicting optimal stimulus parameters and settings in a computer model, based on neural mass models that represent the individual electrode space, and is self-adapting.

Study design

This is an observational study in 20 patients. Each patient will undergo the two routine classic SPES sessions during chronic EEG monitoring. In the first 10-15 patients, the classic SPES will be used to build a computer algorithm. In this algorithm, several settings for SPES will be tested. The settings with the highest sensitivity, specificity and speed will be tested in these patients in a third, extra SPES session for which we ask permission. The next 5-10 patients are part of the validation set. In these patients, the computer will build a SPES protocol itself with the algorithm, without using information from the classic SPES recordings.

Study burden and risks

The extra SPES session will be performed while the patient has no obligations. The patient does not notice anything during SPES and does not require any

instruction. This means that there is no burden and the risks are negligable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

all patients having grid recordings in the UMCU

Exclusion criteria

Not capable of speaking the Dutch language sufficiently to understand the study information

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-08-2016
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	22-07-2015
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	06-04-2016
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
CCMO	NL53390.041.15