# Non-invasive detection of potential epileptogenic cortical brain lesions

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1. Increase detection and localization of epileptogenic lesions using non-invasive TMS stimulation of suspect region's2. Decrease invasiveness and/or improve the accuracy of the presurgical evaluation by comprehensive noninvasive testing of...

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

## Summary

### ID

NL-OMON48843

**Source**
ToetsingOnline

**Brief title**
TMS insult induction / TMS II

### Condition

- Seizures (incl subtypes)

**Synonym**
convulsions, epilepsy

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Stichting Epilepsie Instellingen Nederland
**Source(s) of monetary or material Support:** Nederlands Epilepsie Fonds (NEF)

## Intervention

**Keyword:** Epilepsy, Epileptogenic Zone, Transcranial Magnetic Stimulation

## Outcome measures

### Primary outcome

Positive predictive value of the TMS evoked seizures for successfully

localizing the epileptogenic zone.

### Secondary outcome

Congruency of the TMS evoked epileptiform abnormalities with the epileptogenic

zone as determined in positive surgical outcome cases:

- Epileptiform afterdischarges

- TMS-EEG excitability parameters

Other parameters:

- Type, depth and extension of lesion

- Pathological assessment of lesion

- Type of epilepsy, clinical semiology of seizures

- Result of the pre-surgical evaluation

- Post-surgical outcome

# Study description

### Background summary

Epilepsy surgery is considered when patients are not responding to anti-epileptic drug treatment. The presurgical evaluation for epilepsy surgery is designed to locate the epileptogenic zone (the location of the epileptic abnormality) and to determine if normal brain function will be affected

postoperatively.

If the epileptic focus is not adequately identified with noninvasive investigations, long-term video-EEG monitoring with the use of intracranial EEG (iEEG) may be required. iEEG requires neurosurgical placement of a grid of electrodes in the surface of the brain. iEEG monitoring is physically and psychologically demanding for the patient and his/her family.This procedure carries the risk of severe complications, such as intracranial or intracerebral haemorrhage or infection. Furthermore, placement of the electrodes can be inaccurate and limited in scope resulting in a reduced chance to acquire the required information.

The benefits of a non-invasive, safe and more patient-friendly technique to determine the epileptogenic zone are manifold. It will allow for more accurate placement of iEEG electrodes, or make invasive iEEG redundant and thus reduce patient burden and risk of complications significantly.

**Study objective**

1. Increase detection and localization of epileptogenic lesions using non-invasive TMS stimulation of suspect region's

2. Decrease invasiveness and/or improve the accuracy of the presurgical evaluation by comprehensive noninvasive testing of suspected epileptogenic regions using TMS-EEG

**Study design**

Prior to admittance to the EMU for pre-surgical evaluation lasting 5 days, the medical files of patients will be reviewed by the neurologists involved in this study. Suspect regions will be determined using the MRI. Participants will undergo a total of two TMS-EEG evaluation sessions of the suspect region during their stay at the EMU: on the day of admission and one measurement in the morning of the day where AED dose was tapered to its lowest point.

Using navigated TMS, the suspect region's are activated. The response to this activation can be objectified using the electroencephalogram (EEG). This allows for non-invasive determination of the epileptogenicity of the suspect region's. After the second TMS-EEG measurement, a seizure induction protocol will be started with the goal to evoke a seizure using TMS stimulation. This measurement will be performed not at the point of lowest AED dose, but after an appropriate increase in AED dosage to prevent unwanted non-habitual seizure provocation. The protocol will be performed bed-side. The information gathered with this research may reduce the extent or increase the accuracy of the more invasive intracranial EEG measurements.

**Study burden and risks**

The TMS-EEG measurements will be performed during a patient's regular stay at the EMU for the pre-surgical evaluation. Participation consists of two 30 minute TMS sessions. The regular duration of the registration (5 days) will not be influenced by this research.The TMS stimulation itself can be experienced as a small shock with an accompanying muscle twitch. The seizure induction protocol will be given in a ramping-up manner, with continuous patient feedback to determine comfort, tolerability, and effects of the stimulation trials.

TMS is a safe technique. The first and most significant complication of TMS in literature is seizure induction in itself, especially when medication is being tapered (2.8% chance with regular TMS protocols). While this could be seen as an adverse effect, this is not the case in this pre-surgical setting where patients are admitted especially for seizure recordings and in this proposals case the aim of the study. To increase the chance on seizures it is common practice to taper medication during a patient's stay at the EMU. The EMU is a setting designed for optimal safety of patients in case of seizure events. In the EMU setting, seizures are warranted and TMS evoked seizures may give valuable clinical information that influences the decision-making process for that patient.

# 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

- Admitted to the epilepsy monitoring unit for presurgical evaluation
- Suspect superficial MRI region(s) reachable with TMS stimulation (depth < 3.5cm under the scalp)
- Aged 18 years or over
- Be able to understand the Dutch language
- Be able to understand the study (mentally capacitated)

## Exclusion criteria

- Pregnancy
- Mentally incapacitated
- Major radiological evidence of asymmetry between hemispheres
- Individuals with a cochlear implant, Pacemaker, deep brain stimulator or other implanted electronic devices
- Metal and/or metal fragments in head

# Study design

## Design

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|---|---|
| Study type: | Observational non invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 05-03-2019 |
| Enrollment: | 18 |
| Type: | Actual |

### Medical products/devices used

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| Generic name: | Transcranial Magnetic Stimulator |
| Registration: | Yes - CE outside intended use |

## Ethics review

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|---|---|
| Approved WMO<br>Date: | 21-02-2019 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

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|---|---|
| Not approved<br>Date: | 13-01-2020 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

## 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 | NL64812.058.18 |