Transcranial Magnetic Stimulation combined with electromyography and electroencephalography as a diagnostic and prognostic tool in Juvenile Myoclonus Epilepsy.

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

Summary

ID

NL-OMON41514

Source
ToetsingOnline

Brief title
TMS-EMG/EEG as clinical tool in JME

Condition

- Seizures (incl subtypes)

Synonym
Epilepsy, Seizures

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Epilepsie Instellingen Nederland
Source(s) of monetary or material Support: Christelijke Vereniging voor de Verpleging van Lijders aan Epilepsie (Nederland)

Intervention

Keyword: Cortical excitability, JME (Juvenile Myoclonus Epilepsy), TMS (Transcranial Magnetic Stimulation), TMS-EEG (Transcranial Magnetic Stimulation - electroencephalography)

Outcome measures

Primary outcome

Study parameters: change in conventional cortical excitability parameters

(motor threshold, MEP (motor evoked potential) amplitude, cortical silent

period, recovery curve, short and long intra-cortical inhibition,

intra-cortical facilitation).

Endpoints: Seizure reduction: seizure free intervals, reduction of days with

myoclonus, number of generalised tonic-clonic seizures and seizure recurrence

within a year (with aid of seizure diary).

Secondary outcome

Not applicable

Study description

Background summary

Juvenile Myoclonic Epilepsy (JME) is one of the most common forms of generalised epilepsy in children and young adults. It is characterised by myoclonus, generalised seizures and an increased vulnerability to psychiatric complaints. Although seizure freedom is achieved in most with anti-epileptic

drugs (AED) after several trials, more than 10% of patients continue to have seizures.
Increased cortical excitability has emerged as a general feature of epilepsy that is also present in JME. Cortical excitability can be measured safely and non-invasively with Transcranial Magnetic Stimulation (TMS). Previous research with TMS in people with JME and other types of epilepsy has shown that AED lowers cortical excitability. Substantial decrease after initiation of AED treatment positively correlates with seizure reduction on group level.
Currently, AED treatment initiation is based on the clinical experience of the treating physician. There are indications that early effective AED treatment is of great importance, as this influences the prognosis. Cortical excitability changes upon AED treatment may help guide rational selection of the appropriate drug and dosage for an individual person. If this is proven feasible, TMS may revolutionise epilepsy treatment, as it will offer a means to measure and predict treatment effectiveness, which is as of yet impossible.
The cause of psychiatric vulnerability in people with JME is incompletely understood. It is plausible that pathologic changes in cortical excitability, especially in the frontal cortex, underlie this characteristic of the disease. Altered cortical excitability may also alter functional connectivity in people with JME compared to healthy controls. New techniques such as TMS-EEG, offer the opportunity to investigate these changes.

Addition 17-6-2015
It has long been known that there is a bidirectional association between epilepsy and migraine. However, it is unclear what the pathophysiological basis of this association is. It is possible that this has to do with altered cortical excitability. In migraine, cortical excitability was so far not assessed using TMS-EEG.

Study objective

The aim of the proposed research is twofold:
1) To investigate whether TMS can help guide individual AED treatment to improve response.
a. in people with first seizures
b. in people who (temporarely) want to lower or stop medication
2) To investigate cortical excitability changes with TMS-EEG to shed light on the relation between cortical excitability and psychological disturbances in JME patients.

Study design

Controlled observational study

Study burden and risks

Participants with JME will come 2 to 7 times for measurements that will take between 80 and 150 minutes.

Healthy participants will be asked to come twice, with a year in between. The measurement sessions will take about 120 minutes.

Participants will be asked to fill in a screening list before participation, which consists of questions on medical and neurological history, including symptoms that could be indicative of migraine, family history of migraine and epilepsy, use of medication and lifestyle.

Prior to each measuring session participants will be asked whether they are pregnant and about their lifestyle in the hours preceding the measurements.

After each session, participants will be asked to rate their comfort/discomfort during the measurents (TMS and EMG).

A neuropsychological evaluation will be carried out twice. This will include the Strooptest, Trail making test, Word fluency test, Digit span and a impulsiveness rating scale. During the first and last session, people with epilepsy will be asked to fill in the Quolie-89, to evaluate any changes in quality of life.

All participants with epilepsy will be asked to keep a seizure diary.

All participants will be asked to abstain from drinking alcohol and using drugs in the 24 hrs preceding the sessions, not to smoke in 12 hours preceding the sessions and not to drink coffee in the 6 hours preceding the sessions.

Nerve conductionstudies can lead to local discomfort, but carries no known long-term risks.

A blooddrop test is the least invasive way to obtain blood for pharmacologic evaluations. Aside from local discomfort, no risks are associated.

Electromyography can lead to slight discomfort during the procedure. Infrequently, the needle can cause a muscle hemohrrage. This carries no long-term risks.

TMS can lead to slight discomfort during the evaluation, and some subjects report local pain on the scalp that is not severe and only lasts while the experiment lasts. In rare cases, syncope has been reported. Very rarely, a seizure may be triggered by TMS. The risk amongst people with epilepsy is 0-3.6%. Most seizures during TMS were reported in people with refractory temporal lobe epilepsy who were undergoing pre-surgical evaluation and in whom anti-epileptic drugs were tapered. This type of epilepsy is different from JME. It is more difficult to treat, and the setting is very different as a

pre-surgical evaluation is aimed at triggering seizures. We expect, based on literature, that the probability of a TMS-triggered seizure in people with JME is well below 3.6%, and nil in healthy controls.

Contacts

Public
Stichting Epilepsie Instellingen Nederland

Achterweg 5
Heemstede 2103 SW
NL
Scientific
Stichting Epilepsie Instellingen Nederland

Achterweg 5
Heemstede 2103 SW
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In generally good health
Normal cognitive functioning
Speaking Dutch, English, French, German
1st epileptic seizure OR >2 years seizure free
Diagnosis of JME confirmed

12 years or older;for migraine:
18 years or older
Migraine with aura (3/10 attacks) diagnosed according to ICHD-III criteria
One or more attacks per year
<8 attacks per month or <15 headache days per month (chronic migraine)
At least 1 attack in the year prior to the investigation.
The measurement will take place in the interictal phase, so a participant should not have had an attack 3 days prior or 3 days after the measurement.

Exclusion criteria

Use of medication with known effect on ion channel function (i.e. b-blocker)
Previous head/skull surgery (ferromagnetic material)
Diabetes mellitus (affects peripheral nervous system)
pregnancy (alters cortical excitability)
Neurological condition other than JME
Treated with anti-epileptic drugs before
Any neurological condition (including migraine)
Any psychiatric condition
1st degree family members with epilepsy;for migraine:
Use of prophylactic medication up to 4 weeks prior to measurement
Use of attack medication less than 3 days prior to the measurement
Headache on the day of measurement

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2014

Enrollment:	122
Type:	Actual

Ethics review

Approved WMO Date:	30-10-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL45032.078.13