Longitudinal Early Epilepsy Study

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1) To study cognition in children with absence epilepsy and the development of functional brain organization.2) To find prognostic factors in terms of clinical, 24h-video-EEG or/and MRI characteristics for cognitive deterioration and/or poor seizure...

Ethical review	Not available
Status	Recruiting
Health condition type	Seizures (incl subtypes)
Study type	Observational non invasive

Summary

ID

NL-OMON53316

Source
ToetsingOnline

Brief title
LEES

Condition

- Seizures (incl subtypes)

Synonym
Childhood Absence Epilepsy; Primary generalized seizures

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Absence, Children, Cognitive, Epilepsy, MRI

Outcome measures

Primary outcome

The main study parameters are:

1. Functional MRI parameters.

2. Neuropsychological parameters for neurocognitive development and behaviour, i.e. cognitive capacities, language, memory, visual (spatial) & motoric skills, attention/concentration, academic skills and behaviour.

3. Clinical characteristics (a priori defined characteristics are listed in form C1, page 25):

i. Seizure semiology

ii. Seizure control.

iii. 24h-video-EEG (including standard hyperventilation and photic stimulation test) characteristics (frequency, type and localisation of diurnal and nocturnal epileptiform EEG discharges).

4. Educational development, educational delay (discrepancy score), results of the *Leerling Volgsysteem* (i.e. CITO score).

5. General behavioural (by proxy) assessment using a set of questionnaires.

Secondary outcome

Secondary study parameters are:

1. Multimodal MRI parameters (structural, DTI and IVIM).

2. Demographic characteristics: age, gender, ethnicity, handedness, height, weight, regular teaching.

3. Other epilepsy related factors and other clinical parameters: age at onset,

seizure semiology, seizure types, time between seizure onset and start AED treatment, seizure frequency before start AED, response to first AED, response to second AED etc., duration in years of seizures corrected for years in which seizures were controlled, type and dose of medication per kg, medical history.

Study description

Background summary

The most prevalent pediatric epilepsy is absence epilepsy, which is an idiopathic generalized epilepsy in otherwise healthy children characterized by daily occurring episodes of brief loss of consciousness (staring spells). In contrast to previous beliefs of the benign nature of absences, recent research has identified deficits across a wide range of cognitive abilities and poor seizure control in about 30% of patients with absence epilepsy. So far, little information is available about the possible underlying changes of brain maturation, brain reorganization and change of structure. Understanding the cognitive development of these children and being able to identify children prone to cognitive deterioration or poor seizure control is vital.

Most of our knowledge on absence epilepsy and interrelated factors are derived from cross-sectional cohort studies and post-hoc analyses of age effects, whereas only a few studies investigate the absence epilepsy longitudinally. Firstly, it is unclear whether cognitive deficits are present at onset and how cognitive abilities develop over time in patients with absence epilepsy. Secondly, brain development may follow an altered course. Prior cohort studies from our group on frontal lobe epilepsy (FLE) in children, suggest early changes of functional brain organization, followed by changes of structural connectivity.
Thirdly, certain features may be able to predict if a patient will have poor response to treatment or will experience cognitive decline. Brain characteristics on MRI may correlate with future cognitive deterioration or poor seizure control. In addition, other clinical factors (i.e. semiology, EEG charcteristicscharacteristics, seizure control) may as well have a prognostic value.

In this study we aim to study the altered cognitive and brain development of children with childhood absence epilepsy. In addition, we aim to identify prognostic factors for cognitive deterioration and/or poor seizure control.

Study objective

1) To study cognition in children with absence epilepsy and the development of functional brain organization.
2) To find prognostic factors in terms of clinical, 24h-video-EEG or/and MRI characteristics for cognitive deterioration and/or poor seizure control in patients with absence epilepsy.

Study design

2 year prospective longitudinal, controlled, comparative, clinical, follow up.

Study burden and risks

This study adheres to the *not unless* principle based on WHO guidelines for research involving minors. There are no risks involved with EEG recordings or cognitive assessments and the total burden will be kept to a minimum. The risks of an MRI-scan are negligible because it is a magnetic field, does not involve ionizing radiation and does not require contrast agents or anaesthetics. The subjects are screened beforehand and excluded when they have claustrophobia or any other contraindications for MRI investigations. Participants will be prepared using a thorough preparation protocol, and if necessary with use of a mock scanner, before scanning takes place.

Contacts

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Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Children (2-11 years)

Inclusion criteria

1. Primarily presented with daily occurring episodes of brief loss of consciousness (absences) in an otherwise normal child in the previous 2 years.
2. An EEG showing 3 Hz (2.5-4.5 Hz) generalized rythmic spike-and-wave complexes with a discharge duration of at least 3 seconds on a present or former EEG.
3. Early absence epilepsy , defined as a confirmed diagnosis or seizures within 2 years.
4. Aged 6-12 years at inclusion
5. Permitted accompanying factors:
- A few generalized tonic-clonic seizures (assessed individually according to ILAE statements);
- Mild myoclonic eye(lid) movements
- Co-morbidities: Attention deficiency/concentration disorders, autism, dyslexia and anxiety. These do not form exclusion criteria as this is frequently seen in children with absence seizures and it might be uncertain if the co-morbidity is a manifestation of the absence epilepsy., Age-gender matched controls
- Overall healthy (do not have any of the exclusion criteria) and following a regular school without major problems, which makes a normal intelligence likely.
- Aged 6-12 years on inclusion

Exclusion criteria

* A diagnosis according to ILAE criteria of the following epilepsy syndromes: Juvenile Absence Epilepsy; Eylide myoclonia with absences; Dravet syndrome; Epilepsy with myoclonic-atonic seizures; Epilepsy with Myoclonic Absences; Lennox-Gastaut syndrome; Frontal Lobe Epilepsy or other focal epilepsy.
* A confirmed diagnosis of epilepsy/seizures for more than 2 years (58).
* Recent hospitalizations in the last months or a history which might limit participation in or completion of the study protocol.
* Behavioural characteristics which might hamper the gathering of useful MRI data.
* Intellectual disability or other diseases/causes that may underlie cognitive impairment (i.e. neurodegenerative diseases).
* History of major head trauma or head/brain surgery.
* MRI lesions on (previous) structural brain MRI- or CT-scans or symptomatic epilepsies (e.g. epilepsy related to tumours, vascular abnormalities, congenital dysgenesia).
* MRI contra-indications: claustrophobia, anxiety for an MRI scan, or presence of metallic objects (e.g. prostheses, pacemakers, metal clips on blood vessels,

metal parts in the eye). Dental braces are no exclusion criterion for absence patients.
* Regularly using drugs of abuse (asked during screening session).
* Parents or participants (aged*12 years) not willing to provide informed consent.
* Parents or participants (aged*12 years) who do not want to get informed whenever structural abnormalities are found during imaging.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-11-2016
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO

Date:	04-07-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Not available

Date:	14-12-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Not available Date:	09-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL55455.068.15