IMAGINE-study (Imaging study in epilepsy)
Is there a neuronal correlate for cognitive impairment and response to antiepileptic drugs in children with frontal lobe epilepsy?

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Objectives: In this study we investigate possible correlations between cognitive impairment as well as response to AED treatment in children with FLE and abnormalities in brain micro-structure, function and neuronal connectivity. Therefore, we apply...

Ethical review	Not approved
Status	Will not start
Health condition type	Seizures (incl subtypes)
Study type	Observational non invasive

Summary

ID

NL-OMON32514

Source
ToetsingOnline

Brief title
IMAGINE-Study (Imaging study in epilepsy)

Condition

- Seizures (incl subtypes)

Synonym
epilepsy, seizure

Research involving

Human

Sponsors and support

Primary sponsor: Epilepsie Centrum Kempenhaeghe
Source(s) of monetary or material Support: Kempenhaeghe

Intervention

Keyword: Antiepileptic drugs, Cognition, Frontal lobe epilepsy, MRI

Outcome measures

Primary outcome

Main study parameters/endpoints: These new techniques may reveal structural

abnormalities that are related to FLE or cognitive impairment or refractoriness

or all.

So endpoints are the macro-structural, micro-structural and functional

integrity, seizure history, IQ, and response to anti-epileptic drug treatment.

Secondary outcome

Patient-related and epilepsy-related factors responsible for cognitive

deterioration and refractoriness

Study description

Background summary

Rationale: Frontal lobe epilepsy (FLE), i.e. epilepsy with a frontal epileptic focus, represents a substantial proportion of all partial epilepsies. After the diagnosis FLE is made, the prognosis is still uncertain. Part of the children responds well to antiepileptic drug (AED) treatment, while others will become refractory and have frequent and disabling seizures. A second problem next to response to medication is that part of the children with FLE will suffer from cognitive impairment. The nature and severity of this impairment is highly variable. Up to now, no clear patient or epilepsy-related factors responsible for refractoriness and cognitive changes have been identified, and structural

MRI scans often reveal no abnormalities. Therefore, no currently known markers enable clinicians to recognise this patient category. Hence, a tool for the recognition of patients at risk for refractory epilepsy and cognitive impairment is needed to increase our understanding of the neuronal substrate and thus aetiology of refractoriness as well as cognitive impairment. This, in turn, may open new possibilities for pro-active therapy, including drug development.
As micro-structural and functional changes at the cellular level expectedly precede macro-structural changes, we hypothesize that new MRI techniques, diffusion tensor imaging (DTI) task related functional magnetic resonance imaging (fMRI) and resting state fMRI, are potentially more suitable to identify any neuronal changes associated with cognitive decline and/or refractoriness relative to structural MRI.

Study objective

Objectives: In this study we investigate possible correlations between cognitive impairment as well as response to AED treatment in children with FLE and abnormalities in brain micro-structure, function and neuronal connectivity. Therefore, we apply new MRI-techniques, including DTI, task related fMRI and resting state fMRI.

Study design

Study design: Cohort study

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The purposed MRI-techniques are non-invasive, the burden minimal. The risks are negligible because we do not use contrast agents or anaesthetics. The main burden is that children have to lay down quietly in the noisy MRI scan for one hour.
Though, in theory, it is possible that structural abnormalities will be found during MRI in the healthy control group. Therefore, study participation will only be allowed if people give their approval that whenever structural abnormalities are found, they and their general practitioner will be informed.
Recruitment of children is essential to the subject matter of the study, as frontal lobe epilepsy is basically a disease of childhood. The core aspects of our study, the emergence of cognitive impairment as well as refractoriness, are both observed early in the course of FLE, thus at childhood. Both conditions have a lasting impact on mental and social functioning. To elucidate their causative mechanisms demands their study during their time of emergence.
The study of possible neuronal correlates of cognitive impairment and refractoriness in FLE demands the inclusion of an age-matched control group. The imaging of the normally developing brain provides a baseline for

comparisons, both with FLE and FLE complicated by cognitive impairment or refractoriness.

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

calibration study:
• Adults aged 18 years or older
• Normal intelligence;Patients with frontal lobe epilepsy:
• Patients aged 8 to18 years
• Clinical and electroencephalographic evidence of seizures originating from the frontal lobe.

When EEG is not informative, we require the recording of more than one seizure with clinical evidence of seizures originating from the frontal lobe (Provini et al (1)).
• Non-symptomatic epilepsy;Healthy control group:
• Children aged 8 to 18 years
• Normal intelligence/following regular schools

Exclusion criteria

Exclusion criteria for the healthy adult group for the calibration study:
• Medical history of head trauma or other diseases/ causes that may underlie cognitive impairment (i.e. psychiatric diseases, unable to speak/understand the Dutch language)
• Vision less than +4.5D or - 4.5D
• Claustrophobia
• Metal implants or other contraindication for MRI
• Persons who do not want to get informed whenever structural abnormalities are found during imaging;Exclusion criteria for children with FLE:
• Multiple seizure foci involving more than one lobe of the brain documented on previous EEG studies
• Frontal lobe seizures thought to be a result of spread to the frontal lobes
• MRI lesions on previous structural brain MRI- or CT-scans or symptomatic epilepsy (e.g. tumours, vascular abnormalities, congenital dysgenesia)
• Full scale IQ<70 on the Wechsler Intelligence Scale for Children-Third Edition (Wechsler 1991).
• Progressive neurological disorders
• Other diseases/ causes that may underlie cognitive impairment (i.e. psychiatric diseases, unable to speak/understand the Dutch language)
• Cognitive deterioration directly after starting with AED, or treatment with Topiramate or Phenobarbital
• Vision less than +4.5D or - 4.5D
• Claustrophobia
• Metal implants or other contraindication for MRI
• Parents not willing to provide informed consent;Exclusion criteria for the healthy control children:
• Medical history of head trauma or other diseases/ causes that may underlie cognitive impairment (i.e. psychiatric diseases, unable to speak/understand the Dutch language)
• Vision less than +4.5D or - 4.5D
• Claustrophobia
• Metal implants or other contraindication for MRI
• Parents not willing to provide informed consent
• Parents 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:	Will not start
Enrollment:	130
Type:	Anticipated

Ethics review

Not approved

Date:	28-08-2008
Application type:	First submission
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	NL23987.068.08