Neuronal correlates of post-stroke epilepsy and the associated cognitive impairment

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Rationale and Objective: Up till now, neuronal correlates of post-stroke epilepsy and the comorbid cognitive dysfunction in patients are largely unknown. Therefore, the aim of this study is to unravel imaging biomarkers of post-stroke epilepsy. We...

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

Summary

ID

NL-OMON46873

Source
ToetsingOnline

Brief title
PoSECI-7T

Condition

- Seizures (incl subtypes)

Synonym
epilepsy after brain infarction, post-stroke epilepsy

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: cognition, epilepsy, MRI, stroke

Outcome measures

Primary outcome

- BBB permeability as determined by DCE-MRI to assess the leakiness of the cerebral vasculature by dynamically measuring the rate of contrast agent transfer from blood into the interstitial space (leakage rate; units: mL / (min 100 g tissue)). We will compare BBB permeability in PSE patients with non-PSE patients and healthy controls.

- Perfusion as determined by DSC MRI. With this method we obtain information about the CBF, the cerebral blood volume (CBV), and mean transit time (MTT). We will compare these in PSE patients with non-PSE patients and healthy controls.

- Resting state functional MRI: connectivity measures, locally as well as whole brain network analysis (using graph theoretical measures) as well as DTI connectivity measures, locally (mean diffusivity/fractional anisotropy) and anatomical features (measured by standard T2, SWI and FLAIR sequences: gliosis, iron deposits microbleeds, dilated perivascular spaces, and cortical and subcortical ischemic lesions).

Secondary outcome

- Stroke and post-stroke epilepsy outcome will be assessed using the NIHSS.

- All patients and healthy controls will undergo cognitive testing:

• To assess level of function Raven's Progressive Matrices is used.

• To assess central processing speed the CVST will be used.

• In addition the highest premorbid educational level will be determined.

Laesional deficits (such as dysphasia) will be tested at inclusion.

Study description

Background summary

Post-stroke epilepsy is a major health concern, especially in an ageing population as in the Netherlands. Stroke ranks number one in the elderly as a cause for epilepsy, accounting for up to 33% of new cases.1 80% of stroke patients have a brain infarct, whereas 20% have an intracranial hemorrhage. Although an intracranial hemorrhage carries a somewhat higher risk for epilepsy as compared to a brain infarct, brain infarcts are the dominant cause of post-stroke epilepsy in the general population, because of the higher incidence of brain infarcts. There are a number risk factors known for the development of epilepsy after an infarct, including cortical involvement, location and size. Also blood-brain barrier permeability may play a significant role. Furthermore post-stroke epilepsy patients are known to have more cognitive problems compared to stroke patients without epilepsy.

Study objective

Rationale and Objective: Up till now, neuronal correlates of post-stroke epilepsy and the comorbid cognitive dysfunction in patients are largely unknown. Therefore, the aim of this study is to unravel imaging biomarkers of post-stroke epilepsy. We will assess blood brain barrier (BBB) properties, perfusion properties and brain network formation in patients with and without post-stroke epilepsy (PSE), and healthy controls.

Hypothesis:
1. Stronger BBB leakage in the peri-infarct region is associated with post-stroke epilepsy.
2. Decreased perfusion in the peri-infarct region is seen in the post-stroke epilepsy and stroke patients.
3. More aberrant brain plasticity in the peri-infarct region is associated with post-stroke epilepsy.
4. BBB permeability and the extent of aberrant brain plasticity relate to the cognitive decline.

Study design

Study design: This is an observational cross-sectional study. We will use high field neuroimaging (7T MRI) to determine BBB permeability (using the DCE technique), perfusion (using the DSC technique) as well as brain remodeling (using DTI and rs-fMRI techniques). All patients will undergo cognitive testing using Raven*s Progressive Matrices and the CVST.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients will undergo 7T. MRI imaging including gadolinium contrast enhancement . 7T imaging is safe, an adverse reaction to the intravenous contrast agent is a rare complication, which is very well treatable.

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

- Patients suffering from stroke (and post-stroke epilepsy), including both brain infarction, cerebral hemorrhage and clinically significant hemorrhagic transformation of stroke (or a primary intracerebral hemorrhage)
- Patients suffering from post-stroke epilepsy after cortical stroke defined as one or more unprovoked epileptic seizures occurring more than one week after the stroke, according to International League Against Epilepsy criteria.
- Patients suffering from cortical stroke, with the onset of acute stroke symptoms more than 4 months prior to inclusion.
- Age > 18 years

Exclusion criteria

-onset of stroke (and epilepsy for post-stroke epilepsy patients) less than 4 months ago
-In case of the PSE group: onset of epilepsy within a week or 2 years after the onset of stroke.
-previous history of epilepsy
-history of another cerebral disorder (neurodegenerative diseases, tumours)
-inability to provide informed consent
- any contraindication for MRI: metallic foreign body, pacemaker, claustrophobia, pregnancy, tattoos, permanent make-up.
- known contrast allergy to gadolinium, insufficient kidney function (eGFR<=30).
- A history of topiramate use as an anti-epileptic drug, because of its known cognitive effects.

Study design

Design

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

Recruitment

NL
Recruitment status: Completed

Start date (anticipated):	21-09-2018
Enrollment:	72
Type:	Actual

Ethics review

Approved WMO Date:	21-06-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-08-2018
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	NL57690.068.16