The RVCL-MRI study: neuroimaging findings and cerebrovascular reactivity in preclinical and clinical disease stages of Retinal Vasculopathy with Cerebral Leukodystrophy (RVCL), in migraine patients and healthy controls.

Published: 18-03-2014
Last updated: 23-04-2024

1. To assess neuroimaging hallmarks of RVCL disease stages;2. To evaluate cerebrovascular reactivity as a biomarker of endothelial (dys)function in RVCL patients, in migraine patients and healthy controls;3. To identify shared pathophysiological...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON38389

Source
ToetsingOnline

Brief title
RVCL-MRI study

Condition

- Neurological disorders congenital
- Headaches
- Vascular disorders NEC

Synonym
Retinal Vasculopathy with Cerebral leukodystrophy & migraine

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO/ZonMW,FP-7 NIMBL; Hersenstichting

Intervention

Keyword: cerebral vascular reactivity, Migraine, MRI, RVCL

Outcome measures

Primary outcome

1. The prevalence and distribution of disease specific structural and

functional MRI abnormalities, including (i) brain (non-)lacunar infarcts, (ii)

white matter hyperintensities (deep and periventricular), (iii) widened

perivascular spaces, (iv) microbleeds, (v) cerebral *pseudotumor* mass lesions,

(vi) permeability of the blood brain barrier, (vii) white matter connectivity,

(viii) brain activity in rest.

2. Cerebrovascular reactivity after inducing hypercapnia as a measure of

endothelial function

Secondary outcome

not applicable

Study description

Background summary

Retinal Vasculopathy with Cerebral Leukodystrophy (RVCL) is caused by mutations in the TREX1 gene and manifests itself as a microangiopathy with a retinal

vasculopathy and in addition a wide range of cerebral and systemic conditions, including migraine. Because of this association with migraine, RVCL is considered a monogenic vascular model for migraine. The consecutive stages of the disease, especially the early stages, remain to be identified. Previous studies have suggested that dysfunction of endothelium is part of the pathophysiologic pathway through which mutated TREX1 protein leads to the small vessel disease manifestations of RVCL. Endothelial dysfunction is also suggested to play a role in migraine.

We want to investigate if markers of RVCL are also involved in the more common types of migraine. By unravelling how TREX1 mutations cause disease we hope to obtain insights in the pathophysiology of migraine and other (neuro)vascular disorders such as stroke and vascular dementia, and possibly to define new treatment targets for these currently incurable diseases.

Study objective

1. To assess neuroimaging hallmarks of RVCL disease stages;
2. To evaluate cerebrovascular reactivity as a biomarker of endothelial (dys)function in RVCL patients, in migraine patients and healthy controls;
3. To identify shared pathophysiological pathways of RVCL and migraine.

Study design

We will perform an observational cross-sectional study in RVCL patients. Patients with migraine and age and sex matched control subjects will be included as control groups.

Study burden and risks

MRI scans will be made after careful screening for contraindications for MRI and obtaining written informed consent. MRI scans involve a negligible risk to the participants* health. To further minimize the burden the total scan time is limited to 60 minutes. Relatives of RVCL patients who wish to remain unaware of their genetic status can participate on a research basis, and test results will not be reported in the patients* hospital records or to treating physicians that participate in the study.
The study is observational and aims to elucidate neuroimaging hallmarks of disease stages, pathophysiological mechanisms and endothelial function in RVCL an migraine. The LUMC can contribute significantly to the worldwide RVCL research, as the Dutch RVCL population is the largest of the few populations that have been identified so far. Identifying neuroimaging hallmarks for recognizing (pre)clinical disease stages and possibly for predicting outcome or future progression would be valuable for these patients. By including migraine patients and healthy subjects as control groups, we hope to define whether findings are specific to RVCL or whether there is an overlap between RVCL and

migraine. Overlapping results may help to elucidate (new) mechanisms in migraine pathophysiology. Ultimately we hope that a better understanding of the pathophysiology of RVCL as vascular migraine model will enable us to define new treatment targets for these incurable diseases. Altogether we feel the advantages of this study outweigh the minimal risks.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patient group (RVCL and migraine):
- age >=18 years
- Diagnosed with :
i) RVCL with proven TREX1 mutation; AND/OR
ii) migraine with or without aura according to the criteria of the International Headache

Society (IHS)
- ability and willingness to provide written informed consent;control subjects:
-age >=18 years
- Not genetically related to an RVCL patient OR genetic testing has ruled out TREX1 mutations
- no (history) of migraine attacks
- age and sex matched with the patients
- Ability and willingness to provide written informed consent

Exclusion criteria

All subjects:
- Subjects who do not want to be informed about unexpected findings that are considered serious, with prognostic or therapeutic consequences. This does not concern genetic test results.
- History of severe kidney dysfunction
- Previous allergic-like reaction to gadolinium-containing contrast agents
- Contraindications to MR Imaging (such as presence of metal objects in/on the body that cannot be removed);Migraine patients and control subjects:
- Presence of known (cerebro) vascular diseases such as overt manifestations of hypertensive/ atherosclerotic vascular disease, excessive anticoagulation (INR >3.0), CNS disorders, vasculitis, blood dyscrasia, diabetes mellitus, severe clinical relevant carotid artery stenosis. ;Specific exclusion criteria for participants in the cerebrovascular reactivity measurements:
- Severe asthma
- COPD
- Seizures within the previous year

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:	Recruitment stopped
Start date (anticipated):	10-10-2014
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	18-03-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL47197.058.13