Clarifying the Vascular Aspects of Dementia; natural history study

Published: 02-06-2023
Last updated: 21-09-2024

To investigate longitudinal changes in VR in patients with subjective cognitive impairment (SCI), mild cognitive impairment (MCI) and AD dementia compared with controls. To investigate whether VR predicts progression of disease severity (cognitive...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON53357

Source
ToetsingOnline

Brief title
Vascular aspects in dementia: part 2

Condition

- Other condition
- Vascular haemorrhagic disorders

Synonym
Alzheimer's disease, dementia

Health condition

hersenaandoening

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Gisela Thier Fellowship 2022

Intervention

Keyword: Cerebral amyloid angiopathy, Dementia, functional MRI, small vessel disease

Outcome measures

Primary outcome

1) 3T MRI: the amplitude of the BOLD response in percentage signal change between stimulus on and off, time-to-peak response (sec), and time-to-baseline (sec) after discontinuation of the visual stimulus, classic signs of CAA (intracranial hemorrhage, lobar microbleeds, subarachnoidal hemorrhage and superficial siderosis) and SVD markers (number of small subcortical infarcts and lacunes, volume of white matter hyperintensities (WMHs), perivascular spaces in the basal ganglia and centrum semiovale, number and location of deep microbleeds and grey matter volume). 2) Neuropsychological assessment 3) Baseline characteristics, 4) DNA: APOE * genotype.

Secondary outcome

NA

Study description

Background summary

Cerebral amyloid angiopathy (CAA), a common cerebrovascular small vessel disease (SVD),is a frequently (98%) found co-morbidity at autopsy in patients with Alzheimer*s disease (AD). Current in vivo hallmarks of CAA represent changes relatively late in the disease process and leaves CAA in AD often undetected. Recently, we found that decreased vascular reactivity (VR) measured

with blood oxygen level dependent (BOLD) MRI, after visual stimulus, is an early CAA marker. In my previous research (P19.039), I used BOLD-MRI to detect decreased VR in different stages of AD, showing that increasing stages of AD associate with decreasing VR independent of age, classic SVD markers and atrophy. Moreover our data show that VR is associated with cognitive deficits. Therefore, cross-sectional data indicate that decreased VR is an important co-morbidity already in early stages of AD with an independent effect on disease severity. In this respect, we aim to determine the decrease of VR in both controls and (early stage) AD patients to monitor AD disease progression. This is an essential step to aid in the development and application of effective treatment as it is expected that CAA can cause/worsen AD pathology.

Study objective

To investigate longitudinal changes in VR in patients with subjective cognitive impairment (SCI), mild cognitive impairment (MCI) and AD dementia compared with controls. To investigate whether VR predicts progression of disease severity (cognitive decline) over a time period of 3 years and to investigate if decreased VR at baseline predicts increasing severity of other MRI markers for AD and SVD-markers at follow-up.

Study design

an longitudinal observational case - control study.

Study burden and risks

This is a non-therapeutic group relatedness study in only capacitated subjects. In order to achieve the aim of the study AD patients are needed. Vascular reactivity has potential to determine the role of the vascular aspects in AD. The risks of this research are minimal (risk of every day life), because there are no consequences to the health of the participant. We will keep the charges at a minimum. The research will consist of a 60 minutes MRI scan, a neuropsychological assessment of 1 hour and collection of 2 ml saliva (if not already collected at baseline).

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

In order to be eligible to participate in this study, a subject must meet the inclusion all of the following criteria. For this study three different routes for inclusion exists. Inclusion criteria for each group separately are shown below.:

1. Participants who were included in our previous CASCADE study (P19.039).
* Capable of giving informed consent (see appendix)

2. Patients who attended the memory clinic of the Leiden University Medical Center/ Haaglanden MC within one year ago
• Diagnosed with (mixed) probable AD
• Diagnosed as MCI
• Diagnosed as SCI
• Age between 50-90 years
• Capable of giving informed consent (see appendix)

3. Control subjects
• Healthy adults without memory complaints
• Age aged between 50-90 years old
• Capable of giving informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study. For this study three different routes for inclusion exists. Exclusion criteria for each group separately are shown below.

1. Participants who were included in our previous CASCADE study (P19.039).
• No MRI at previous CASCADE study (P19.039)

2. Patients who attended the memory clinic of the Leiden University Medical Center/Haaglanden MC within one year ago
- Contra-indication to MRI scanning:
• Claustrophobia
• Pacemakers and defibrillators
• Nerve stimulators
• Intracranial clips
• Intraorbital or intraocular metallic fragments
• Cochlear implants
• Ferromagnetic implants
• Hydrocephaluspump
• Intra-utrine device (not all types)
• Permanent make-up
• Tattoos above the shoulders (not all)

- Specific contraindications to fMRI
• Seizure within prior year.
• Noncorrectable visual impairment.

- MMSE < 19 points (measured at moment of screening or at memory clinic with a maximum of 6 months in retrospect) (this cutoff was also used in the Leiden 85-Plus study14)
- Severe physical restrictions (completely wheelchair dependent)
- Age above 90

3. Control subjects
- Contra-indication to MRI scanning:
• Claustrophobia
• Pacemakers and defibrillators
• Nerve stimulators
• Intracranial clips
• Intraorbital or intraocular metallic fragments
• Cochlear implants
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- Severe physical restrictions (completely wheelchair dependent)
- Age above 90

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-09-2023
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	02-06-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	12-02-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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	NL83653.058.23