Blood-brain barrier leakage in dementia A dynamic contrast-enhanced MRI study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44871

Source
ToetsingOnline

Brief title
Blood-brain barrier leakage in dementia

Condition

- Other condition

Synonym
dementia

Health condition

neurodegeneratieve aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: collectebusfonds: Alzheimer Nederland

Intervention

Keyword: Blood-brain barrier, Cognition, DCE-MRI, Dementia

Outcome measures

Primary outcome

The main study measures are blood brain barrier permeability as measured by T1-weighted dynamic contrast MRI; and cognitive performance as measured by the neuropsychological assessment of the standard diagnostic procedure of the memory clinic, including global cognition (Mini Mental State examination), memory performance (Verbal Learning Test), mental speed (Letter Digit Substitution Test), and attention (Stroop task and Concept Shifting Test). Another outcome measure is the status of MRI visible cerebrovascular pathology (i.e. white matter hyperintensities, lacunar infarctions, microbleeds).

Secondary outcome

Gray matter atrophy

Study description

Background summary

Alzheimer*s disease (AD) and vascular dementia (VaD) are the most common forms of dementia. Yet, the cause of these diseases is still unknown. A potentially important initiating factor is a disrupted blood-brain barrier. This can initiate cerebral microangiopathy, which has frequently been associated with VaD. Nevertheless, also in most AD patients a substantial increase of vascular damage has been observed. The present study investigates the correlation between blood-brain-barrier breakdown and cognitive decline in AD and VaD. An

innovative dynamic contrast-enhanced MRI scan that has recently been developed and tested at our institute, will be used to measure blood-brain barrier permeability (see previous METC dossier no NL36156.068.11).

Study objective

We will investigate the relationship between this permeability measure and (i) cognitive performance and (ii) the status of MRI visible cerebrovascular pathology (i.e. white matter hyperintensities, lacunar infarctions, microbleeds) in the most common forms of dementia.

Study design

The present study is a cross-sectional observational MRI study.

Study burden and risks

Individuals with contraindications for MRI and the contrast agent Gadovist (eGFR > 30 mL/min) will be excluded. Risks associated with participants are therefore negligible. The burden for patients is restricted to two test sessions. The first test session lasts approximately 85 minutes and includes a 1-hour MRI scan (max. 45 minutes scanning plus preparations), blood pressure measurement and blood tests for haematocrit levels and ApoE genotype. The second test session includes a 1-hour MRI scan (max. 45 minutes scanning plus preparations) with contrast administration. From the standard diagnostic procedure of the memory clinic, we will obtain performance on neuropsychological tests, blood creatinine level and clinical history. Healthy control participants will follow the same procedure; except that the first test session lasts 100 minutes (including also a blood creatinine test and clinical history) and the second session lasts 120 minutes (including also neuropsychological tests).

From experience with our previous study NL36156.068.11, we know that this is doable for patients.

For the 20 participants who will be invited for the follow-up examination, we will plan two sessions: the first session lasts 15-75 minutes (depending on the need of a neuropsychological assessment), the second session consists of the MRI scan en will last 75 minutes (actual scanning takes maximally 55 minutes). Participants who agree to undergo an additional scan 2-4 hours later, will have an additional 20 minutes MRI scan.

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 (baseline):
* Informed consent before participation in the study
* Age of 55 and older
* Diagnosed with AD, VaD, mixed AD and VaD, mild cognitive impairment, vascular cognitive impairment and subjective cognitive impairment
* MMSE * 20 and patients are mentally competent (in general, individuals with an MMSE *18 are considered mentally competent) ;Healthy participants (baseline):
* Informed consent before participation in the study
* Age of 55 and older
* No Diagnosis of dementia, prodromal dementia, or mild cognitive impairment.
* MMSE * 26
* No substantial memory complaints (according to participant)

* Average age, gender and education is similar to the patient groups.;Follow-up participants with leakage:
* Informed consent before participation in the follow-up study
* MMSE * 20
* Participation in baseline study
* Blood-brain barrier leakage is apparent on baseline post-contrast FLAIR sequence ;Follow-up participants without leakage:
* Informed consent before participation in the follow-up study
* MMSE * 20
* Participation in baseline study
* Blood-brain barrier leakage is not apparent on baseline post-contrast FLAIR sequence
* Average age, gender and diagnosis is similar to the follow-up participants with leakage group.

Exclusion criteria

* Contraindications for MR scanning (e.g. brain surgery, cardiac pacemaker, metal implants, claustrophobia, large body tattoos)
* Contraindications for contrast agent Gadovist (renal failure) as determined by the estimated Glomular Filtration Rate eGFR < 30 mL/min; or known allergy to Gadovist.
* Major vascular disorders (e.g. stroke<3 months ago, unstable heart disease <3 months ago. Because AD and VaD and their preceding stages are associated with both stroke and heart disease (such as myocardial infarction) we will exclude participants when these occurred <3 months before inclusion).
* Psychiatric or neurological disorders: Major depression (< 12 months); history of schizophrenia; bipolar disorder; psychotic disorder NOS or treatment for a psychotic disorder (< 12 mnd); epilepsy; Parkinson*s disease; MS; brain surgery; brain trauma; electroshock therapy; kidney dialysis; Meniere*s disease; and brain infections.
* Structural abnormalities of the brain
* Absence of reliable informant (for patient groups)
* cognitive impairment due to alcohol abuse or other substances

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):	06-11-2014
Enrollment:	140
Type:	Actual

Ethics review

Approved WMO Date:	25-04-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-10-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-05-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-08-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-07-2017
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
Other	Bij clinicaltrials.gov: Protocol ID NL46089.068.13
CCMO	NL46089.068.13

Study results

Date completed: 26-03-2018

Actual enrolment: 101

Summary results
Trial ended prematurely