WHIte MAtter hyperintensity Shape (WHIMAS) Study

Published: 21-07-2022
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Our overall aim is to study how different pathological mechanisms in cerebral SVD influence WMH shape.Primary objectiveTo study the association of a more complex WMH shape with abnormalities in small vessel morphology.Secondary objectiveTo study the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Dementia and amnestic conditions
Study type	Observational non invasive

Summary

ID

NL-OMON54365

Source
ToetsingOnline

Brief title
WHIMAS Study

Condition

- Dementia and amnestic conditions

Synonym
dementia; cerebral small vessel disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Alzheimer Nederland grant WE.03-2019-08

Intervention

Keyword: cerebral small vessel disease, dementia, glymphatics, White matter hyperintensity shape

Outcome measures

Primary outcome

In order to postulate underlying mechanisms related to WMH shape variations we will study the association between a more complex WMH shape and structural and functional markers of cerebral SVD (such as lacunes and microbleeds).

WMH shape is assessed as follows: Convexity, solidity, concavity index, and fractal dimension are calculated for periventricular/confluent WMHs. A lower convexity and solidity, and higher concavity y index and fractal dimension indicate a more irregular shape of periventricular/confluent WMH23. For deep WMHs, fractal dimension and eccentricity are determined. A higher eccentricity and fractal dimension indicate a more complex shape of deep WMH.

Secondary outcome

We want to investigate WMH shape parameters and the association with cognition (mini-mental state exam, clinical dementia rating and cognitive domain scores). Another endpoint is to investigate if different WMH phenotypes can be identified (by machine learning models). Moreover, we want to investigate the association between SVD markers/cognition and novel glymphatics markers (such as size of perivascular spaces, CSF mobility and 4th ventricle CSF flow dynamics).

Study description

Background summary

In a society with increased life expectancy, the economic, social and personal burden of dementia increases. Dementia is often caused by a combination of neurovascular and neurodegenerative diseases. Impaired brain clearance is suggested to be closely related to dementia development, as waste products (e.g. amyloid beta) accumulate in the brain, leading to neurodegeneration. The most common mixed pathology is Alzheimer*s dementia and the neurovascular disease of cerebral small vessel disease (SVD). SVD even contributes to the clinical dementia phenotype in around 45% of patients with a diagnosis of Alzheimer*s dementia. White matter hyperintensities of presumed vascular origin (WMH) are the key brain MRI manifestation of cerebral SVD. There is evidence that the currently known and MRI-visible WMH are landmarks of an already progressed stage of the underlying pathology. The pathophysiology of WMH has been attributed to multiple underlying mechanisms, such as hypoperfusion, defective cerebrovascular reactivity and blood-brain barrier dysfunction. Furthermore, different anatomical locations and different types of WMH are related to different underlying pathological changes. Using ultra-high field 7 T MR imaging techniques WMH lesions can be detected with a higher sensitivity and resolution than on 3 T MRI. Our hypothesis is that different pathological mechanisms of cerebral SVD lead to variations in the complexity of WMH shape. Moreover, the brain clearance (*glymphatic*) system of the brain appears to be tightly connected to dementia pathology. Thus, novel markers of glymphatic activity could aid to describe and understand the pathology.

Study objective

Our overall aim is to study how different pathological mechanisms in cerebral SVD influence WMH shape.

Primary objective

To study the association of a more complex WMH shape with abnormalities in small vessel morphology.

Secondary objective

To study the association between WMH shape and cognition/other cerebral SVD markers. To study the association of novel MRI markers of glymphatics with cerebral small vessel disease markers and cognition.

WMH shape is assessed as follows: Convexity, solidity, concavity index, and fractal dimension are calculated for periventricular/confluent WMHs. A lower

convexity and solidity, and higher concavity index and fractal dimension indicate a more irregular shape of periventricular/confluent WMH. For deep WMHs, fractal dimension and eccentricity are determined. A higher eccentricity and fractal dimension indicate a more complex shape of deep WMH.

Study design

Cross-sectional study that will be conducted at the Leiden University Medical Center (LUMC).

Study burden and risks

The study group will not directly benefit from the results of the study. However, their contribution to the study will add important information about the pathophysiology of the cerebrovascular pathology that contributes to dementia. Therefore, it is not possible to study the research question in a different population group. The ultra-high field 7 T MRI system is widely used in a research setting and since its first introduction in the 1990s no serious adverse events have been reported. Important temporary side-effects are vertigo, nausea and involuntary eye motion due to forces on ion currents in the semicircular loops. As all MRI scans are performed within a maximum of 60 minutes and without any contrast agents, the participant burden is seen as a non-substantial burden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

• Admitted to the memory or the geriatric clinic of the LUMC
• From 65 years of age
• Eligible for MRI
• Native or native-level Dutch speaker

Exclusion criteria

• Claustrophobia
• Contraindications for MRI such as metal implants and pacemaker
• Use of benzodiazepines
• Initiated treatment with antidepressants less than 6 weeks prior to inclusion
• Not being able to provide written informed consent (assessed by the treating physician)
• Individuals that have been declared mentally incapacitated*
• Other severe neurological disease besides dementia related
• Cognitive impairment due to known other neurological disease
• Previous brain surgery

*A declaration of mental incapacity has wide going consequences for the subject. Discussion about participation in this study should not be used as a basis for such a decision. The treating physician assesses at the study visit if the patient is able to sign informed consent and is able to participate in the study based on his/her own free will.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-01-2023
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	7 Tesla Philips Achieva MRI Scanner
Registration:	No

Ethics review

Approved WMO

Date:	21-07-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	21-09-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	11-10-2024
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	NL78641.058.21