Amyloid pathology and vascular disease in focus: exploring interaction in two pathways towards neurodegeneration

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To study in a population-based setting, in persons free of dementia, the interplay between amyloid-* pathology and vascular pathology. We hypothesize that higher overall load and progression of vascular pathology will relate to a higher burden of...

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

Summary

ID

NL-OMON46142

Source
ToetsingOnline

Brief title
Amyloid pathology and vascular disease in neurodegeneration

Condition

- Other condition
- Structural brain disorders

Synonym
Dementia, vascular pathology

Health condition

neurodegeneratieve aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Piramal Imaging Limited

Intervention

Keyword: Amyloid pathology, Neurodegeneration, Population-based, Vasculair disease

Outcome measures

Primary outcome

How (progression of) systemic vascular pathology and vascular brain pathology

relate to amyloid-* pathology; how amyloid-* and vascular pathologies interact

in their association with cognitive function and decline over time.

Secondary outcome

N/A

Study description

Background summary

Central to the quest for the etiology of Alzheimer*s disease is insight into how the two prevailing pathways, amyloid-* pathology and vascular pathology, influence disease development in its earliest stage. These pathways could act as independent processes leading to dementia, or alternatively, they may directly influence each other, interact and cause an accelerated disease process. Evidence from the two pathways influencing each other comes from both experimental studies and patient-based studies. Yet, there is a void of studies that use an integrated approach to study both pathways simultaneously, in particular in a preclinical setting. Technical developments in imaging amyloid-* deposition non-invasively with use of radioactive PET tracers has greatly advanced the possibility to study amyloid-* pathology in vivo, directly, in presumed healthy individuals. This proposal will make use of the existing infrastructure within The Rotterdam Study, a large on-going population-based study with extensive multiple time-point data (including brain magnetic resonance imaging), enabling a detailed assessment of vascular

pathology.

Study objective

To study in a population-based setting, in persons free of dementia, the interplay between amyloid-* pathology and vascular pathology. We hypothesize that higher overall load and progression of vascular pathology will relate to a higher burden of amyloid-* pathology.

Moreover, we will examine if both pathologies interact in their effect on (decline in) cognitive functioning, by investigating if amyloid pathology leads to a greater cognitive decline in the presence of vascular pathology, or if amyloid deposition and vascular pathology are indirectly related to cognition and cognitive decline. We will in a secondary objective furthermore examine whether Apolipoprotein E4 (APOE4) affects these relations.

Study design

In a sample of 700 persons from the Rotterdam Study, brain amyloid PET imaging will be acquired. To ensure a good representation of different stages of vascular brain pathology, these 700 participants will be selected by random sampling from quartiles of the distribution of white matter lesion volume load, as quantified on previous brain MRI.

Study burden and risks

The main reason to participate in this study would be the contribution to scientific research. This study is particularly relevant as vascular factors are potentially modifiable and thus could prove preventive targets for Alzheimer*s disease, especially when shown to modify amyloid-* pathology. Risks include radiation exposure and potential adverse reactions to the injection of the radionuclide, but are deemed acceptable.

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

- persons are eligible who are non-demented;
- who had at least one previous complete brain MRI examination and assessment of vascular pathology within The Rotterdam Study;
- and who are scheduled for a regular follow-up visit which will include repeat MRI and cognitive testing.

Exclusion criteria

- Contraindications for PET/CT imaging:
· hypersensitivity to the active substance (ascorbic acid or ethanol anhydrous)
· extreme claustrophobia
· inability to lie flat
· pregnancy or breastfeeding (not likely in our population).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2018
Enrollment:	700
Type:	Anticipated

Ethics review

Approved WMO

Date:	16-07-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL65670.078.18