Production of amyloid ß in hereditary cerebral hemorrhage with amyloidosis-Dutch type

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The objective of the study is to determine whether the HCHWA-D gene mutation affects the proteolysis of AßPP with regard to the ratio of the diverse Aß species produced from AßPP.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON29777

Source
ToetsingOnline

Brief title
Aß production in HCHWA-D

Condition

- Central nervous system vascular disorders

Synonym
Aß CAA; Aß amyloid deposition in cerebral blood vessels

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting Rotary

Intervention

Keyword: amyloid ß, cell culture system, cerebral amyloid angiopathy, HCHWA-D

Outcome measures

Primary outcome

Concentrations of the diverse Aß species in the media of cultured fibroblasts

derived from skin biopsy.

Secondary outcome

not applicable

Study description

Background summary

Amyloid ß cerebral amyloid angiopathy (Aß CAA), that is, the deposition of Aß amyloid in the walls of cerebral blood vessels, is associated with cerebral hemorrhage and dementia. Aß CAA is the pathologic hallmark of the rare disease hereditary cerebral amyloid angiopathy-Dutch type (HCHWA-D). HCHWA-D is caused by a mutation in the gene encoding the Aß precursor protein (AßPP). Aß CAA can also occur as a sporadic entity and it is a frequent feature of the pathology of Alzheimer's disease. The pathogenesis of Aß CAA is unknown and the mechanisms by which CAA may lead to cerebral hemorrhage and dementia are not clear. Being a monogenic disorder HCHWA-D is an excellent model for the study of these issues. Recent studies of the brains of HCHWA-D patients and transgenic mice suggest that relative changes in the production of the diverse Aß species from AßPP could play a role in the pathogenesis of Aß CAA.

Study objective

The objective of the study is to determine whether the HCHWA-D gene mutation affects the proteolysis of AßPP with regard to the ratio of the diverse Aß species produced from AßPP.

Study design

Observational study with invasive measurements (skin biopsy).

Study burden and risks

A 4mm skin biopsy will be performed once. The procedure will take 10 minutes. The risks include scarring and a small chance of infection of the wound (1.6-3%).

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

carrier of the HCHWA-D gene mutation

Exclusion criteria

age under 18 years
dementia (MMSE under 25)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL12687.058.06