Amyloid pathology in cognitively normal elderly subjects

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This study has been transitioned to CTIS with ID 2024-518559-41-01 check the CTIS register for the current data. The main objectives are to identify markers for amyloid pathology in cognitively normal subjects, to identify risk factors for amyloid...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Structural brain disorders
Study type	Observational invasive

Summary

ID

NL-OMON55380

Source
ToetsingOnline

Brief title
PreclinAD

Condition

- Structural brain disorders

Synonym
Alzheimer's disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: GE Healthcare,IMI (Europese Unie);Stichting Dioraphte;Stichting Steun Alzheimer centrum Amsterdam (SSAA);anonieme stichting,Janssen-Cilag

Intervention

Keyword: Alzheimer's disease, Amyloid, Cognition, Preclinical

Outcome measures

Primary outcome

The primary study parameters are to identify diagnostic markers for amyloid pathology in cognitively normal subjects, to identify risk factors for amyloid pathology in cognitively normal subjects and to identify prognostic markers for cognitive decline in cognitively normal subjects with amyloid pathology.

Main outcome measure at baseline is the presence of amyloid pathology assessed by CSF analysis or PET scan.

The main outcome at follow-up is cognitive performance after 2 years.

The main outcome at second follow-up is cognitive performance after 4 years and the development and presence of amyloid pathology assessed by CSF analysis or PET scan

The main outcome at third follow-up is cognitive performance after 6 years.

The main outcome at fourth follow-up is cognitive performance after 8 years and the development and presence of amyloid pathology assessed by CSF analysis or PET scan

Secondary outcome

The secundary study parameters are to determine the concordance rate of amyloid and other AD markers between monozygotic twin, to investigate the correlation

between amyloid pathology as assessed in CSF and assessed on PET scan and

identify markers of discordance and to create a control group of healthy

elderly without amyloid pathology.

Study description

Background summary

Alzheimer*s disease (AD) is a neurodegenerative disorder characterised by progressive neuronal loss and eventually death. Abnormal aggregation of beta amyloid (Aβ) is the first event in AD and is present in 20-40% of cognitively normal elderly and can be present up to 20 years before clinical dementia. A better understanding of the pathophysiology of AD in non-demented subjects is needed in order to enable early diagnosis, prognosis and the discovery of novel treatment targets.

Study objective

This study has been transitioned to CTIS with ID 2024-518559-41-01 check the CTIS register for the current data.

The main objectives are to identify markers for amyloid pathology in cognitively normal subjects, to identify risk factors for amyloid pathology in cognitively normal subjects and to identify predictors for cognitive decline in cognitively normal subjects with amyloid pathology. Secondary objectives are to determine the concordance of amyloid and other AD markers in monozygotic twins, to investigate the overlap between amyloid pathology as assessed in CSF and assessed on PET scan and to create a substantial control group of healthy elderly without amyloid pathology.

Study design

A longitudinal observational two-site cohort study.

Study burden and risks

Neuropsychological testing might be tiresome.

Vena puncture: This is a very common procedure therefore there is a lot of knowledge and experience in the medical practice. There is a very small risk of bleeding or infection, however, if this is performed lege artis the risk is negligible. The severity of any infection or hematoma is very low.

CSF collection: This is often performed in neurology. On the screening day at the Alzheimer Center it is basically performed in any patient. An lumbar puncture can cause post-punctional headache in less than 5% of cases, this is basically self-limiting, if symptoms persist, then a blood patch can be performed. Other very rare side effects are bleeding or infection, this risk is negligible. The severity of post-puncture headache is light. The severity of an infection or hemorrhage depending on the extent of the complication.

MRI scan: The MRI scan is widely used in medical practice. Therefore, there is a lot of experience and knowledge. It is possible that the narrow space and the loud sounds generate anxiety. The severity of possible adverse effects is negligible.

MEG: The MEG is a relatively new, but it's harmless. The narrow space can be frightening.

The PET scan: The PET flutemetamol scan is performed with a relatively new tracer, which has already been extensively tested and approved. This scan produces a radiation dose of 6.1 mSv with 185 MBq, which is within the standards, and very rarely an allergic reaction to the tracer. However, this risk is negligible. The severity of an allergic reaction to the tracer can vary from mild to moderate. The severity of the radiation exposure is light.

For retinal imaging, pupil dilatation is needed. Pupil dilation at an ophthalmological examination is very common. Therefore there is a lot of knowledge and experience. It gives transient blurred vision, this will be restored after a few hours. The severity of the reduced vision is low.

Tears are sampled using paper Schirmer strips that are gently placed in the lower eyelid. This procedure is not considered uncomfortable. In some cases, insertion of the paper strip causes reflex tearing (excessive tearing similar to tearing in reaction to foreign body, smoke or onions). The procedure is considered harmless.

Regarding the extensive knowledge on the above tests, the probability of the occurrence of unknown risks is virtually zero.
For PET flutemetamolscan there would be a negligible probability of occurrence of unknown risks.

There is a small to very small risk of complications in all the separate parts of the protocol, as described above. The damage that could occur can be called light. The subjects are all healthy, mentally competent elderly for whom we think the burdening is acceptable in the context of the importance of our research. Therefore, we think there is a negligible risk.

To minimize burden, data collection will be concentrated on 2 days at baseline, 1 day at follow-up, 2 days at second follow-up,1 day at third follow-up and 2

days at fourth follow-up. The study will not have any direct benefits for participants, but it will add enormous value to studies on the understanding and diagnosis of AD.

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

- Age 60-100 years - Monozygotic twin - Telephone Interview for Cognitive Status modified (TICSm) >22 - Geriatric Depression Scale (GDS) (15 item) <11 - Consortium to Establish a Registry for Alzheimer*s Disease (CERAD) 10 word list immediate and delayed recall (> -1.5 SD of age adjusted normative data) - Clinical Dementia Rating (CDR) scale of 0 with a score on the memory subdomain of 0

Exclusion criteria

- clinical diagnosis of probable Alzheimer's disease or mild cognitive impairment
- neurological problems like Parkinson's disease, Huntington disease, severe head trauma, braintumour, stroke with physical impairment, epilepsy currently using antiepileptic drugs, braininfection
- known uncontrolled diabetes, thyroid disease, vitamin B12 deficiency
- psychiatric disorder like psychosis or schizophrenia

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-12-2014
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]Flutemetamol
Generic name:	[18F]Flutemetamol

Ethics review

Approved WMO

Date:	28-08-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-518559-41-01
EudraCT	EUCTR2014-000219-15-NL
CCMO	NL47359.029.14