Finding the biological basis of lost brain connections in Alzheimer*s Disease

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON54226

Source
ToetsingOnline

Brief title
Finding lost connections

Condition

- Neurological disorders NEC

Synonym
Alzheimer's disease, mild cognitive impairment

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: (prodromal) Alzheimer Disease, Biological mechanisms, Brain connectivity, Proteomics

Outcome measures

Primary outcome

Main predictor: baseline and longitudinal biological processes measured with

CSF proteomics.

Main endpoints: decline in brain network measures over time compared to

baseline.

Secondary outcome

Secondary endpoints:

- Decline in cognitive functioning over time compared to baseline as measured

with a neuropsychological test battery

- Progression to dementia

Study description

Background summary

The most common cause of dementia is Alzheimer*s disease (AD). AD starts with amyloid beta aggregation in the brain, 20 years before the onset of dementia. This long time period provides opportunities to prevent dementia. We have previously developed methodology to measure brain connectivity using a routine structural MRI scan. Our research showed that loss of brain connectivity is central to the clinical manifestation of AD. We propose to investigate the biological processes associated with disrupted brain connectivity in AD to find new leads for dementia prevention.

We will use a combined cerebrospinal fluid (CSF) proteomics and multimodal magnetic resonance imaging (MRI) approach to identify biological processes in the brain that are associated with loss of brain connections in early AD.

Study objective

The aim of this research is to study which biological processes precede and can predict loss of brain connectivity in a longitudinal study in 55 individuals with predementia AD, for whom a potential intervention may have maximal effect.

This research will generate new knowledge on the biological processes that underlie disrupted brain connectivity in AD, which is crucial for developing novel treatments that delay or even prevent dementia.

Study design

This study is a 3-year prospective longitudinal study

Study burden and risks

Before inclusion from the memory clinic, patients have been screened at the Alzheimer Center Amsterdam, including comprehensive neuropsychological testing, MRI imaging and collection of blood and CSF. When patients participate in this study, they will receive repeated MRI imaging and CSF withdrawal three times within approximately 2 years. If possible, visits will be planned consecutively to routine clinical follow-up which includes neuropsychological testing. The lumbar puncture is a common procedure in neurology practice. Our researchers have a lot of experience in the procedure and it has been proven to be safe. An MRI scan is a widely used imaging technique in medical practice. It can cause discomfort but the risks are negligible. There is no direct benefit for the participant. Participants will contribute valuable information to dementia research, which will be a benefit for future patients with AD. As the risks are low and the outcome of the project is very valuable for dementia research, we consider the burden to be 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

- Clinical diagnosis of mild cognitive impairment due to Alzheimer's Disease
- Abnormal CSF biomarker for aggregated amyloid
- Signed informed consent for Amsterdam Dementia Cohort (ADC) (P2016.061) and Amsterdam Dementia Biobank (P2017.315)
- Age >=50 years

Exclusion criteria

- No CSF collection or MRI-imaging at screening at memory clinic
- Clinical diagnosis of dementia or subjective cognitive decline
- Other neurological diagnosis, such as Parkinson*s disease, symptomatic stroke, mental retardation, brain tumor or infection, likely to be cause of cognitive impairment
- Major psychiatric disorder, such as psychosis, schizophrenia, depression with vital signs, severe personality disorder, abuse of alcohol or other substances, likely to be cause of cognitive impairment
- Use of (oral) anticoagulants or other contraindications for lumbar puncture
- Contraindications for MRI scan (e.g., metal implants, pacemaker)

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:	Recruiting
Start date (anticipated):	03-10-2022
Enrollment:	55
Type:	Actual

Ethics review

Approved WMO Date:	14-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2023
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
CCMO	NL77598.029.21