

# Study to identify early signs of Alzheimer's disease in healthy elderly people

<b>Submission date</b> 16/04/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 20/04/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 04/08/2022	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Alzheimer's disease is a common type of dementia. Dementia is a syndrome (a group of related symptoms) associated with an ongoing decline of brain functioning. It can affect memory, thinking skills and other mental abilities.

In the current study the researchers aimed to develop an algorithm based on less-invasive biomarkers for Alzheimer's Disease (AD) pathology, to pre-select subjects who can be expected to have, abnormal, lowered cerebrospinal fluid (CSF) Amyloid beta ( $A\beta$ ) levels consistent with the presence of AD pathology. This algorithm could be used to identify these presymptomatic AD subjects for potential trial participation.

### Who can participate?

Males and females, aged 65 and older (inclusive).

### What does the study involve?

All study participants visit the unit twice, once for a medical screening and once for the study day. During the study day participants are asked to perform multiple neurocognitive tasks and neurophysiological tasks. Also, blood is taken at three times and one CSF sample is taken.

### What are the possible benefits and risks of participating?

This is a study without an intervention (e.g. novel drug administration) which makes the risk of injuries or side effect from drug administration none. Taking blood samples can be an unpleasant procedure and can lead to bruises. The CSF sampling could be an uncomfortable procedure and may lead to side effects, for instance post-dural puncture headache or bruising. There is no benefit for the subjects who participate in the study.

### Where is the study run from?

Centre for Human Drug Research (CHDR) (Netherlands)

### When is the study starting and how long is it expected to run for?

September 2017 to November 2018

Who is funding the study?  
Investigator initiated and funded

Who is the main contact?  
Samantha Prins, sprins@chdr.nl

## Contact information

### Type(s)

Public

### Contact name

Miss Samantha Prins

### ORCID ID

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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Protocol serial number

CHDR1633

## Study information

### Scientific Title

Observational, correlational study aiming to identify healthy elderly subjects with Alzheimer pathology more efficiently

### Study objectives

Develop an algorithm based on less-invasive biomarkers for AD pathology, to be used for pre-selection of subjects who are suspected of lowered, abnormal, CSF A $\beta$  levels ("A $\beta$  positive subjects") consistent with the presence of AD pathology.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 08/09/2017, Medisch Ethische Toetsing Commissie (Medical Research Ethics Committee) of the LUMC (Secretariaat METC-LDD, postzone P5-P Postbus 9600, 2300 RC Leiden, Netherlands; +31 (0)71 5263241; metc-ldd@lumc.nl), ref: P17.148

## **Study design**

Single-centre single occasion observational correlational study

## **Primary study design**

Observational

## **Study type(s)**

Screening

## **Health condition(s) or problem(s) studied**

Healthy subjects with Alzheimer biomarkers/pathology

## **Interventions**

In total subjects are asked to visit the research unit twice. Screening to determine eligibility will take place within 21 days before the study day. This study involves a single study day, which will take place during the day and will not involve an overnight stay. Screening takes 2 hours, the study day takes 4 hours.

Subjects are randomized over time of day, morning/afternoon.

CSF and plasma: abeta1-40/1-42, total tau, NFL, YKL-40 and exploratory biomarkers.

Blood genetics: apoe e4

Neurocognitive, neurophysiological and neuropsychological assessments.

Handgrip strength

## **Intervention Type**

Other

## **Primary outcome(s)**

Performed as training to reduce learning effect during screening and once during the study day.

1. Attention measured using the Adaptive tracking test
2. Memory measured using the Visual Verbal Learning Test (VVLТ)
3. Spatial measured using working memory the Milner Maze test
4. Episodic measured using memory the Face encoding and recognition test
5. Working measured using memory the N-back test
6. Vigilance measured using the Sustained Attention to Response test (SART)
7. Motor activation and fluency measured using the Finger tapping task

Performed once during the study day only:

8. Level of cognitive impairment measured using the Clinical Dementia Rating scale (CDR)
9. Level of independence measured using the Instrumental Activities of Daily Living scale (IADL)
10. Handgrip strength of dominant hand measured using the JAMAR hydraulic hand dynamometer
11. Several biomarkers in CSF and plasma related to dementia/AD measured using:
  - 11.1. A $\beta$  concentration (1-40, 1-42 and 1-42/1-40 ratio)
  - 11.2. T-Tau and p-Tau concentrations
  - 11.3. NfL concentration.
12. Genetic disposition for developing Alzheimer's disease measured using blood sample to determine APOE  $\epsilon$  genotype

13. Three blood samples were taken during the study day to determine several biomarkers related to dementia/AD:

13.1. Synaptic loss; Neurogranin

13.2. Glial inflammation; YKL-40

13.3. Levels of p-Tau181 in extracts of neutrally-derived blood exosomes

13.4. MicroRNAs [MiR-155, MiR-107 and MiR-29]

**Key secondary outcome(s)**

None

**Completion date**

13/11/2018

## Eligibility

**Key inclusion criteria**

1. Aged 65 and older (inclusive)

2. Willing and able to perform the cognitive tests, as evidenced by performance on the training session of the cognitive tests

3. Willing and able to give written informed consent and to comply with the study procedures

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Senior

**Sex**

All

**Total final enrolment**

200

**Key exclusion criteria**

1. Legal incapacity or inability to understand or comply with the requirements of the study

2. Evidence of cognitive deterioration, as indicated by a diagnosis of a cognitive disorder (including but not limited to MCI, Alzheimer's disease, Lewy Body Dementia, Fronto-temporal Dementia)

3. History or symptoms of significant psychiatric disease in the past 3 years (including but not limited to clinical depression, schizophrenia);

4. A Mini Mental State Examination (MMSE) score of  $\leq 24$

5. A Geriatric Depression Scale – 15 (GDS) score of  $\geq 6$

6. Presence of drug abuse, or positive urine drug screen (UDS) at screening or occasion

7. Presence of severe alcohol abuse (daily alcohol consumption exceeding 2 standard drinks per day on average for females or exceeding 3 standard drinks per day on average for males (1 standard drink = 10 grams of alcohol)), or a positive breath alcohol test at screening or occasion

8. Any contradictions for a lumbar puncture as judged by the principal investigator

9. Any other reason that it is not safe or ethical to allow a subject to participate in the study in the opinion of the investigator

**Date of first enrolment**

01/09/2017

**Date of final enrolment**

02/11/2018

## **Locations**

**Countries of recruitment**

Netherlands

**Study participating centre**

**Centre for Human Drug Research (CHDR)**

Zernikedreef 8

Leiden

Netherlands

2333CL

## **Sponsor information**

**Organisation**

Centre for Human Drug Research

**ROR**

<https://ror.org/044hshx49>

## **Funder(s)**

**Funder type**

Other

**Funder Name**

Investigator initiated and funded

## **Results and Publications**

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are not expected to be made available due to participants not giving consent for this.

### IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		17/07/2021	19/07/2021	Yes	No
<a href="#">Results article</a>		03/08/2022	04/08/2022	Yes	No
<a href="#">Protocol file</a>		16/08/2017	18/05/2020	No	No