ISRCTN79036545 https://doi.org/10.1186/ISRCTN79036545

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

Submission date	Recruitment status	[_] Prospectively registered
16/04/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/04/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/08/2022	Nervous System Diseases	

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 (Aβ) 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
https://orcid.org/0000-0002-3882-7906

Contact details
Centre for Human Drug Research
Zernikedreef 8
Leiden
Netherlands
2333CL
+31 715246419
sprins@chdr.nl

Additional identifiers

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 Aβ levels (“Aβ 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

Primary study design
Observational

Study design
Single-centre single occasion observational correlational study

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 (VVLT)
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. Aβ 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 ε 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-derives 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 ≤24
5. A Geriatric Depression Scale – 15 (GDS) score of ≥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?
Results article		17/07/2021	19/07/2021	Yes	No
Results article		03/08/2022	04/08/2022	Yes	No
Protocol file		16/08/2017	18/05/2020	No	No