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

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44173

Source
ToetsingOnline

Brief title
Observational study to identify AD pathology in healthy elderly

Condition

- Other condition

Synonym
Alzheimer's disease, Dementia

Health condition

Neurodegenerative disorders

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Centre for Human Drug Reseach - Clinical Research Organization

Intervention

Keyword: Alzheimer, Biomarkers, Healthy elderly

Outcome measures

Primary outcome

NeuroCart assessments

- Adaptive tracking test;

- Visual Verbal Learning Test (VVLT);

- Milner Maze test;

- Face encoding and recognition test;

- N-back test;

- Sustained Attention to Response test (SART);

- Finger tapping.

Neurophysiological NeuroCart assessments

- 21 leads electroencephalogram (EEG);

- Smooth and saccadic eye movement.

Neuropsychological tests

- Clinical Dementia Rating scale (CDR);

- Instrumental Activities of Daily Living scale (IADL).

Handgrip strength

- JAMAR hydraulic hand dynamometer

Biochemical outcome variables

CSF biomarkers

- A* concentration (1-40, 1-42 and 1-42/1-40 ratio);

- T-Tau and p-Tau concentrations;

- NfL concentration.

Plasma biomarkers

- A* concentration (1-40, 1-42);

- T-Tau and p-Tau concentrations;

- NfL concentration.

Genetics

- APOE * genotype.

Secondary outcome

Exploratory biomarkers including but not limited to:

- Synaptic loss; Neurogranin [24],

- Glial inflammation; YKL-40 [25],

- Levels of p-Tau181 in extracts of neutrally-derives blood exosomes [26],

- MicroRNAs [MiR-155, MiR-107 and MiR-29 [27]]).

Study description

Background summary

While the definite diagnosis for AD can only be made post-mortem by investigating the presence of amyloid beta (A*) plaques and neurofibrillary tangles, recent advances in neuroimaging, cerebrospinal fluid (CSF) assays, and other fluid biomarkers now provide the ability to detect evidence of the AD pathophysiological process in vivo [3]. Furthermore, emerging data in otherwise healthy elderly individuals suggest that biomarker evidence of A* accumulation and neurofibrillary tangles are associated with functional and structural brain alterations, consistent with the patterns of abnormality seen in patients with mild cognitive impairment (MCI) and AD prior to the clinical expression of symptoms [4]. These observations are confirmed by clinical cohort studies which suggest that there may be very subtle cognitive alterations that are detectable years before meeting clinical criteria for MCI, and which predict progression to AD [5].
Based on extensive longitudinal biomarker studies [6, 7] a specific pattern of deterioration of AD specific biomarkers has been proposed, which reflects the underlying progressive neuropathology of the disease. In this model, described by Jack et al., (2013) concentrations of A* in CSF start decreasing decades before clinical symptoms appear. Changes in total and phosphorylated tau (t-Tau, p-Tau) concentrations have been shown to occur in CSF up to 15 years prior to the clinical onset of AD [8]. As the disease process progresses, cognitive functions start to decline; at first only noticeable through sophisticated neuropsychological testing, but eventually also clinically evident.

Study objective

Main objective of the study is to define an algorithm based on the plasma biomarkers: A*40, A*42, t-Tau, p-Tau, NfL and APOE * status and NeuroCart tests, age, grip strength and level of education that distinguishes between positive and negative A* CSF in healthy elderly.

Study design

Single-centre, observational, correlational study.

Study burden and risks

NA

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

1. Males and females, 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.

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.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2017
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	08-09-2017
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	NL62138.058.17