An fMRI and EEG study in patients with mild to moderate Alzheimer*s disease and healthy elderly controls

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1. To determine the feasibility of performing a few functional magnetic resonance imaging (fMRI) tasks and clinical neurophysiological measurements in patients with mild to moderate AD.2. To validate the visual perception fMRI task in healthy…

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

Summary

ID

NL-OMON48923

Source
ToetsingOnline

Brief title
fMRI and EEG study in Alzheimer patients

Condition

- Neurological disorders NEC

Synonym
Alzheimer's Disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: CHDR

Intervention

Keyword: Alzheimer's disease, EEG, fMRI

Outcome measures

Primary outcome

Biomarker:

* Picture recognition task (Episodic memory) probing novelty and subsequent memory (Maass et al., 2014, Nature Communications)

o Blood oxygen level dependent (BOLD) fMRI activity in the hippocampus and entorhinal layers/sub-regions

o Subsequent memory performance (i.e .hit rate)

* Visual perception task probing layer specific memory processing (Meppelink et al., 2009, Brain)

o Blood oxygen level dependent (BOLD) fMRI activity in the visual areas

* Resting state fMRI

o functional connectivity within the default mode network (DMN)

* Clinical neurophysiology

o 40 Hz Auditory steady state response * gamma oscillations

- Gamma-band intertrial phase coherence

- Gamma-band evoked power

o MMN

- MMN amplitude

- MMN latency

o P300

- P300 amplitude

- P300 latency

o Visual Evoked Potentials (VEP) based technique to measure LTP

- N75 amplitudes and latencies

- P100 amplitudes and latencies

- N135 amplitudes and latencies

Safety:

- (serious) adverse events ((S)AEs).

- Concomitant medication

Secondary outcome

N/A

Study description

Background summary

Alzheimer*s disease (AD) is characterised by a significant and progressive loss of acetylcholine neurons in the brain, specifically cholinergic innervation to the cortex and hippocampus is progressively lost. This is correlated with cognitive deficits, disturbance in visual perception and neuropsychiatric (e.g. hallucinations) symptoms. Selective acetylcholine receptor agonists and modulators targeting type 1 and type 4 muscarinic acetylcholine receptors (M1 and M4 mAChR) are being developed as therapy for AD. Both these M1 and M4 receptors are present in the visual cortex. For the early phase development of M1 and M4 receptor agonists, suitable biomarkers are required to measure the drug effects.

In this study of several fMRI and EEG based measurements the feasibility to function as a biomarker and the difference between patients with mild to moderate AD and healthy elderly will be assessed.

Study objective

1. To determine the feasibility of performing a few functional magnetic resonance imaging (fMRI) tasks and clinical neurophysiological measurements in patients with mild to moderate AD.
2. To validate the visual perception fMRI task in healthy subjects.

Study design

The total duration of the study for each subject will be maximal 42 days.
* Screening: medical screening will take place within 42 days prior to inclusion
* Study day (Day 1): On this day clinical neurophysiological measurements and the fMRI scan will be performed
* No follow-up visit is planned

Study burden and risks

During this study the participants will have 2 study visits:
-screening visit: medical screening with medical history, physical examination, questionnaires (MMSE, GDS NPI and CDR (first in AD patients only))
study time visit:
- urine drug screening
- breath alcohol test
- One blood sample will be taken to determine APOE genotype.
- fMRI measurement
- clinical neurophysiological measurements (incl. EEG)

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. Aged 50- 80 years;
2. Ability to communicate well with the investigator in the Dutch language;
3. Willing to give written informed consent and to comply with the study restrictions;
Additional inclusion criteria for the AD subjects are:
4. Diagnosed with probable AD according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria confirmed by the treating physician;
5. MMSE score 18-26 (inclusive);
6. CDR global rating score of 0.5 or 1.0 or 2 at screening;
Additional inclusion criteria for the healthy controls are:
7. MMSE score * 27.

Exclusion criteria

1. Any contra-indications for MRI (prostheses, implants, claustrophobia, pacemakers, etc.);
2. Presence or history of alcohol abuse, or 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 upon admission to the Clinical Research Unit (CRU);
3. Use of tobacco and/or nicotine-containing products within 30 days of day 1;
4. Positive urine drug screen at screening or day 1;
5. Unable to refrain from use of (methyl) xanthine (e.g. coffee, tea, cola, chocolate) from 24 hours prior to day 1 until discharge from the CRU;
6. Use of concomitant medication which reduces the level of alertness;
7. Concussion or other acute head trauma in the past six months.
8. A Geriatric Depression Scale * 15 (GDS) score *6;
Exclusion criteria for AD subjects are:

9. Clinically relevant history of abnormal physical or mental health, other than AD, interfering with the study as determined by medical history taking obtained during the screening visit and/or at the start of day 1 as judged by the investigator (including (but not limited to), neurological, psychiatric, endocrine, cardiovascular, respiratory, gastrointestinal, hepatic, or renal disorder).
10. Use of cholinesterase inhibitors, Memantine or herbal treatments such as Ginkgo Biloba in patients with mild AD.
Exclusion criteria for healthy subjects:
11. Clinically relevant history of abnormal physical or mental health interfering with the study as determined by medical history taking and physical examinations obtained during the screening visit and/or at the start of day 1 as judged by the investigator (including (but not limited to), neurological, psychiatric, endocrine, cardiovascular, respiratory, gastrointestinal, hepatic, or renal disorder).

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-08-2018
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	06-06-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-11-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL65882.056.18