Imaging the retina for early diagnosis in Alzheimer's disease

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This proof-of-concept study aims to non-invasively detect amyloid-beta (Aβ)-plaques in the retina of AD patients using a Heidelberg Spectralis scanner with Curcumin as labeling fluorophore. The retinal Aβ-plaques will be related to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Structural brain disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50349

Source
ToetsingOnline

Brief title
I-READ

Condition

- Structural brain disorders

Synonym
Alzheimer's disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,STW,Alzheimer Nederland;VUMC Fonds tbv Alzheimercentrum,Heidelberg Engineering

Intervention

Keyword: Alzheimer, amyloïd-beta, diagnosis, retina

Outcome measures

Primary outcome

Detection of Aβ-plaques in the retina of AD patients.

Secondary outcome

Comparison of Aβ-plaques in the retina with other AD biomarkers. Analysis of

sensitivity and specificity.

Study description

Background summary

Alzheimer*s disease (AD) is by far the most important cause of dementia. The diagnosis of AD is based on clinical criteria supported by either magnetic resonance imaging (MRI), positron emission tomography (PET) or cerebrospinal fluid (CSF) analysis. These ancillary investigations are expensive and/or invasive. What is needed is a non-invasive, cheap and fast, patient friendly method, suitable for use in an outpatient setting. The eye is a direct protrusion from the brain and the retina has many structural similarities with the brain. The retina is easily accessible for ophthalmological examination. As such, the retina can be of interest as a *window to the brain* and offers a potential new diagnostic method for early diagnosis of AD and/or follow-up of possibly therapeutic agents in the future.

Study objective

This proof-of-concept study aims to non-invasively detect amyloid-beta (Aβ)-plaques in the retina of AD patients using a Heidelberg Spectralis scanner with Curcumin as labeling fluorophore. The retinal Aβ-plaques will be related to currently used AD biomarkers such as hippocampal atrophy on MRI, Aβ1-42-level in CSF and amyloid-PET imaging.

Study design

Proof of concept diagnostic observational clinical cross sectional study.
During the first visit we will conduct a thorough baseline ophthalmological

examination including baseline cfSLO, which will take around 60-80 minutes. During the 10 days prior to the third visit patients will take an oral daily dose of Curcumin followed by examination with the Spectralis scanner. This will take around 30 minutes.

Study burden and risks

Patients will have three extra site visits, next to the regular visits for patient care in the VUmc Alzheimer Center. The first to obtain baseline ophthalmological characteristics, the second for short medical check and bloodsampling and the third to perform Spectralis scanning after 10 days of Longvida administration prior to this visit. Longvida dose levels up to 4000 mg have been given to humans without safety concerns and without side effects. For standard ophthalmological examination and to improve the quality of the optical coherence tomography (OCT) and Spectralis images, pupil dilatation is necessary with a topical mydriatic (Tropicamide). Pupil dilatation may cause a modest amount of transient photophobia and blurred vision in some participants, lasting several hours. This may interfere with car driving, so patients are advised not to drive themselves. Adverse ocular or systemic side effects of Tropicamide are very rare. Baseline ophthalmological investigations include OCT, Frequency Doubling Technology (FDT) and the Heidelberg Retinal Tomograph II (HRTII). Both these and the Heidelberg Spectralis scanner are non-invasive optical eye examinations in which light is used to examine the posterior part of the eye. The used wavelength and the overall energy level of the light is well below the safety margins and is harmless and without risks.

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

-Study cases: patients with alzheimer's disease fulfilling the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria.
-Controls: age and gender matched controls with Subjective Memory Complaints(SMC) and/or AMD (Age related Macula Degeneration) and no evidence of amyloid pathology according to CSF or amyloid PET scan analysis.
-Patients need to be fully capacitated and able to give informed consent themselves, with an mini-mental state examination (MMSE)-score of at least 17/30.

Exclusion criteria

+ Subject with ophthalmological conditions:
- Media opacities interfering with optimal imaging
- Narrow angle (with risk of acute angle close glaucoma)
- History of glaucoma, uveitis, retinal detachment, retinal dystrophy)
- History of chronic illness, with chronic medication, like reuma, sarcoidosis, inflammatory bowel disease, diabetes mellitus
- Recent ocular surgery within 6 months prior to study examinations
- Any ocular surgery of the vitreous / retina (vitrectomy, retinal detachment, macular hole, pucker). Late stages of Age related Macular Degeneration (AMD) or extensive drusen in the retina
+ MMSE <=16
+SMC with Aβ-pathologie
+ Multiple sclerosis, Parkinson's disease or other neurodegenerative diseases

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-04-2016
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Spectralis-SN9367
Registration:	No

Ethics review

Approved WMO Date:	07-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2015
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2020
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	NL52237.029.15