Glymphatic dysfunction in cognitive impairment: a memory clinic study

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1. Seven Tesla MRI can identify abnormalities of the glymphatic system associated with dementia and its preclinical stages relative to cognitively normal control (i.e. neurotypical) subjects. 2. More severe signs of dementia are associated with...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON29030

Bron
NTR

Verkorte titel
GlyM

Aandoening

Alzheimer's disease, Mild cognitive impairment

Ondersteuning

Primaire sponsor: Maastricht University Medical Center
Overige ondersteuning: Alzheimer Nederland and MUMC+

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoints are the interstitial fluid characteristics, the derived cerebral blood flow pulsatility index, and other derived MRI measures.

Toelichting onderzoek

Achtergrond van het onderzoek

Alzheimer's disease (AD), the most frequent neurodegenerative disorder and most common cause of dementia in the elderly, is characterized by the accumulation of amyloid-β (Aβ) plaques and neurofibrillary tangles. Solute clearance in the brain is not only dependent on transport across the blood-brain barrier (BBB), but also on the clearance of interstitial fluid (ISF) in the brain tissue and the perivascular spaces by a waste clearance system, the so-called glymphatic system [1-3]. In addition is the brain highly vulnerable to the (kinetic) energy deposition of the arterial pulsatility which is increased due to the low resistance of brain arterioles and age-related hardening of arterial walls. Reduction in vascular elasticity and increased arterial pulsatility affect the perivascular clearance of waste products in the ISF [4], altering the physiologic transport of catabolites out of the brain including Aβ [2]. Therefore, a link between glymphatic function and AD has been hypothesized.

The number of patients with AD will increase dramatically in the upcoming decades [5]. The cause remains to be elucidated and effective options for treatment are therefore not yet developed. The current study aims to obtain a better understanding of glymphatic dysfunction in dementia of the Alzheimer's type and its preclinical stages. In addition, non-invasive imaging of the glymphatic system might provide an early biomarker of patients at risk (i.e. before the onset of overt symptoms).

Seven Tesla (7T) MRI provides high signal to noise and spatial details, and the unique opportunity to noninvasively assess various features of the glymphatic system by quantifying the volumetric fraction and dynamics of the ISF (using intravoxel incoherent motion imaging, IVIM) and measuring the pulsatility of small perforating lenticulostriate arteries (LSA) and other supplying arteries (using velocity sensitive MRI). We hypothesize that these features of glymphatic dysfunction can be linked to cognitive impairment. We will investigate the relationship between MRI-derived metrics indicative of the glymphatic system, namely interstitial fluid (ISF) characteristics and arterial pulsatility, with (1) brain tissue markers, (2) cognitive performance, and (3) AD biomarkers (Aβ/tau) in a memory clinic population.

The aim of this study is to discover how these metrics are affected in different stages of cognitive impairment. In a cross-sectional observational study, 120 individuals with different states of cognitive condition will be included. This will include 40 healthy cognitively normal controls, 40 patients with Mild cognitive impairment and 40 patients with mild AD dementia.

Doel van het onderzoek

1. Seven Tesla MRI can identify abnormalities of the glymphatic system associated with dementia and its preclinical stages relative to cognitively normal control (i.e. neurotypical) subjects.

2. More severe signs of dementia are associated with more affected glymphatic metrics: increased interstitial fluid fractions and arterial pulsatility are associated with

neurodegeneration and more impaired cognitive performance.

Onderzoeksopzet

One session at one time point

Onderzoeksproduct en/of interventie

Control subjects will undergo the following study specific measurements:
-the 7T MRI scan
-the blood pressure measurement
-questionnaires (CHAMPS, PSQI) and questionnaires on medical and demographic information
-neuropsychological testing
-blood sampling via venepuncture
-tear fluid collection

The participating patients (MCI and AD) will undergo the following study specific measurements:
-the 7T MRI scan
-the blood pressure measurement
-questionnaires (CHAMPS, PSQI).
For the participating patients (MCI and AD), information will be retrieved from the BBACL-cohort concerning neuropsychological test results, medical and demographic information, blood- and tear fluid measurements, and CSF measurements (if a lumbar puncture is performed for diagnostic purposes and CSF-values are registered within the BBACL).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Patients with mild Alzheimer's disease dementia, patients with mild cognitive impairment (MCI), and healthy subjects will be included.

In order to be eligible for the AD dementia-group, a subject must meet all of the following criteria:
- Mentally competent (MMSE≥18) and able to give informed consent
- Informed consent before participation in the study
- Age > 55 years
- Diagnosis of dementia of the AD type

Criteria for the MCI-group:
- Mentally component (MMSE ≥18) and able to give informed consent
- Informed consent before participation in the study
- Age > 55 years
- Diagnosis of MCI or diagnosis of Mild Neurocognitive Disorder (DSM V)

Criteria for the control (cognitively normal) group:
- Mentally component (MMSE ≥18) and able to give informed consent
- Informed consent before participation in the study
- Age > 55 years
- MMSE ≥ 26
- Average age and gender is similar to the patient groups

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Any significant disease or unstable medical condition that could influence neuropsychological testing (with the exception of a MCI or AD diagnosis)
- Major depression (according to the DSM IV) (< 12 months ago)
- Psychiatric history (schizophrenia, schizoaffective disorder, bipolar disorder or any history of electroconvulsive therapy)
- Vascular dementia
- Ischemic or valvular heart disease or electrocardiographic evidence of atrial fibrillation
- Recent transient ischemic attacks and ischemic or haemorrhagic stroke or cerebrovascular accident (< 2 years or paired with cognitive decline within 3 months after incident)
- Obstructive sleep apnoea syndrome

- Normal Pressure Hydrocephalus, M. Huntington, Parkinson’s disease, Frontotemporal dementia, Motor neuron diseases, Multiple sclerosis, Epilepsy
- Systemic inflammation, such as active rheumatoid arthritis
- Diabetes
- Cognitive impairment due to alcohol/drug abuse
- Structural abnormalities of the brain, such as tumours or stroke lesions
- Inability to provide informed consent
- Any contraindication for MRI: metallic implants, pacemaker, claustrophobia, pregnancy, tattoos in the head/neck region
- Unwillingness to be informed about potential abnormal MRI-findings

Additional exclusion criteria for the control group:
- A known diagnosis of mild cognitive impairment, prodromal dementia or dementia
- Substantial memory complaints (according to participant)

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Enkelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	24-07-2020
Aantal proefpersonen:	120
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	24-07-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 56079
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8798
CCMO	NL72269.068.19
OMON	NL-OMON56079

Resultaten