The Effect of a Nutritional Intervention on brain Glucose Metabolism in early Alzheimer*s disease

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

Summary

ID

NL-OMON44286

Source
ToetsingOnline

Brief title
NL-ENIGMA

Condition

- Neurological disorders NEC

Synonym
early Alzheimer's disease

Research involving
Human

Sponsors and support

Primary sponsor: Alzheimercentrum
Source(s) of monetary or material Support: NWO,Nutricia

Intervention

Keyword: 18F-fluorodeoxyglucose, Alzheimer's disease, Positron Emission Tomography, Souvenaid

Outcome measures

Primary outcome

Main exploratory parameters:

- Quantitative absolute FDG uptake as assessed by 18F-FDG-PET using arterial sampling and kinetic analysis

- Relative semi-quantitative 'standardized uptake value' (SUV) ratios with a normalisation region (cerebellum and pons) at a predefined standard uptake time interval of 45-60 minutes post injection.

Secondary outcome

Additional exploratory parameters

* Semi-quantitative SUV and SUV ratio (normalization regions cerebellum and pons) as assessed by 18F-FDG-PET using different time windows post injection

* MRI biomarkers:

- 3D T1 weighted MRI: atrophy rates in different brain regions

- rs-fMRI: mean synchronisation likelihood of the whole brain

- DTI: mean fractional anisotropy of voxels in white matter skeleton

- structural brain networks based on DTI data (analysed using graph theory)

- ASL measures: mean cerebral blood flow in Alzheimer ROIs

- q-flow: blood flow in the large arteries to the brain

* Blood biomarkers:

- vitamin E

- homocysteine (Hcy)

- fatty acid profile in erythrocytes

- other markers like nutritional parameters might be analysed

* CSF markers (optional):

- A*1-40 and 1-42, total tau (tau) and tau phosphorylated at threonine-181

(ptau) will exploratory be analysed

- Other markers like nutritional CSF parameters might be analysed

* Cognition:

- RAVLT immediate and delayed recall and recognition test

- Executive functioning using TMT-A and TMT-B

Study description

Background summary

Alzheimer Disease (AD) is associated with synapse loss. The medical food Souvenaid® contains Fortasyn® Connect, a combination of nutrients designed to enhance synapse formation and function in AD. Two earlier studies demonstrated memory improvement in mild AD dementia patients after Souvenaid intervention for 12 and 24 weeks. The 24-week study also showed effects on brain network organisation measured with electroencephalography (EEG), which strengthens the hypothesis that Souvenaid affects synaptic formation and function.

Study objective

To provide further insight into Souvenaid*s hypothesised mode of action, the current NL-ENIGMA study explores brain glucose metabolism in mild cognitive impairment (MCI) and mild dementia due to AD, using Positron Emission Tomography with 18F-FDG-PET as indicator for synapse function. Additionaly, MRI measurements, blood markers, CSF markers and cognitions will be explored.

Study design

The NL-ENIGMA study is an exploratory, randomised controlled study. Drug-naïve subjects with MCI or mild dementia due to AD (MMSE * 20 and presence of amyloid burden) will be 1:1 randomised to receive either Souvenaid (containing Fortasyn Connect) or an iso-caloric control product (without Fortasyn Connect) for a 24-week period, n = 40 completers. At baseline and after 24 weeks, participants will undergo quantitative 18F-FDG-PET imaging including arterial sampling. To collect further information on the mode of action of Souvenaid, additional assessments include relative and absolute 18F-FDG-PET imaging, magnetic resonance imaging (MRI) (i.e. structural MRI, resting-state functional MRI, diffusion tensor imaging (DTI), graph theory based on DTI data, arterial spin labelling and q-flow for measuring afferent blood flow in large arteries to the brain), cerebrospinal fluid (CSF) and the assessment of blood parameters.

Intervention

Daily intake of Souvenaid or placebo (isocaloric product without specific ingredients) for the duration of the follow-up.

Study burden and risks

1. Radiation exposure;
2. Idiosyncratic reaction to the tracer;
3. Discomfort or complications related to placement of the intra-arterial catheter;
4. Discomfort and complications related to blood and CSF sampling;
5. Discomfort during PET or MRI assessment.

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

- diagnosis MCI or mild dementia
- with CSF biomarker profile or amyloid PET-scan indicating underlying Alzheimer's disease
- age 50*85 years (inclusive)
- Mini-Mental State Examination score * 20
- informed consent form signed by subject
- available reliable study partner (informant) who agrees to monitor administration of study product

Exclusion criteria

* Diagnosis of significant neurological and / or psychiatric disease other than AD, including vascular dementia according to NINDS-AIREN criteria, cerebral tumour, Huntington*s disease, Parkinson*s disease, normal pressure hydrocephalus (NPH), seizures, delirium, schizophrenia, major depression and other entities relevant for brain function.
* Diagnosis of diabetes or use of anti-diabetic medication. Non-fastening blood glucose concentration * 10.0 mmol/l at screening is an exclusion criterion, unless blood glucose concentration is < 7.0 mmol/l when measurement is repeated when patient is in fasting state.
* Diagnosis of stroke, intracranial hemorrhage, mass lesion, NPH or white matter hyperintensities according to Fazekas scale 3 on MRI. MRI must not be older than one year.
* Use within three months prior to baseline, or expected need during the study, of donepezil, rivastigmine, galantamine and / or memantine
* Contraindications to PET or MRI (e.g., claustrophobia, pacemaker, metallic implants, current use of anticoagulants)
* Haemoglobin (Hb) level in blood < 7.5 mmol/l (women) or < 8.5 mmol/l (men) at screening
* Alcohol or drug abuse
* Use within three months prior to baseline of Souvenaid

* Use within two months prior to baseline of:
- omega-3 fatty acid containing supplements
- oily fish (when consumed more than twice a week)
* Use within one month prior to baseline of:
- atropine, scopolamine, tolterodine, hyoxcyamine, biperiden, benztropine, trihexyphenidyl, oxybutynin
- antipsychotics
- vitamins B, C and / or E > 200% RDI
- high energy and/or protein nutritional supplements / medical foods
- benzodiazepines
- other investigational products
* Change in dose within one month prior to baseline of:
- lipid lowering medication
- antidepressants
- antihypertensive medication
* Investigator's uncertainty about the willingness or ability of the patient to comply with the protocol requirements.
* Participation in any other studies involving investigational or marketed products concomitantly or within two weeks prior to entry into the study
* Participation in the LipiDiDiet study within three months prior to baseline

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-03-2015
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	12-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-10-2016
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

ID: 24193
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	4718
CCMO	NL49949.029.14
OMON	NL-OMON24193