In vivo imaging of brain metabolism in ALS

Published: 10-02-2016
Last updated: 19-04-2024

To study the role of brain metabolites and macromolecules in relationship to pathogenesis, structural brain changes and clinical phenotype of ALS. This will reveal underlying molecular mechanisms of pathogenesis, structural brain changes and...

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

Summary

ID

NL-OMON43668

Source
ToetsingOnline

Brief title
ALS brain metabolism

Condition

- Neuromuscular disorders

Synonym
Amyotrofic lateral sclerosis, Lou Gehrig's disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: collectebusfondsen

Intervention

Keyword: ALS, brain, molecular mechanisms, spectroscopy

Outcome measures

Primary outcome

Main study parameters are the level of brain metabolites as obtained with 1H-MRS and 31P-MRS that should discriminate between ALS patients, familiar persons and healthy persons.

• Quantification of metabolites related to energy metabolism, such as Creatine, Glutamate, Glutamine (1H-MRS) and phosphocreatine, ATP and ADP (31P-MRS).

• Quantification of metabolite levels related to neuronal/glial loss, such as N-Acetylaspartic acid, Choline, Creatine and Myo-Inositol (1H MRS).

• Relation of these metabolite levels in regions with cortical thickness.

• Quantification of neurotransmitter levels such as GABA (inhibitory neurotransmission) and Glutamate and Glutamine (excitatory neurotransmission) (1H MRS) and their relation with cartical thinning and clinical phenotype.

• The relation of these metabolites levels to each other to discover a pattern of metabolic involvement in ALS.

Secondary outcome

• Clinical parameters including age, gender, age at onset of disease, site of onset, El Escorial criteria, disease severity (as measured by ALSFRS questionnaire), disease duration and progression rate, and presence of cognitive impairment (as measured by ECAS, as explained in the next section) in relation with brain metabolites.

Study description

Background summary

Pathological studies as well as imaging studies have shown alterations in the brain of patients with amyotrophic lateral sclerosis (ALS). Distinct molecular mechanisms play a role in the pathogenesis of ALS. Using Magnetic Resonance Spectroscopy (MRS) techniques, the metabolites, neurotransmitters and macromolecules involved in those molecular mechanisms can be quantified. This opens opportunities to study the role of brain metabolites in ALS pathogenesis in vivo in (presymptomatic) ALS patients. This will result in new knowledge about pathophysiology of ALS and might offer new targets for future therapies.

Study objective

To study the role of brain metabolites and macromolecules in relationship to pathogenesis, structural brain changes and clinical phenotype of ALS. This will reveal underlying molecular mechanisms of pathogenesis, structural brain changes and clinical phenotype in vivo.

Study design

Observational case-control study

Intervention

All subjects will receive a MRI scan with a ttotal duration of approximately 60 minutes including 10 minutes for preparation and planning. MRI protocol consists of a T1 weighted 3D anatomical scan, 1H-MRS with water and fat suppression and 31P-MRS.

Study burden and risks

Participants will undergo a clinical assessment and MRI examination at the University Medical Center (UMC) Utrecht. Standardized 7T MRI checklists will be used to ensure MRI safety. The burden for the patient includes the time the patient will spend for making the 7T MRI scans and travel time to the hospital. Patients will be compensated for travel costs made for the visits to the hospital for the 7T MRI examination. There are no direct benefits for the individual participant. Information acquired by this research project provides new insights in molecular pathways that might become involved in ALS.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subjects
a. ALS patients: definite, probable, probable-laboratory supported or possible ALS according to the revised El Escorial criteria (Brooks 2000);
- familar ALS is defined only if there is a family history of ALS.
b. Healthy control subjects without ALS: including family members of ALS patients with and without an established mutation, without any sign of ALS.
2. Age 18 - 80 years (inclusive)
3. Capable of thoroughly understanding the study information given; has signed the informed consent.
4. Capable of climbing up the stairs, so the patient is able to climb up the MRI table

Exclusion criteria

• Tracheostomy, tracheostomal ventilation of any type, (non)-invasive ventilation.
• Any history or presence of brain injury, epilepsy, psychiatric illness and other cerebral disease (not related to ALS).
• Any intoxication or medication known to have an association with motor neuron dysfunction, which might confound or obscure the diagnosis of motor neuron disease.
• Presence of pronounced swallowing disorders or orthopnoea (which make it dangerous to lie supine in the MRI scanner).
• Contra-indications to MRI scanning according to hospitals 7T MRI screening guideline of the UMC Utrecht.
• Pregnancy

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-05-2016
Enrollment:	130
Type:	Actual

Ethics review

Approved WMO

Date:	10-02-2016
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL55287.041.15