Dynamic imaging of brain metabolism in ALS

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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	Pending
Health condition type	Neuromuscular disorders
Study type	Observational invasive

Summary

ID

NL-OMON56544

Source
ToetsingOnline

Brief title
Dynamic brain metabolism in ALS

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: Stichting ALS

Intervention

Keyword: ALS, Brain, Deuterium, Spectroscopy

Outcome measures

Primary outcome

Main study parameters are the level of brain metabolites as obtained with 1H-MRS, 2H-MRS, that should discriminate between ALS patients, asymptomatic family members of patients with ALS and healthy controls. This will be used to derive the main outcome:

-TCA-cycle rate.

Main parameters from MRS.

- Glutamate, glutamine, glucose, lactate,

Main parameters from blood.

- Glucose, lactate, % deuterium enrichment.

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 in relation with brain metabolites.

Other MRS parameters

-N-acetyl aspartate (NAA), choline (Cho), creatine (Cr)

The primary outcome measure will be related to secondary parameters as well as

parameters as acquired in earlier studies, mainly the anatomical MRI data as

acquired in Imaging MND 11-552. e.g. cortical thinning.

Study description

Background summary

Pathological studies and 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. Magnetic Resonance Spectroscopic imaging (MRSI) techniques can quantify the metabolites and neurotransmitters involved in those molecular mechanisms. 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 the pathophysiology of ALS and might offer new targets for future therapies.

The principle of this study has been proven in its predecessor: "In vivo imaging of brain metabolism in ALS". The results of this study (awaiting publication) have shown numerous aspects of metabolic changes in ALS. With this new study design, we want to use new MR techniques to look further into the aspects of brain metabolism which have shown changes and also into new aspects. One of these aspects is the glucose metabolism, deuterium-glucose can be dynamically followed and its metabolites quantified and as such give information about this process in vivo.

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

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, placement of an IV drip and be in fasting state for 6hrs prior to the MR-scan.

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

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1.
a. ALS patients: definite, probable, probable-laboratory supported or possible ALS according to the revised El Escorial criteria (Brooks 2000); only if ALS patients have a family history of ALS, this will be defined as fALS.
b. Healthy control subjects without ALS: including family members of ALS patients with or without an established mutation (i.e. we will not select them based on any knowledge about a mutation they might carry), 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.
5. Willing and able to lie in an MRI scanner uninterrupted for 90 minutes.

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 and/or to drink 2H-glucose).
• Diabetes mellitus
• Contra-indications to MRI scanning according to hospitals 7T MRI screening guideline of the UMC Utrecht.
• Pregnancy
• Any intoxication or medication that could influence the cerebral glucose metabolism as judged by the researcher

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-02-2024
Enrollment:	123
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	25-01-2024
Application type:	First submission
Review commission:	METC NedMec

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	NL85201.041.23