The frontotemporal syndrome in amyotrophic lateral sclerosis: screen, impact, imaging and pathology.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44137

Source
ToetsingOnline

Brief title
The frontotemporal syndrome in amyotrophic lateral sclerosis

Condition

- Other condition
- Neuromuscular disorders

Synonym
amyotrophic lateral sclerosis (ALS), Motor neuron disease (MND)

Health condition

binnen zenuwstelsel aandoeningen: dementie van het frontotemporale type (FTD)

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: meerdere fondsen

Intervention

Keyword: Amyotrophic lateral sclerosis, Cognitive impairment, Frontotemporal dementia

Outcome measures

Primary outcome

1. A validated, short cognitive screening instrument for ALS patients.

2. Differences in structural and functional brain networks (connectivity

measures) between patients with and without a frontotemporal syndrome.

Secondary outcome

1. An estimate of the impact of ALS and the frontotemporal syndrome on the

patient and their carers.

2. A brainbank of phenotyped ALS patients.

Study description

Background summary

Amyotrophic lateral sclerosis (ALS) is a devastating disease, affecting the central and peripheral motor neurons, rendering them to wheelchair dependence and death due to respiratory insufficiency three years after the onset of symptoms. Recently, focus has been shifting to involvement of frontotemporal brain regions in up to 50% of the patients leading to a frontotemporal syndrome (i.e. mild to moderate cognitive and behavioral changes or frontotemporal dementia, FTD). The frontotemporal syndrome has a negative impact on survival, on the decision to opt for life-prolonging therapies and, possibly on the relationship between patients and carers, and is therefore an important syndrome to recognise. In addition, the correct classification of ALS patients (phenotyping) is essential for clinical trials and for the interpretation of genetic and pathological findings.

Study objective

The main objectives are:
1. to develop a diagnostic tool for the assessment of the frontotemporal syndrome.
2. To investigate the structural and functional brain networks of ALS patients with and without a frontotemporal syndrome, in order to gain understanding of the pathophysiology of ALS.

The secondary objectives are:
1. to examine the impact of the frontotemporal syndrome of ALS on the carers.
2. to correlate clinical signs and symptoms with pathological findings.

Study design

Step 1: Development of an easy-to-administer screening instrument to detect frontotemporal cognitive dysfunction in ALS
Step 2: Examination of the clinimetric properties of the new screen (ALS-FTD-Cog)
Step 3: Examination of the quality of life of patients and caregivers
Step 4: Classification of patients into three groups, based on the results of the neuropsychological examination and the score on the ALS-FTD-Q: no, moderate or severe frontotemporal syndrome.
Step 5: In a subgroup (N=102) an MRI of the brain and an MEG recording will be performed.
Step 6: Six months later, a repeat MRI scan, MEG recording and neuropsychological examination will be performed in this subgroup (N=102).
Step 7: Neuropathological examination in patients who consent to autopsy

Study burden and risks

Group benefits
The aim of this study is to develop and improve diagnostic tools for the detection of the frontotemporal syndrome of ALS. For future clinical trials and the interpretation of basic scientific studies (genetics and pathology), it will be beneficiary to be able to accurately phenotype patients within the spectrum of ALS-FTD, i.e. ALS without cognitive or behavioural disturbances, ALS with cognitive impairment, ALS with behavioural changes or ALS with cognitive impairment and behavioural changes.
Also, we aim at clarifying the pathophysiology of ALS, by investigating the structural and functional brain networks of ALS patients with and without a frontotemporal syndrome. This might result in possible new drug targets.

Risks and burden
In a subgroup of patients and controls MRI scans of the brain will be performed. There is a small chance that there will be incidental findings on

the MRI, such as old infarction, a meningeoma, a vascular anomaly or a brain tumour. On the magnetoencephalogram epileptic activity might be observed. Incidental findings will not be communicated to the participants, unless it concerns a lesion for which further evaluation or treatment is warrented, e.g a lesion suspicious for malignancy or an aneurysm. Patients will be refered to a neurologist. All suspicious lesions will be examined by a radiologist (Prof. Dr. C. Majoie).

ALS is a devastating disease with a median survival of 3 years after diagnosis. A subgroup of patients will undergo 2 neuropsychological examinations, 2 MRI scans and MEG recordings. We realize that this study will consume some of their time. We calculated that this study will cost patients 7 hours at most, not including travel time. We tried to limit the number of hospital visits and related inconvenience in this study by including a home visit.

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

Age >= 18 years, speak Dutch fluently, have a proxy (partner, family member or close friend) who speaks Dutch fluently and is willing to fill in the questionnaires.
Furthermore, ALS patients must have sporadic or familial (fALS), probable, probable-laboratory supported or definite ALS, as defined by the El Escorial criteria, with a symptom duration of less than 12 months. ALS-FTD and behaviour variant-FTD patients must have sporadic or familial, probable or definite bv-FTD, as defined by the Neary criteria and the revised criteria by Rascovsky et al.

Exclusion criteria

Any neurological or psychiatric condition with cognitive impairment or behavioural changes, use of psychopharmaca, excessive alcohol intake, i.e. >= 5 drinks per day, forced vital capacity < 70% of the predicted value in the upright position, at the time of inclusion (ALS patients), incapacitated person.

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:	Recruitment stopped
Start date (anticipated):	02-07-2013
Enrollment:	181
Type:	Actual

Ethics review

Approved WMO Date:	10-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2014
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	NL42161.018.12