Neuromuscular model for MND: Quantifying the effect of motor neuron disease on neural and non-neural properties of the lower limbs

Published: 14-08-2019
Last updated: 10-04-2024

The key objective of the study is to assess the validity of a quantitative uniform examination technique for estimating physiological properties in MND patients, to better examine the neuromuscular properties from which defective motor behavior...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neuromuscular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON48095

Source
ToetsingOnline

Brief title
Neuromuscular model for MND

Condition

- Neuromuscular disorders

Synonym
Lou Gehrigs disease, Motor neuron disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: ALS Stichting Nederland

Intervention

Keyword: Amyotrophic lateral sclerosis, Human motor control, Motor neuron disease, Neuromechanics

Outcome measures

Primary outcome

A set of neuromuscular properties determined from the uniform examination

protocol which is performed on the Wristalyzer.

Secondary outcome

A set of clinical scores of characteristic symptoms in MND, derived in

neurological examination.

Study description

Background summary

Motor Neuron Disease (MND) is a group of terminal neurodegenerative disease, leading to progressive loss of motor function. Treatment of MNDs such as Amyotrophic Lateral Sclerosis (ALS), progressive muscular atrophy (PMA) and primary lateral sclerosis (PLS), remains an unresolved challenge despite intensive research into diagnosis, prognosis and therapy. New therapeutics, and the quality of care after diagnosis can be enhanced by early, more personalized diagnosis at individual patient level, enabling tailored care and individualized treatment.
To personalize the diagnosis, there is a need for reliable quantitative biomarkers, for early detection of disease onset and to distinguish the different sub-types of the disease with different symptoms and progression rates. Several quantitative biomarkers have been investigated for use in MND, including Motor Unit Number Estimation (MUNE), Motor Unit Number Index (MUNIX), Cortical Excitability in Transcranial Magnetic Stimulation (TMS), electromyography (EMG) Inter-muscular Coherence, Magnetic Resonance (MR) and other imaging techniques, and EEG signatures. However, these biomarkers cannot appropriately identify the complex interplay of neuromuscular factors contributing to motor dysfunction in individuals. To examine these factors, a proper quantification of motor and sensory factors and their behavior during

systematic manipulation of task conditions is required. This study will apply parameter estimation paradigms to a non-linear neuromuscular model of the human wrist from measurements of EMG, force and motion. The estimated parameters are expected to function as a set of novel neuromuscular biomarkers, beyond what is currently attainable from clinical neurological examination and other quantitative measurement techniques in MND.

The proposed study is significant from several neurological perspectives:
- it aims to enhance the qualitative measures of disease progression with quantitative measures
- it recognises the heterogeneity of the disease by assessing a set of neuromuscular biomarkers to quantify the different dimensions of the disease;
- and it is based on neuro-electric activity measures that are non-invasive and can be employed inexpensively with patients participating in clinical trials.

Study objective

The key objective of the study is to assess the validity of a quantitative uniform examination technique for estimating physiological properties in MND patients, to better examine the neuromuscular properties from which defective motor behavior originates, both at a group level and at the individual level. Therefore, we would like to measure the neuromuscular properties of patients, controls and asymptomatic carriers with the use of a wrist manipulator. In doing so, our aim is to advance understanding of MND pathology and identify novel, inexpensively measured biomarkers that can distinguish MND patients based on neural and non-neural properties. Such biomarkers have applications in disease prognostics and measurements of therapeutic activity of neurotherapeutic candidates. Successful discrimination between neuromuscular properties can be used to diagnose MND, which may also be useful for better patient care and for the development of novel neuro-motor rehabilitation.

Study design

Prospective observational study, cross-sectional design.

Study burden and risks

The MND community is in great need of a technique that allows patient wide uniform assessment of high resolution quantitative biomarkers of factors contributing to MND symptoms. This protocol will align with current clinical practice and therefore will not interfere in clinical decision making.
The protocol uses additional measurements of motor function, through the use of a single-axis haptic robot (Wristalyzer; MOOG FCS, Nieuw Vennep, the Netherlands) for very accurate assessment of wrist movements. The measurements will be performed during visiting days of the *Imaging in MND* study (METC

protocol number 11-552). No follow-up visits are required for any of the subjects.
Measurements are non-invasive and bear minimal risks. Active participation of the subjects is required, though tasks will mostly involve submaximal efforts and small movements. The measurement protocol takes around 45 minutes, but patients are offered extra rest periods if necessary.
The Wristalyzer is safeguarded by hard- and software bounds, which are adapted to each individual. In addition, task intensities are adapted to strength level of each patient to ensure that the range of movement does not exceed 3 degrees from the neutral wrist position.

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. a. MND patients: definite, probable, probable-laboratory supported or possible ALS according to the El Escorial criteria (Brooks, 2000), PMA or PLS.
b. Control subjects: no diagnosis of MND or ALS mimics and age- and gender-matched to patient groups, intact physical ability to take part in the experiment.
c. Asymptomatic carriers: carriers of MND-related gene mutations with no neurological symptoms associated with MND.
2. Age:18 and older
3. Capable of performing active tests with their right hand; muscle strength should be above 3 on the medical research council (MRC) scale27.
4. Capable of thoroughly understanding the study information given; has signed the informed consent.

Exclusion criteria

Exclusion criteria are for all participants:
1. a history of major head trauma or other neurological conditions that could affect cognition,
2. alcohol dependence syndrome, current use of neuroleptic medications or high dose psychoactive medication.
3. History of reaction or allergy to recording environments, equipment and the recording gels.
4. Tracheostomy, tracheostomal ventilation of any type, (non)-invasive ventilation.
5. Pregnancy.

Further exclusion criteria for healthy controls and asymptomatic carriers:
6. History of neuromuscular, neurological or active psychiatric disease

Further exclusion criteria for patients:
7. The presence of any active psychiatric disease, and any medical condition associated with neuropathy (e.g. diabetes).
8. Any history or presence of brain injury, epilepsy, psychiatric illness and other cerebral disease.
9. Any intoxication or medication known to have an association with motor

neuron dysfunction,
which might confound or obscure the diagnosis of MND.

Study design

Design

Study type:	Observational non 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):	12-09-2019
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Date:	14-08-2019
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	NL70328.041.19