Neuroimaging biomarkers in Huntington*s Disease after 16 years of disease progression

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Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON57274

Source
ToetsingOnline

Brief title
HD16MR: Neuroimaging biomarkers in HD; 16 years later.

Condition

- Neurological disorders congenital
- Movement disorders (incl parkinsonism)

Synonym
Huntington's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bontius Stichting

Intervention

Keyword: biomarkers, disease progression, Huntington's Disease, neuroimaging

Outcome measures

Primary outcome

The main study parameters are the neuroimaging markers, starting with the primary outcome measurement:

1. Atrophy of subcortical regions such as caudate nucleus and putamen, and cortex

2. Measures of iron accumulation in the basal ganglia and cortex

3. Levels of metabolites, especially neuroinflammation metabolites, in the putamen.

We will compare these measures with the previous MRI outcome measurements from TRACK-HD.

Secondary outcome

The secondary parameters are the clinical outcome measures, derived from the clinical assessments during this study, during TRACK-HD and the years in between during the Enroll-HD study.

Study description

Background summary

Huntington*s Disease (HD) is a rare autosomal dominant inherited progressive neurodegenerative disorder, caused by a CAG repeat expansion of exon 1 in the HTT gene on chromosome 4. The disease typically manifests at an age at onset between 30 and 50 years old and is characterized by a variety of motor disturbances (mainly chorea and dystonia), cognitive impairment and behavioral changes.

There have been multiple neuroimaging studies showing pathophysiological changes in the brain during the course of Huntington*s Disease. One of the most common findings in neuroimaging studies is striatal atrophy, studied with structural MR imaging. Volume changes seem to start in the striatum, years before clinical onset and spreads throughout the brain during the manifest stages, affecting widespread regions of the grey and white matter. There are also other MRI sequences that have proved to be of value in assessing disease progression in HD, such as diffusion tensor imaging (DTI) which have assessed microstructural changes in the white matter, Magnetic Resonance Spectroscopy (MRS) that show pathophysiological mechanisms like increased neuroinflammation and iron sensitive sequences which show an increased iron accumulation in certain regions of the brain.

An important limitation of most of the neuroimaging studies in HD, is the lack of longitudinal follow-up. Most of the longitudinal studies that have been performed so far, have followed participants up to 30-72 months (resp. IMAGE-HD and TRACK-HD. A longitudinal follow-up after 16 years has never been performed and is therefore extremely valuable. Therefore, we will follow-up the participants who participated in TRACK-HD in the LUMC at least at baseline in 2008, with a follow-up MRI and clinical assessments to assess disease progression with MRI and clinical characteristics. These data combined will show a long intra-individual progress of disease progression, which will add information to a huge gap of knowledge in neuroimaging studies.

Study objective

Our primary objective is to compare neuroimaging markers on a 3T MRI-scan with the MRI-scans that were performed during TRACK-HD in 2008-2011. We will assess the following neuroimaging markers, starting with the most important marker:
1. Structural neuroimaging; volume of regions such as the caudate nucleus, putamen, and cortex.
a. To assess atrophy in the brain
b. Compare the findings with earlier results from TRACK-HD to evaluate the progression of this neuroimaging marker
2. Iron sensitive MRI; quantification of iron levels in regions such as the basal ganglia and cortex.
a. To assess iron accumulation in the brain
b. Compare the findings with earlier results from TRACK-HD to evaluate the progression of this neuroimaging marker
3. Magnetic Resonance Spectroscopy (MRS); measurement of metabolites level in the putamen.
a. To assess neuroinflammation in the brain
b. Compare the findings with earlier results from TRACK-HD to evaluate the progression of this neuroimaging marker
4. Diffusion Tensor Imaging (DTI): measuring microstructural tracts in the white matter
a. To evaluate microstructural differences

b. Compare the findings with earlier results from TRACK-HD
to evaluate the progression of this neuroimaging marker

Secondary Objectives:
In addition to the course of neuroimaging markers during intra-individual disease progression, we would like to analyse the clinical characteristics of these participants during this study, during TRACK-HD and in between the neuroimaging timepoints, to add multiple extra timepoints with clinical data.

Study design

This is a cross-sectional study in which we perform clinical assessments and a 3T MRI-scan of the brain on participants who have participated in TRACK-HD in the LUMC. This will be added to the data of TRACK-HD which included clinical assessments and a yearly 3T MRI-scan of the brain during the period 2008-2011. This study will include one visit in which we perform clinical assessments and a 50-minute 3T MRI-scan. The clinical assessments include a short motor assessment, psychological and functional assessments. Before these assessments are performed, the patient needs to sign an informed consent. All together this visit will take around 3 hours.

Study burden and risks

This is a non-therapeutic group relatedness study. Before the study assessments participants have to give informed consent. The study days consists of a 3T MRI scan and short motor, functional, and neuropsychological assessments, which have no consequences for the health of the participants. Contra-indications for MRI will be carefully checked per subject to minimize the risks. Burden will be kept at a minimum by using short protocols and breaks in between.

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

Individuals with an age of 21 years or above, whom have participated in TRACK-HD at the Leiden-site, with the ability to give informed consent and undergo MRI scanning.

Exclusion criteria

• Inability to understand the information about the protocol;
• Severe chorea that, in the investigator*s judgment, precludes the patient*s participation in and completion of the MRI.
• Contra-indication to MRI scanning, such as:
- Claustrophobia;
- Pregnancy;
- Pacemakers and defibrillators;
- Nerve stimulators;
- Intracranial clips;
- Intraorbital or intraocular metallic fragments;
- Cochlear implants;
- Ferromagnetic implants;
- Hydrocephalus pump;
- Intra-utrine device (not all types);
- Permanent make-up (not all);
- Tattoos above the shoulders (not all).

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:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2024
Enrollment:	48
Type:	Anticipated

Ethics review

Approved WMO

Date:	18-10-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL86229.058.24