Ultra- High field ImaGing in Huntington*s Disease

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To determine early and subtle MRI changes in premanifest and early manifest HD patients which distinguish them from the healthy population. This includes both structural/quantitative MRI data and MRI-signs of blood-brain barrier (BBB) breakdown. And...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON54262

Source
ToetsingOnline

Brief title
Ultra-HIGH-D

Condition

- Movement disorders (incl parkinsonism)
- Psychiatric and behavioural symptoms NEC

Synonym
autosomal dominant neurodegenerative disease, Huntington's chorea

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 7T MRI, Blood brain barrier, Huntington's disease, MRI changes

Outcome measures

Primary outcome

- The main study endpoint will be the structural and functional changes of the premanifest compared to early manifest and healthy family or gene negative controls, which will be assessed on 7T ultra-high field MR images. We will also use quantitative MRI approaches, since this enables us to detect small structural and anatomical differences which cannot be detected on qualitative MRI acquisitions.

- BBB permeability as determined by DCE-MRI to assess the leakiness of the cerebral vasculature by dynamically measuring the rate of contrast agent transfer from blood into the interstitial space (leakage rate; units: ml.min 1.100g). We will compare BBB permeability in early manifest HD with pre-manifest HD participants.

Secondary outcome

We will assess the relationship between the imaging measures and clinical scores/ disease burden with regression analysis.

We will investigate if gadolinium, injected during MRI, enters tear fluid.

We will investigate if the level of gadolinium correlates with the level of BBB leakage on MRI.

Study description

Background summary

Accurate estimation of clinical disease onset in Huntington*s Disease (HD) remains difficult because motor symptoms develop insidiously and may be subtle, and neuropsychiatric symptoms may precede the onset of motor symptoms by up to 10 years. Reliable biomarkers such as those obtained by ultra-high field magnetic resonance imaging (MRI) may be useful in determining disease onset and course and may be used as a diagnostic biomarker for novel treatment therapies. Furthermore, tear fluid is a source of biomarkers in HD as well. Determining gadolinium in tears may help to discover early blood-brain barrier (BBB) breakdown without MRI.

Study objective

To determine early and subtle MRI changes in premanifest and early manifest HD patients which distinguish them from the healthy population. This includes both structural/quantitative MRI data and MRI-signs of blood-brain barrier (BBB) breakdown. And also to lay the foundation for a longitudinal cohort study that allows to investigate the prognostic implications of these MRI changes. Furthermore, to investigate if gadolinium, injected during MRI, enters tear fluid and to investigate if the level of gadolinium correlates with the level of BBB leakage on MRI.

Study design

This is an observational study in which all participants will be assessed only once. However, patients will be asked for the consent to be contacted about follow-up studies.

Study burden and risks

The MRI that will be performed is non-invasive, but in 1:100/1000 subjects, possible problems can occur on the first contrast solution. Tear fluid collection is painless and without risks, but may be uncomfortable. The eyes may feel dry for a few minutes to hours.

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

General inclusion criterium:
- Between 18 years and 75 years of age

Inclusion criteria pre-manifest participants:
- An UHDRS motor score <= 5
- CAG repeat size of 36 or more
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Inclusion criteria manifest participants:
- An UHDRS motor score > 5
- Disease Stage 1 or 2
- CAG repeat size of 36 or more
- TFC between 7 and 13 (disease stage 1 or 2)

Inclusion Criteria gene negative controls
- a CAG repeat size of 35 or less

Exclusion criteria

- Subjects with contra-indications for a MRI-scan as defined in the MRI screening form of SCANNEXUS such as claustrophobia, subjects carrying

incompatible metallic devices, subjects who have an allergy for intravenous contract or subjects who are pregnant.
- Manifest participants who are not capable of consenting
- Manifest patients not capable of undergoing MRI because of involuntary movements.
- Genotype unknown
- Current participation in a drug trial
- Not agreeing to be informed about incidental findings on the MRI scan
- Known kidney insufficiency

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-09-2023
Enrollment:	60
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	18-07-2022
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-07-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL79009.068.21