NEurodegeneration: Traumatic brain injury as Origin of the Neuropathology

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Encephalopathies
Study type	Observational invasive

Summary

ID

NL-OMON51986

Source
ToetsingOnline

Brief title
NEwTON

Condition

- Encephalopathies

Synonym
boxing dementia, Chronic traumatic encephalopathy (CTE), dementia pugulistica

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Stichting Dioraphte

Intervention

Keyword: Athletes, Chronic Traumatic Encephalopathy (CTE), Neurodegeneration, Repetitive head injury

Outcome measures

Primary outcome

- Neuropsychological performance

- Psychiatric/behavioral symptoms

- Neuropsychological and psychiatric/behavioral progress

- Determination of potential biomarkers CSF

- Collection of MRI data, including DTI. Measurement of cortical atrophy, cavum

septum pellucidum, cortical thinning, white matter changes, spatial

distribution of magnetic susceptibility (QSM) and resting state cortical

activity

Secondary outcome

-

Study description

Background summary

Traumatic brain injury is associated with a higher risk for neurodegenerative disorders later in life. Specifically, repetitive head injury is the cause of the neurodegenerative disorder: chronic traumatic encephalopathy (CTE), which is characterized by accumulation of hyperphosphorylated tau (p-tau), found perivascular at the depths of the sulci in the cerebral cortex. The clinical manifestation of CTE is highly variable, with a range of impairments in cognition, behavior and mood, but no definite consensus about clinical diagnostic criteria for CTE has been reached yet, in order to diagnose CTE during life. Furthermore, the role of (neuro-imaging) biomarkers in CTE diagnostics remain unclear.

Study objective

The primary goal of NEwTON is to study the link between repetitive head injury and neurodegeneration, leading to cognitive, psychiatric and behavioral symptoms as found in CTE. We will collect a prospective cohort of patients at high risk of CTE, with symptoms related to traumatic encephalopathy syndrome (TES) with a history of repetitive head injury and compare this group to matched controlled subjects.
We aim to extensively phenotype the study population, identify the clinical progression, identify potential biomarkers in cerebrospinal fluid (CSF), determine neuro-imaging features.

Study design

The NEwTON study is a single center prospective obervational cohort study

Study burden and risks

The first baseline tests take an average of 6-8 hours for patients from external, 2,5-4 hours for patients who has already visited the memory clinic previously and 2,5 hours for controls subjects, with another two follow-up visits of approximately 2,5 hours for patients. Follow-up tests will include neuropsychological testing and questionnaires. The testing is organized in similar way as in regular memory clinic care. There is no direct benefit for participants, but they will highly contribute to research into CTE
Neuropsychological testing and questionnaires might be considered tiresome, but this depends on the mental resilience of the participant.

CSF collection by a lumbar puncture is also a common procedure in neurology practice (only for patients form external) and we gained a lot of experience in the memory clinic, where all patients undergo a lumbar puncture. A lumbar puncture can cause post-punctional headache in less than 5% of the cases. which is basically self-limiting, however in a few percentage of the cases, a blood patch is needed.
An MRI scan is widely used medical practice. The narrow space and the loud noise can cause some discomfort, but the risk of MRI scans are negligible (when contra-indications are asked well)

Concluding, because of the minimal to negligible risks and the valuable nature of this project (this will be the research first project to CTE in the Netherlands), we consider this burden to be acceptable for participants.

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

Patient:
Repetitive head injury
Age 30 + years
Symptoms have changed from premorbid functioning
Clinical duration of symptoms >12 months
At least 1 core feature
- Cognitive symptoms
- Neurobehavioral dysregulation

Controls:
- Age 30+ years
- No history of participation in organized contact/collision sports,

professional military service
- No reported neurologic, psychiatric or cognitive disorder or symptoms
- No history of clinical significant TBI and/or concussion

Exclusion criteria

- Insufficient knowledge of Dutch language
- Not mentally competent to give informed consent
For patients: MMSE <=18
For patients: A documented concussion or traumatic brain injury within one year before inclusion
For controlgroup: contra-indication for MRI scan according to hospital protocol

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:	Recruiting
Start date (anticipated):	15-07-2021
Enrollment:	115
Type:	Actual

Ethics review

Approved WMO

Date:	28-05-2021

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-02-2023
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	NL74662.029.20