PET imaging of neuroinflammation in mild traumatic brain injury

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON38412

Source
ToetsingOnline

Brief title
Neuroinflammation in mTBI

Condition

- Neurological disorders NEC

Synonym
mild traumatic brain injury, neurological disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Mild traumatic brain injury, Neuroinflammation, Positron Emission Tomography

Outcome measures

Primary outcome

The [11C]-PK11195 binding potential in the brain, and the performance in the neuropsychological tests will be the primary parameters.

Secondary outcome

Secondary study parameters are white matter integrity, MRI Spectroscopy and serum proteins indicative of inflammation.

Study description

Background summary

Mild Traumatic Brain Injury (mTBI) represents approximately 85% of the hospital admissions for traumatic brain injury, which make it the most common neurological disorder generated by external trauma. Almost all mTBI patients (86%) report one or more symptoms the day after the injury, and 15% of them still report symptoms after a year. These cognitive disturbances have a major impact on their lives, e.g. return to work and/or not able to participate in social activities. The reason for the persistence of symptoms may be an inflammatory process in the brain in response to the injury. This inflammation can pass unnoticed by standard imaging techniques, such as computed tomography (CT) and structural magnetic resonance imaging (MRI), but may be visualized by Positron Emission Tomography.

Study objective

The primary objective of this study is to determine if neuroinflammation is present in patients with mild traumatic brain injury, using [11C]-PK11195 PET. The secondary objective is to determine if there is a correlation between [11C]-PK11195 binding and the degree of cognitive deficits, white matter integrity and serum proteins indicative of inflammation.

Study design

This is a observational, cross-sectional study, designed to identify if neuroinflammation is present in patients with mTBI. Such patients will be recruited by the Neurology Department of the University Medical Center Groningen 4 to 6 weeks after the injury, during the follow-up. Patients, that still have complaints at that time, will be asked by their neurologist to participate in the study. Healthy volunteers will be recruited via advertisement in public buildings and local newspapers. Interested subjects will be approached by the researchers and will receive both oral and written information about the study. Subjects will have two weeks time for reflection to decide whether or not to participate in the study. Those that volunteer to participate are asked to sign the written informed consent and it will be determined if they meet the inclusion and exclusion criteria.
Patients with continuing complaints 4 to 6 weeks, after the accident, will undergo a structural MRI and neuropsychological tests, as part of the normal follow-up procedure. Patients will undergo extra neuropsychological tests if specific tests are not part of the normal follow-up procedure. At this point subjects with abnormalities in the MRI, or with underachievement or depression results during the neuropsychological test will be excluded from the study. Those patients that surpass all the exclusion criteria will be scheduled for PET and MRI scans within 8 to 12 weeks after the injury, with a maximum of one week between the PET and MRI scan. During the PET scan, blood samples will be taken, to measure serum markers of inflammation.
From healthy volunteers that are willing to participate a blood sample will be taken to determine C-reactive protein (CRP) and will also undergo the same neuropsychological tests. Those subjects with serum values of CRP above 10mg/L will be excluded from the study. In addition, subjects that show underachievement or depression during the neuropsychological tests will also be excluded. The remaining volunteers will undergo PET and MRI scans, with a maximum of one-week interval. Blood samples will also be taken during PET scan.

Study burden and risks

The subjects have to fill in a questionnaire and undergo neuropsychological tests, a MRI scan and a PET scan. A total of 170 ml of blood will be taken for determination of serum markers of inflammation and for PET scan data-analysis. For the PET scan, the arterial catheterization can cause discomfort and the subjects are exposed to radioactivity with minor to moderate risk. The patients will not obtain direct benefit from the study but, if positive results are obtained, it may lead to new therapies and diagnosis techniques for mTBI.

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

All subjects:
-Age above 18 and below 50 years.
-Written informed consent for participation.;Patients only:
-Diagnosis of mild traumatic brain injury.
-No abnormalities in the structural MRI during neurologist follow-up, 4-6 weeks after the injury.

Exclusion criteria

All subjects:
-The use of benzodiazepines.
-The use of anticoagulants or having coagulation disorder.
-Use of somatic medication that may affect the immune system.
-Use of any investigational drug.
-Current or recent (<1 year) alcohol or substance abuse.
-Current or recent (<4 weeks) infectious or inflammatory disease.
-Current systemic disease.

-Major metabolic disease.
-Somatic, organic or neurological disorder (other than mTBI for patients).
-Participation in a scientific research study (<1 year) involving radiation.
-Claustrophobia.
-Presence of materials in the body that can be magnetized.;For healthy volunteers:
-Presence of infection of inflammation.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-03-2013
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	1-(2-chlorophenyl)-N-[11C]methyl-N-((R)-1-methylpropyl)-3-isoquinoline carboxamide
Generic name:	[11C]-PK11195

Ethics review

Approved WMO

Date:	24-07-2012

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-10-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2012-001153-44-NL
CCMO	NL36770.042.12