In vivo imaging of neuroinflammation in Parkinson's disease: A first in human purinergic P2X7 receptor PET study

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To assess the potential of the PET-tracer [11C]SMW139 to investigate the role of P2X7R, a cell surface receptor upregulated in activated microglia, in neuroinflammation in PD. The aim is to find the optimal tracer kinetic model which can be used to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON44519

Source
ToetsingOnline

Brief title
P2X7R-PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Michael J. Fox Foundation

Intervention

Keyword: Neuroinflammation, P2X7 receptor, Parkinson's disease, Positron Emission Tomography (PET)

Outcome measures

Primary outcome

The primary outcome is the difference in [11C]SMW139 binding between the patient group and the healthy controls, and to identify the optimal tracer kinetic method for quantification of [11C]SMW139 in vivo binding.

Secondary outcome

Secondary, in the patient group [11C]SMW139 binding will be determined for disease specific regions of interest. A last objective is a possible correlation between [11C]SMW139 binding and clinical motor impairments (UPDRS motor score and modified Hoehn & Yahr stage) in the patient group.

Study description

Background summary

Microglia activation can be used as an indirect marker to assess the contribution of neuroinflammation to the pathophysiology of PD. For the past twenty years there have been studies on neuroinflammation and its impact on several pathologies of the central nervous system using TSPO PET tracers. However, TSPO as a microglial imaging target has several limitations such as intracellular localization, and various polymerization states resulting in binding differences.

Study objective

To assess the potential of the PET-tracer [11C]SMW139 to investigate the role of P2X7R, a cell surface receptor upregulated in activated microglia, in neuroinflammation in PD. The aim is to find the optimal tracer kinetic model which can be used to understand the in vivo tracer kinetics both in PD patients

and healthy subjects.

Study design

We included 7 Parkinson's disease patients and 7 healthy controls to have complete data of 5 patients and 5 controls. For both the PD patients and healthy controls this study will consist of three parts:
1. First study visit at the neurology outpatient clinic for a neurological and physical examination, questionnaires and venous blood sampling.
2. MR scan will be acquired.
3. [11C]SMW139 PET-CT scan with arterial blood sampling.

Intervention

N/A

Study burden and risks

Risks associated with participation in this study are related to 1) radiation exposure, 2) idiosyncratic reaction to the tracer, 3) placement of in intra-venous and intra-arterial catheter, 4) discomfort during the scanning, 5) blood sampling, 6) coincidental finding.

1) The [11C]SMW139 PET-CTscans will result in a total radiation burden of 3 mSv. This falls in the International Commission on Radiological Protection (ICRP) risk category lib. Radiation exposure in this category is justified if it is directly aimed at the cure or prevention of disease, as is the case for this protocol.
2) Based on the extensive experience with PET-tracers in our center, idiosyncratic reaction to the venously administered tracer [11C]SMW139 is not rendered likely. During each injection of the tracer a physician will be present.
3) Intravenous and intra-arterial cannulation is associated with a very small risk of infection and bleeding. This will be prevented by the use of proper techniques by experiences personal.
4) It may be uncomfortable to lie motionless in the MRI and PET scanners and it may cause some subjects to fell anxious. Subjects will be made acquainted with the surroundings beforehand. Moreover, our staff will be available to provide support, reduce anxiety, optimise the comfort of subjects and if requested remove subjects from the scanner.
5) Adverse effects of blood sampling will be minimised by exclusion of subjects with low haemogolibin levels (in males Hb < 8.0 mmol/litre, in females Hb < 7.0 mmol/litre). No more than 250 ml blood will be withdrawn during the total PET procedure and screening.
6) With the blood tests and MRI-scan a coincidental finding may occur. lf such a new finding has consequences for the subject, the subject and his/her general

practitioner will be informed.If a patient or healthy control does not want to be informed on such a coincidental finding, this subject can not partake in this trial.

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

For healthy control subjects:
- Subject is between 45 and 80 years (male/female).
- Subject is judged to be in good health by the investigator on the basis of medical history, physical examination including vital signs and clinical laboratory tests.
- No clinical evidence of a movement disorder as evidenced by careful neurological examination by a neurologist or an MD instructed by a movement disorder specialist.;For Parkinson's patients:

- Subject is between 45 and 80 years (male/female)
- Subject has a clinical diagnosis of Idiopathic Parkinson*s Disease (IPD) according to UK PD brain bank criteria, with at least 2 of the cardinal signs of the disease: resting tremor, bradykinesia or rigidity
- Subject has a modified Hoehn and Yahr stage * 3

Exclusion criteria

- Subject has parkinsonism not caused by IPD (e.g. drug-induced, metabolic disorders, encephalitis, vascular PD, atypical PD)
- Subject has a history of another major neurological disorder or history of significant brain lesion (e.g. tumor, stroke)
- Subject has significant structural brain lesions on T1 or T2 MRI, unrelated to IPD.
- Subject has a history of any major disease that may interfere with radiotracer investigations (especially liver and kidney disease, or uncontrolled diabetes).
- Subject chronically uses anti-inflammatory medication (steroids, non-steroidal anti-inflammatory drugs (NSAIDs), aspirine, paracetamol,...)
- Previously subject has had exposure to ionizing radiation (> 11 mSv) in other research studies within the last 12 months.
- Inability to undergo PET and MRI scans (eg: metal objects in or around the body, claustrophobia or cannot tolerate confinement during PET or MR scanning procedures, unable to lie sufficiently still in the scanner for 90 minutes, or has tremor with significant head movements)
- Subject has had surgery, significant blood loss (> 500 ml), donated blood or participated in another clinical trial using investigational drug(s) within 30 days prior to the imaging day.
- History of alcohol and/or drug abuse
- Subject has a known allergy to lidocaine (which may be used as a local anesthetic for the placement of the arterial catheter).
- Subjects has an allergy including, but not limited to, hay fever, dust mite allergy and allergies to cats or dogs.
- Subjects has asthma ;Additionally for healthy controls: Subject has an elevated likelihood for hereditary Parkinson*s disease as assessed by family history

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-12-2017
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[11C]SMW139
Generic name:	NA

Ethics review

Approved WMO Date:	20-09-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2017
Application type:	First submission
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
EudraCT	EUCTR2017-002415-33-NL
CCMO	NL62257.029.17