Assessing cholinergic innervation in Parkinson*s disease using the PET imaging marker [18F]Fluoroethoxybenzovesamicol

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

Summary

ID

NL-OMON43478

Source
ToetsingOnline

Brief title
Cholinergic PET imaging in Parkinson*s disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson, Parkinson's disease

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: Cholinergic, Parkinson's disease, PET imaging

Outcome measures

Primary outcome

The main endpoint of this study is the difference in VAChT brain binding on a [18F]FEOBV PET-scan between PD patients and healthy control subjects.

Secondary outcome

The secondary endpoints of this study are:

- the correlation between (1) distribution volume (VT) and binding potential (BP) as quantitative endpoints and (2) the uptake, expressed as SUV, in selected brain regions. This is to determine the best time point for short static scanning as an alternative for extensive dynamic scanning and confirm previous literature findings.
- The percentage change in mean SUV between test and retest to assess test-retest variability.
- Neuropsychological assessment

Study description

Background summary

Cholinergic neurons play an important role in neurotransmission within the central nervous system (CNS). They are involved in complex functions like memory, learning, recognition, attention, consciousness, regulation of sleep-wake cycles and maintenance of posture and gait. Cholinergic neuron

degeneration in the neocortex and hippocampus of the CNS, is an important neurochemical change observed in several neurodegenerative diseases, including Parkinson*s disease (PD) and Alzheimer*s disease (AD). Therefore, assessment of the vesicular acetylcholine transporter (VAChT) as an important molecular target in the cholinergic circuit, has sparked interest in the development of radiotracers for studying this target in vivo. Preclinical studies show the VAChT tracer (-)-5- [18F]Fluoroethoxybenzovesamicol ([18F]FEOBV) to be potentially useful in detecting cholinergic lesions in vivo. A previous [18F]FEOBV PET study confirms that the tracer binds to VAChT with the expected in vivo human brain distribution. The use of [18F]FEOBV as a PET imaging marker of cholinergic innervations has, however, only been studied in healthy human volunteers and no data is available on patients.

Study objective

The main objective of this study is to evaluate the differences in [18F]FEOBV binding between PD patients and healthy control subjects, in order to evaluate the clinical feasibility of [18F]FEOBV as a cholinergic imaging ligand in PD.

Secondary objectives are:
- Confirming previous findings on [18F]FEOBV validation, in order to establish an optimal scan protocol for a static scan.
- The assessment of test-retest variability in both healthy control subjects and PD patients.
- Explorative analysis of the relationship between neuropsychological performance and cholinergic innervation

Study design

In order to establish the difference in [18F]FEOBV binding between PD patients and healthy control subjects, the study will be conducted in three parts.
The first part of the study is to establish [18F]FEOBV as a PET tracer for application in clinical research by confirming previous findings on [18F]FEOBV validation. This will include dynamic scanning of 3 healthy control subjects in 3 imaging sessions (0-120, 150-180, 210-240 min after injection of [18F]FEOBV). From this part of the study, the optimal short static scan period will be determined by comparing relative uptake values with the results of kinetic analysis.
Part 2 of the study is to evaluate differences in [18F]FEOBV in Parkinson*s disease and healthy controls. For this, the three dynamic scans of part 1 will be used and an additional 7 healthy control subjects and 10 PD patients will be included for a simple static scan (period determined after part 1 of the study).

All 20 subjects included in Part 1 and 2 of the study will undergo a neuropsychological assessment. This assessment will take 30-45 minutes and will

be performed on the same day as the PET or the MRI scan.

In part 3, test-retest variability is evaluated in both groups. Of each group, 5 patients will undergo a short second static scan.
All subjects will be screened within 30 days before the PET scan for demographic information and detailed clinical history.

Study burden and risks

Burden: Participating in the study will take 1 or 2 visits of the subjects to University Medical Center Groningen (UMCG). Participants will undergo one brain MRI, a neuropsychological assessment and one or two [18F]FEOBV PET-scan of the brain.
Risks: The risks involved in this study is related to the PET imaging. The [18F]FEOBV PET scan will result in a radiation dose of 4.6 mSv for one scan, after administration of 200 MBq. For subjects undergoing two scans in order to evaluate test-retest variability, radiation dose is 9.2 mSV (ICRP risk category IIb).

Benefits: With this study we will quantify the differences in cholinergic function between PD patients and healthy aged-matched volunteers. In addition we will determine the test-retest variability. By combining this information we will be able to perform power calculations for the assessment of longitudinal changes. This is essential to follow the normal clinical development as well as to investigate the effect of therapeutic approaches once they become available. An additional benefit of [18F]FEOBV is that it provides a direct and specific measurement of presynaptic cholinergic function only rather than both pre- and post-synaptic expression. This gives a more specific measurement of cholinergic functioning and can be helpful in determining underlying pathology of neurodegenerative diseases.

Group relatedness: Cognitive impairment in Parkinson*s Disease is associated with cholinergic and dopaminergic deficiencies in the brain. Although dopaminergic neuronal degeneration is quite well established, the rate and extent of the cholinergic neuronal degeneration in the course of PD is unknown. It is also unclear how cholinergic degeneration contributes to cognitive deficits found in early and more advanced PD. The use of [18F]FEOBV as a PET imaging marker offers the opportunity to study cholinergic innervation in vivo in Parkinson*s disease and other neurodegenerative disorders.

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

Control Subjects:
- Age between 45 - 65 years
- Willingness to cooperate and sign written informed consent
- No prior history of neurologic or psychiatric illness
- Able and fit enough to participate in this study;Patient Group:
- Diagnosis Parkinson*s disease
- Disease duration between 3 and 10 years.
- Age between 45 - 65 years
- Willingness to cooperate and sign written informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- The refusal to be informed about an unforeseen clinical finding
- Pregnant women, breast feeding
- Exhibition to a radiation dose for other reasons (e.g. participation in other research trial),

exceeding the maximum annual dose.
- Anticoagulant medication, antiplatelet agents used in the 5d before the imaging visit
- Contra-indication for MRI-scanning (metal parts in the body)
- Other neurological conditions, more specifically neurodegenerative disorders and brain lesions.
- Treatment with deep brain stimulation

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:	Recruitment stopped
Start date (anticipated):	19-10-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]-Fluoroethoxy-benzovesamicol
Generic name:	[18F]-Fluoroethoxy-benzovesamicol

Ethics review

Approved WMO

Date:	24-05-2016
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-09-2016
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	EUCTR2015-005679-26-NL
CCMO	NL56173.042.15