Relation of short-latency afferent inhibition to the cholinergic system

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To validate SAI as a measure for cholinergic innervation by relating SAI directly to [18F]FEOBV PET imaging. The secundary aims are as follows: - To assess the correlation between SAI and cognitive functioning, motor symptoms, RBD, walking speed,...

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

Summary

ID

NL-OMON49949

Source
ToetsingOnline

Brief title
SAICS

Condition

- Movement disorders (incl parkinsonism)
- Cognitive and attention disorders and disturbances

Synonym
hypokinetic rigid syndrome, Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Acetylcholine, FEOBV, Parkinson's disease, SAI

Outcome measures

Primary outcome

The main study parameter resulting from the SAI-measurement is percentage of conditioned motor evoked potential (MEP) versus unconditioned MEP. The main study parameter resulting from [18F]FEOBV PET imaging is the mean cortical tracer binding. We will perform a correlation analysis between these parameters as a main outcome measure.

Secondary outcome

- Tracer binding in different ROIs and per voxel.

- Outcome of all questionnaires and clinical tests as mentioned under E4.

- Resting-state functional connectivity.

Study description

Background summary

Parkinson*s disease (PD) is a complex neurodegenerative disorder, involving multiple neurotransmitter systems. It has been shown that degeneration of the cholinergic system in PD is related to both motor and nonmotor symptoms, including cognitive impairment, REM-sleep behavioural disorder (RBD), visual hallucinations (VHs), hyposmia, postural instability and gait disorder. Several methods exist for imaging of the cholinergic system in vivo, although they are not routinely performed in clinical practice due to their cost, limited availability and radiation burden for the patient. Short-latency afferent inhibition (SAI) might be a relatively cheap and non-invasive alternative for fast in vivo assessment of the cholinergic system.

Study objective

To validate SAI as a measure for cholinergic innervation by relating SAI

directly to [18F]FEOBV PET imaging. The secundary aims are as follows:
- To assess the correlation between SAI and cognitive functioning, motor symptoms, RBD, walking speed, VHs, olfactory function and speech.
- To explore the accuracy of resting-state functional connectivity as a reflection of cholinergic innervation in Parkinson*s disease.
- To explore to what extend SAI and resting-state functional connectivity can pick up changes in cognitive functioning, motor symptoms, RBD, walking speed, VHs, olfactory function and speech that result from active perturbation of the cholinergic system.

Study design

This is a method-comparison study aiming to assess the correlation between SAI and [18F]FEOBV PET.

Study burden and risks

In de PET imaging, 200 MBq is injected, resulting in a radiation burden of 4.6 mSv. For attenuation correction a low-dose CT is added to each PET scan performed. This accounts for an additional radiation burden of 1.5 mSv. According to recommendations from the International commission of radiological protection (ICRP) a dose of 1-10 mSv in one year for volunteers for biomedical research, falls in a moderate risk category (The 2007 recommendations of the international commission on radiological protection. ICRP publication 103.2007). There are no known risks of paired-pulse TMS, although it may lead to a mild transient headache due to contraction of scalp muscles. (Rossi et al. 2009).
For the PD-D patients, treatment with rivastigmine (the ChEI of choice) may be delayed until after the measurements. This delay includes the time of the patient to consider participation and the time to schedule the measurements. This means that the symptoms that are supposed to be treated with rivastigmine might persist longer. However, rivastigmine is not prescribed in an acute setting and there is no reason to believe that rivastigmine can halt the underlying pathology of the symptoms.

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

- Willingness to cooperate and sign written informed consent
Patients:
- Clinical diagnosis of idiopathic Parkinson*s disease by a neurologist.

Exclusion criteria

- Incapable to provide informed consent
- Treatment with anticholinergics
- Current or recent treatment with ChEIs
- Presence of deep brain stimulation implants
- (Suspected) pregnancy
- Migraine
- Epilepsy
- Participation in a scientific research study during the past year involving radiation
- MRI contra-indications, e.g.
o Ferrous objects in or around the body (e.g. braces, pacemaker, metal fragments)
o Claustrophobia
- Insufficient knowledge of the Dutch language
Control subjects:
- History of neurological or neurodegenerative disorder
Parkinson Disease Dementia:

- Unsafe or irresponsible to postpone treatment with cholinesterase inhibitor, according to treatment provider

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):	10-06-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	10-03-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-11-2020
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-08-2021
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
CCMO	NL72060.042.19
Other	NL7838