Follow-up of FDG-PET imaging in idiopathic REM Sleep Behavior Disorder (RBD)

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PDRP expression in iRBD patients increases over time and may be used to track / predict phenoconversion to parkinsonism.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27392

Bron
NTR

Verkorte titel
REMPET2

Aandoening

idiopathic Rapid Eye Movement Sleep Behavior Disorder (iRBD), Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB), Multiple System Atrophy (MSA)

Ondersteuning

Primaire sponsor: Stichting Parkinsonfonds Nederland + Parkinsonfonds Deutschland
Overige ondersteuning: Stichting Parkinsonfonds Nederland + Parkinsonfonds Deutschland

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Increase in absolute PDRP score saying something about disease state / progression

Toelichting onderzoek

Achtergrond van het onderzoek

Neurodegenerative brain diseases can be difficult to diagnose, particularly in the early stages. [18F]FDG-PET allows for visualization of cerebral glucose metabolism. If, say, a cohort of healthy controls and a cohort of disease patients are taken, a (mathematical) multivariate spatial covariance method known as Scaled Subprofile Model / Principal Component Analysis (SSM/PCA) can identify specific brain regions with relative hyper- or hypometabolism in the disease relative to healthy subjects. This is known as a "disease-related metabolic brain pattern"; these have been identified in a number of different disorders. The expression of these patterns can then be quantified in new subject scans; scores tend to increase with disease progression and decrease with effective treatment. In the UMCG, in collaboration with Prof. David Eidelberg's group at the Feinstein Institute in NY, we have implemented the SSM/PCA method, and have defined a number of patterns -- including for Parkinson's disease (PD), Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP), Alzheimer's Disease (AD), and Dementia with Lewy Bodies (DLB).
Idiopathic rapid eye movement sleep behavior disorder (iRBD) is a parasomnia, characterized by loss of muscle atonia during REM sleep, resulting in (often violent) dream-enacting behaviors such as shouting, hitting, and kicking. In 80-90% of cases, iRBD is known to be prodromal for alpha-synucleinopathies / parkinsonian disorders such as PD, DLB, or more rarely, MSA. This makes iRBD patients an important group for potential parkinsonian disease-modifying drug trials. By using the SSM/PCA method, we can investigate whether iRBD patients exhibit pathological expression of these disease-related patterns. We also wish to see if and how pattern expression can be used to predict phenoconversion to parkinsonism.
In the previous study (REMPET1: METC2012/442) which served as a baseline proof-of-principle, it was shown that over half of the (non-demented, non-parkinsonian) iRBD patients already expressed the PD-related metabolic brain pattern (PDRP). In some of the subjects, the pattern was even expressed without reduced nigrostriatal dopaminergic transporter (DAT)-binding as seen on DAT-SPECT scans (see: www.doi.org/10.1002/mds.27094).
REMPET2 has longitudinally repeated FDG-PET scans in 20 iRBD subjects from REMPET1; preliminary results show that PDRP expression increases over time and is correlated to . Additionally, we are currently busy with recruiting more subjects in this multicenter study, with a goal of including 100 iRBD patients.

Doel van het onderzoek

PDRP expression in iRBD patients increases over time and may be used to track / predict phenoconversion to parkinsonism.

Onderzoeksopzet

REMPET1: Baseline FDG-PET imaging occurred between 2014-2015.
REMPET2: Follow-up FDG-PET imaging of 20 iRBD subjects from REMPET1 occurred in 2018.
Inclusion of new subjects: 2018-present.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

-Age between 40 and 80 years old
-(For women) postmenopausal (> 1 year no menses)
-Intellectual capacity to understand the study
-Diagnosis of RBD according to the criteria of International Classification of Sleep Disorders (ASDA Criteria 2005): The subject has a complaint of violent or injurious behavior during sleep. Limb or body movement is associated with dream mentation. At least one of the following occurs: Harmful or potentially harmful sleep behaviors. Dreams appear to be “acted out.” Sleep behaviors disrupt sleep continuity. Video-polysomnographic (PSG) monitoring demonstrates at least one of the following electrophysiological measures during REM sleep: Excessive augmentation of chin electromyography (EMG) tone. Excessive chin or limb phasic EMG twitching, irrespective of chin EMG activity, and one or more of the following clinical features during REM sleep: excessive limb or body jerking; complex, vigorous, or violent behaviors; absence of epileptic activity in association with the disorder. The symptoms are not associated with mental disorders, but may be associated with neurological disorders. Other sleep disorders (e.g., sleep terrors or sleepwalking) can be present, but are not the cause of the behavior.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

-Claustrophobia (for the MRI scan, further contraindications are given)
-Abuse of drugs or alcohol at present or in the past (as determined by disclosed medical history)
-Kidney diseases with elevated levels of blood creatinine, liver diseases with elevated levels of blood transaminases (at least 3 times as high than normal), or an elevated blood level of gamma-GT (at least 5 times higher than normal)
-Hyperglycemia before the FDG PET scan (> 7 mmol/l)
-Use of benzodiazepines during the day before the FDG-PET scan
-Structural cerebral lesion or any other neurological disease which can interfere with the analysis of the image data (for example, a stroke in the past)
-Diagnosis of any parkinsonism or dementia before baseline FDG-PET imaging
-If subjects do not want to be informed about an unforeseen clinical finding

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-01-2018
Aantal proefpersonen:	100
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	30-09-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8057
Ander register	METC UMCG : MECT2017/225

Resultaten

Samenvatting resultaten
from REMPET1: www.doi.org/10.1002/mds.27094, www.doi.org/10.2967/jnumed.117.202242
(First REMPET2 manuscript currently in progress)