Clinical follow-up on the development of impulse control disorders in Parkinson's disease

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON47691

Source
ToetsingOnline

Brief title
Follow-up ICD in PD

Condition

- Other condition
- Movement disorders (incl parkinsonism)
- Mood disorders and disturbances NEC

Synonym
shaking palsy

Health condition

impulsscontrolestoornissen

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Parkinson Vereniging

Intervention

Keyword: depression, impulse control disorders, impulsivity, Parkinson's disease

Outcome measures

Primary outcome

- Striatal dopamine transporter availability (measured with DaT SPECT) at

baseline

- presence and severity of symptoms of impulse control disorders at baseline

and follow-up

Secondary outcome

- course of the symptoms of depression, anxiety, impulsivity and executive

functioning with progression of the disease and possible effects of treatment.

- temporal relation between the symptoms of depression, anxiety, impulsivity

and cognitive functioning.

Study description

Background summary

Parkinson's disease (PD) is a neurodegenerative disorder that is associated with progressive degeneration of dopaminergic neurons (Groenewegen et al. 1997). Apart from the characteristic motor symptoms such as bradykinesia, rigidity, tremors and postural instability, PD is also associated with neuropsychiatric symptoms such as depression, anxiety and impulse control disorders (ICD) (Aarsland et al. 2012). The neuropsychiatric disorders often have a higher impact on the quality of life than the motor symptoms (Mamikonyan

et al. 2008). The prevalence of ICD in PD is approximately 14% (Voon et al. 2011). ICD enclose a spectrum of disorders that show commonalities with obsessive-compulsive and related disorders and substance use disorders (van den Heuvel et al., 2010). ICD are frequently described as behavioral addictions in which patients no longer have the ability to suppress an impulse, drive or urge that is potentially dangerous to the patients themselves and/or their surrounding (American Psychiatric Association, 1994; van den Heuvel et al., 2010). Examples of ICD include compulsive shopping, compulsive eating, pathological gambling, hypersexuality, punding and dopamine dysregulation syndrome (van den Heuvel et al. 2010; Voon et al. 2011). Risk factors associated with ICD in PD are young age, an early disease onset, male gender, depression, novelty-seeking personality traits and a positive (family) history of substance abuse (Voon et al. 2009; Wu et al. 2009). ICD seldom occur on their own in PD but seem to be a consequence of dopamine replacement therapy, mainly dopamine agonists (van den Heuvel et al. 2011; Voon et al. 2011). Dopaminergic projections from the ventral tegmental area have an important neuromodulatory role in the limbic fronto-striatal circuit that connects cortical areas, such as the anterior cingulate cortex and orbitofrontal cortex with the ventral striatum, i.e. caudate nucleus and nucleus accumbens (Groenewegen et al. 1997; Groenewegen and Trimble 2007; Leh et al. 2007; Haber and Calzavara 2009). The ventral striatum seems to have an important role in the pathophysiology of both depression and ICD in PD (Voon et al. 2011; Vriend et al. 2013; Vriend et al. 2013) and is also involved in the initiation of addictive behavior (Everitt et al. 2008). In a recently published review we describe a model in which degeneration of mesolimbic dopamine projections from the ventral tegmental area towards the ventral striatum can directly result in symptoms of depression. Degeneration of ventral striatal dopaminergic projections combined with dopamine replacement therapy could subsequently lead to the disturbance of reward-related processes and could in that way lead to the development of ICD. This model is corroborated by studies, including those from our own research group, that show that depressive symptoms as well as ICD symptoms are associated with reduced striatal dopamine transporter (DaT) availability (Weintraub et al. 2005; Rektorova et al. 2008; Hesse et al. 2009; Cilia et al. 2010; Lee et al. 2013; Voon et al. 2013; Vriend et al. 2013; Vriend et al. 2013). DaT availability, measured with a SPECT scan, is an in vivo marker for the integrity of dopaminergic projections. Nevertheless, studies on the association between ICD and DaT availability were conducted in relatively small sample sizes. Moreover, to our knowledge no prior study has investigated the course of neuropsychiatric symptoms in a PD patient cohort for an extended period of time; from diagnosis and the start of dopamine replacement therapy until four years into the disease. Our study design also allows us to investigate the (temporal) relation between the symptoms of ICD, depression and anxiety, something that has so far received little scientific attention.

If our previous results of reduced striatal DaT availability in PD patients with ICD symptoms are confirmed, DaT SPECT scans can in the future be utilized

to screen PD patients on their predisposition and risk to develop ICD after commencing dopamine replacement therapy. These patients can thereafter receive a distinct treatmentplan to avoid the development of these symptoms. We expect that patients that develop an ICD after commencing dopamine replacement therapy will exhibit reduced DaT availability at baseline compared with PD patients that do not develop an ICD and will also show higher incidences of symptoms of depression and anxiety. Furthermore, we are interested in the relation between these neuropsychiatric symptoms (ICD, depression and anxiety) and cognitive functioning, most notably executive functioning. Although it has previously been found that executive functioning is disturbed in patients with ICD but without PD (Goudriaan et al. 2004), no study has yet investigated this in PD.

Study objective

the primary aim of this research is to investigate whether the development of ICD in PD after commencing dopamine replacement therapy can be predicted with baseline DaT availability. We also want to look at the (temporal) relation between the symptoms of ICD and deficits in impulsivity, executive functioning and de presence of symptoms of depression and anxiety.
The results of this study can contribute to:
1) a better understanding of how the DaT SPECT scan, that is often acquired as part of the diagnostic process, can be used in the clinic to help determine what the risk is of developing ICD in PD patients prior to commencing dopamine replacement therapy. This is relevant for the type of dopamine replacement therapy that is prescribed and/or the intensity of routine psychiatric evaluations.
2) insight into the course of, and the temporal relation between the symptoms of ICD, anxiety and depression to allow the formulation of a more effective (and simultaneous) treatment for these frequently co-occuring neuropsychiatric symptoms in PD.

Study design

Follow-up on medication-naive Parkinson patients from which a SPECT scan was acquired at baseline as part of the diagnostic process with a [123I]N-*-Fluoropropyl-2*-carbomethoxy-3*-(4-iodophenyl)nortropane ([123I]FP-CIT) tracer that binds to the dopamine transporter (DaT). These patients are subsequently prescribed dopamine replacement therapy. Follow-up measurements are acquired at six months, 1 year, 2 years and 4 years after the DaT SPECT scan. The follow-up measurements will be planned as close as possible to the ideal date, which will be defined from the date of day screening. A maximal deviation of a month from this ideal date will be utilized. At each timepoint patients are asked to fill out a number of questionnaires that determine the presence and severity of neuropsychiatric symptoms (ICD, depression, anxiety). The frequency and the duration of the follow-up (measurements) has been chosen in such a way that it maximizes the detection of

ICD symptoms. The average latency for developing ICD symptoms after commencing dopamine replacement therapy was in previous research 11.4 months (Vriend et al. 2014), although other research shows that there is al lot of inter-individual variability and ranges from a few months to several years (Bastiaens et al. 2013). Moreover, the duration of our follow-up also allows us to study the course of the symptoms of depression, anxiety and impulsivity and cognitive functioning during a longer period of disease progression.

Study burden and risks

In this observational study only questionnaires and computertasks are added to the regular treatment of Parkinson's disease. There's no intervention. The study has been classified as 'negligible risk' since we do not expect any adverse effects of filling out questionnaires and executing (computer)tasks which, for the most part, are also performed as part of routine clinical care. In a period of four year subjects are asked to visit the outpatient clinic of the VU University medical center four times.At one timepoint patients are asked to fill out questionnaires at home and post it back. If patients perceive the burden of traveling to the hospital as too high, the measurements can also be performed in the patients home. Every visit to the VU University medical center will take approximately one to two hours. the total time investment for all the visits sums up to eight hours in a period of four years. The burden for patients is therefore quite low. To further decrease the burden we will try to schedule the visits so that they are on the same day as the regular outpatient visits or perform the measurements at the patient's home.

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

medication-naive (de novo) Parkinson's disease patients who underwent a dopamine transporter SPECT scan and MRI scan at baseline in the VU University medical center.

Exclusion criteria

use of medication at baseline that influences DaT tracer binding (including serotonin reuptake inhibitors).

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-09-2014

Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	16-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2019
Application type:	Amendment
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
CCMO	NL47913.029.14