The influence of deep brain stimulation on reward and attention in Parkinson*s disease

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

Summary

ID

NL-OMON40948

Source
ToetsingOnline

Brief title
Parkinson*s disease and reward

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit
Source(s) of monetary or material Support: ERC-2012-AdG 323413-REWARDVIEW (Theeuwes PI)

Intervention

Keyword: attention, deep brain stimulation, Parkinson's disease, reward

Outcome measures

Primary outcome

Primary study parameters are reaction time and accuracy (first block), and

perseveration/response reversal of earlier choices (block 2).

Secondary outcome

Not applicable

Study description

Background summary

Parkinson*s disease is primarily a movement disorder stemming from a loss of dopamine producing cells in the substantia nigra. Symptoms, such as tremor, rigidity, postural instability and slowness of movements, arise when a large fraction of these neurons is lost. However, as dopamine networks are widespread throughout the brain, emotion and cognition also change as a function of reduced dopamine signalling. Dopamine replacement therapy can ameliorate these symptoms but may also lead to impulse control behaviors (ICBs), which have a reward-oriented aspect, such as addiction to dopaminergic medication, pathological gambling and increased sexual and eating desire. This is not surprising as dopamine is involved in the circuits that control motivation (Berridge 2007), reward-processing (Wise 1998; Kapogiannis, Campion et al. 2008; Cools, Frank et al. 2009; Buckholtz, Treadway et al. 2010), and attention (Chamberlain, Robbins et al. 2007). The prevalence of ICBs is thought to be 6% in patients not using dopamine replacement therapy and 17% in patients using dopamine agonist treatment (Voon, Hassan et al. 2006; Weintraub, Siderowf et al. 2006; Weintraub, Koester et al. 2010). Why certain patients develop ICBs is not yet fully understood, although important leads have recently emerged (Djamshidian, Averbeck et al. 2011). Some of these factors relate to premorbid personality features (Djamshidian, O'Sullivan et al. 2011): while Parkinson*s patients without ICBs are typically risk averse and anhedonic (Ishihara and Brayne 2006), those who develop ICBs appear to be more novelty seeking (Voon, Thomsen et al. 2007). Reducing ICBs requires a reduction in dopamine replacement therapy, which is possible in combination with deep brain stimulation (DBS), for instance of the subthalamic nucleus (STN). With this

technique, patients are implanted with an electrode that runs from a subcutaneously placed pulse generator directly to a specific brain region such as the STN. Patients with Parkinson*s disease can benefit greatly from stimulation of the STN. Unfortunately, DBS of the STN may also result in hypersexuality (Doshi and Bhargava 2008), mania (Kulisevsky, Berthier et al. 2002), and impulsivity (Frank, Samanta et al. 2007; Ballanger, van Eimeren et al. 2009). This suggests that even when dopaminergic medication is reduced, stimulation of a node in a dopaminergic pathway (e.g., STN) may result in impulsive, reward-oriented behavior. Therefore, we wish to investigate the effects of STN DBS on how rewards steer visual selective attention. While many studies on Parkinson*s disease focus on alterations in higher order cognition (Cools, Barker et al. 2001; Cools, Stefanova et al. 2002; Cools, Miyakawa et al. 2010; Obeso, Wilkinson et al. 2011), only a few studies have examined automatic (bottom-up) attention in Parkinson*s disease (Cools, Rogers et al. 2010). One of these studies (Cools, Rogers et al. 2010) showed that rigidity in set-shifting tasks are accounted for by greater automatic capture of attention by salient information. Although they interpreted this finding in terms of reduced top-down control, the authors acknowledged that it might also argue for a disproportionate influence of automatic bottom-up attention (Cools, Rogers et al. 2010). In our study, the main focus will be on attentional processes that are independent of strategic top-down control. In light of the reward-oriented aspect of ICBs in Parkinson*s disease, we will focus on the interplay between reward and selective attention. It was for instance recently shown that previously rewarded stimuli capture attention more strongly (Hickey, Chelazzi et al. 2010). This shows that rewards may act to change the salience of stimuli at the level of the visual cortex (Hickey, Chelazzi et al. 2010; Anderson, Laurent et al. 2011; Anderson, Laurent et al. 2013). This mechanism may account for reward-driven behaviors associated with dopamine replacement therapy and STN DBS in Parkinson*s patients. In turn, better understanding of the mechanisms through which these behaviors arise may lead to better treatment and patient care.

Study objective

The main goal of this study is to investigate the side effects of deep brain stimulation in Parkinson's disease. An important aspect of these side effects is the reward-oriented behavior. For this reason, patients will be administered psychological tests which will provide valuable information on the different components of this reward-oriented behavior.

Study design

Patients with Parkinson's disease will be enrolled. Based on various test, a cognitive profile of each individual patient will be made. This study involves a within-subjects design, consisting a 4 parts with which it possible to see the influence of the STN on different components of the learning reward

contingencies

Intervention

please see protocol

Study burden and risks

For this research it is required that DBS is turned on or off during certain blocks of the experiment. Patients will only be tested when they are in their on-phase. In the on-phase patients respond well to medication resulting in few symptoms (patients will remain on their prescribed medication). When patients are in the on-phase, switching DBS off will result in few side-effects (Odekerken, van Laar et al. 2013). We therefore anticipate a minimal burden for patients. However, patients will be explicitly instructed to directly notify the experimenter should any symptoms manifest.
One clear benefit will be a better understanding of the mechanisms through which ICBs may manifest in patients with Parkinson*s disease. Secondly, the role of the STN in reward-oriented behaviors in general, and in Parkinson*s patients in particular will be clarified. Third, we will also look at effects of stimulation of the ventral vs dorsal STN which will increase our understanding of the effects of stimulation of subcomponents of the SNT (see page 13 and 14 for further explication). In the future, this knowledge should lead to better treatment for patients with Parkinson*s disease but also for other patient groups in which reward-driven behaviors are present and DBS may constitute a treatment option (e.g., addiction).

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

- Patients implanted with a DBS device for the treatment of Parkinson*s.
- Written Informed Consent
- Age > 18 years
- clearly defined on-phase
- Patients with bilateral electrode implants will only be included if the stimulation is generated by one external pulse generator (Kinetra, ActivaPC, or ActivaRC).
- Absence of dementia or major psychiatric illness

Exclusion criteria

- Color blindness
- Patients who use dopamine agonists (e.g., ropinirole, pramiprexol will not be enrolledallowed, only L-dopa will be allowed.
- Anticholinergic medication (e.g., trihexiphedidyl, benzhexol etc.)
- History of psychiatric illnesses (e.g., psychosis, bipolar disorder)
- Previous functional stereotactic neurosurgery

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-06-2015
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO Date:	26-08-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2016
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	NL48414.018.14