Baseline Dopamine Dependent Drug Effects of Methylphenidate and Sulpiride on Brain and Behaviour: A PET, Pharmaco-fMRI Study

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Ethical review	Approved WMO
Status	Completed
Health condition type	Cognitive and attention disorders and disturbances
Study type	Observational invasive

Summary

ID

NL-OMON43196

Source
ToetsingOnline

Brief title
Baseline dopamine and cognition

Condition

- Cognitive and attention disorders and disturbances

Synonym
distractability, lack of motivation

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen

Source(s) of monetary or material Support: NWO VICI grant

Intervention

Keyword: Cognitive control, decision-making, dopamine, striatum

Outcome measures

Primary outcome

Baseline dopamine synthesis capacity measured with [18F]-DOPA PET; BOLD signal measured with fMRI; behavioural performance on computerized tasks (measuring reward sensitivity, working memory, reversal learning, reinforcement learning, cognitive effort, the influence of affective information on goal-oriented behaviour, and creativity); subjective measurements (e.g. self-report questionnaires, visual analogue scales); psychophysiological recordings (e.g., blood pressure, heart rate, respiration, elctrocardiography); blood and saliva sample to assess dopamine genes for pathway-based genetics analysis.

Secondary outcome

All tasks in the cognitive testing battery (computerized tasks) result in both outcomes of primary interest (see section 7.1.1 in the study protocol) and additional outcomes (see section 7.1.2 in the study protocol). Our secondary objective is to further our understanding of the relationship between baseline dopamine synthesis capacity and baseline measures - such as working memory, genetic differences, impulsivity and eye-blink rate * to assess how baseline levels of dopamine mediate the effects of the drug on the secondary outcomes from the cognitive testing battery.

Study description

Background summary

Failures of cognitive control are common, not only in neuropsychiatric disorders, but also in the healthy population. These failures can be remediated with dopaminergic drugs, such as methylphenidate and sulpiride, but there is huge individual variability in the direction and extent of dopaminergic drug effects. Dopamine is known to play a role in many psychological functions, such as cognitive control, learning, motivation and memory. However, at present our ability to predict dopaminergic drug effects on behaviour across individuals and different task demands is limited.

Study objective

We aim to develop a proxy-model of baseline dopamine based on machine learning methods which would provide us with behavioural predictors of the effects of dopaminergic drugs on brain and cognition that maximally generalize to new participants.

Study design

A within-subject, double-blind, placebo-controlled cross-over design will be employed. All subjects will visit the department of Radiology and Nuclear Medicine of the Radboud UMC for one PET scan, and Donders center for cognitive neuroimaging for one screening session and three pharmaco-fMRI testing sessions. During the pharmaco-fMRI sessions subjects will receive oral capsules of methylphenidate, sulpiride, and oral placebo capsules. In order for the fMRI data acquisition to coincide with the time-window of maximal drug effects represented by a combination of plasma kinetics and physiological effects we will administrate the drugs at two different time points prior to fMRI data acquisition by employing a double-dummy design. Thus, participants will receive two capsules on two separate time points per test session. Participants will receive placebo or methylphenidate ~80 minutes after receiving placebo or sulpiride. Order of administration will depend on testing session: sulpiride/placebo, placebo/methylphenidate and placebo/placebo. During the visit at the department of Radiology and Nuclear Medicine of the Radboud UMC all subjects will receive oral capsules of carbidopa and entacapone, and an F-DOPA intravenous injection for PET acquisition.

Study burden and risks

Subjects will attend five study days; one screening session (3h), three pharmaco-fMRI session (MPH, sulpiride and placebo; 6h each) and one session for PET acquisition (carbidopa, entacapone and F-DOPA; 2.5h). Subjects will

complete a baseline battery measure, questionnaires, a structural MRI scan, donate a saliva sample (2ml) and a blood sample (12.5ml) for pathway-based genetics analysis, and complete a battery of computerized tests in and outside of the fMRI scanner. On the day preceding a test session, subjects will have to adhere to some simple restrictions with respect to medication, alcohol and drug intake. On the day of testing subjects will have to refrain from smoking and stimulant containing drinks. Methylphenidate, sulpiride, carbidopa, entacapone and F-DOPA can be administered safely without any relevant risk of serious adverse events and have been approved for clinical use in the Netherlands.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy volunteers between 18 and 45 years of age

Exclusion criteria

Neuropsychiatric disorders; history of drug abuse; heart problems; metal objects in or around the body (see section 4.3 in research protocol (C1) for full list of exclusion criteria)

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-02-2017
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	27-09-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	09-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-12-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28994
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL57538.091.16
OMON	NL-OMON28994

Study results

Date completed:	20-06-2019
Results posted:	04-01-2021
Actual enrolment:	100

First publication
12-09-2020