Dopaminergic mechanisms of gating working memory, learning, and motivation: A pharmaco-fMRI study

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The primary objective of this study is to unravel the effects of dopamine D2 receptor stimulation on gating of working memory, reinforcement learning, and reward-based motivation, and their associated physiological changes (measured with fMRI and...

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

Summary

ID

NL-OMON52146

Source
ToetsingOnline

Brief title
Dopamine and cognitive function

Condition

- Cognitive and attention disorders and disturbances

Synonym
distractibility, lack of motivation

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: KNAW Ammodo Award and a NWO Vici award

Intervention

Keyword: dopamine, learning, motivation, working memory

Outcome measures

Primary outcome

Behaviour on cognitive tasks (working memory, reward learning & perceptual decision making, and effect of motivation on cognitive control), and associated physiological measures:

• working memory: BOLD signal (measured with fMRI)

Secondary outcome

Our secondary aim is determine how relevant interindividual differences (impulsivity, working memory capacity) may moderate drug effects. For this we will assess the relationship of behavioural performance on computerized tasks (as above) with i) subjective measurements (self-report questionnaires); ii) performance on neuropsychological tests (WM capacity

Study description

Background summary

Dopamine is a catecholamine neurotransmitter that plays a central role in flexible and self-directed thought and action: Our ability to think and make plans about stimuli that are not physically present (working memory), to learn from new information (reinforcement learning), and to make choices based on prior learning and our current environment (incentive motivation), all critically rely on dopamine. Dopamine dysregulation also plays a central role in many disorders, including Parkinson*s Disease, schizophrenia, AHDH, and depression. The mechanisms by which dopamine influences diverse cognitive processes in healthy and patient populations has been theorized using biologically-plausible computational models; however further empirical investigation is needed.

Furthering our mechanistic understanding of the role of dopamine in these processes is beneficial, both for refining theories and computational models of cognition, and for providing insights that can improve treatment of dopamine-related disorders.

Study objective

The primary objective of this study is to unravel the effects of dopamine D2 receptor stimulation on gating of working memory, reinforcement learning, and reward-based motivation, and their associated physiological changes (measured with fMRI and eyetracking).

Study design

A double-blind placebo controlled within-subject design will be employed, in which young healthy participants are tested twice, once on placebo, and once on a low oral dose (400mg) of the D2 receptor antagonist sulpiride. This design and drug dose is commonly used in our lab without side effects. All participants will complete one screening sessions and 2 pharmaco-fMRI sessions, all of which will take place at the Donders Centre for Cognitive Neuroimaging. During each pharmaco-fMRI sessions, subjects will receive an oral dose of sulpiride or placebo, and the order of sulpiride vs. placebo will be counterbalanced across subjects.

Study burden and risks

Participants will take part in 3 test sessions. One intake session (3 hours) and two pharmaco-fMRI sessions (6 hours each) and will complete several questionnaires at home (1 hour total). The intake session will involve a medical and psychiatric screening interview, neuropsychological tests, an ECG measure, and some training on the tasks for the pharmaco-fMRI sessions. On the days preceding the pharmaco-fMRI sessions participants will have to adhere to some simple restrictions with respect to medication, alcohol, and drug intake. On the morning of each test session participants will have to refrain from smoking and caffeinated drinks. During the pharmaco-fMRI sessions participants will receive 400mg sulpiride or placebo, and will be asked to complete some questionnaires and perform tasks testing learning and memory, inside and outside of the fMRI scanner. Sulpiride can be administered safely without any relevant risk of serious side effects and has been approved for clinical use in the Netherlands.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Healthy volunteers between 18-45 years of age.
- Right-handed

Exclusion criteria

Neuropsychiatric disorders; history of drug abuse; heart problems; metal objects in or around the body (see section 4.3 in the 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:	Recruiting
Start date (anticipated):	19-10-2021
Enrollment:	46
Type:	Actual

Ethics review

Approved WMO Date:	22-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-02-2022
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

No registrations found.

In other registers

Register	ID
CCMO	NL76159.091.21