DOPAGATE

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON57489

Source
Onderzoeksportaal

Brief title
DOPAGATE

Condition

- Schizophrenia and other psychotic disorders

Synonym
cognitive impairment, working memory problems

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO Open competition grant to Prof. Dr. Roshan Cools

Intervention

- No intervention

Explanation

N.a.

Outcome measures

Primary outcome

BOLD signal measured with laminar fMRI; behavioural performance on cognitive tasks.

Secondary outcome

Behavioural performance on cognitive tasks/questionnaires.

Study description

Background summary

The ability to flexibly adapt current goals and use them to guide purposeful behavior is a hallmark of human cognition and one key building block of this ability is working memory (WM). WM deficits, however, are commonly seen in many brain disorders, including Parkinson’s disease and schizophrenia, where WM deficits contribute to failures to direct behavior at currently relevant goals. WM is well known to implicate brain dopamine and accordingly, WM deficits in schizophrenia and Parkinson’s disease have been shown to be, respectively, alleviated and simulated by the administration of common antipsychotics that target the dopaminergic system, The mechanisms by which dopamine receptor modulation acts to change working memory are unclear. This causes a major problem for neurology and psychiatry because there is huge variability in the direction and extent of dopamine’s effects across different individuals and task demands. Therefore, unraveling these mechanisms in the current study promises to inform future clinical studies aimed at identifying key factors that contribute to the large variability in treatment efficacy. The current cognitive study with young healthy volunteers aims at uncovering the neural mechanisms by which dopamine receptor modulation changes working memory subprocesses. To elicit selective changes in dopamine receptor stimulation, we will utilize a well-established product to elicit such changes: the registered and commonly used antipsychotic sulpiride, a D2 receptor antagonist the clinical, pharmacological, and pharmacodynamic effects of which are well-established already. Once established, these mechanisms can be leveraged in future clinical studies to predict the cognitive effects of sulpiride in patients with schizophrenia, and thus for individual tailoring of pharmacological treatment.

Study objective

The primary objective of this study is to isolate effects of dopamine receptor manipulation on distinct forms of working memory (WM) gating and their associated physiological changes in distinct layers of prefrontal cortex (measured with high-resolution fMRI). We will test the hypothesis that dopamine receptor manipulation changes working memory output gating and associated deep cortical layers, where dopamine receptors are abundant, but not working memory input gating and associated superficial cortical layers, where dopamine receptors are sparse.

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 after intake of a product well established to affect dopamine receptors: sulpiride (oral, 400mg). Sulpiride is a registered in the Netherlands and commonly used antipsychotic and this design and drug dose is commonly used in our lab without side effects.

Intervention

This is not a clinical trial, thus there is no investigational product. Participants will receive either 400mg sulpiride or placebo in the pharmaco-fMRI session, in separate sessions in a counterbalanced order.

Study burden and risks

Participants will attend 3 study sessions: A screening session and 2 pharmaco-fMRI sessions (sulpiride and placebo). Participants will complete a baseline battery of tasks and questionnaires, a structural MRI scan, as well as a battery of tasks both in and outside the scanner. On the day preceding each pharmaco-fMRI session, participants 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. Sulpiride can be administered safely without any relevant risk of serious adverse events and has been approved for clinical use in the Netherlands.

Contacts

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Trial sites

Trial sites in the Netherlands

Radboud Universiteit Nijmegen
Target size: 34

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy volunteers between 18 and 45 years of age

Predominant right-handedness

18.5 < BMI < 30

Exclusion criteria

Neuropsychiatric disorders; Relevant medical disorders; History of drug abuse; Pregnancy; Metal objects in or around the body (see section 4.3 of the Research Protocol C1 for full list of exclusion criteria)

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
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):	21-05-2025
Enrollment:	34
Duration:	1 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.

IPD sharing statement

Plan to share IPD: Yes

Plan description
Data will be shared using the Radboud Data Repository under registered access.

Ethics review

Approved WMO

Date:	18-03-2025
Application type:	First submission
Review commission:	METC Oost-Nederland

Approved WMO

Date:	19-05-2025
Application type:	Amendment

Review commission: METC Oost-Nederland

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
Research portal	NL-009546