Dopaminergic mechanisms of inference for language: a pharmaco-fMRI study

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

Summary

ID

NL-OMON53778

Source
ToetsingOnline

Brief title
Dopamine' s role in linguistic inference

Condition

- Other condition

Synonym
brain

Health condition

Neuroscience research (basic science)

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: NWO (Nederlandse Organisatie voor Wetenschappelijk Onderzoek);Language in Interaction

Intervention

Keyword: Dopamine, fMRI, Inference, Language

Outcome measures

Primary outcome

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

Secondary outcome

Subjective measurements (e.g., self-report questionnaires, visual analogue

scales)

Study description

Background summary

Humans are flexible and efficient at inferring meaning during language processing. Similar capacity has also been observed in making novel decisions drawing from past experience, for example in spatial relations.

Dopamine is the key neural candidate posited to play a crucial role in drawing inferences in non-linguistic domains. Dopamine is a catecholamine neurotransmitter that is known to play a central role in flexible and self-directed thought and action: our abilities to think about and make plans based on stimuli that are not physically present (working memory), to learn from new information and stimulus-response associations (reinforcement learning), and to make choices based on prior and current environment (incentive motivation), all critically rely on dopamine. Particularly, dopamine stimulation leads to flexible and adaptive behaviour, making it a likely component for inferential reasoning.

Besides its role in flexible behaviour, dopamine has also been linked to language processing: previous research has shown the importance of dopamine in amplifying the salience of linguistic information (e.g. enhancing semantic

processing). This is consistent with the idea that dopamine increases signal-to-noise ratio between specific signals and background noise.

This study addresses fundamental questions about the neural mechanisms that are central to our capacity to infer meanings flexibly and efficiently during language processing, broadening the role of dopamine from action and spatial planning to linguistic relations.

Study objective

The primary objective of this study is to investigate whether increases in brain dopamine enhance novel meaning inference in language processing, and what cognitive and neural mechanisms underlie this. We will test the hypothesis that dopamine promotes the building of novel word meaning representations and increases the signal to noise ratio of existing word meaning representations in the hippocampus and prefrontal cortex.

Study design

A double-blind placebo-controlled between-subject design will be employed: Healthy participants are tested once, either on placebo or on a low oral dose (150mg) of the dopaminergic precursor, levodopa, in order to increase brain dopamine. Similar pharmacological designs, albeit with other dopaminergic pharmacological challenges, are commonly used in our lab. The proposed dose of levodopa has been widely used without side effects in other studies with comparable study populations.

Study burden and risks

Participants will attend two study sessions: a screening session and a pharmaco-fMRI session (levodopa or placebo). On the pharmaco-fMRI session, participants will complete questionnaires, structural and functional MRI scans, as well as a battery of tasks both in (during the fMRI scans) 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 pharmaco-fMRI day, subjects will have to refrain from smoking and stimulant-containing drinks. Levodopa 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

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy volunteers between 18 and 45 years of age;
Dutch native speaker;
Predominant right-handedness;

Exclusion criteria

Neuropsychiatric disorders; history of drug abuse; 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:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-11-2022
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	21-07-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-07-2023
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	NL80626.091.22