The effects of increased levels of dopamine on the activation in the dopaminergic system.

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1) To investigate if it is possibility to measure neural activation (CBF) in the DA brain stem nuclei and the functionally associated brain regions with ASL. 2) To investigate the effect of increased DA on activation in the DA system during resting...

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

Summary

ID

NL-OMON33408

Source
ToetsingOnline

Brief title
The dopaminergic system

Condition

- Cognitive and attention disorders and disturbances

Synonym
n.v.t.

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dopamine, Functional MRI, Gambling task, Methylphenidate

Outcome measures

Primary outcome

1) Regional cerebral blood flow (method: arterial spin labeling MRI) during resting state in the cortex, sub cortical and brain stem regions.

2) Regional blood oxygenated level dependent (BOLD) response (method: BOLD functional MRI) during resting state and during task performance, in the cortex, sub cortical and brain stem regions.

3) Task performance; the number of correct response and the reaction time.

Secondary outcome

1) The levels of Ritalinic acid in the blood

2) Mood and physical complaints (method: questionnaire)

3) Hart and breathing rate (assessed during the scan session)

Study description

Background summary

Dopamine (DA), a brain chemical that modulates the signaling between brain neurons (neurotransmitter), is known to be involved in reward and punishment processing. DA is released by DA neurons (located in the DA nuclei in the brain stem) into cortical and sub cortical projection regions. D*Ardenne et al. (2008) showed that with an adapted MRI sequence it is possible to measure the blood oxygen level dependent (BOLD) response (indirect measure for neuronal activation) in the DA nuclei. Since the BOLD response is confounded by drug induced changes in the neurovascular response, further methodological improvements are needed to be able to study the effects of drugs on activation in the DA nuclei. In this study, we will use arterial spin labeling (ASL), a noninvasive method to measures cerebral blood flow (CBF), to investigate the functioning of the DA system (nuclei and projection regions) during resting

state. When the BOLD response is complimented with baseline CBF measures, the interpretation of drug induced changes in BOLD response can be improved.
So far, it is unknown what the effects of a DA stimulant are on the activation of the DA system. In this study, we will investigate the effects of methylphenidate (MPH; Ritalin) on the activation of the DA system (brain stem nuclei and projection regions) during resting state and during the performance of a task that is known to increase the activation of the DA system: a gambling task in which the participants receive unexpected high rewards.
Thirdly, previous research has shown that personality characteristics can interact with the effects of drugs on brain activation during task performance.

Study objective

1) To investigate if it is possibility to measure neural activation (CBF) in the DA brain stem nuclei and the functionally associated brain regions with ASL.
2) To investigate the effect of increased DA on activation in the DA system during resting state
3) To investigate the effect of increased DA on brain activation during reward and punishment processing.
4) To investigate the relation between the personality trait *reward dependence* and the effect of increased DA, on the functioning of the DA system.

Study design

This study has have a double-blind randomized placebo-controlled design.

Study burden and risks

Before inclusion the participants will complete a medical questionnaire (15 min) and will undergo a medical screening (45 min; two blood samples, a urine sample and an electrocardiogram). When included, the participants will visit the laboratory three times: for a training session (1 hour) and two test sessions (3.5 hours each). During each test session the participants will complete two questionnaires (5 min) at two different time and will perform a cognitive tasks (36 min) inside the MRI scanner (scan session in total 75 min). Furthermore in each test session two blood samples will be taken. In total, the study will take 9 hours to complete. The participants will be paid in total 74 euros as compensation.
The risk sof MRI scanning and the administration of methylphenidate are negligible.

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

Good health, right-handedness, male, between 23 and 35 years of age, no history of mental illnesses or neurological disorders, no history of drug or alcohol abuse, no use of medication.

Exclusion criteria

MRI contra-indications, such as claustrophobia and metal parts in the body, cardiovascular abnormalities as assessed by standard 12-lead electrocardiogram (ECG), excessive drinking and hypertension.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-06-2010
Enrollment:	20
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Ritalin
Generic name:	Methylphenidate hydrochloride
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-08-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-11-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-02-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2009-014731-20-NL
CCMO	NL29192.068.09
Other	Not yet received