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

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1. We hypothesize that methylphenidate will decrease the activation in the dopaminergic nuclei and will increase the activation in the dopaminergic projection regions during rest and during reward processing during the gambling task; 2. We...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28941

Bron
NTR

Verkorte titel
The dopaminergic system

Aandoening

Disorders related to disturbed dopaminergic functioning.

Ondersteuning

Primaire sponsor: Maastircht University
Overige ondersteuning: Maastricht University

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

SUMMARY:

Rationale: 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 brain activation. 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 experimentally induced increased DA 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 DA: a gambling task.
Thirdly, previous research has shown that personality characteristics can interact with the effects of drugs on brain activation during task performance.

Main study objective:

1. To measure activation in the DA brain stem nuclei and the projection regions with ASL;

2. To investigate the effect of increased DA on activation in the DA system during baseline;

3. The effect of increased DA on brain activation during reward and punishment processing;

4. The relation between the personality trait reward dependence and the effect of increased DA on brain activation in the DA system.

Study design: This study will have a double-blind randomized placebo-controlled design. Twenty male healthy volunteers (23 – 55 years) will be tested after placebo and after a capsule of 40 mg of MPH.

Main study parameters/endpoints are:

1. CBF during resting state in the cortex, sub cortical and brain stem regions;

2. The BOLD response 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.

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 the training session, study procedures will be explained by the researcher, the cognitive fMRI task will be trained in a dummy scanner, and a personality questionnaire will be completed. During each test session the participants will complete three questionnaires (5 min) at two different times 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 75 euros as compensation. The risk of MRI scanning and the administration of methylphenidate are negligible.

Doel van het onderzoek

1. We hypothesize that methylphenidate will decrease the activation in the dopaminergic nuclei and will increase the activation in the dopaminergic projection regions during rest and during reward processing during the gambling task;

2. We hypothesize that in people that score high on reward dependence (low baseline dopamine) methylphenidate will increased brain activation to a lesser extend than in people that score low in reward dependence (higher baseline dopamine).

Onderzoeksopzet

The participants will be tested twice in the MRI scanner. Once starting 90 minutes after the administration of methylphenidate, and once starting 90 minutes after the administration of a placebo capsule. The test session will be at least one week apart.

Onderzoeksproduct en/of interventie

This study will have a cross-over design. Twenty healthy male volunteers (mainly students) will be tested after placebo and after 40 mg of methylphenidate (order of treatment will be randomized). Methylphenidate MPH (and placebo) will be administrated 90 min before the

commencement of the fMRI scans to ascertain peak plasma concentrations during the acquisition of the MRI images. A blood sample will be taken before treatment and before and after scanning. Three questionnaires (physical complaints VAS scales, the Profile of Mood State questionnaire (POMS) and the Bond and Lader questionnaire) will be completed before treatment, and before and after scanning.

The MRI scanning (exactly the same for the methylphenidate and placebo session) will last about 75 min and will consist of two resting state blocks, 4 task blocks in which participants perform a gambling task and a structural scan. During the scanning session breathing rate and heart rate will be constantly monitored, to guard the wellbeing of the participants and to be able to correct for motion artifacts in the fMRI analysis. In total, a test session will last for about 3.5 hours. The minimum period between successive test sessions will be one week.

Before the two test sessions participants will come to the lab for a training session (duration 1 hour). In this session explanations and instructions for the test session will be given, the gambling task that will be performed in the scanner will be trained, and the personality questionnaire will be filled in.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen

(Inclusiecriteria)

1. Healthy, right handed, male, between 23 and 35 years of age;

2. No history of mental illness or neurological disorders;

3. No history of drug abuse or alcohol abuse;

4. No use of medication.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. MRI contra-indications, such as claustrophobia and metal parts in the body;

2. Cardiovascular abnormalities as assessed by standard 12-lead electrocardiogram (ECG);

3. Excessive drinking;

4. Recreational drug use;

5. Hypertension;

6. Contraindications to methylphenidate (as defined in the methylphenidate SmPC).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland	
Status:	Werving nog niet gestart

(Verwachte) startdatum:	01-02-2010
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	28-09-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1916
NTR-old	NTR2033
Ander register	METC University Maastricht : MEC 09-3-052
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A