The role of dopamine in visuospatial attention.

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It is expected that dopaminergic antagonism by haloperidol 2mg or 3mg wil result in specific inhibition of both bias and disengagement related activity as measured by EEG in combination with computertasks. Specifically, we expect that, dopamine...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26886

Bron
Nationaal Trial Register

Verkorte titel
The role of dopamine in visuospatial attention

Aandoening

Methylphenidate, frequently prescribed in the treatment of ADHD, increases the central availability of both dopamine and noradrenaline. The roles of dopamine and noradrenaline in attention and inhibition are yet unclear. It is of importance to investigate the role of these neurotransmitter systems since at least 20 percent of patients do not benefit from methylphenidate or have undesired side effects.

Ondersteuning

Primaire sponsor: Utrecht University
Overige ondersteuning: NWO open competitie (MAGW)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Behavioural measures:
1. In the VSC (Visual Spatial Cueing) paradigm: The validity effect in ms (RT valid cued target - RT invalid cued target). A larger validity effect reflects either more bias, or less disengagement;
2. In the stop task paradigm, the time needed (in milliseconds) to abort a prepotent response: The Stop Signal Reaction Time (SSRT); SSRT reflects inhibition and related disengagement but is also dependent on bias.

Neurophysiological (Event Related Potentials, task related brain activity) endparameters in the VSC:
1. Parietal cue Event Related Potential (ERP) components. These are the Anterior Directing Attention Negativity (ADAN) and the Late Directing Attention Positivity (LDAP). Both are related to bias;
2. P1 ERP (following a validly cued target); associated with bias;
3. Late Positive Deflection (LPD) ERP (following an invalidly cued target); associated with disengagement.

Neurophysiological (ERP) endparameters in the stop task:
1. N2 ERP (following the onset of a stopsignal), associated with disengagement;
2. LPD ERP (following the onset of a stopsignal), associated with disengagement.

Toelichting onderzoek

Achtergrond van het onderzoek

Two central mechanisms underlying attention and inhibition are bias and disengagement. Overly simplified, bias refers to the (result of) focusing of attention whereas disengagement refers to the decoupling of attention. Methylphenidate is a standard psychopharmacological treatment for ADHD. Methylphenidate promotes the central availability of both dopamine and noradrenalin and affects both bias and disengagement. However, the roles of these neurotransmitter systems in bias and disengagement remain unknown. This still unsolved question is important to answer, since many patients still have many undesired side-effects following methylphenidate administration. In our previous study we set out to investigate the role of the noradrenergic system in bias and disengagement. In the current study we investigate the role of the dopamine system in bias and disengagement. One study suggests that noradrenergic antagonism affects only bias. Hence, dopamine (ant)agonism must affect disengagement. This is indeed supported by a study showing that stopping behaviour correlates with dopamine metabolites. However, scrutinizing behavioural measures, it seems that dopamine antagonism also negatively affects bias. Integrating the literature we expect that, firstly dopamine antagonism by haloperidol negatively affects bias. Secondly, with

respect to disengagement, we expect that dopamine antagonism will affect a right frontal mechanism, but not a more posterior mechanism involved in disengagement. Since behavioral outcome reflects activity in both, disengagement and bias related mechanisms, studying brain activity is crucial. Therefore we incorporate EEG in combination with two computer tasks to investigate bias and disengagement associated brain indices (i.e., event-related potentials; ERPs). Participants will be presented two sessions (placebo/haloperidol, sessions are separated by at least a week). In each session, before and after haloperidol or placebo intake, participants will be assessed with respect to disengagement and bias. The total sample will consist of a maximum of 38 male participants. Initially 2 mg haloperidol and placebo will be administered to 8 participants. Subsequently, an interim analysis will be performed to estimate the effect size. Depending on the effect size of this dose, we either continue with the 2 mg dose, or we start with a higher dose of haloperidol (3 mg) after which we re-estimate the sample size after another 8 participants. This design is implemented to minimize the burden for participants due to unnecessary side effects.

Doel van het onderzoek

It is expected that dopaminergic antagonism by haloperidol 2mg or 3mg wil result in specific inhibition of both bias and disengagement related activity as measured by EEG in combination with computertasks. Specifically, we expect that, dopamine antagonism by haloperidol negatively affects all bias related measures (P1 effect ERP. and the parietal cue response EDAN and LDAP ERPs) Secondly, with respect to disengagement, we expect that dopamine antagonism will attenuate a right frontal mechanism (Stop N2 ERP), but not a more posterior mechanism involved in disengagement (LPD ERP).

Onderzoeksopzet

Before administration of haloperidol/placebo, a small version of the computertasks is performed (baseline measurement). At 180 min post haloperidol/placebo administration, computertasks are performed and EEG is recorded. Total duration of each session (placebo / haloperidol) is approximately 6.5 hours.

Spontaneous motor activity is measured continuously using an actigraph. Dyskinesia is measured using Velocity Scaling before and after haloperidol/placebo administration.

Onderzoeksproduct en/of interventie

Dopaminergic antagonism by 2mg (and possibly 3mg) haloperidol.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age 18 – 45;

2. Male.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Any of the following (assessed by interview):

1. History of cardiovascular problems;

2. Liver disease;

3. Use of any medication;

4. History of cocaine use;

5. Diagnosed psychopathology;

6. Hypersensitivity to haloperidol;

7. Hyperthyroidism;

8. History of epilepsy.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-08-2011
Aantal proefpersonen:	38
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

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	NL2778
NTR-old	NTR2918
Ander register	CCMO : 37109
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A