

Why methylphenidate is not successful in cocaine-dependent ADHD patients: A SPECT study comparing DAT before and after methylphenidate treatment in ADHD patients with and without cocaine dependence.

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1. Does baseline dopamine transporter (DAT) binding differ in ADHD patients with (ADHD+SUD) and without substance use disorders (ADHD-SUD)? A possible explanation for the difference in treatment response is that ADHD patients with and without...

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

Samenvatting

ID

NL-OMON24052

Bron
NTR

Verkorte titel
ADHD-SUD study

Aandoening

ADHD, substance use dependence, SUD, cocaine

Ondersteuning

Primaire sponsor: Academic Medical Centre, University of Amsterdam

Overige ondersteuning: ZonMW/NIDA

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Dopamine transporter (DAT) availability before and after 2 weeks MPH treatment, assessed using 123I-FP-CIT single photon emission computed tomography (SPECT).

Toelichting onderzoek

Achtergrond van het onderzoek

Attention deficit hyperactivity disorder (ADHD) may play a role in the etiology and pathogenesis of substance use disorders (SUD) although its relationship to substance abuse is not fully understood.

The dopamine transporter (DAT) plays a fundamental role in both ADHD and SUD. Dopamine transporter (DAT)-selective medications, such as methylphenidate (MPH), have been shown to successfully block the DAT in ADHD patients (Krause et al., 2000; Dresel et al., 2000), and DAT occupancy has been associated with clinical effectiveness (Vles et al., 2003; van Dyck et al., 2002). In ADHD patients with SUD, however, these medications are not very effective, neither for treating ADHD nor SUD.

Thus, ADHD patients with SUD are often not responsive to MPH. This raises two important questions: why are patients with ADHD with SUD not responsive to adequate doses of MPH and how does this relate to SUD?

This study is an attempt to investigate one of the most plausible reasons for the difference in effectiveness of MPH in the treatment of adult ADHD patients with and without SUD. It is hypothesized that adult ADHD patients with SUD generally have higher baseline DAT availability in the basal ganglia (Jacobsen et al., 2000; Little et al., 1998, 1999; Malison et al., 1998), and that similar doses of MPH result in lower occupancy rates in adult ADHD patients with SUD compared to adult ADHD patients without SUD. It remains unclear whether baseline DAT density and DAT occupancy following MPH treatment differs between ADHD patients with and without SUD. These are relevant concerns since answers to these questions may shed light on the lack of efficacy of MPH for the treatment of ADHD symptoms and drug use in ADHD patients with comorbid SUD.

Doel van het onderzoek

1. Does baseline dopamine transporter (DAT) binding differ in ADHD patients with (ADHD+SUD) and without substance use disorders (ADHD-SUD)?

A possible explanation for the difference in treatment response is that ADHD patients with and without comorbid SUD differ in their baseline DAT density. We expect higher baseline striatal DAT expression in patients with cocaine dependence compared to patient without comorbid cocaine dependence;

2. Does methylphenidate (MPH) affect DAT binding differently in ADHD+SUD and ADHD-SUD patients?

Another possible explanation for the difference in treatment response between ADHD patients

with and without comorbid SUD is that MPH differentially affects striatal DAT binding in ADHD+SUD compared to ADHD-SUD patients. We expect 10-20% lower occupancy in ADHD patients with cocaine addiction compared to those without addiction following treatment with identical dosages of MPH;

3. Does MPH differentially affect ADHD symptoms and ADHD associated cognitive functions in ADHD patients with and without cocaine dependence?

We expect that identical dosages of MPH are less effective in the reduction of ADHD symptoms and associated cognitive functions in ADHD patients with cocaine addiction compared to patients without cocaine addiction;

4. Does DAT occupancy affect drug craving and drug use in ADHD+SUD patients?

We expect MPH to increase striatal DAT occupancy and possibly reduce drug craving in ADHD patients with cocaine dependence compared to their baseline measures.

Onderzoeksopzet

All outcome measurements (questionnaires and 123I-FP-CIT single photon emission computed tomography (SPECT) scans) are assessed at baseline, and following two weeks treatment with methylphenidate.

Onderzoeksproduct en/of interventie

Patients with ADHD with and without cocaine dependence will be treated with a fixed dose of methylphenidate for 2 weeks (slow-release methylphenidate, 54 mg tablets). Patients will be scanned using 123I-FP-CIT single photon emission computed tomography (SPECT) to assess possible differences in dopamine transporter availability at baseline, and differences in dopamine transporter occupancy following fixed-dose methylphenidate treatment.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Male, age 18-60 years;
2. Current DSM-IV diagnosis of adult ADHD for all participants;
3. For the ADHD+SUD group: Current DSM-IV diagnosis of cocaine dependence, but abstinent from cocaine use for at least 1 week;
4. Able to provide written informed consent and to comply with all study procedures;
5. Negative urine analyses for MPH, amphetamines and cocaine.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1. Currently dependent on any substance other than cocaine or nicotine;
2. Severe neurological or psychiatric disorders or diseases (e.g., psychosis, bipolar depression, Parkinson's disease, or dementia) that require psychotropic medications;
3. Serious medical illnesses that would make participation hazardous, such as cardiovascular disease or ECG abnormalities;
4. Known hypersensitivity or allergy to MPH;
5. Under therapy with drug known to influence binding to DATs, including antipsychotics, MPH, bupropion, and dexamphetamine within 30 days prior to randomization;
6. Received a drug with known potential for toxicity to a major organ system within the month prior to entering treatment;
7. Clinically significant abnormal laboratory values (3x normal) as measured by the Arkin Mental Health and Addiction treatment center;
8. Any disease of the gastrointestinal system, liver, or kidneys which could result in altered metabolism or excretion of the study medication;
9. Hypersensitivity to iodine;
10. Any contraindications to perform MR imaging (e.g., pacemaker, or any piece of metal in the body).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland
Status: Werving gestart
(Verwachte) startdatum: 01-10-2011
Aantal proefpersonen: 30
Type: Verwachte startdatum

Ethische beoordeling

Positief advies
Datum: 31-10-2011
Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 33367
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2979
NTR-old	NTR3127
CCMO	NL27983.018.09
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON33367

Resultaten

Samenvatting resultaten

N/A