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

Published: 20-08-2009
Last updated: 19-03-2025

This study is an attempt to seriously 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.

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON33367

Source
ToetsingOnline

Brief title
Methylphenidate in ADHD patients with and without cocaine dependence

Condition

- Other condition
- Psychiatric disorders

Synonym
ADHD, hyperactivity disorder

Health condition

verslaving

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: ADHD, cocaine, DAT, methylphenidate

Outcome measures

Primary outcome

Does baseline DAT binding differ in ADHD+SUD and ADHD-SUD patients?

Does MPH affect DAT binding differently in ADHD+SUD and ADHD-SUD patients?

Secondary outcome

Does MPH differentially affect ADHD symptoms and ADHD associated cognitive

functions in ADHD patients with and without cocaine dependence?

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

Study description

Background summary

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. DAT-selective medications, such as methylphenidate (MPH), have been shown to successfully block the DAT in ADHD patients and DAT occupancy has been associated with clinical effectiveness. 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?
It is hypothesized that adult ADHD patients with SUD generally have higher baseline DAT availability in the basal ganglia, 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.

Study objective

This study is an attempt to seriously 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.

Study design

Our hypotheses will be tested using [123I]FP-CIT single photon emission computed tomography (SPECT) to assess DATs in-vivo in two groups of adult ADHD patients, one with a comorbid diagnosis of cocaine dependence (ADHD+SUD, n=30) and one without a comorbid substance use disorder (ADHD-SUD, n=30).

Intervention

We will use [123I]FP-CIT single photon emission computed tomography (SPECT) to assess DATs in-vivo before and after MPH treatment

Study burden and risks

The burden for the participant consists of exposures to 2 SPECT scans, questionaires and neuropsychological testing. Also, 4 blood samples (1 during each SPECT scan, 1 for genetics, and 1 at the end of treatment to check for study compliance and MPH plasma levels) and weekly urine tests will be obtained. Participants will also ingest methylphenidate daily during 3 weeks.
The risks for the participants include: exposure to the radiotracer, and possible side effects of methylphenidate (see protocol pg 8).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male, age 18-60 years;
2. Current DSM-IV diagnosis of adult ADHD for all participants;
3. For the ADHD+cocaine dependent 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 methylphenidate, amphetamines and cocaine.

Exclusion criteria

1. Currently dependent on any substance other than cocaine or nicotine;
2. History of severe depression, i.e. depression necessitating hospitalization, a history of 2 or more recurrent episodes of depression or previous suicide attempts;
3. Severe neurological or psychiatric disorders or diseases (e.g., psychosis, bipolar depression, Parkinson*s disease, or dementia) that require psychotropic or ECG abnomedications;
4. Serious medical illnesses that would make participation hazardous, such as cardiovascular disease;

5. Known hypersensitivity or allergy to methylphenidate;
6. Under therapy with drug known to influence binding to DATs, including antipsychotics, MPH, bupropion, and dexamphetamine within 30 days prior to randomization;
7. Received a drug with known potential for toxicity to a major organ system within the month prior to entering treatment;
8. Clinically significant abnormal laboratory values (*3x normal) as measured by the treatment center;
9. Any disease of the gastrointestinal system, liver, or kidneys which could result in altered metabolism or excretion of the study medication;
10. Hypersensitivity to Iodine.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2009
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Concerta
Generic name:	methylphenidate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-08-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24052
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2009-012261-61-NL
CCMO	NL27983.018.09
OMON	NL-OMON24052