Effects of methylphenidate on the developing brain.

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Administration of MPH during brain development, but not in adulthood, results in an altered outgrowth of the dopaminergic system. This long-lasting disturbance of the dopaminergic system may result in behavioral abnormalities, such as anxiety and...

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

Samenvatting

ID

NL-OMON20266

Bron
Nationaal Trial Register

Verkorte titel
ePOD - MPH

Aandoening

Effect of methylphenidate treatment on the outgrowth of the dopaminergic system in children and young adults with attention-deficit hyperactivity disorder.
Effect van de behandeling met methylfenidaat op de uitgroei van het dopamine systeem in kinderen en jong volwassenen met ADHD

Ondersteuning

Primaire sponsor: Academic Medical Center Amsterdam
Overige ondersteuning: eerste geldstroom (Geld van Ministerie van OC&W aan universiteiten)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. phMRI: % change in ASL signal from baseline in response to acute oral MPH challenge before and after 16 weeks of MPH treatment;
2. DTI: % change in FA and MD values from baseline after 16 weeks of MPH treatment;
3. Resting state fMRI (rs-fMRI): % change in functional connectivity (FC) within specific (DA) neuronal networks;
4. % change of above mentioned outcome parameters during treatment vs. baseline and post-treatment.

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

50-90% of prescribed pediatric drugs have never been tested or licensed in children, only in adults. Approximately 100 million children in the European Union are prescribed off-label or unauthorized drugs and in doing so risk adverse reactions or do not respond to treatment at all. In fact, medication doses used in children are no more than ‘guestimates’. Clearly, there are potential dangers in assuming that children will have the same response to therapy as adults. Methylphenidate (MPH) is primarily used as treatment for attention deficit hyperactivity disorder (ADHD), effectively reducing symptoms of inattention, hyperactivity, and impulsivity in up to 70% of children. It is assumed MPH does this by blocking the DA transporter (DAT) thus increasing extracellular DA in the brain. Its efficacy and safety has been documented in many studies. However, there is still a gap of knowledge concerning the influence of MPH on brain development and its effect on brain structure and function. Studies in animals raise serious concerns and call for further investigation of possible effects on brain structure and function.

Primary objective of the study:

To report on the effectmodification by age of MPH treatment on the outgrowth of the DA system using state-of-the-art Magnetic Resonance Imaging (MRI) techniques.

Secondary objectives:

1. To report on the effectmodification by age of MPH on the outgrowth of the DA system

using several functional outcome measures (functional MRI (fMRI), neuropsychological test battery);

2. To report on the effects of MPH on restless legs syndrome (RLS) symptoms and insomnia.

Study design:

A pharmacological MRI (phMRI) study for assessment of dopaminergic function and connectivity in an 18-week multicenter randomized, double-blind, placebo-controlled trial with methylphenidate in 100 children-, and adult male ADHD patients in which the effect of age is investigated before and after treatment. Patients will be stratified into two age groups: adolescents (10-12 years of age) and adults (23-40 years of age) and randomly assigned to receive a flexible dose of either MPH or placebo, resulting in four groups consisting of 25 subjects each.

Study population:

50 adolescent (10-12 years of age) and 50 adult (23-40 years of age) male outpatients diagnosed with combined type ADHD (combined type) as defined in the DSM-IV, and in need of pharmacotherapy according to existing guidelines.

Intervention:

1. Random assignment to a flexible dose of methylphenidate or placebo drug treatment for a period of 16 weeks with a 1 week washout period;

2. 3.0 Tesla MRI scan. Total duration 2 x 30 minutes (with a 90 minute break in between scans) including a pharmacological phMRI (phMRI), diffusion tensor imaging (DTI), functional connectivity (rs-fMRI) and task-related fMRI scans before and after a DA challenge with oral MPH (0.5 mg/kg). Before, during and after trial end. The MRI scan during the trial will last 30 minutes, without a DA challenge;

3. Assessment of a neuropsychological (NPO) test battery and questionnaires (duration approximately 1 hour), Before, during and after trial end. The NPO during the trial will last 30 minutes;

4. Assessment of sleep architecture using a questionnaire, actigraph and a sleep log during 3 x 5 days: Before, during and after trial end.

Doel van het onderzoek

Administration of MPH during brain development, but not in adulthood, results in an altered outgrowth of the dopaminergic system. This long-lasting disturbance of the dopaminergic system may result in behavioral abnormalities, such as anxiety and depression.

Onderzoeksopzet

1. Screening;

2. Baseline: Week 0;

3. Midtreatment: Week 8;

4. Washout: Week 16;

5. Post-treatment: Week 17.

Onderzoeksproduct en/of interventie

1. Random assignment to a flexible dose of methylphenidate or placebo drug treatment for 16 weeks, followed by a medication-free wash-out period of one week;

2. 3.0 Tesla MR imaging including diffusion tensor imaging (DTI), task-related functional MRI (fMRI) and pharmacological MRI (phMRI) following dopaminergic challenge with oral methylphenidate (0.5 mg/kg);

3. Assessment of a neuropsychological test battery and short questionnaires;

4. Assessment of sleep with actigraphy.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Male outpatients (ages 10-12 and 23-40) newly diagnosed with ADHD as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV, American Psychiatric Association 1994) and as determined by a structured interview: Diagnostic Interview Schedule for Children fourth edition (DISC-IV; Ferdinand et al., 1998) in parents or Diagnostic Interview voor ADHD bij volwassenen (DIVA; Kooij andFrancken, 2010) in adults.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Co-morbid Axis I psychiatric disorders requiring treatment with medication at study entry;

2. Major medical illness, such as a history of epilepsy and traumatic brain injury;

3. IQ < 80;

4. Current or previous (including prenatal) dependency of drugs or medications that influence the dopamine system before age 23

5. Any contraindications to methylfenidate treatment or MRI proceedings.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-05-2011
Aantal proefpersonen:	100
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	13-10-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 39033
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2955
NTR-old	NTR3103
CCMO	NL34509.000.10
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON39033

Resultaten

Samenvatting resultaten
N/A