Mapping dopaminergic function using pharmacologic Magnetic Resonance Imaging (phMRI)

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-to assess the reliability of phMRI (BOLD-, PWI and ASL based phMRI) in assessing cerebral DA function when compared to dopamine transporter (DAT) SPECT.-to assess which MRI technique (BOLD-, PWI or ASL) is best in assessing cerebral DA function...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON33010

Source
ToetsingOnline

Brief title
Dopamine-MRI

Condition

- Other condition

Synonym
not applicable

Health condition

kinder en jeugd psychiatrie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: amphetamine, dopamine, MRI, SPECT

Outcome measures

Primary outcome

BOLD: % change in BOLD SI from baseline (ROI)

PWI: % change in ratio from baseline (ROI: rCBV/white matter rCBV)

ASL: % change in CBF from baseline (ROI CBF/100 mg tissue)

SPECT: DAT ratio (striatal ROI binding/binding in cerebellum)

Secondary outcome

Amphetamine Interview Rating Scale

Study description

Background summary

Rationale: Little is known about the pathophysiology of neuropsychiatric diseases in which dopamine (DA) plays an important role in children and adolescents, as positron emission tomography (PET) and single photon emission computed tomography (SPECT) research studies are hardly allowed in the pediatric population because of radiation exposure. Recent work suggests that DA function can also be evaluated non-invasively using magnetic resonance imaging (MRI) by measuring hemodynamic changes following an amphetamine challenge, called pharmacological MRI (phMRI). There are three ways of assessing pharmacological-induced changes in hemodynamic responses with MRI: using BOLD (blood oxygenation-level dependent) contrast, perfusion weighted imaging (PWI) and arterial spin labelling (ASL). However, the reliability of these techniques in assessing DA function have not yet been assessed and directly compared to each other. Therefore, this study will assess the reliability of BOLD-, PWI and ASL based phMRI by assessing cerebral DA function when compared to dopamine transporter (123I-FP-CIT) SPECT in 10 healthy male

volunteers, and identifies the best phMRI technique in doing so. Ultimately, it is expected that DA phMRI will open a new horizon in the diagnosis and treatment of children suffering from neuropsychiatric disorders, such as attention deficit hyperactivity disorder (ADHD).

Study objective

-to assess the reliability of phMRI (BOLD-, PWI and ASL based phMRI) in assessing cerebral DA function when compared to dopamine transporter (DAT) SPECT.
-to assess which MRI technique (BOLD-, PWI or ASL) is best in assessing cerebral DA function when compared to DAT SPECT.

Study design

BOLD-, PWI and ASL DA-phMRI studies will be conducted and compared to a DAT SPECT scan as reference (gold standard). A DAT SPECT scan will be conducted. With an interval of 2-3 weeks, the BOLD and ASL DA-phMRI studies can be studied in one scan session following a low dose challenge with amphetamine. In a second MRI study with gadolinium (PWI based phMRI), again a low dose amphetamine challenge will be given.

Study burden and risks

No serious side effects are foreseen. MRI itself is a non-invasive imaging modality. In this study, a low dose amphetamine challenge (0.3 mg/kg i.v.) will be administered during the two MRI studies, along with a contrast agent during the PWI MRI study. There is no risk associated with participation. Gadobutrol (Gadovist) is routinely administered for contrast enhanced MRI studies at the departments of Radiology worldwide, also in healthy human volunteers. Furthermore, low dose amphetamine (0.3 mg/kg) is nowadays frequently administered in PET and SPECT studies, to study amphetamine induced dopamine release. The pharmacy of the AMC will provuide the d-amphetamine, conform GMP annex 13 criteria. No serious side effects of the low dose d-ampehtamine are foreseen. It has been shown that while some subjects experience large increases in happiness, restlessness and energy, other subjects experience almost no subjective effects following 0.3 mg/kg, and that the quality and intensity of the subjective responses to low dose amphetamine were similar during a second exposure (Abi-Dargham 2003). The radiation exposure of the SPECT scan is classified as category II, and routinely conducted at the AMC also in healthy human volunteers. Moreover, [123I]FP-CIT is a registated radioligand, which is produced routinely using GMP-criteria.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male adult volunteers, aged between 20 and 35.

Exclusion criteria

Contraindications for MRI (e.g. osteosynthetic material, pacemaker, artificial cardiac valves); claustrophobia. Symptomatic cardiovascular disease, moderate-to-severe hypertension, hyperthyroidism, glaucoma, hypersensitivity or idiosyncrasy to sympathomimetic amines, agitation, and history of drug abuse, or use of psychotropic drugs that affect DA function, such as methylphenidate and cocaine (anamnestic). Finally, cardial conduction disorder (abnormal ECG) en renal disease (serum creatinine * 110 mmol/L).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2009
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

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

No registrations found.

In other registers

Register	ID
CCMO	NL26449.018.09