Biperiden pharmacological-MRI as a tool to assess the function of the central cholinergic system: a validation study

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

Summary

ID

NL-OMON43422

Source
ToetsingOnline

Brief title
biperiden-phMRI

Condition

- Other condition
- Cognitive and attention disorders and disturbances

Synonym
NA

Health condition

centrale cholinerge systeem

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ERA-NET PrioMedChild (FP6)

Intervention

Keyword: acetylcholine, muscarine M1 receptor, pharmacological MRI, SPECT

Outcome measures

Primary outcome

- M1 receptor availability in the ACC, striatum and hippocampus.

- Change in free choline concentrations in the ACC and striatum

Secondary outcome

NA

Study description

Background summary

At present brain neurotransmission is typically visualized using positron emission tomography (PET) and single photon emission computed tomography (SPECT), techniques that involve radiopharmaceuticals. However, a recently developed technique called, pharmacological Magnetic Resonance Imaging (phMRI), allows measuring effects of pharmaceuticalspharmaca on the brain in a non-radioactive manner. Because with MRS it is possible to measure metabolite changes induced by a pharmacological challenge, radioactive compounds are not necessary. This novel approach yields a lot of information on how pharmaceuticals moderate brain function and how this response is altered in patients with a psychiatric disorder such as major depression, attention-deficit hyperactivity disorder (ADHD) or neurodegenerative disorders as Alzheimer*s or Parkinson*s disease.

Study objective

We aim to validate MRS with a cholinergic challenge as method to investigate muscarinic M1 receptor functioning. To investigate the relationship between the response to a muscarinic receptor antagonist with biperiden phMRI and

[123I]IDEX SPECT imaging.

Study design

The study is a cross-sectional single blind placebo-controlled study. All participants will receive SPECT imaging using [123I]IDEX on one occasion to assess brain M1 receptor availability. Participants will then undergo two MRS scanning sessions to measure concentrations of free choline: once under a cholinergic challenge with biperiden, and once after receiving a placebo.

Study burden and risks

MRS is a non-invasive imaging tool, which can also be used to measure drug-induced responses. Mild reversible unwanted effects have been found at 4 mg of biperiden administration (i.e. dry mouth, obstipation, concentration difficulties) but these are transient if occur. The radiation exposure of the SPECT scan is classified as category IIb (intermediate), and frequently conducted at the department of nuclear medicine AMC both in patients and in healthy human volunteers. Moreover, [123I]IDEX will be produced according to GMP criteria quality benchmark. Therefore, the risk involved in participating in this study should be considered negligible. The nature of the burden is classified as moderate considering that subjects will have to come to the AMC on 2 separate occasions and undergo 2 different types of scans. For the SPECT scan the nature of the burden is 1 venous puncture and for the MRI scan participants will be given biperiden orally as cholinergic challenge. No serious side effects of biperiden are foreseen

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

- For men: age 40 years and older. For women: 50 years and older
- Mentally competent to sign informed consent.

Exclusion criteria

- Use of anticholinergic medication
- Contraindications for MRI (e.g. metal implants, pacemaker etc.)
- Severe neurological, endocrine or psychiatric disorders (e.g., depression, bipolar illness)
- Pregnancy
- Current use of recreational drugs; participants must have abstained from using recreational drugs such as cannabis for at least 4 weeks prior to participation.
- Contraindications for biperiden
- Contraindications for potassium iodide

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2016
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	29-03-2016
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	NL56179.018.15