Pharmacological Magnetic Resonance Spectroscopy

Published: 22-09-2020
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To demonstrate that combined phMRI/phMRS can characterize the dose-dependent neurometabolic response to S-ketamine.

Ethical review	Approved WMO
Status	Completed
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Observational invasive

Summary

ID

NL-OMON49551

Source
ToetsingOnline

Brief title
phMRS

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
There is no specific disease being investigated

Research involving
Human

Sponsors and support

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

Intervention

Keyword: neuroimaging, pharmacology

Outcome measures

Primary outcome

* Change in levels of GABA, glutamate, and lactate in the mPFC;

* phMRI signal in the mPFC.

Secondary outcome

* Functional connectivity, with the prefrontal cortex as important region of interest

* Score on a VAS, to quantify the subjective effect of S-ketamine

* CADSS to monitor changes in dissociative state due to placebo or ketamine administration.

* Blood samples will be obtained at several time points to assess the plasma concentration of S-ketamine and its active metabolite norketamine.

Study description

Background summary

Pharmacological magnetic resonance imaging (phMRI), which measures the blood flow response to drug-induced neuronal activation, is a promising technique to non-invasively assess the brain*s response to psychotropic medication. However, phMRI measures are blood flow based and therefore often contaminated by (systemic) cardiovascular effects frequently induced by psychotropic medication. Magnetic resonance spectroscopy has been suggested as a technique to more directly assess drug-induced neuronal activity and therefore allow a more complete characterization of the brain response to psychotropic medication. We hypothesise that concurrent measurements of the hemodynamic response and glutamate/GABA levels (with MRS) during drug administration will provide the much-needed information to interpret the underlying neuronal contribution to the phMRI signal. The aim of the proposed study is to provide evidence for this hypothesis.

Study objective

To demonstrate that combined phMRI/phMRS can characterize the dose-dependent neurometabolic response to S-ketamine.

Study design

The study is a single-blind double-dose counterbalanced placebo-controlled randomized crossover design.

Study burden and risks

After an initial intake session, participants will visit the laboratory site 3 times. Each visit they will receive a sub-anaesthetic dose of S-ketamine or placebo intravenously, during a phMRS/phMRI scan.

On the day before each visit all participants will have to adhere to some simple restrictions regarding medication, alcohol and drug intake, as this may affect phMRI/phMRS scans. In the morning of each visit participants will have to refrain from smoking and stimulant containing drinks. During each experimental session, two IV lines will be placed to facilitate blood sampling and S-ketamine administration. The most common side effects of sub-anaesthetic doses of S-ketamine include nausea and psychotomimetic effects such as dream-like states and vivid imagery. Importantly, the above-mentioned adverse events rapidly decrease after discontinuation of administration of S-ketamine. Considering the low dose (five to nine times lower than anaesthetic dose), extensive exclusion criteria, screening procedure and constant monitoring of the subjects, no serious side effects are expected. Additionally, a (resident) anaesthesiologist will supervise S-ketamine administration. MRI is a safe method with no long-term side effects.

Though the participants of this study will have no direct benefits from participating, the results contribute to the exploration of the highly promising imaging technique phMRS. The overall nature and extent of the added risk associated with participation in the current study is to be classified as negligible and the burden can be considered minimal.

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 volunteers between 18 and 55 years old;
* BMI between 18.5 and 25;
* Male or female;
* If female: using oral contraceptives and not in hormone-free week during scanning.

Exclusion criteria

* (History of) psychiatric treatment, for which prescription medication is used;
* First-degree relative with (history of) schizophrenia or major depression;
* (History) of neurological disorders (including stroke, convulsion, epilepsy) as well as concussion with loss of consciousness
* Contraindications for S-ketamine (e.g. allergy for S-ketamine, or one of the inactive ingredients of this product, high BP (RRsystolic > 180 mmHg or diastolic >100 mmHg), use of xantiderivatives or methylergometrine);
* Contraindications for 7T MRI (e.g. claustrophobia, osteosynthetic material, pacemaker, artificial cardiac valves);
* (History of) drug (opiate, LSD, (meth)amphetamine, cocaine, solvents, cannabis, or barbiturate) or alcohol dependence;
* Used psychotropic medication, or recreational drugs over a period of 1 week prior to each test session;

* Used alcohol within the last 24 hours prior to each test session;

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-04-2021
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	22-09-2020
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: 29216
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL74447.018.20