An Investigation of the Test-Retest Variability of Measures of the Fractional Enrichment of Glutamate/Glutamine in Healthy Adults Measured Using Selective Proton Observed, Carbon Edited (selPOCE) MRS

Published: 25-11-2020
Last updated: 08-04-2024

The purpose of this study is:To investigate how glutamate is processed in the brain using magnetic resonance, a non-invasive technique used to see images of your brain. Glutamate is a chemical that sends signals between nerve cells in the brain.

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

Summary

ID

NL-OMON51033

Source
ToetsingOnline

Brief title
Study of selPOCE MRS Measures of Glutamate Flux in Healthy Adults

Condition

- Other condition
- Dementia and amnestic conditions

Synonym
Alzheimer□s disease, schizophrenia

Health condition

Depressed mood disorders and disturbances, Schizophrenia and other psychotic disorders

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Glutamate, Healty volunteers, MRS

Outcome measures

Primary outcome

- Part 1 - Objective: Determine the infusion parameters required to stably maintain plasma glucose concentrations of ~7-10 mM with an IV infusion of dextrose.

- Part 2- Objective: Evaluate the parameters (infusate concentration, rate and duration of infusion) for maintaining plasma glucose concentrations of ~7-10 mM over a typical scan period using a [U-13C] glucose infusion.

- Parts 2, 3 - Evaluation: Determine the fractional enrichment of 13C-glutamate, glutamine in the brain that can be achieved using an IV [U-13C] glucose infusion that maintains total plasma glucose at ~7-10 mM.

- Part 3-Objective: Assess the intra-subject test/retest variability around measures of the maximal fractional enrichment of 13C-labeled Glu and Gln levels in the prefrontal cortex of healthy adults using selPOCE MRS.

- Hypothesis: The mean difference in the maximal fractional enrichment of 13C-labeled Glu and Gln determined on 2 scan dates >=2 weeks apart under

baseline conditions (without pharmacologic intervention) in healthy adults is

<=25%.

Secondary outcome

- All parts: Monitor the safety and tolerability of glucose infusions

- Part 3 - Objective: Determine Vcycle and VTCA in the prefrontal cortex of

healthy adults using selective, proton observed, carbon edited magnetic

resonance spectroscopy

Study description

Background summary

This study will investigate a new, non-invasive technique to measure changes in glutamate. Glutamate plays an important role in learning and memory and may play a role in many disorders such as Alzheimer*s disease, schizophrenia, depression, substance use disorders, seizures, and other brain disorders.

Study objective

The purpose of this study is:
To investigate how glutamate is processed in the brain using magnetic resonance, a non-invasive technique used to see images of your brain. Glutamate is a chemical that sends signals between nerve cells in the brain.

Study design

If The volunteer does participate, this will last a total of 6.5 to 8.5 weeks (from screening until the follow-up visit) for the volunteer, depending on which part of the study the volunteer participate in.

The volunteer will be treated with the study intervention 1 or 2 times, depending on the part the volunteer participates in. The study will consist of 3 parts. The volunteer will participate in either Part 1, Part 2, Part 3, or (if the volunteer choose) both Parts 1 and 2.

The volunteer will receive an infusion into a vein in his arm, hand, leg, or foot, for up to 2 hours of a sugar, which is the study intervention. The volunteer will either receive dextrose, a simple sugar found in corn (subjects

in Part 1), or 13C glucose (subjects in Parts 2 or 3).

Intervention

The volunteer will receive an infusion into a vein in his arm, hand, leg, or foot, for up to 2 hours of a sugar, which is the study intervention. The volunteer will either receive dextrose, a simple sugar found in corn (subjects in Part 1), or 13C glucose (subjects in Parts 2 or 3).

Study burden and risks

The study intervention may cause side effects/adverse effects.

Disadvantages of participating in the study may be:
- Possible side effects of the study intervention;
- Possible adverse effects or discomforts of the evaluations in the study;
- Administration of study intervention according to strict procedures;
- Disadvantages for your partner/those living with you;
- Participation in the study may lead to incidental findings about your health. You may not wish to know this.
- Covid test

Contacts

Public
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US
Scientific
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New Jersey 08889-0100
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Is in good health based on medical history, physical examination, VS measurements and ECGs performed prior to randomization (referring to Appendix 9 of the protocol).
2. Is in good health based on laboratory safety tests obtained at the screening visit (referring to Appendix 2 and 10 of the protocol).
3. Have a fasting blood glucose <=110 mg/dL and a Hb1Ac <= 6.1%.
4. Have a BMI <=30 kg/m2, inclusive.
5. Is male, from 18 years to 50 years of age inclusive, at the time of signing the informed consent.
6. The participant provides written informed consent/assent for the study, including for future biomedical research.
7. Has acceptable venous access.
8. Is willing to comply with the study restrictions.

Exclusion criteria

1. Has a history of clinically significant endocrine, gastrointestinal, cardiovascular, hematological, hepatic, immunological, renal, respiratory, genitourinary, or major neurological (including stroke and chronic seizures) abnormalities or diseases.
• Candidates with Type 1 or 2 diabetes are specifically excluded.
Participants with a remote history of uncomplicated medical events (eg, uncomplicated kidney stones, as defined as spontaneous passage and no recurrence in the last 5 years, or childhood asthma) may be enrolled in the study at the discretion of the investigator.
2. Is mentally or legally incapacitated, has significant emotional problems at the time of pre-study (screening) visit or expected during the conduct of the study or has a history of clinically significant psychiatric disorder of the last 5 years. Participants who have had situational depression may be enrolled in the study at the discretion of the investigator.
3. Has a history of cancer (malignancy).
Exceptions include adequately treated non-melanomatous skin carcinoma or other malignancies which have been successfully treated with appropriate follow up and are therefore unlikely to recur for the duration of the study, in the opinion of the investigator and with agreement of the Sponsor (eg, malignancies which have been successfully treated >=10 years prior to the pre-study

[screening] visit).
4. Has a history of significant multiple and/or severe allergies (eg, food, drug, latex allergy), or has had an anaphylactic reaction or significant intolerability (ie, systemic allergic reaction) to prescription or non-prescription drugs or food.
5. Is positive for hepatitis B surface antigen, hepatitis C antibodies or HIV.
17. Parts 2 and 3 only: Has implanted metal objects (including pacemakers, neurostimulators, vascular clips, cochlear or other auditory implants, hydrocephalus/insulin/medicine pumps, vascular stents, etc), works with metal (ie, welder), or has any other exclusion criteria that prevents participation in an MRI scan.

For complete overview see the protocol.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-12-2020
Enrollment:	28
Type:	Actual

Ethics review

Approved WMO

Date:	25-11-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	30-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL75257.056.20