The role of glutamate in cognition in adults with chromosome 22q11 deletion syndrome

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON47173

Source
ToetsingOnline

Brief title
Glutamate and cognition in adults with 22q11DS

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Cognitive and attention disorders and disturbances

Synonym
DiGeorge syndrome, Velo-Cardio facial syndrome (VCFS)

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 22q11DS, glutamate, Magnetic Resonance Spectroscopy (MRS), riluzole

Outcome measures

Primary outcome

The main study parameter will be hippocampal, striatal and ACC glutamate concentrations as measured with [1]H MRS after a glutamate challenge and after placebo.

Secondary outcome

A secondary outcome measure is cognitive functioning, measured with a standardized cognitive battery (CANTAB). A cognitive composite score will be computed using the mean scores of the CANTAB subtests. This score will represent cognitive functioning and will be correlated with glutamate concentrations in the ACC and striatum.

Study description

Background summary

22q11 deletion syndrome (22q11DS) is a genetic disorder caused by a microdeletion on the long arm of chromosome 22. Subjects with this syndrome have an increased risk of developing a variety of psychiatric disorders, particularly schizophrenia and other psychotic disorders. One of the genes located at the deleted region in 22q11DS is known to be involved in glutamatergic neurotransmission. This gene encodes proline dehydrogenase (PRODH), also known as proline oxidase. This enzyme is implicated in converting proline to glutamate. Glutamate, i.e. the major excitatory neurotransmitter in the brain, has been associated with the pathophysiology of psychosis, particularly the cognitive symptoms. Since 22q11DS is associated with progressive cognitive and functional deterioration in combination with psychosis, it could be hypothesized that a neurodegenerative process, as a consequence of chronic high (neurotoxic) concentrations of glutamate could result in neuronal damage. This suggests that abnormal glutamatergic

neurotransmission could explain the vulnerability for psychopathology and cognitive decline in 22q11DS.

Study objective

The main objective of this (pilot) study is to investigate the role of glutamate in cognitive functioning in adults with 22q11DS using a glutamatergic challenge (riluzole)and high-field MRS. We will relate glutamate concentrations in the striatum and anterior cingulate cortex (ACC) with performance on a cognitive test battery (CANTAB).

Study design

This study is a double-blind, cross-over placebo controlled (pilot) study. To measure in-vivo glutamate concentrations in the brain, all participants will receive a MRS scan on two occasions, one following placebo and one following a glutamatergic challenge (riluzole, 50 mg.). The order of placebo and drug will be counterbalanced. On the first day, a cognitive test battery (CANTAB) will be assessed prior to the MRS scan.

Intervention

On two occasions, non-invasive 7.0 Tesla MRS recordings will be conducted, once following a glutamate challenge (riluzole, 50 mg.) and once following placebo, administered orally.

Study burden and risks

The study protocol will be explained to the participants and they will be asked for consent for participation. [1]H-MRS is a non-invasive measuring apparatus. Little unwanted effects have been found at 50 mg of riluzole oral administrationin healthy subjects and these are transient if occur. Therefore, the risks are negligible and the burden of participation to the study is minimal. This study will be carried out with adults with a confirmed diagnosis of 22q11DS. The study is group related; it is only possible to extent the knowledge of 22q11DS and associated cognitive function and psychopathology using this unique population.

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 participants with 22q11DS:
• Confirmed diagnosis of 22q11DS established by FISH, microarray or MLPA analysis.
• Age 18 and older and mentally competent to give informed consent.
• No psychopharmacological treatment at the time of inclusion .
• No presence of a physical/medical condition that may interfere with the study.
• No contraindication for MRI;For healthy controls:
• Healthy subjects will be matched for age, gender and ethnicity.
• No use of any psychopharmacological treatment at the time of inclusion.
• No presence of a physical/medical condition that may interfere with the study.
• No contraindication for MRI

Exclusion criteria

For participants with 22q11DS:
• Other chromosomal abnormalities
• Current substance abuse / dependence
• Comorbid psychiatric / neurologic disorder
• Contraindications for Riluzole;For healthy controls:

• Any chromosomal abnormalities
• Current substance abuse / dependence
• A psychiatric or neurologic disorder
• Contraindications for riluzole

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-03-2015
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	19-01-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-08-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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: 29680
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL49834.068.14
OMON	NL-OMON29680