Glutamate and cognition in adults with 22q11DS

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29680

Source
NTR

Health condition

22q11 deletion syndrome
cognition

Sponsors and support

Primary sponsor: Maastricht University
Source(s) of monetary or material Support: Maastricht University

Intervention

Outcome measures

Primary outcome

The main study parameter will be 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.

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.

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 hippocampus, striatum and anterior cingulate cortex (ACC) with performance on a cognitive test battery (CANTAB).

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 both occasions, a cognitive test battery (CANTAB) will be assessed after the MRS scan.

Study objective

It is hypothesize that

-performance on a cognitive test battery (CANTAB) will be negatively associated with brain glutamate concentrations in adults with 22q11DS

-Cognitive functioning will improve after riluzole administration compared to placebo.

Study design

2 weeks

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.

Contacts

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Eligibility criteria

Inclusion criteria

• 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

Exclusion criteria

•Other chromosomal abnormalities

•Current substance abuse / dependence

•Comorbid psychiatric / neurologic disorder

•Contraindications for Riluzole

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2015
Enrollment:	10
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	11-03-2015

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 47173
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4841
NTR-old	NTR5095
CCMO	NL49834.068.14
OMON	NL-OMON47173

Study results