Brain glutamate levels in patients who experienced a psychosis: The GLUP study

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Objectives: Primary objective: - To investigate whether high-resolution glutamate levels in the brain of patients that experienced a psychosis differ from healthy individuals.Secondary objectives:- To compare the high resolution glutamate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational invasive

Summary

ID

NL-OMON47254

Source
ToetsingOnline

Brief title
GLUP

Condition

- Schizophrenia and other psychotic disorders

Synonym
psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NARSAD en NWO

Intervention

Keyword: glutamate, MRS, psychosis, symptoms

Outcome measures

Primary outcome

Primary study parameter:

- High-resolution brain glutamate levels.

Secondary outcome

Secondary study parameters:

- Symptom severity in patients who experienced a psychosis

o Short cognitive test battery

o Positive and negative symptoms (Positive and Negative Symptoms Scale (PANNS))

o Functional impairment (using the Manchester Short Assessment of Quality of

Life)

- Structural (brain volumes) and functional (resting state BOLD signal) brain

parameters.

- (epi)Genetic variation in glutamatergic genes.

Study description

Background summary

Rationale: An increasing number of studies point to a role for glutamatergic dysfunction in the pathophysiology of psychosis. In vivo glutamate levels can be non-invasively measured with proton magnetic resonance spectroscopy (1H-MRS). A major methodological drawback is the fact that glutamate levels are currently measured in one rather large preselected voxel (usually around 8 cm3). This sharply contrasts with the ubiquitous presence of glutamate across the brain and the convincing evidence for altered glutamate functionality in psychotic disorders in cortical, limbic, and striatal regions. This study uses

a novel spectroscopy approach to investigate high-resolution in vivo glutamate levels across the brain in psychosis using a multichannel crusher coil. Therefore, we can now investigate how glutamatergic dysfunction in after an episode of psychosis affects glutamate levels across the brain at high resolution, including the possibility to map interlinked regions.

Study objective

Objectives:
Primary objective:
- To investigate whether high-resolution glutamate levels in the brain of patients that experienced a psychosis differ from healthy individuals.
Secondary objectives:
- To compare the high resolution glutamate distributions to
o symptom severity in first episode psychosis patients (cognitive and psychotic symptoms, as well as functional impairment)
o structural (brain volumes) and functional (resting state BOLD signal) brain parameters of all participants.
- To investigate whether (epi)genetic variation in glutamatergic genes affects glutamate levels in both patients and healthy controls.

Study design

Study design:
A small monocenter study in patients who experienced a psychosis (N=50) and healthy individuals (N=50). Participants will undergo one scanning session in the 7T scanner (duration around 60 min) and complete a cognitive test battery.

Study burden and risks

Risks for participants are minimal. Participation consists of some questionnaires taking approximately half an hour, and one session with a duration of approximately 3,5 hours and sufficient time for breaks. No direct benefits are present for participants. All participants will be given a reimbursement of ¤40,- for their cooperation and time. Also potential travel costs will be reimbursed.

The visit includes:
- Inclusion, collection of a blood sample (duration around 60-90 min, depending on whether PANSS interview is needed)
- Completion of cognitive test battery (duration around 60 min).
- One MRI scan in the 7Tesla scanner (duration around 60 min).

Regarding a risk analysis, a negligible risk for participants is estimated. One scanning session with a duration of 60 minutes in the 7T scanner has often been

applied without any known disadvantageous effects as reviewed in literature

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:;Inclusion criteria for all subjects (patients and healthy controls):
* 16-40 years old.
* Written informed consent of the subject;Patients who experienced a psychosis:
* Psychosis (ICD-10 criteria for any functional psychotic illness: F10-19, excluding coding F1x.0 for Acute intoxication; F20-29 and F30-39, psychotic codings).

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;General exclusion criteria for all individuals:
- Use of certain drugs and medication
- Any previous neurosurgery or neurological disorder, including epilepsy
- Any contraindications for MRI
- Subjects who do not fully comprehend the purpose or are not competent to make a rational decision whether or not to participate
- Patients who were admitted to a psychiatric unit involuntarily after being given an *inbewaringstelling* (IBS). Patients with *rechterlijke machtigingen* (RM) may be included, but only if they are mentally competent (see section on mental competence and decisional capacity above). The reasons for including these patients are that this will increase the likelihood of attaining the projected number of study participants and that inclusion of these patients will contribute to assembling a study population representative of all Dutch patients.
;Additional exclusion criteria for healthy controls:
- Current Axis-I psychiatric disorder

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-09-2017
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	27-01-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-03-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL55796.041.15