Predicting Treatment Resistance in Schizophrenia

Published: 18-04-2018
Last updated: 19-03-2025

1. To assess whether a. Neuromelanin-sensitive MRI (nMRI) is a suitable biomarker for TRb. Plasma DDC activity is a suitable biomarker for TR2. To increase our insight in the role of glutamate in the anterior cingulate cortex (ACC) in TR and assess...

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

Summary

ID

NL-OMON48828

Source
ToetsingOnline

Brief title
TREVOS

Condition

- Schizophrenia and other psychotic disorders

Synonym
first episode psychosis, schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: veni subsidie van dr. E.M. van de Giessen

Intervention

Keyword: dopa decarboxylase, neuromelanin MRI, schizophrenia, treatment resistance

Outcome measures

Primary outcome

- Treatment resistance

- Neuromelanin contrast ratio on nMRI

- Glutamate/Creatine ratio on MRS in ACC

- Plasma DDC activity

- [18F]DOPA influx (Ki) value (for subgroup of 40 patients)

Secondary outcome

- Side effects of antipsychotics

- Symptom scores on PANSS

- Neuropsychological ratings

Study description

Background summary

Treatment resistance (TR) in schizophrenia is a major clinical problem with 20-35% of psychotic patients showing non-response to antipsychotic treatment. This leads to months to years of delay in effective treatment, resulting in hospitalization and unnecessary side effects of ineffective antipsychotics. We need a biomarker that could be used to switch TR patients at an early stage to clozapine, the only antipsychotic with recognized superior effectiveness in TR. A well-established finding in schizophrenia, using [18F]F-DOPA positron emission tomography (PET) imaging, is increased striatal dopamine synthesis, but interestingly TR patients don*t show altered synthesis. PET imaging however is too costly and invasive to use for TR screening. A novel neuromelanin-sensitive MRI sequence (nMRI), which indirectly measures striatal dopamine synthesis, has great potential as biomarker for TR. nMRI indeed shows increased signal in schizophrenia patients, but has not yet been tested in TR. Another potential biomarker is a recently developed plasma measure of dopa

decarboxylase (DDC) activity, an enzyme required for dopamine synthesis. Furthermore, the role of other neurotransmitters than dopamine in TR is underexposed, of which glutamate is a likely candidate.

Study objective

1. To assess whether
a. Neuromelanin-sensitive MRI (nMRI) is a suitable biomarker for TR
b. Plasma DDC activity is a suitable biomarker for TR
2. To increase our insight in the role of glutamate in the anterior cingulate cortex (ACC) in TR and assess whether it is a potential biomarker for TR

Study design

Prospectief

Study burden and risks

Patients will be assessed on two separate occasions:
(1) Interview, MRI (eventual questionnaires, neuropsychological tasks, blood draw)
(2) interview, MRI (eventual questionnaires, neuropsychological tasks and blood draw) (6 months later).
A subgroup of 40 participants will have an additional visit at baseline for an [18F]F-DOPA PET scan.
Risks: For the subgroup of 40 patients, the radiation dose for this study is 3.9 mSv and falls within category IIb (minor to intermediate) and is lower than most diagnostic CT scans.

Healthy controls will be assessed on one occasion:
(1) Interview, MRI, questionnaires and neuropsychological tasks

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9

Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For patients:
- First episode psychosis
- Age 18-35 years old;For healthy contols:
- Age 18-35 years old

Exclusion criteria

- Antipsychotic use longer than one year
- Dependence on other substances of abuse than nicotine or cannabis
- Use of amphetamine, cocaine or medication for ADHD (attention deficit hyperactivity disorder), since these drugs influence the dopamine system
- Neurological disorder (e.g. epilepsy) or evidence of brain damage
- Inability to provide informed consent;In addition to the exclusion criteria mentioned above, healthy control subjects are not allowed to have any kind of psychiatric disorder;Exclusion criteria directly related to MRI scanning:
- Contra-indications for MRI (including pacemaker, ferromagnetic implants, claustrophobia)
- Pregnancy;Exclusion criteria directly related to PET/CT scanning (for subgroup of 40 patients):
- Participation in a scientific examination where radiation was used, in the last year.
- Positive urine drug screen on the day of the PET/CT scan. Participants will be tested on cannabis, amphetamine, XTC, cocaine and opiates. Only recent cannabis use will be accepted.
- In women: positive pregnancy test on the day of the PET/CT scan and lactation.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	29-05-2018
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	18-04-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	18-02-2020
Application type:	Amendment
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: 21525
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	7430
CCMO	NL63410.018.17
OMON	NL-OMON21525