An Imaging and Cognition Study of Positive Valence Systems in Psychotic Syndromes

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To examine the PVS domain, and in particular reward circuits and behaviour, in large genetically informative cohorts comprising 500 individuals (including 125 SCZ patients, 125 BP patients, 125 relatives and 125 controls) already ascertained in the...

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

Summary

ID

NL-OMON54698

Source
ToetsingOnline

Brief title
Brain Function of Individuals with Psychotic Disorders and Bipolar Disorder

Condition

- Schizophrenia and other psychotic disorders

Synonym
Psychosis; manic depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: National Institute of Mental Health;United States

Intervention

Keyword: Bipolar disorder, Brain function, Positive valence, Psychotic disorders

Outcome measures

Primary outcome

Estimates of brain activation during task performance.

Secondary outcome

Performance on the 3 PVS tasks, answers to questions (collected via self-report and interviews) on current demographics, clinical situation, motivational behaviour, and personality.

Study description

Background summary

The Research Domains Criteria (RDoC) initiative aims to identify more valid dimensions, spanning multiple biological and psychological levels, to advance basic understanding of mental disorders and their treatments. One of the core components of RDoC is focused on reward circuits and behavior. Reward circuitry is central to the formulation of the RDoC Positive Valence Systems (PVS) domain, which has been linked to diverse psychiatric disorders including schizophrenia and bipolar disorder.
There is consensus that schizophrenia (SCZ) and bipolar disorder (BP) share substantial genetic risk and multiple overlapping phenotypic variations at the levels of corticostriatal brain circuits, cognitive functions, and behavior.
Yet, it remains unknown precisely whether reward circuitry and behaviour is similar.

Study objective

To examine the PVS domain, and in particular reward circuits and behaviour, in large genetically informative cohorts comprising 500 individuals (including 125 SCZ patients, 125 BP patients, 125 relatives and 125 controls) already ascertained in the Netherlands. Using functional MRI (fMRI) we aim to characterize the neural correlates of the ventral striatum of the reward circuit during the Monetary Incentive Delay (MID) task in relation to diagnostic category and symptom dimensions. In addition, we aim to characterize

the PVS system using 3 online assessments. "

The primary objective is to identify differences in ventral striatum (VS) activity during reward anticipation between 125 patients with SCZ, 125 patients with BP and 125 controls.

The secondary objectives are:
1. to characterize the neural correlates of the VS of the reward circuit in relation to symptom dimensions in 250 patients, 125 relatives and 125 controls
2. to identify differences in VS activity during reward anticipation in relatives of patients as compared with patients and controls
3. to identify differences in the other three primary PVS components (reward valuation, effort valuation, Action Selection/Decision Making), assessed using an online tool, between patients, relatives and controls.

Study design

This is an observational study.

Study burden and risks

Study participation involves one visit to the Erasmus MC which will take approximately 5.5 hours in total. At the Erasmus MC, the participant will conduct an online cognitive assessment (1 hour) and will be interviewed (patients: to assess current state and lithium, lamotrigine and clozapine response, 45 minutes; relatives and controls: to assess psychiatric symptoms, 30 minutes). In addition, we ask for a fecal sample for biobanking, we measure height, weight and blood pressure, a blood sample will be drawn (8 ml in 2 EDTA tubes). Blood samples will be taken from the participating subjects and stored at the biobank of the Erasmus MC. On request, the skin can be locally anesthetized prior to the venapuncture. Since the amount and number of blood samples is limited, the burden for participating subjects is expected negligible. Participants are asked to fill out questionnaires on current demographic and clinical situation, lithium and lamotrigine reponse, motivational behaviour and personality (1 hour, these questionnaires can be filled out from home). In addition, a magnetic resonance imaging (MRI) scan session will be performed (1 hour). Technically MRI is a non-invasive technique (i.e., nothing is inserted into the body). However, the CCMO marked MRI as an invasive technique to heighten the safety regulations. There are no known risks associated with MRI acquisition, so there is no need for special preparation for the subject on top of the Erasmus MC standard procedure. The data are primarily used for research purposes. However, a radiologist will provide a neurodiagnostic evaluation. When the specialist finds that medical treatment is indicated, then the subject will be notified. Also, subjects may become anxious during the scan. The subject can communicate this by means of a push button, and he/she will be taken out of the scanner.

The risk assessment for participation to this study is minimal. Subjects will experience no direct benefits from our study. In the long run, increased understanding of the etiology and pathophysiology of SCZ and BP may contribute to diagnosis, early detection, and/or prediction of treatment outcome.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

For patients:
1. Diagnosis of a psychotic disorder or bipolar disorder

For all participants:
1. In case of participants from the GROUP or Bipolar Genetics study; provided past consent to be re-contacted for future studies.
2. Give written informed consent for the current study

3. Age 18 years or older
4. First degree family members of the included patients can participate, irrespective of having a psychiatric diagnosis or not.
5. Controls subjects must not have an affective or non-affective diagnosis, nor in their first-degree family members.

Exclusion criteria

- No demonstration of adequate understanding of the purpose, procedures, risks, benefits, emergency contacts, and payment issues.
- Unable to give consent to all aspects of the study.
- Ferrous objects in or around the body (e.g. braces, tattoos, piercings, metal fragments; small braces are allowed
- Pacemaker or other stimulatory devices/leads that are not temporarily removable from the body without health hazards
- Claustrophobia
- History of closed head injury
- History of neurological illness or endocrine dysfunction
- Neurological abnormalities as well as structural brain abnormalities that may interfere with the measurements, identified through neurodiagnostic evaluation

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:	Completed
Start date (anticipated):	21-12-2020
Enrollment:	500
Type:	Actual

Ethics review

Approved WMO Date:	18-02-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-09-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL70380.078.19