Genetic vulnerability to stress across psychiatric diagnoses. Schizophrenia and Major Depressive Disorder

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Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON31500

Source
ToetsingOnline

Brief title
Stress and brain in psychiatry

Condition

- Other condition

Synonym
mood disorder, psychosis

Health condition

psychiatrische aandoeningen

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: genetic susceptibility, major depressive disorder, schizophrenia, stress

Outcome measures

Primary outcome

The main study parameter is the relationship between susceptibility to stress

(cortisol response after a psychosocial stressor) and structural and functional

brain measurements, and how this association is medicated by genotype (COMT,

5HTTLPR).

Secondary outcome

n/a

Study description

Background summary

One of the most extensively studied and replicated gene-by-environment interactions is the interaction between life stressors and a genetic sensitivity to stress, often used to conceptualize the pathogenesis of affective illnesses. Recently, it was shown that the polymorphisms in the serotonin transporter promoter region (5-HTTLPR) and COMT are related to sensitivity to stress. The association between both 5-HTTLPR and COMT and increased sensitivity appears related to the interaction between medial prefrontal cortex (mPFC), amygdala and hippocampus.
Interestingly, the hippocampus, which is highly affected by prolonged increased levels of cortisol, is found to be decreased in both schizophrenia and major depressive disorder (MDD). Moreover, schizophrenia and MDD share abnormal structure and function of the amygdala and mPFC, as well as clinical and genotypic features.

Study objective

In the current proposal we hypothesize that vulnerability to stress is a non-specific risk factor for developing either schizophrenia or MDD. Increased stress sensitivity is hypothesized to be related to reduced prefrontal functioning, leading to diminished inhibition of the amygdala which consequently shows increased activation. As a result of this these subjects will also show smaller hippocampal volumes than subjects not at genetic risk. Being exposed to stressful life events in combination with a genetic sensitivity to stress is expected to reinforce these effects.

Study design

This study is a three-group experimental study, in which diagnosis is the between-subjects grouping variable. Within-subject variables are stress susceptibility (i.e., cortisol-responsiveness after a psychosocial stressor), brain volume and density measures of mPFC, hippocampus and amygdala as measured with sMRI, white matter integrity and connectivity as measured with MTR and DTI, task related brain activity as measured with fMRI (expressed in BOLD-signal changes), and the occurrence of life-events.

Study burden and risks

Two MRI scan sessions of approximately 50minutes each will be performed: MRI is a non-invasive technique, so there is no need for special preparation for the subject. There are no known risks associated with the MRI acquisition and the data are solely used for research purposes. However, structural cerebral pathology may be noticed. If medical treatment is indicated, the subject will be notified.

From each participant a small amount (4 x 10 ml) of EDTA blood will be taken, by means of a venapuncture. On request, the skin can be locally anesthetized prior to the venapuncture. If the participant refuses the puncture, a cotton swab of buccal mucosa can be taken. Since the number of blood samples is limited and the samples are small, the burden for participating subjects is expected to be negligible.

No immediate benefits are to be expected from participation in this study for the subjects. In the long run, increased understanding of the etiology and pathophysiology of psychiatric illness in general and schizophrenia and major depression in particular, 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)
Elderly (65 years and older)

Inclusion criteria

Subjects have to satisfy the following criteria in order to participate in the study:
- Give written informed consent
- Aged between 18-65 years of age;Specific for schizophrenia patients:
- Do have a DSM-IV diagnosis of Schizophrenia
- Do not chronically use medication, other than psychiatric medication
- Are not in an acute psychotic episode, but stable for at least 6 months;Specific for MDD patients:
- Do have a DSM-IV diagnosis of Major Depressive Disorder
- Do not chronically use medication, other than psychiatric medication
- Are not in an acute depressive episode, but stable for at least 6 months
- Have had at least two depressive episodes and at least one hospital admission due to affective symptoms

Exclusion criteria

- Ferrous objects in or around the body (e.g. braces, pacemaker, metal fragments)
- Claustrophobia
- Drug or alcohol abuse over a period of six months prior to the experiment
- History of closed-head injury
- History of neurological illness or endocrinological dysfunction
- A pacemaker;Specific for the healthy individuals:
- A psychiatric history
- Chronic use of medication
- A first-degree family member with a psychiatric illness

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:	Will not start
Enrollment:	90
Type:	Anticipated

Ethics review

Not approved

Date:	23-12-2008
Application type:	First submission
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	NL18121.041.08