stress and functional connectivity in bipolar disorder

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Primary objective: Investigate the effects of a stress task on resting state and task-induced functional connectivity in patients with bipolar I disorder. Secondary objective: - Correlate the endocrine response to mental challenge to resting state...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42774

Source
ToetsingOnline

Brief title
BiCONNECT

Condition

- Other condition
- Psychiatric disorders NEC

Synonym
stress-related psychiatric disorders

Health condition

effect van stress op connectiviteit in het brein

Research involving
Human

Sponsors and support

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

Intervention

Keyword: bipolar disorder, functional connectivity, MRI, stress

Outcome measures

Primary outcome

Effects of mental challenge on functional connectivity in the brain during rest

and during emotion and reward processing.

Secondary outcome

- Change in levels of cortisol, alpha-amylase, heart rate and perceived stress

levels

- (epi)genetic variation in a number of genes involved in stress

Study description

Background summary

Bipolar I disorder (BP1) is characterized by recurrent manic and depressive episodes. Stress increases the risk for these symptoms. It is currently unknown how stress causes these detrimental effects and what the underlying biological mechanisms are. Multiple neuroimaging studies have established impairments of both structural and functional connectivity within emotional networks in patients with bipolar disorder. The overall aim of this study is to investigate how stress affects the brain of euthymic BP1 patients by examining functional connectivity. This provides a unique opportunity to investigate how acute stress affects connectivity in the diseased brain in which connectome abnormalities are already present.

Repeatedly measuring brain activity with functional MRI (fMRI) allows the assessment of both the spatial and temporal characteristics of stress on neuronal connectivity. This is relevant as the effects of stress follow a distinct temporal pattern. Immediately after stress, catecholamines and fast

(non-genomic) effects of corticosteroids promote instrumental and short-term behavior. In contrast, in the aftermath of stress, behavior is aimed at restoring higher cortical functions with more flexible behavior. Examining the temporal effects of stress on the brain by repeatedly measuring functional connectivity patterns can provide a dynamic readout of stress vulnerability in BD1 patients.

Study objective

Primary objective: Investigate the effects of a stress task on resting state and task-induced functional connectivity in patients with bipolar I disorder.
Secondary objective:
- Correlate the endocrine response to mental challenge to resting state and task-induced functional connectivity
- Investigate the association between (epi)genetic variation in genes involved in emotional control and functional connectivity in the brain during rest and task.

Study design

A small monocenter intervention study in healthy individuals (N=40) and BP1 patients (N=40). Participants will be randomized to either the stress condition (Trier Social Stress Test, TSST) or a validated control condition, resulting in the following 4 groups:
- healthy individuals * control test (N=20)
- healthy individuals * stress test (N=20)
- BP1 patients * control test (N=20)
- BP1 patients * stress test (N=20)

Intervention

All participants will be subjected to either the stress or control condition of the Trier Social Stress Test, a validated and standardized test to induce a psychosocial challenge in laboratory settings.

Study burden and risks

Risks for participants are minimal. Participants are invited to the UMCU two times with a duration of approximately 4 hours and sufficient time for breaks. No direct benefits are present for participants. All participants will be given a reimbursement of ¤60,- for their cooperation and time. An additional reimbursement of ¤15,- will be received after the reward task. Also potential travel costs will be reimbursed.

The visit includes:
- Inclusion, collect a blood sample, complete several questionnaires

- Three MRI scans in the 3T scanner before and after the Trier Social Stress Test (TSST)
Total duration: 265 min (of which 60 min in the 3T scanner).

Regarding a risk analysis, a negligible risk for participants is estimated. The stress test involves a speech test and/or a short arithmetic test that does not lead to extreme perceived stress levels. The stress test has often been applied without any known lasting disadvantageous effects as reviewed in literature (Dickerson & Kemeny, 2004). This includes previous studies from our group (the CHOICE study [METC 11-222) and Epistress [METC 11-259] and COLUMBUS [METC 12-563]) and an ongoing stress study measuring functional connectivity in siblings of schizophrenia patients, which show no detrimental effects and the feasibility of repeated scans in the MRI scanner.

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

Age between 18 and 50 years old
Diagnosed with bipolar I disorder (patient group only)

Exclusion criteria

General exclusion criteria for all subjects:
- Any previous neurosurgery or neurological disorder, including epilepsy
- History of head injury resulting in unconsciousness lasting at least 1 hour
- Mental retardation
- Any contraindications MRI
- Subjects who do not fully comprehend the purpose or are not competent to make a rational decision whether or not to participate
- Lack of fluency in the Dutch language
- Speech impairments
- Self-reported current or past drug use in the last week
- Positive urine screen on the presence of amphetamines (including MDMA), cannabinoids, cocaine and opiates)
- Current neurological or endocrine disorder including alcohol or drug abuse or dependence
- claustrophobia
- Any acute illness
- Physical exertion within the last 2 hours
- Use of medication which might influence the stress response, such as beta blockers and any hormonal treatment (including steroids).;Additional exclusion criteria for healthy controls:
- Current Axis-I psychiatric disorder
- First-degree relative with a current Axis-I psychiatric disorder

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-06-2016
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	22-01-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-07-2016
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	NL55314.041.15