Functional Connectivity in the Brain after Cognitive Load: the CONNECT Study

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Primary objective: Investigate the effects of acute stress on resting state and task-induced connectivity in the brain of healthy individuals and unaffected siblings of schizophrenia patients. Secondary objectives: - Correlate the endocrine stress...

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

Summary

ID

NL-OMON44499

Source
ToetsingOnline

Brief title
CONNECT

Condition

- Other condition

Synonym
Stress-related psychiatric disorders

Health condition

effecten van stress op connectiviteit van 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

Intervention

Keyword: functional connectivity, MRI, siblings of schizophrenia patients, stress

Outcome measures

Primary outcome

Task-induced and resting state functional connectivity between the prefrontal

cortex and amygdala

Secondary outcome

- Basal and stress-induced levels of cortisol, alpha amylase, heart rate and

perceived stress levels.

- (Epi)genetic variation in a limited number of stress genes.

Study description

Background summary

Stress increases the risk for psychotic symptoms, both in schizophrenia and in the general population. It is currently unknown how stress causes these detrimental effects and what the underlying neurobiological mechanisms are. The overall aim of this study is to investigate how stress affects the brain by examining functional connectivity.
Recent neuroimaging studies at the UMCU have established impairments of both structural and functional connectivity in unaffected siblings of schizophrenia patients. Therefore, this study will also study unaffected siblings of schizophrenia patients. This provides a unique opportunity to investigate how acute stress affects connectivity in the vulnerable 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. Investigating the temporal effects of stress on the brain by repeatedly measuring functional connectivity patterns can provide a dynamic readout of stress vulnerability.

Study objective

Primary objective: Investigate the effects of acute stress on resting state and task-induced connectivity in the brain of healthy individuals and unaffected siblings of schizophrenia patients.

Secondary objectives:
- Correlate the endocrine stress response to resting state and task-induced functional brain connectivity parameters.
- Investigate the association between (epi)genetic variation in stress-related genes and stress-related functional connectivity.

Study design

A small monocenter intervention study in healthy individuals (N=40) and unaffected siblings of schizophrenia 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)
- unaffected siblings * control test (N=20)
- unaffected siblings * stress test (N=20)

Functional connectivity is repeatedly measured in the brain before and after an experimental stress/control test using fMRI in a 3Tesla scanner.

Intervention

Participants are randomized to either a stress test or a control test.
o Stress: the Trier Social Stress Test (TSST), a validated and standardized test to induce psychosocial stress in laboratory settings.
o Control: a validated protocol with no psychosocial stress components.

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. Also potential travel

costs will be reimbursed.

During visit:
- Inclusion, collect a blood and urine sample, complete several questionnaires
- Three MRI scans in the 3T scanner before (1x) and after (2x) either the Trier Social Stress Test (TSST) or a control protocol.
- Saliva samples
- Total duration: 250 min (of which 65 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 control protocol also consists of a speech and/or short arithmetic task, but without the psychosocial stress components. The stress test has often been applied without any known lasting disadvantageous effects as reviewed in literature.1 This includes two previous studies from our group outside the MRI scanner (the CHOICE study [METC 11-222) and Epistress [METC 11-259]) and an ongoing stress study measuring GABA and glutamate levels in the 7T-MRI scanner (Columbus study [METC 12-563]) which show no detrimental effects of the combination of stress and 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 55 years old
- 1st degree family member with schizophrenia (unaffected sibling group only)

Exclusion criteria

General exclusion criteria:
- Incapability of giving informed consent
- Lack of fluency in the Dutch language or speech impairments
- Irregular sleep/wake rhythm (e.g., regular nightshifts or cross timeline travel).
- Use of medication which might influence the stress response, such as psychotropics, beta blockers, ACE inhibitors and any hormonal treatment.
- Major medical history including history of closed or open head injury.
- Acute minor medical illness within the three weeks prior to testing
- Current psychiatric, neurological or endocrine disorder including claustrophobia and alcohol abuse or dependence
- Epilepsy in 1st degree family
- Psychiatric illness in 1st degree family (only in healthy control group)
- Self-reported current or past drug use in the last 2 weeks
- Ferrous objects in or around the body according to default checklist present ;Acute exclusion criteria:
- Any acute inflammatory disease
- Physical exertion within the last 2 hours
- Drink other than water or any food within the last 2 hours
- Any alcohol use in the last 24 hours
- Positive urine screen on the presence of amphetamines (including MDMA), barbiturates, cannabinoids, benzodiazepines, cocaine and opiates)

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):	08-02-2015
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	24-09-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-03-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-04-2016
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	NL48978.041.14