Effects of Childhood Trauma on Stress Reactivity: an MR study

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Primary objective: - Investigate the effects of childhood maltreatment on basal and stress-induced in vivo metabolite concentrations in the brain measured with 7T-MRS. Secondary objectives: - Correlate the endocrine, autonomic and subjective stress...

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

Summary

ID

NL-OMON40873

Source
ToetsingOnline

Brief title
MRS and Childhood Trauma

Condition

- Other condition

Synonym
Childhood-trauma associated psychiatric disorders

Health condition

effecten van stress op MRS metabolieten bij jeugdtrauma

Research involving
Human

Sponsors and support

Primary sponsor: Psychiatrie
Source(s) of monetary or material Support: Ministerie van OC&W,VENI subsidie

Intervention

Keyword: Childhood maltreatment, Spectroscopy, Stress

Outcome measures

Primary outcome

Primary parameter: Concentrations of glutamate, glutamine, GABA, choline, NAA,

creatine, myoinositol and lactate as measured by 7T-MRS.

Secondary outcome

Secondary parameters:

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

- Perceived stress levels.

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

- Plasma GABA levels

Study description

Background summary

Childhood maltreatment has a substantial impact on the brain during a critical developmental period and is a major risk factor for the development of almost all psychiatric disorders. However, the neurobiological mechanisms in the brain underlying these detrimental effects are not well understood. Magnetic resonance spectroscopy (MRS) non-invasively measures biologically important molecules in the living brain, yielding quantitative information on neurotransmitters, energy metabolism, and neuronal integrity. Therefore, this in vivo technique can probe the neurochemical correlates of childhood maltreatment. In light of the profound and long-lasting effects of childhood maltreatment on the stress system, this study integrates neuroimaging with an experimental stress design. Repeatedly measuring MRS metabolites prior to and

following exposure to acute stress provides a dynamic readout of stress vulnerability.

Study objective

Primary objective:
- Investigate the effects of childhood maltreatment on basal and stress-induced in vivo metabolite concentrations in the brain measured with 7T-MRS.

Secondary objectives:
- Correlate the endocrine, autonomic and subjective stress response with stress-induced changes of MRS metabolites.
- Investigate the association between (epi)genetic variation in stress-related genes and stress-induced changes in the MRS metabolites.
- Investigate the association between plasma GABA levels and childhood trauma

Study design

A small monocenter intervention study in healthy male individuals. Two experimental groups (n=60 each) are formed based on low and high exposure to childhood maltreatment. MRS levels of various in vivo metabolites are measured in the brain under basal and acute stress conditions using 7T-MRS. A between-subject design will be applied and participants will be randomized to either the stress condition (Trier Social Stress Test, TSST) or a validated control condition.

Intervention

Stress test or a control test randomized.
o Stress: the Trier Social Stress Test (TSST), an 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 maximum duration of 3 hours and 50 minutes and sufficient time for breaks. No direct benefits are present for participants. All participants will be given a reimbursement of ¤50,- for their cooperation and time, also potential travel costs will be reimbursed.

- Screening
- Potential participants can fill in questionnaires via a website (General screening list, MRI screening list, Life Stressor Checklist Revised (LSC-R), Childhood Trauma Questionnaire (CTQ) en State Trait Anxiety Inventory (STAI).

Identity of the subject will be encoded on this questionnaire, in a way that the identity can only be known by the researcher. Participants will be selected, based on their answers on these questionnaires.

- First visit
- Inclusion, collect blood samples, complete several questionnaires, and perform a first short scan to acquaint subjects with the 7T scanner.
- Total duration: 85 min (of which 15 min in the 7T scanner)

- Second visit
- Two 45 min MRS scans in the 7T scanner before and after either the Trier Social Stress Test (TSST) or a control protocol.
- Total duration: 145 min (of which 90 min in the 7T 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 7T scans and the feasibility of repeatedly measuring metabolites in the MRI scanner. The scan protocol will be carried out in accordance with this protocol and protocol 07-235 (*MRI development for 7T (and lower field strengths)*).

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

- Male sex
- Age between 18 and 40 years old
- Either low or high levels of childhood maltreatment

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
- History of any psychiatric, neurological or endocrine disorder including claustrophobia and alcohol abuse or dependence
- Self-reported current smoking in the last 2 weeks
- Self-reported current or past drug use in the last 2 weeks
- Ferrous objects in or around the body according to default checklist present at 7T scanner (version defined by METC protocol 07-235: *MRI development for 7T (and lower field strengths)* ;Acute exclusion criteria on 2nd and 3rd visit:
- 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):	02-10-2014
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	01-07-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-07-2014
Application type:	Amendment
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)

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	NL48847.041.14