Stress system dynamics in childhood trauma-related depression

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON51711

Source
ToetsingOnline

Brief title
REACT

Condition

- Mood disorders and disturbances NEC

Synonym
Depression, mood disorder

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Childhood trauma, Depression, Stress dynamics, Stress system

Outcome measures

Primary outcome

The main study parameters are the laboratory stress system dynamics measured by resting state brain function directly (0 - 40 minutes) and later (60-100 minutes) after the stress (TSST) or control (placebo-TSST) test.

Secondary outcome

Secondary study parameters are stress system dynamics measured through task-related fMRI activity and behavior, endocrine responses during stress, perceived stress and anxiety during stress, and (psycho)physiological responses, as well as daily life stress reactivity, including physiological and psychological measures, measured by ecological momentary and physiological assessment.

Study description

Background summary

Childhood trauma (CT) is a significant risk factor for several psychiatric disorders including major depressive disorder (MDD). Not only does it increase the risk of onset, but CT-related depression has been shown to critically differ from non-CT-related depression in its earlier emergence, more severe and recurrent symptoms, and worse treatment outcomes. While a wealth of evidence demonstrates altered stress system functionality across the life span following exposure to CT in relation to depression, it is currently unknown which CT-related changes in development of the stress system explain why individuals with CT-related depression have poor outcomes at adult age. Recent work has made clear that dynamic functionality of the stress system is key to an adequate and coordinated stress response, spanning across several modalities including endocrine responses, brain functions/networks, and behavioral

responses. We hypothesize that impaired dynamics in the stress response is central in the persistent vulnerability of patients with CT-related depression. Specifically, we hypothesize that mood disorder patients with CT have a reduced proficiency for dynamic adaptation of brain function, which is necessary after stress. This would then result in an impaired response to stress compared to non-CT mood disorder patients and healthy controls, with lower stress-induced (de)activation and connectivity of the salience network, executive control network, and default mode network. We expect that this loss of normal stress-related functional network dynamics also relates to altered physiological and psychological responses to stress in daily life.

Study objective

The primary objective is to investigate if the stress-induced dynamics across stress systems are impaired in patients with CT-related depression compared to non-CT-related depression and healthy controls. The secondary objective is to examine how stress system dynamics in the laboratory translate to real-life stress in daily life in these three groups.

Study design

The study is designed as a randomized cross-over study with two experimental conditions (stress condition and placebo-stress condition, separated by at least 2 weeks).

Intervention

Participants will undergo the trier social stress test (TSST) and a placebo version of the trier social stress test (placebo-TSST).

Study burden and risks

A moderate risk for participants is estimated. Participants will have to complete several questionnaires which may be perceived as a burden; however, research has shown that the burden is low, including questionnaires related to CT, and that participants experience their participation as positive and beneficial. In addition, the stress test (Trier Social Stress Test; TSST) is a validated and standardized test to induce mild psychosocial stress in a laboratory setting and is often applied without any known lasting disadvantageous effects, on its own as well as in combination with MRI, including in patient groups with psychiatric disorders (e.g., schizophrenia, bipolar disorder, and depression). In the MRI scanner, participants will be exposed to a magnetic field for less than 1.5 hours. This is not dangerous and poses no risk as long as no metal objects are located on the participant, as these can be heated or magnetized. Therefore, all participants will be informed in advance and checked for the presence of metal in or on the body. The time

spent in the laboratory is limited to 4 hours per visit and participants have sufficient time for breaks and will be compensated for their time. Participants will provide their saliva five times per visit (10 times in total) by chewing on a cotton pad for 1 minute, which they can do independently. Written instructions on how this works are shared with all participants beforehand, but the researcher will also be present in case any further assistance is needed. Tools used for physiological and psychological assessment of daily life stress reactivity are safe and cause limited interference with daily activities.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

General inclusion criteria:
- Mastery of Dutch language
- Age of >= 18 years

- Willingness and ability to give written informed consent
- Normal or corrected-to-normal vision

Additional inclusion criteria for the patient groups (i.e., MDD+CT and MDD-CT):
- Moderate to severe depression
- Score >= 26 on the Inventory of Depressive Symptoms-Self Report (IDS-SR) (Rush et al., 2000)
- DSM-5 diagnosis of major depression disorder (MDD), confirmed with clinical interview (MINI (Sheehan et al., 1997))

Additional inclusion criteria for the MDD+CT group:
- Moderate to severe childhood trauma (CT) before the age of 18
- Score above validated cut-off for moderate to severe CT using the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1994):

Exclusion criteria

General exclusion criteria:
- Speech impairments
- Other lifetime severe psychiatric comorbidity (bipolar disorder, psychotic disorder) or current alcohol/drug dependence
- Primary diagnosis of post-traumatic stress disorder (PTSD) or Acute Stress Disorder (ASD)
- Lifetime diagnosis of borderline personality disorder (BPD)
- Any acute somatic or acute endocrine disease (e.g., acute asthma)
- Taking any medication known to influence endocrine systems
- Chronic benzodiazepine use (and sporadic use on the days of the lab visits)
- Neurological disorder
- Known contraindications for MRI investigations, such as the presence of metal objects (e.g., pacemaker, arteriovenous clips) or severe claustrophobia.

Additional exclusion criteria for healthy controls and MDD-CT patients:
- Moderate to severe childhood trauma (CT) before the age of 18
- Score above validated cut-off for moderate to severe CT using CTQ (see cutoff scores above)

Additional exclusion criteria for healthy controls:
- Past or present psychiatric condition.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2023
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	26-04-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL81663.029.22