REStoring mood after Early life Trauma - the effectiveness of trauma-focused therapy in patients with depression and childhood trauma

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The main objective is to investigate whether trauma-focused therapy (TFT), as an addition to *treatment as usual* (TAU), is more effective compared to TAU only in reducing depression symptom severity in patients with CT-related depression.

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

Summary

ID

NL-OMON54461

Source
ToetsingOnline

Brief title
RESET-psychotherapy

Condition

- Mood disorders and disturbances NEC

Synonym
Childhood Trauma, Depression, Major Depressive Disorder

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Stichting tot Steun VCVGZ

Intervention

Keyword: Childhood trauma, Depression, Trauma treatment

Outcome measures

Primary outcome

The primary outcome measure is defined as depression symptom severity after 12 weeks treatment (post-treatment), measured with the Inventory of Depressive Symptomatology - Self Rated; IDS-SR.

Secondary outcome

1. Effectiveness of TAU + TFT compared to TAU by looking at: 1) remission in CT-related depression after 12 weeks of treatment (post-treatment), 2) depression symptom severity during the 12 week treatment, 3) depression symptom severity and remission after 6 weeks of treatment, and 4) depression symptom severity and remission at 6 months post-treatment (follow-up)

2. Other clinical outcomes related to TFT response: anxiety, disability, insomnia, subjective stress and suicidal ideation and behavior

3. Descriptive variables (clinical factors and previous and current care), and potential moderators and mediators related to TFT response

4. Stress-related biomarkers (to better understand how and for who TFT works):

• Hair cortisol levels: at baseline and post-treatment.

• Blood: at baseline and post-treatment for research on inflammatory and

(epi)genetic markers in relation to TFT response.

fMRI substudy

In a subgroup of 60 participants (matched for treatment allocation, age, and sex), stress-related brain activity is measured with a +/- 60 minute fMRI assessment before treatment and after 12 weeks of treatment, to better understand the brain mechanisms of trauma-focused psychotherapy.

Study description

Background summary

Depression is a recurrent, debilitating psychiatric disorder with a lifetime prevalence of 25%. Even though antidepressants and psychotherapy are often effective, a substantial proportion of patients does not respond to currently used evidence-based treatments. The heterogeneous nature of depressive symptoms is a major obstacle for the development of novel, effective treatments and targeted treatments for depression are currently lacking. There is increasing evidence that depression related to childhood trauma (CT) is critically different from non-CT related depression: it emerges earlier in life with more severe and recurrent symptoms and has worse treatment outcomes. With a prevalence of 25% in depressed patients, there is a large and unmet need for novel therapeutic strategies for CT-related depression. Effective, evidence-based trauma treatments, such as Eye Movement Desensitization and Reprocessing (EMDR) and Imagery Rescripting (ImRs), are well investigated treatments for trauma-related disorders, such as posttraumatic stress disorder (PTSD). Currently, there is no targeted treatment available for CT-related depression. Given the major role of trauma in CT-related depression, it is plausible that trauma-focused psychotherapies may be effective in this depression subtype. Therefore, this study investigates whether trauma-focused therapy is effective in reducing depression and increasing remission in CT-related depression. It is expected that trauma-focused therapy will be a safe and rational strategy to enhance resilience and improve depression outcomes for patients with CT-related depression.

Study objective

The main objective is to investigate whether trauma-focused therapy (TFT), as

an addition to *treatment as usual* (TAU), is more effective compared to TAU only in reducing depression symptom severity in patients with CT-related depression.

Study design

RESET-psychotherapy is a 12-week randomized controlled clinical trial (single-blind RCT), in which TFT in combination with TAU will be compared to TAU only at (various) sGGZ units of mental health care institutions GGZ inGeest, HSK Groep, Altrecht, PsyQ and Pro Persona. Treatment allocation is performed via simple randomization and blinded for assessors. As patients in the intervention group (TAU+TFT) group) will receive more treatment sessions compared to patients in the control group (only TAU), patients in the control group will be offered extra contact moments with a researcher in order to reduce the chance of an *attention effect*.

Intervention

After randomization, patients that are assigned to the TFT+TAU condition will receive 6-10 sessions of trauma-focused therapy (TFT) in addition to regular depression treatment (TAU). As part of TFT, treatment protocols for EMDR and ImRs (EMDR if there was predominantly abuse and violence in childhood and ImRs if there was predominantly neglect in childhood) with a focus on trauma reprocessing of CT-related memories are followed, adapted to depression in accordance to previously published treatment protocols.

Study burden and risks

Patients in the TFT+TAU condition will be offered 6-10 sessions of TFT added to their regular depression treatment (TAU). Data will be collected during multiple assessments: at baseline (T0), after 6 weeks (T1), after 12 weeks (T2; post-treatment), and after 6 months post-treatment (follow-up, T3). The baseline assessment will take approximately two hours. Completion of T1, T2, and T3 measurements will take approximately 45 minutes. In addition, to obtain information about depression symptom severity during treatment, patients are asked to complete the IDS-SR online (duration 5 minutes) once in every two weeks and only in those weeks that they do not already have a study assessment. To better understand how and for who TFT works, stress-related biomarkers are examined. Cortisol levels are assessed by collecting hair samples (baseline and T2). At baseline and at post-treatment (T2), blood samples are taken for measurements of inflammatory and (epi)genetic markers in relation to TFT response. A sub-group of patients (N=60, 30 per intervention group) will be asked to undergo a fMRI scan before the start of treatment and after 12 weeks of treatment, to measure stress-related brain activity (approximately 60 minutes per fMRI session).

Patients are informed that they can cancel their participation at any time without disclosing reasons for their cancellation and without negative consequences for their future care. Participation in the study is associated with a moderate amount of risks for patients. Both TAU and TFT will be offered by experienced and qualified therapist.

The current study does not directly benefit participating patients. However, by participating, the patient does help in the search for a better treatment for people with depression and childhood trauma.

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 >=18 years

• Score >=26 on Inventory of Depressive Symptoms Self-Report (IDS-RS; moderate to severe depression)
• DSM-5 diagnosis of major depressive disorder (MDD) confirmed with the Mini International Neuropsychiatric Interview - Simplified; MINI-S for DSM-5
• Moderate to severe childhood trauma (CT): score above validated cut-off for moderate to severe CT on one or more of the following domains using the Childhood Trauma Questionnaire (CTQ): physical neglect: score >=10; emotional neglect: score >=15; sexual abuse: score >=8; physical abuse: score >=10; emotional abuse: score >=13.
• Sufficient mastery of Dutch language
• Patient is inclined to participate in a randomization process
• Patient in inclined to give written informed consent

Exclusion criteria

• Previous trauma-focused therapy on childhood trauma
• Other lifetime severe psychiatric comorbidity (psychotic disorder, bipolar 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

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-11-2021
Enrollment:	158

Type:	Actual

Ethics review

Approved WMO Date:	02-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2024
Application type:	Amendment
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	NL74405.029.20