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Mechanism-based modular psychotherapy vs. cognitive-behavioural therapy for adolescents and young adults with childhood trauma experiences: Study protocol for a feasibility trial within the German Center for Mental Health

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Abstract

Introduction: Patients with mental disorders and a history of childhood trauma show an early onset of psychopathology and often a poor response to standard disorder-specific treatments. They represent a patient group which requires more personalized interventions targeting the transdiagnostic mechanisms related to early trauma and their functional consequences. The mechanism-based, modular psychotherapy (MeMoPsy) approach is conceptualized as an innovative framework for psychotherapy development. It comprises independent, flexibly applicable interventions from various theoretical backgrounds and evidence-based programs within a systematic treatment algorithm, thereby tailoring module selection to the specific needs of traumatized adolescents. *Methods and analysis*: In a randomized controlled feasibility trial (RCT), N=80 outpatients between 15 and 25 years of age diagnosed with various mental disorders will receive 28 individual sessions with MeMoPsy or standard Cognitive Behavioral Therapy (CBT). MeMoPsy includes a basic module that addresses trauma history and three additional modules focusing on functional impairments known to be associated with childhood trauma, that is rejection sensitivity, emotion regulation, and relationship difficulties. These modules are selected based on a self-report algorithm. Techniques from Mentalization-Based Psychotherapy (MBT), Cognitive Behavioral Analysis System of Psychotherapy (CBASP), Dialectical-Behavior Therapy (DBT), and Systemic Therapy (ST) are integrated in this personalized modular procedure. This proof-of-concept study aims to provide initial evidence for acceptability, feasibility, and preliminary evidence for efficacy (post-treatment and three months follow-up) of MeMoPsy and to elucidate mechanisms of change, using psychotherapy process research, Ecological Momentary Assessment, and functional magnetic resonance imaging. *Ethics and dissemination:* This RCT obtained approval from independent ethic committees of participating centres and is accompanied by a data and safety monitoring board. Findings will be communicated within the research community as well as with patients and the public by the dissemination strategies of the German Center for Mental Health (DZPG). *Registration*: German Clinical Trials Register DRKS00034058

Strengths and limitations of this study

- This is the first study to investigate the feasibility of a modular, mechanism-based psychotherapy for difficult to treat adolescents and young adults with various diagnoses and with a history of early trauma.
- Besides feasibility, this RCT aims to provide preliminary evidence for the efficacy of modular, mechanism-based psychotherapy and to generate pilot data for a subsequent multicentre confirmatory trial.
- Experimental research, ecological momentary assessment (EMA), qualitative interviews as well as regular assessments of the psychotherapy process in patients and therapists will act synergistically to understand the mechanisms of change processes.
- Using Cognitive Behavioural Therapy (CBT) as an active treatment comparator represents a strong comparator for a rigorous evaluation of MeMoPsy with impact for dissemination in mental health care services.
- Since no a priori values are established, the algorithm cut-offs for module selection used here are based on general population means of self-rated questionnaires (according to pre-study of our group; (1))

Administrative information

Please note that the numbers in square brackets in this protocol refer to the item numbers of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 Checklist (2).

Title [1]: Mechanism-based modular psychotherapy vs. cognitive-behavioral therapy for adolescents and young adults with childhood trauma experiences: Study protocol for a feasibility trial within the German Center for Mental Health

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Introduction

Background and rationale [6]

Childhood trauma experiences such as abuse and neglect are well-established risk factors for mental health problems (3, 4). Systematic reviews and meta-analyses consistently indicate robust associations between childhood trauma experiences and a broad range of mental disorders (5, 6), such as depression (7, 8), anxiety disorders (9), eating disorders (10), substance use disorders (11), psychosis (12), and borderline personality disorder (13). Many of those mental disorders first appear before the age of 24 (14), making adolescence and young adulthood particularly vulnerable periods.

Since “one size fits all”-treatments are not optimal for most patients, innovative approaches focus on more personalized interventions that target the specific functional impairments of patients and associated psychological and neurobiological mechanisms. Patients with mental disorders and childhood trauma experiences are characterized by an earlier onset of psychopathology, more chronic and recurrent symptoms and higher comorbidity rates (15), and – most importantly – they show poorer treatment responses than patients without such trauma experiences (e.g., 15, 16-19). Thus, the question arises as to why current evidence-based psychotherapeutic treatments appear to be less effective for these patients, as compared to patients without childhood trauma experiences. One possible reason is that the mechanisms linking childhood trauma experiences to mental disorders are not sufficiently understood and are therefore not adequately addressed in current psychotherapeutic treatments (20). In recent years, numerous mechanisms have been proposed through which childhood trauma experiences could be translated into risk for different mental disorders (e.g., 21, 22, 23). Some of the most prominent transdiagnostic mechanisms underlying childhood trauma experiences and mental disorders encompass 1.) rejection hypersensitivity (24), 2.) emotion dysregulation (23), as well as 3.) difficulties in (close) interpersonal relationships (25).

First, individuals with childhood trauma experiences exhibit biases in social information processing, specifically a hypersensitivity towards interpersonal rejection (23, 24). Individuals

with high levels of rejection sensitivity tend to anxiously expect, readily perceive, and overreact to signs of interpersonal rejection (26). According to a recent meta-analysis including 16 studies and 5335 participants, rejection hypersensitivity is linked to childhood trauma experiences, specifically emotional abuse, regardless of age or sex of those affected (24). Moreover, rejection hypersensitivity is associated with specific mental disorders, including depression, anxiety disorders, eating disorders, and borderline personality disorder (24, 27).

Second, individuals with childhood trauma experiences are characterized by difficulties in emotion and stress regulation (23). Childhood trauma experiences are linked to low emotional awareness, i.e. a diminished ability to identify and differentiate one's own emotions (28). Low emotional awareness may, in turn, contribute to emotion regulation difficulties or emotion dysregulation (23). Emotion dysregulation has been defined as patterns of emotional experiences and/or expressions interfering with appropriate goal-directed behaviours (29). Studies suggest that individuals with childhood trauma experiences are more likely to use maladaptive emotion regulation strategies such as rumination, suppression, and impulsive responses (23, 30). Likewise, individuals with childhood trauma experiences tend to have more difficulties engaging in adaptive emotion regulation strategies such as acceptance and cognitive reappraisal (23, 30). In addition, emotion regulation difficulties emerge in numerous mental disorders, including mood, anxiety, eating, personality, and schizophrenia spectrum disorders (31, 32).

Finally, and closely associated with rejection hypersensitivity and emotion dysregulation, individuals with childhood trauma experiences tend to have more difficulties in (close) interpersonal relationships (25). Specifically, individuals with childhood trauma experiences report more dissatisfaction with current relationships (33), less intimacy (34, 35), less social support (36-38), less empathy (39) as well as more loneliness and social isolation (40) than individuals without such experiences. Interestingly, difficulties in (close) interpersonal relationships are not only linked to different mental disorders (41), but could also mediate the relationship between childhood trauma experiences and mental health symptoms (e.g., 42).

Taken together, a growing body of evidence suggests robust associations between childhood trauma experiences, mental disorders and underlying transdiagnostic mechanisms (i.e., rejection hypersensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships). It thus appears promising to target these mechanisms in order to improve current psychotherapeutic treatments for individuals with mental disorders affected by childhood trauma experiences (43).

The Centre for Psychosocial Medicine at Heidelberg University together with the Central Institute of Mental Health Mannheim and the Freie Universität Berlin therefore developed a personalized, mechanism-based, modular psychotherapeutic approach (MeMoPsy) for individual outpatient settings. Our MeMoPsy approach builds upon a recent proof-of-concept randomized controlled trial conducted in collaboration between our research group and Elisabeth Schramm's research group (44). In this study, 70 adult outpatients between 18 and 65 years with a primary diagnosis of major depressive disorder, at least one comorbid mental disorder and childhood trauma experiences received 20 sessions of either standard cognitive-behavioural therapy alone (CBT) or CBT plus modular-based psychotherapy (MoBa). MoBa is based on psychotherapeutic modules, defined as independent but combinable sets of functional units which target common transdiagnostic mechanisms and teach skills to improve processes such as emotion regulation or theory of mind. In the MoBa approach, three psychotherapeutic modules focus on transdiagnostic childhood trauma-related dysfunctions, specifically social threat hyperresponsivity and social avoidance behaviour, emotion dysregulation as well as lack of empathy and theory of mind. To select these modules in the MoBa condition, a personalized treatment algorithm was applied using empirical cut-off values for self-report measures of childhood-trauma related dysfunctions. First encouraging results indicate the feasibility, safety and efficacy of the MoBa approach, with advantages related to patients' and therapists' satisfaction and different clinical outcomes (1).

Building on this recent proof-of-concept randomized controlled trial (1), we aim to assess the feasibility of MeMoPsy in a multicentre, proof-of-concept randomized controlled

trial. We will compare our MeMoPsy approach with standard, non-manualized CBT, as CBT represents one of the most prominent treatments as usual in psychotherapeutic health care (45). While MoBa targeted adult patients aged up to 65 years with depression, comorbid disorders and childhood trauma, MeMoPsy shifts its focus to the needs of a particularly vulnerable patient group, i.e. adolescents and young adults aged 15 to 25 years with various mental disorders and childhood trauma experiences. Similar to MoBa, the psychotherapeutic modules of MeMoPsy focus on mechanisms underlying the association between childhood trauma experiences and mental disorders (i.e., rejection hypersensitivity, emotion dysregulation, difficulties in interpersonal relationships). Further, the personalized treatment algorithm which was used in our previous proof-of-concept study will also be applied in the current study to enable an evidence-based systematic selection of psychotherapeutic modules. We believe that our personalized treatment algorithm represents an advantage as compared to the common clinical practice of intuitively selecting psychotherapeutic interventions according to the clinical judgement, expertise and preferences of the treating therapists. Furthermore, the accompanying process research with regular questionnaires on psychopathology and quality of the therapeutic alliance will enable adaptions to patients´ current needs (within the selected modules) depending on patients´ feedback.

Objectives [7]

The aim of this multicentre, proof-of-concept randomized controlled trial is to investigate the feasibility of a newly developed mechanism-based, modular psychotherapeutic approach (MeMoPsy) for adolescents and young adults with various mental disorders and childhood trauma experiences as compared to standard non-manualized CBT offered in German mental health care services. Specifically, this study aims to (1) examine the acceptability of the MeMoPsy approach for patients and therapists, (2) determine the feasibility of study-related measurements, (3) provide preliminary evidence for the efficacy of MeMoPsy compared to CBT, and to elucidate mechanisms of change using psychotherapy process research, Ecological Momentary Assessment (EMA), and functional magnetic resonance imaging (fMRI).

Trial design [8]

The study is designed as a randomized, controlled, multicentre feasibility trial with two parallel arms (*N* = 80), comparing MeMoPsy with routine non-manualized CBT. Randomization will be performed as block randomization stratified by study site (i.e., Heidelberg, Mannheim, Berlin) with a 1:1 allocation.

Methods and Analysis

Study setting [9]

The study will be conducted at three urban German sites, i.e. the Centre for Psychosocial Medicine at Heidelberg University, the Central Institute of Mental Health Mannheim, and the Institute of Clinical Child & Adolescence Psychology and Psychotherapy of the Freie Universität Berlin.

Eligibility criteria [10]

Eighty outpatients between 15 and 25 years of age with one or more mental disorder and childhood trauma experiences will be recruited. Patients in the MeMoPsy or CBT condition will be treated by licensed adult and children psychotherapists or psychotherapists in training with at least 2 years of practical experience in treating patients with mental disorders. Key inclusion and exclusion criteria for patients are:

Inclusion criteria:

1. Age eligibility: 15-25 years
2. One or more mental disorders according to DSM-5 as assessed with the Diagnostic Short-Interview for Mental Disorders (Mini-DIPS; 46), and the Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5-PD; (47) and The Structured Clinical Interview for DSM-5, Clinical Version (SCID-5-CV; (48) for ADHD.

3. Childhood trauma experiences: at least moderate to severe in one or more of the five subscales of the Childhood Trauma Questionnaire (CTQ, 49; i.e., emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect), as defined by Häuser et al. (50)
4. Meeting the cut-off of at least one mechanism-based treatment module (module 1 to module 3)
5. Statutory health insurance to cover the costs for the psychotherapeutic outpatient treatment
6. Fluent in German
7. Written informed consent

Exclusion criteria:

1. Acute risk of suicide, assessed by Mini-DIPS (interview)
2. One or more mental disorders requiring diagnosis-specific treatment as assessed by clinical judgement and applying the Mini-DIPS (46) or the 10-item version of the Autism Spectrum Quotient (AQ-10; 51), including posttraumatic stress disorder; moderate or severe substance use disorder with the exception of cannabis use disorder; acute psychotic or manic symptoms; autism spectrum disorder
3. No ability or willingness to abstain from substance use over the course of treatment
4. Severe cognitive impairment (i.e., IQ < 70) as assessed with the mini-q (52)
5. Other ongoing psychotherapy
6. Serious medical condition that interferes with regularly attending therapy sessions
7. Change in current psychotropic medication or initiation of new psychotropic medication for at least two weeks before inclusion (3 weeks for fluoxetine)

Interventions [11]

The MeMoPsy condition comprises 28 individual psychotherapy sessions over 24 weeks of treatment (twice weekly in weeks 1-4, then once per week in weeks 5-24). Each

patient receives a basic module and up to three mechanism-specific therapy modules (Figure 1). The application of the modular interventions is preceded by a diagnostic assessment of the patient's impaired transdiagnostic mechanisms (s. secondary outcomes, Table 1). If the cut-off values (based on general population means and according to prior experiences from Elsaesser et al. (53)) are exceeded, the respective module will be used for that patient. Each module comes with a defined series of interventions, some of which are mandatory, while others are optional for the psychotherapist to use during the course of the therapy. MeMoPsy is a personalized treatment in the sense of an algorithm-driven selection of therapy modules. Furthermore, as feedback on therapeutic processes is an integral part of MeMoPsy (54), a routine outcome monitoring (RoM) procedure is established, with study therapists receiving access to their patients' questionnaire scores (Brief Symptom Inventory BSI; 73) regarding the therapeutic process and psychopathology throughout the treatment.

The therapy modules are as follows:

- The basic module, which is mandatory for every patient, encompasses a detailed mental health history, psychoeducation and information about the therapy and the therapy focus, the identification and integration of traumatic experiences, and the improvement of mentalization and interpersonal functioning. The therapeutic approach is validating, cooperative, and influenced by the curious and not-knowing stance from mentalization-based therapy (MBT; (55)). Therapists aim to establish a sustainable therapeutic alliance and pay close attention to potential conflicts and ruptures in it. They coregulate the level of emotional arousal where necessary and identify problematic relationship patterns which may arise as a consequence of trauma. Therefore, therapists use interventions such as the lifeline (56), the window of tolerance model, as well as further techniques from the rupture-repair model (57) and mentalization-based therapy(55).
- Module 1 is administered if patients score ≥ 9.88 on the RSQ (58). It targets interpersonal rejection sensitivity and avoidance behaviour in social situations. It draws on techniques from the Cognitive Behavioral Analysis System of Psychotherapy

(CBASP) (59) such as the significant other history, interpersonal discrimination exercises, and situation analyses, and in addition strategies of MBT.

- Module 2 is administered if patients score ≥ 46.97 on the State Difficulties in Emotion Regulation Scale (S-DERS) (60). It aims at improving emotional awareness and stress regulation and draws on techniques from Dialectical Behavior Therapy (DBT; (61), such as emotion-specific psychoeducation, anti-dissociative or distress tolerance skills, mindfulness exercises, and the ability to observe, describe, and regulate aversive emotions.
- Module 3 is administered if patients score ≥ 13 on the OQ-45 (social role subscale) (62). It aims at strengthening resources, resilience, and solution-focus within the social system of close interpersonal relationships, employing basic principles of systemic trauma therapy (63) such as task and goal orientation, resource orientation, and solution-focused interventions, but also genograms or relationship maps. This module may take place in an individual therapy setting, but also in multi-person settings with caregivers or other persons of reference if appropriate.

The modules are not simply added as separate and serial components, but therapists will be trained and supervised to integrate them into the dynamic course of the therapeutic process in preferably equal measure. Consequently, the amount of time spent with a single module will be reduced if more modules are indicated for an individual patient. Therapists will document the time spent with each module.

The control condition is a treatment-as-usual, non-manualized brief CBT at cooperating psychotherapy training institutes. Patients receive a total of 28 treatment sessions and 3 preparatory meetings, corresponding to the reimbursement scheme of the German statutory health insurance for psychotherapy. Common CBT elements are, for example, psychoeducation, behavioural activation, cognitive restructuring, and exposition.

All psychotherapists in both study conditions are supervised by board-certified clinical psychologists or physicians with specialization in the respective psychotherapy approach, with supervision taking place on average every fourth therapy session, i.e. there will be in total

seven supervision sessions within a therapy. Psychotherapists in the MeMoPsy condition must complete an intensive training course (four 90-minutes online theory lessons, three days of practical training) held by board-certified clinical psychologists or physicians with specialization in the respective psychotherapy approach, as well as a pilot therapy of at least 15 sessions with at least six additional supervision sessions by the same module experts. In addition, all therapy sessions are recorded on video for the purpose of quality and adherence assurance and can be used as part of supervision.

Outcomes [12]

Due to the exploratory nature of this feasibility trial, three primary outcomes were defined: (1) the acceptability of MeMoPsy to patients and therapists, (2) the feasibility of study-related measures, and (3) preliminary evidence for the efficacy of MeMoPsy compared to standard CBT treatment. Furthermore, a number of secondary outcomes will be explored, including the assumed transdiagnostic mechanisms underlying the link between childhood trauma experiences and mental disorders (i.e., rejection sensitivity, emotion dysregulation, difficulties in interpersonal relationships), psychopathological symptoms and psychotherapeutic processes. Please refer to Table 1 for all primary and secondary outcomes and corresponding measures.

Psychotherapy process research will be used to study the course of transdiagnostic mechanisms of change. On a macroscopic level, we will investigate ongoing change, therapeutic relationship and intersession experiences. On a microscopic level, we will address change events, difficult episodes and therapeutic interventions. Findings will be integrated to analyse the action of therapy modules on the course of general psychopathology and well-being as well as rejection sensitivity, emotion regulation and relationship dynamics.

Furthermore, EMA allows to further operationalize and investigate the assumed mechanisms: First, the dynamics of the mechanisms in everyday life and the connection with the respondents' well-being can be investigated. Second, potential moderators (e.g. personality characteristics) that strengthen or weaken this relationship will be investigated.

Third, the intervention effects of the three MeMoPsy modules will be examined experimentally (see below) and in everyday life. Saliva sampling of the stress dependent hormone cortisol will be linked to ambulatory assessment. All primary and secondary outcomes and corresponding measures are described in Table 1. Please note that the time points of assessments are given only for the primary outcomes. For a detailed overview of all assessments, please refer to Table 2.

In addition, neurobiological measurements using functional magnetic resonance imaging (fMRI) will be performed to elucidate the mechanisms of change initiated by MeMoPsy. Participants complete three tasks in two fMRI testing sessions, one before the start of the treatment and one immediately after the end of treatment. First, the attention bias (i.e. increased sensitivity to rejection) is recorded during fMRI using an emotion classification task, in which emotional faces have to be matched (64). Second, the assumed interpersonal difficulties will be measured using an fMRI task on empathy and theory of mind (ToM) skills (EmpaToM (65)). Empathy and ToM are considered core competencies of social relationship building. The EmpaToM-Y paradigm consists of videos of young actors and actresses reporting specific social settings. This video set enables independent manipulation and assessment of empathy and ToM. Third, the assumed increased sensitivity to rejection and problems in establishing interpersonal relationships are tested using a task on social information processing. This task represents an adaptation and combination of previous studies in which participants rate themselves on character traits and imaging getting feedback for these traits (66), (67).

Table 1. Primary and secondary outcomes and corresponding measures

Outcome	Measure
Primary outcomes	
Acceptability	
Patients' satisfaction	8-item Fragebogen zur Patientenzufriedenheit (ZUF-8), the German adaptation of the 8-item Client Satisfaction Questionnaire (CSQ-8; 69), rated by patients at the end of treatment (T2)
Therapists' satisfaction	Acceptability of Intervention Measure (AIM) and Feasibility of Intervention Measure (FIM) (70), two 5-item scales rated by therapists at the end of treatment (T2)
Negative psychological treatment effects	20-item Negative Effects Questionnaire (NEQ; 71), rated by patients at the end of treatment (T2)
Adherence	Number of therapy sessions attended and number of intervention dropouts, determined by study personnel at the end of treatment (T2)
Feasibility	
Recruitment	Number of patients recruited per month (i.e., recruitment speed) and percentage of suitable patients who agree to participate in the study (i.e., recruitment rate), determined by study personnel at the end of treatment (T2)
Completeness of online data collection	Percentage of online questionnaires completed by patients and therapists before (T0), during (T1) and at the end of treatment (T2), determined by study personnel at T2
Dropout rate	Number of patients terminating their study participation prematurely and their reasons for premature termination as assessed by the self-rated 25-item Reasons for Termination Scale (Roe; 72)
Quality of module-specific cut-off values	Percentage of patients receiving 1, 2 or 3 modules (i.e., module allocation rate), determined by study personnel at the end of treatment (T2)
Efficacy	
Self-rated severity of psychopathology	53-item Brief Symptom Inventory (BSI; 73), rated by patients at the end of treatment (T2)
Interviewer-rated severity of psychopathology	Global Assessment of Functioning (GAF; 74) a 100-point scales rated by trained and blinded diagnosticians at the end of treatment (T2)
Secondary outcomes	
Transdiagnostic mechanisms of change, targeted by psychotherapeutic modules	

Rejection sensitivity (Module 1)	Module questionnaire: The Rejection Sensitivity Questionnaire (RSQ; 26) assesses the anxious-expectations component of rejection sensitivity. The RSQ encompasses 20 hypothetical interpersonal interactions, characterized by the potential of being rejected by others. For example, patients are asked to imagine asking someone from their workplace out for coffee. Patients rate each hypothetical interpersonal interaction on two scales: first, they indicate their concern or anxiety that they will be rejected on a 6-point Likert scale ranging from 1 (very unconcerned) to 6 (very concerned). Then, they indicate the likelihood that the other person will engage in non-rejecting behavior toward them on a 6-point Likert scale ranging from 1 (very unlikely) to 6 (very likely). The psychometric properties of the German version have been found to be good (75).
Emotion dysregulation (Module 2)	Module questionnaire: The 28-item State Difficulties in Emotion Regulation Scale (S-DERS; 76) allows to assess different dimensions of emotion dysregulation repeatedly over brief periods of time. The S-DERS consists of four subscales including Nonacceptance (i.e., non-acceptance of current emotions), Modulate (i.e., momentary difficulties modulating emotional and behavioral reactions), Awareness (i.e., limited awareness of current emotions), and Clarity (i.e., limited clarity about current emotions). Patients rate statements such as “My emotions feel overwhelming” on a 5-point Likert scale ranging from 1 (not at all) to 5 (completely). Preliminary evidence supports the psychometric properties of the measure (76).
Difficulties in (close) interpersonal relationships (Module 3)	Module questionnaire: The 45-item Outcome Questionnaire-45 (OQ-45; 77) is recommended for routine outcome monitoring in a wide range of mental health service settings (78). The OQ-45 consists of three subscales, including Symptom Distress (25 items), Interpersonal Relations (11 items), and Social Role (9 items). Patients rate statements such as “I am concerned about family troubles” on a 5-point Likert scale ranging from 0 (never) to 4 (almost always). To determine difficulties in (close) interpersonal relationships, only the OQ-45 subscale Interpersonal Relations is used, which refers to the patient’s friendships, family life and romantic relationships. The psychometric properties of the German version have been found to be acceptable to good (79).
Psychopathology	
Severity of personality disorder	36-item Personality Inventory for DSM-5 – Brief Form Plus Modified (PID-5-BF+M; 80) and 12-item German version of the Level of Personality Functioning Scale-Brief Form 2.0 (LPFS-BF; (81)), both rated by patients
Severity of borderline personality disorder (BPD) symptomatology	14-item Fragebogen zu Gedanken und Gefühlen (FGG-14, engl.: Questionnaire on Thoughts and Feelings; 82) and 23-item Borderline Symptom List (BSL-23; 83), both rated by patients

Dissociation	4-item Dissoziations-Spannungs-Skala (DSS-4, engl.: 4-item Dissociation Tension Scale; 84), rated by patients
Mentalizing	20-item Certainty about Mental States Questionnaire (CAMSQ; 85), rated by patients
Social support	5-item ENRICHD Social Support Inventory (ESSI; 86), rated by patients
DZPG minimum dataset	Dataset designed by experts of the German Centre of Mental Health (Deutsches Zentrum für Psychische Gesundheit, DZPG) to measure core patients' characteristics. Single items have been selected from existing questionnaires to assess sociodemographics, the exposome, and dimensions of the Research Domain Criteria (RDoC) Hierarchical Taxonomy of Psychopathology (HiTOP), and everyday functioning such as mental health and quality of life. Items are rated by patients.
Clinical impression of global functioning	Clinical Global Impressions (CGI; 87), two 7-point scales assessing severity of psychopathology (CGI-Severity, CGI-S) and change since initiation of treatment (CGI-Improvement, CGI-I), rated by therapists
Qualitative interviews	At the end of treatment, qualitative interviews are conducted with the patients and therapists in the MeMoPsy condition in order to explore the experiences made with the therapy and the assessment of its usefulness from the perspective of both. For the therapists, the extent to which they have used the available interventions is also investigated as well as their expectations concerning the implementation of tailor-made therapy for clients. For the selection of interview partners, either "maximal variation sampling" or "stratified purposeful sampling" (88) is used to consider a wide range of patients and therapists (e.g., age, gender, socio-economic background, previously used therapy methods, professional experience).
Psychotherapeutic processes	
Therapeutic homework	Self-designed items to assess compliance with therapeutic homework, rated by patients and therapists
Therapeutic interventions	Self-designed Therapeutic Elements Checklist to assess all therapeutic interventions in the MeMoPsy and CBT condition, including the time spent on those interventions, rated by therapists
Medication	Self-designed items to assess medication before, during and at the end of treatment, rated by patients
Continuous process monitoring	
Therapeutic mechanisms	12-item Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie (89), rated by patients (STEP-P) and therapists (STEP-T)
Therapeutic alliance	12-item Working Alliance Inventory – Short Revised (90), rated by patients (WAI-P) and therapists (WAI-T)
Symptom distress	11-item Symptom Checklist (SCL-K11; 91), rated by patients

Mental wellbeing	7-item Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS; 92), rated by patients
Patients' intersession experiences	Self-designed 16-item Experiences Between Psychotherapy Sessions Questionnaire (EBPSQ), targeting intersession experiences, rated by patients
Course of transdiagnostic mechanisms of change	12 module-specific items, taken from the RSQ, S-DERS, and OQ-45 subscale Interpersonal Relations and Reflective Functioning Questionnaire (RFQ (90)), to assess state aspects of changes in rejection sensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships, and reflective functioning, rated by patients
Therapist-rated severity of psychopathology	Global Assessment of Functioning (GAF) and Global Assessment of Relational Functioning (GARF), two 100-point scales rated by therapists
Additional assessments (optional)	
Ecological Momentary Assessment (EMA)	Daily prompts (26 items) which patients are asked on their smartphone at 8 random times per day over a period of one week before (T0) and at the end of treatment (T2). EMA items assess transdiagnostic mechanisms of change (i.e., rejection sensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships), mental, physical, and social stress, and positive and negative affect. Items are self-designed or taken from the Positive and Negative Affect Schedule (PANAS; 93).
Functional magnetic resonance imaging (fMRI)	Three experimental paradigms performed in the MRI scanner to assess neural changes post (T2) compared to pre-treatment (T0) interpersonal threat sensitivity (94), empathy and theory of mind (95, 96), social feedback processing (66) (97)
Hormone measurements	Saliva samples to determine cortisol levels in patients. Saliva samples are collected 8 times per day to calculate cortisol awakening responses and diurnal profiles on three consecutive days within the one-week EMA period before (T0) and at the end of treatment (T2).

Participant timeline [13]

At enrolment, patients will be screened for eligibility, and written informed consent of all eligible patients will be obtained. If the patient is a minor (i.e., 15-17 years old), informed consent must also be given by a parent or legal guardian. Additionally to the participation in the intervention study, patients are asked to participate in one or more further assessments using EMA, functional magnetic resonance imaging (fMRI), saliva samples to determine cortisol levels, and qualitative interviews. Patients will be randomized to either MeMoPsy or CBT. Data assessments will take place before the beginning of the intervention (baseline, T0), during the intervention (baseline + 16 weeks, T1), at the end of the intervention (baseline + 32 weeks, T2) and at follow-up (baseline + 44 weeks, T3). A comprehensive overview of the frequency and scope of all core trial visits and the continuous outcome monitoring including all assessments and measures is provided in Table 2.

Table 2. Frequency and scope of core trial visits and continuous outcome monitoring

Core trial visits (MeMoPsy and CBT condition)								
Visits			**Screening (T-2)**	**Diagnostics (T-1)**	**Baseline (T0)**	**Mid-Intervention (T1)**	**Post-Interv. (T2)**	**Follow-up (T3)**
Week(s)			**-**	**-**	**0**	**16**	**32**	**44**
	Format	**Measure**						
Diagnostician	I	In-person or telephone screening	●					
		Mini-DIPS		●				
		SCID-5-PD:		●				
		KERF-40-I		●				
		GAF			●		●	
		SCID-5-CV for ADHD		●				
	Q	CTQ	●					
Patient	Q	AQ-10		●				
		mini-q		●				
		RSQ			●	●	●	●
		S-DERS			●	●	●	●
		OQ-45, subscale IR			●	●	●	●
		ZUF-8				●	●	●
		NEQ				●	●	●
		BSI			●	●	●	●
		PID-5-BF+M			●	●	●	●
		LPFS-BF 2.0			●	●	●	●
		FGG-14			●			
		BSL-23			●			
		DSS-4			●	●	●	●

		CAMSQ			●			●			●		●
		ESSI			●			●			●		●
		DZPG MDS*			●			●			●		●
		Homework						●			●		
		WAI-SR						●			●		
		Medication			●			●			●		●
	Optional	EMA			●						●		
		fMRI			●						●		
		Cortisol			●						●		
		Qual. interviews									●		
Therapist	Q	AIM, FIM			●			●			●		
		CGI			●			●			●		
		Therapeutic Elements Checklist						●			●		
		Homework						●			●		
Continuous outcome monitoring (MeMoPsy condition only)													
						Treatment							
Session(s)						**1**	**6**	**11**	**16**	**21**	**26**		
	Format	**Measure**											
Patient	Q	STEP-P**											
		WAI-P				●	●	●	●	●	●		
		SCL-K11				●	●	●	●	●	●		
		SWEMWBS				●	●	●	●	●	●		
		EBPSQ				●	●	●	●	●	●		
		Module-specific items				●	●	●	●	●	●		
Therapist	Q	STEP-T**											
		WAI-T				●	●	●	●	●	●		
		GAF, GARF				●	●	●	●	●	●		

		Time spent on each module**										

Note. AIM, Acceptability of Intervention Measure; AQ-10, 10-item version of the Autism Spectrum Quotient; BSI, Brief Symptom Inventory; BSL-23, 23-item version of the Borderline Symptom List; CAMSQ, Certainty about Mental States Questionnaire; CGI, Clinical Global Impressions; CTQ, Childhood Trauma Questionnaire; DSS-4, 4-item version of the Dissoziations-Spannungs-Skala; DZPG, Deutsches Zentrum für Psychische Gesundheit (German Center for Mental Health); EBPSQ, Experiences Between Psychotherapy Sessions Questionnaire; ESSI, ENRICHD Social Support Inventory; FGG-14, Fragebogen zu Gedanken und Gefühlen; FIM, Feasibility of Intervention Measure; GAF, Global Assessment of Functioning; GARF, Global Assessment of Relational Functioning; I, interview; IR, Interpersonal Relations; KERF-40-I, brief German interview version of the Maltreatment and Abuse Chronology of Exposure scale; MDS, Minimum Dataset; Mini-DIPS, Diagnostic Short-Interview for Mental Disorders; mini-q, brief screening for cognitive abilities; NEQ, Negative Effects Questionnaire; OQ-45, 45-item version of the Outcome Questionnaire; PD, Personality Disorder; LPFS-BF 2.0 Level of Personality Functioning Scale-Brief Form 2.0; PID-5-BF+M, Personality Inventory for DSM-5 – Brief Form Plus Modified; Q, questionnaire; RSQ, Rejection Sensitivity Questionnaire; SCID-5-PD, Structured Clinical Interview for DSM-5 Personality Disorders; SCID-5-CV, Structured Clinical Interview for DSM-5 Clinical Version; SCL-K11, 11-item version of the Symptom Checklist; S-DERS, State Difficulties in Emotion Regulation Scale; STEP-P/STEP-T, Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie, patient (P) or therapist (T) version; SWEMWBS, Short Warwick-Edinburgh Mental Wellbeing Scale; WAI-P/WAI-T: Working Alliance Inventory, patient (P) or therapist (T) version; ZUF-8, 8-item version of the Fragebogen zur Patientenzufriedenheit.

*: Please note that assessments marked with one asterisk are collected only selectively at T1, T2 and T3 after being collected fully at T0. **: Please note that measures marked with two asterisks are administered after each session in the MeMoPsy condition

Sample size [14]

Due to the exploratory nature of this feasibility trial no formal sample size calculation was performed. Rather, the current feasibility trial serves to obtain pilot data that can be used for the sample size calculation a subsequent confirmatory trial. For reasons of feasibility, the number of patients in each group (i.e., MeMoPsy, CBT) was set at $n = 40$, aiming to recruit 4 patients per month over a recruitment period of 10 months. With reference to Cocks and Torgerson (98), a total of 80 patients (assuming 20% dropout) is sufficient to obtain data in order to plan a subsequent confirmatory trial for continuous outcome measures for moderate effect sizes of at least Cohen's $d \geq 0.3$. Significant dropout rates of up to 55% have been reported in clinical trials with children, adolescents, and adults with childhood trauma experiences (99). In our recent proof-of-concept randomized controlled trial (1), however, only 5 out of 70 patients (four in MoBa, one in CBT) discontinued treatment prematurely, which corresponds to a dropout rate of 7%. Building on the latter study, the aim of the current trial is to keep the dropout rate below 20%, which is reasonable given that the MeMoPsy approach focuses on the therapeutic alliance and encompasses regular assessments to keep in contact with the patients.

Recruitment [15]

Patients will be recruited at inpatient and outpatient clinics at three German study sites (i.e., Heidelberg, Mannheim, Berlin). The majority of patients will be recruited at the Centre for Psychosocial Medicine at Heidelberg University Hospital, the Central Institute of Mental Health in Mannheim and the psychotherapeutic outpatient clinic of the Department of Clinical Child and Adolescent Psychology and Psychotherapy at Freie Universität Berlin. In addition, patients will be recruited via posts on social media, flyers in private practices and articles in local newspapers to announce the psychotherapeutic treatment offer within the current feasibility trial. Please refer to Figure 2 for the trial design and flow of patients.

Assignment of interventions: Allocation [16]

Randomization will be performed, stratified by study site (i.e., Heidelberg, Mannheim, Berlin), in a 1:1allocation ratio. The allocation sequence is based on computer-generated random numbers and implemented using the Internet-based software ASMO (*As*sessment and *Mo*nitoring of Mental Health; www.asmo.online), developed and maintained at the Centre for Psychotherapy Research at University Hospital Heidelberg (100). The study staff does not have access to the allocation sequence. Patients will be automatically randomized to either MeMoPsy or CBT after having completed the online baseline assessment. The diagnostician accompanying the baseline assessment will inform another member of the study staff after the patient has finished the online baseline assessment. This person will access the result of the randomized allocation sequence provided by ASMO, and informs the patient about the allocation to either MeMoPsy or CBT. This procedure enables us to keep the diagnostic staff blinded to treatment allocation.

Assignment of interventions: Blinding [17]

Research assistants and diagnosticians involved in recruitment and interview assessments at baseline (T0) and post-intervention (T2) are blinded to treatment allocation. Specifically, blinded diagnosticians will rate the effectiveness of MeMoPsy as compared to CBT using the Global Assessment of Functioning Scale (GAF) at T0 and T2. After baseline assessment, patients receive pseudonymized codes which do not contain any information on treatment allocation. Patients and therapists cannot be blinded regarding treatment allocation due to the nature of the psychotherapeutic interventions. Primary outcomes (except the effectiveness of MeMoPsy as compared to CBT, see above) and secondary outcomes encompass self-report and therapist-report measures and thus cannot be assessed in a blinded manner. Feedback on psychotherapeutic processes is an integral part of modular psychotherapy (43). Therefore, therapists in the MeMoPsy condition are not blinded to all of their patients' ratings. Instead, at every 5th session, therapists in the MeMoPsy condition are given access to their patients' ratings of items measuring changes in the assumed

transdiagnostic mechanisms linked to the psychotherapeutic modules, the therapeutic alliance, and the psychopathological symptom burden. In addition, at the assessment time points T0, T1 and T2, both the therapists in the MeMoPsy condition and the therapists in the CBT condition are given access to their patients' ratings of the psychopathological symptom burden. This procedure allows for adapting the selection of interventions according to patients´ current needs (within the selected modules). Research assistants involved

- in the additional assessments using EMA, fMRI, and saliva samples to determine cortisol levels will be blinded regarding treatment allocation of the patients.
- in qualitative interviews are not blinded regarding treatment allocation since they are only performed in the MeMoPsy condition.
- in the data analysis will be blinded regarding the treatment allocation with the exception of the data collected using continuous process monitoring which is only done in the MeMoPsy condition.

No circumstances are defined under which unblinding is permissible, as both patients and therapists are not blind to treatment allocation.

Data collection, management, and analysis

Data collection methods [18]

All patients will participate in comprehensive clinical and experimental assessments, including psychometrically validated, widely used measures (see Tables 1 and 2).

Screening for initial eligibility (time point T-2) will be performed by trained research assistants using a brief screening questionnaire adapted from a prior large cross-sectional study on childhood trauma experiences (101), including the German version of the CTQ (102). Screening will be conducted in a conventional paper-and-pencil format. Diagnostic assessments (time point T-1) will be conducted by qualified diagnosticians (i.e., with at least a master's degree in clinical psychology) who will receive standardized diagnostic training before the beginning of the study. Diagnostic assessments include different commonly used measures captured in a paper-and-pencil format: (1) childhood trauma experiences will be

assessed with a comprehensive interview, the KERF-40-I (103), which is the brief German interview version of the Maltreatment and Abuse Chronology of Exposure scale (104); (2) mental disorders will be assessed with an efficient interview, the Mini-DIPS (46); (3) avoidant and borderline personality disorders will be assessed with the SCID-5-PD (105, 106) to consider frequently occurring personality disorders in adolescent traumatized individuals; (4) symptoms of autism spectrum disorders will be determined with a self-report questionnaire, the AQ-10 (51); and (5) general cognitive abilities will be measured with a brief screening tool, the mini-q (52). If no exclusion criteria are identified at screening (T-2) and diagnostics (T-1), the software ASMO is used to register the patient and subsequently administer several online questionnaires to measure patients' and diagnosticians' ratings at baseline (time point T0). ASMO is used both for the core trial visits (i.e., mid-intervention T1, 16 weeks after baseline; post-intervention T2, 32 weeks after baseline; follow-up T3, 44 weeks after baseline) and the continuous process monitoring (i.e., patients' and therapists' ratings collected every session or every 5th session in the MeMoPsy condition). ASMO allows to automatically collect data on primary and secondary outcomes. The scientific staff continuously ensures that patients and therapists fill out the online questionnaires at the designated time points and, if necessary, reminds patients and therapists by email to complete online questionnaires on time.

All patients will be encouraged to take part in additional optional assessments (EMA, fMRI, saliva sampling to determine cortisol levels, and qualitative interviews). All additional assessments will be performed by trained scientific staff under the supervision of experts in the corresponding field.

Once a patient is randomized to one of the two treatment conditions, we will make every reasonable effort to promote patient retention and maximize completeness of data collection. We will perform regular assessments with a maximum interval of 16 weeks, remind patients to complete the assessments at the designated time points, and financially reimburse patients for their participation in the assessments of primary and secondary outcomes, and additional assessments and research tools (i.e., EMA, fMRI, hormone measurements, qualitative interviews). Data assessment (T1, T2, and T3) will be administered online, allowing patients

to complete it from home and thus reducing their burden related to additional on-site visits. All patients will be asked to participate in the core trial assessments (i.e., mid-intervention T1, post-intervention T2, follow-up T3), even if they discontinue treatment prematurely, and thus minimize the number of patients lost to follow-up.

Data management [19]

Data management will be performed using ASMO. The respective servers are located at the University Hospital Heidelberg. Data collected digitally guarantee the highest level of data integrity and quality as risks for missing data and false data entry are minimized. ASMO allows for the monitoring of data collection, the continuous documentation of all access logs, the traceability of all entered data (i.e., user and timestamp), and for the restoration of previous states. A Distributed Replicated Block Device (DRBD)-based cluster will ensure synchronous replication of all data during data entry on two separate servers and highest availability. In addition, full and incremental backups will be conducted following a predefined plan. Data storage and data transfer will be encrypted. Access to the data will be password-protected and strictly limited to authorized and trained staff members. Data collected in a paper-and-pencil format (i.e., screening for eligibility, diagnostics via interviews at baseline) will be entered electronically by authorized and trained scientific staff using a pseudonymised electronic case report form in ASMO. Data management for the additional assessments will be performed according to standard procedures within the corresponding field.

Statistical methods [20]

Before conducting the final data analysis, a detailed statistical analysis plan will be prepared. Considering the exploratory nature of our feasibility trial, the final data analysis will be performed only descriptively and in accordance with the intention-to-treat principle (i.e., based on the full analysis set, including all patients randomized to one of the two treatment groups). All primary and secondary outcomes will be described by treatment arm and overall using appropriate indices from the empirical distributions (i.e., arithmetic means, standard

deviations, minimum, 25% quantile, median, 75% quantile, maximum, relative and absolute frequencies). For the primary and secondary outcomes, effect sizes between the two treatment groups (i.e., MeMoPsy, CBT) will be described in absolute differences and Cohen's *d* with corresponding 95% confidence intervals and will be evaluated by unpaired *t*-tests. For the continuous psychotherapy process research within the intervention group, we follow established standards and employ multilevel modelling to account for the temporal and hierarchical structure of the data. Missing values will be described by relative frequencies and will not be imputed. Patient characteristics between patients with and without missing data in the primary outcomes will be compared in order to identify possible bias. Evaluation of the primary outcomes will be performed blinded to treatment allocation.

For the safety analysis, the frequency of serious adverse events in all randomized patients will be tabulated by treatment group (i.e., MeMoPsy, CBT), presumed association with the intervention, and severity.

All analyses will be performed in R v4.4.0 or higher, available under https://www.r-project.org/

Monitoring

Data monitoring [21]

A Data Safety Monitoring Board (DSMB) has been established, which is independent of the investigators, the sponsor, and of competing interests. The role and reporting structure of the DSMB is detailed in a study-specific DSMB charter, which is available from the corresponding author on request. Briefly, the role of the DSMB is to protect the interests of the trial participants and patients, assess the safety of the interventions during the trial period, and monitor the integrity of the trial. In addition, the role of the DSMB is to support and advise the investigators to protect the validity and credibility of the study without violating the underlying study protocol. To this end, the DSMB will meet in person or online on at least three predefined dates (i.e., with start of recruitment, six months and one year after the beginning of the study) and as needed (e.g., in case of potential safety concerns, delays in study progress). In the

DSMB meetings, the recruitment progress, violations of the study protocol, dropout rates, adverse and serious adverse events, and data quality will be discussed. Serious adverse events, high study dropouts or a high incidence of violations of the study plan may indicate potential safety problems.

The DSMB consists of three German scientists with expertise in psychotherapy research and Medical Informatics. The DSMB will be supported by individuals with lived experience, who participated in developing the MeMoPsy approach specifically considering the needs of patients (see also the chapter on Patient and Public Involvement).

No interim analysis will be performed.

Harms [22]

In the current feasibility trial, serious adverse events (SAEs) are defined as death of a patient, child endangerment, acute suicidality and acute aggressiveness with indication for inpatient treatment (i.e., emergency hospital admission). Adverse events (AEs) are defined as symptom deterioration, occurrence of new symptoms, occurrence of passive suicidal thoughts, problems in the patient-therapist relationship, private problems, occupational problems, or other medical conditions. SAEs and AEs are reported by therapists with deterioration of psychopathology also checked by regular session reports. In a comparable, recently published randomized controlled trial on modular psychotherapy (1), no SAE occurred. In the current feasibility trial, all study-related measures (i.e., diagnostics, EMA, fMRI, hormone measurements, qualitative interviews) have already been performed in a similar manner in previous studies by the participating investigators without any SAEs on the study participants. Based on our experiences with psychotherapy trials, we do not expect any SAE to occur in connection with our planned feasibility trial. Should a SAE occur, it must be reported within 24 hours of its occurrence to the principal investigator, Sabine C. Herpertz, who will forward this information to the members of the DSMB. Indications of SAEs and AEs will be followed up by the diagnostician or the psychotherapist in charge in accordance with clinical guidelines and good clinical practice (e.g., consulting with an experienced colleague, initiating child and youth

welfare measures, initiating emergency hospital admission). If there are any indications that an adult patient is at risk (e.g., recent experience of (serious) abuse or violence), the approach is similar to that for child endangerment, and measures are implemented to ensure safety. Patients with acute suicidal tendencies who require immediate crisis intervention are referred to a suitable specialized facility, but can continue the randomized treatment if the duration of the crisis intervention does not exceed 14 days. Patients who leave treatment due to SAEs will continue to be cared for in accordance with good clinical practice until they are no longer clinically conspicuous.

Auditing [23]

See data monitoring

In addition, at the request of the study management protocol review, data analysis or similar will be advised. Due to a feasibility study no external monitoring is planned.

Patient and Public Involvement

The current feasibility trial is part of the German Centre for Mental Health (Deutsches Zentrum für Psychische Gesundheit, DZPG). The DZPG pursues the overarching goal of promoting population mental health based on a comprehensive translational research program of national scope (for a concise overview of the DZPG, please see 107). The DZPG research program is consistently co-created with people with lived experience, and patient and public involvement (PPI) is fostered at all stages of research. In line with this participatory approach, the current feasibility trial has been designed with the support of service users affected by both mental disorders and childhood trauma experiences. Service users have been and will be involved in decision competency in all steps of the research process, which is also reflected by the employment of one service user as an expert by (lived) experience in the current feasibility trial who has checked the study design including outcomes.

Ethics and Dissemination

Research ethics approval [24]

The study protocol, informed consent forms, recruitment materials, participant information on procedures specific to the hormone measurements have been reviewed and approved by the independent Ethics Committees of the Medical Faculty of Heidelberg University (AZ: S-583/2023), and of the Medical Faculty Mannheim of Heidelberg University (AZ:2023-675). The Ethics Committee of Freie Universität Berlin has declared that it will abide by the vote of the Ethics Committee of the managing site in Heidelberg.

Protocol amendments [25]

All relevant modifications have gained approval by the Ethics Committees in Heidelberg, Mannheim and Berlin prior to start of the study and have been implemented in the study registration at the German Clinical Trials Register (Deutsches Register Klinischer Studien, DRKS; DRKS00034058). Each study site is responsible for training their study staff in protocol modifications.

Consent or assent [26]

Informed consent will be obtained by qualified psychologists (at least a master's degree in clinical psychology) trained to ensure adherence to the study protocol. In the informed consent forms approved by the Ethics Committees in Heidelberg, Mannheim and Berlin, patients can consent to the intervention study and the additional measures (i.e., EMA, fMRI, hormone measurements), and qualitative interviews separately.

Confidentiality [27]

All data are subject to medical confidentiality and will be handled in accordance with the European Union General Data Protection Regulation (Datenschutzgrundverordnung, DSGVO) and the German legal regulations concerning data protection and security (Landesdatenschutzgesetz Baden-Wurttemberg, Bundesdatenschutzgesetz). All study-related information will be stored securely at the study sites. All data assessed in a paper and

pencil format will be stored in locked file cabinets in areas with limited access. All data will be pseudonymised (i.e., identified by a coded identification number) to maintain patient confidentiality. All data assessed electronically using ASMO will be transferred to the ASMO servers located at Heidelberg University Hospital. Data storage and data transfer will be encrypted. Access to the data will be password-protected and strictly limited to authorized and trained staff members. Data will be stored for 10 years.

Declaration of interests [28]

The authors report no potential conflicts of interest.

Access to data [29]

All investigators will have access to the final trial dataset.

Ancillary and post-trial care [30]

Patients can get support from our outpatient and inpatient clinics in case of need.

Dissemination policy [31]

We plan to communicate trial results via publications in peer-reviewed journals and conference contributions. We will use the DZPG newsletter, which addresses people with lived experience (i.e., patients and their families), the DZPG website, press releases, LinkedIn and social media for science communication. We will provide access to the full protocol, participant-level dataset, and statistical code on demand.

References

1. Schramm E, Elsaesser M, Jenkner C, Hautzinger M, Herpertz SC. Algorithm-based modular psychotherapy vs. cognitive-behavioral therapy for patients with depression, psychiatric comorbidities and early trauma: a proof-of-concept randomized controlled trial. World psychiatry : official journal of the World Psychiatric Association. 2024;23(2):257-66.
2. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Annals of internal medicine. 2013;158(3):200-7.
3. Baldwin JR, Wang B, Karwatowska L, Schoeler T, Tsaligopoulou A, Munafò MR, et al. Childhood Maltreatment and Mental Health Problems: A Systematic Review and Meta-Analysis of Quasi-Experimental Studies. The American journal of psychiatry. 2023;180(2):117-26.
4. Bellis MA, Hughes K, Ford K, Ramos Rodriguez G, Sethi D, Passmore J. Life course health consequences and associated annual costs of adverse childhood experiences across Europe and North America: A systematic review and meta-analysis. Lancet Public Health. 2019;4(10):e517-e28.
5. Hogg B, Gardoki-Souto I, Valiente-Gómez A, Rosa AR, Fortea L, Radua J, et al. Psychological trauma as a transdiagnostic risk factor for mental disorder: an umbrella meta-analysis. Eur Arch Psychiatry Clin Neurosci. 2023;273(2):397-410.
6. McKay MT, Kilmartin L, Meagher A, Cannon M, Healy C, Clarke MC. A revised and extended systematic review and meta-analysis of the relationship between childhood adversity and adult psychiatric disorder. Journal of psychiatric research. 2022;156:268-83.
7. Humphreys KL, LeMoult J, Wear JG, Piersiak HA, Lee A, Gotlib IH. Child maltreatment and depression: A meta-analysis of studies using the Childhood Trauma Questionnaire. Child abuse & neglect. 2020;102:104361.
8. LeMoult J, Humphreys KL, Tracy A, Hoffmeister JA, Ip E, Gotlib IH. Meta-analysis: Exposure to Early Life Stress and Risk for Depression in Childhood and Adolescence. Journal of the American Academy of Child and Adolescent Psychiatry. 2020;59(7):842-55.
9. Li M, D'Arcy C, Meng X. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: Systematic review, meta-analysis, and proportional attributable fractions. Psychological medicine. 2016;46(4):717-30.
10. Pignatelli AM, Wampers M, Loriedo C, Biondi M, Vanderlinden J. Childhood neglect in eating disorders: A systematic review and meta-analysis. Journal of trauma & dissociation : the official journal of the International Society for the Study of Dissociation (ISSD). 2017;18(1):100-15.
11. Zhang S, Lin X, Liu J, Pan Y, Zeng X, Chen F, et al. Prevalence of childhood trauma measured by the short form of the Childhood Trauma Questionnaire in people with substance use disorder: A meta-analysis. Psychiatry Res. 2020;294:113524.
12. Bonoldi I, Simeone E, Rocchetti M, Codjoe L, Rossi G, Gambi F, et al. Prevalence of self-reported childhood abuse in psychosis: a meta-analysis of retrospective studies. Psychiatry Res. 2013;210(1):8-15.
13. Porter C, Palmier-Claus J, Branitsky A, Mansell W, Warwick H, Varese F. Childhood adversity and borderline personality disorder: a meta-analysis. Acta psychiatrica Scandinavica. 2020;141(1):6-20.
14. Blakemore SJ. Adolescence and mental health. Lancet (London, England). 2019;393(10185):2030-1.
15. Group CTM-AS. Treatment efficacy and effectiveness in adults with major depressive disorder and childhood trauma history: a systematic review and meta-analysis. The lancet Psychiatry. 2022;9(11):860-73.
16. Karatzias T, Murphy P, Cloitre M, Bisson J, Roberts N, Shevlin M, et al. Psychological interventions for ICD-11 complex PTSD symptoms: systematic review and meta-analysis. Psychological medicine. 2019;49(11):1761-75.

17. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. The American journal of psychiatry. 2012;169(2):141-51.
18. Nelson J, Klumparendt A, Doebler P, Ehring T. Childhood maltreatment and characteristics of adult depression: Meta-analysis. The British Journal of Psychiatry. 2017;210(2):96-104.
19. Shirk SR, Deprince AP, Crisostomo PS, Labus J. Cognitive behavioral therapy for depressed adolescents exposed to interpersonal trauma: an initial effectiveness trial. Psychotherapy (Chicago, Ill). 2014;51(1):167-79.
20. Panagou C, MacBeth A. Deconstructing pathways to resilience: A systematic review of associations between psychosocial mechanisms and transdiagnostic adult mental health outcomes in the context of adverse childhood experiences. Clinical psychology & psychotherapy. 2022;29(5):1626-54.
21. Jaffee SR. Child maltreatment and risk for psychopathology in childhood and adulthood. Annual review of clinical psychology. 2017;13:525-51.
22. McCrory E, Ogle JR, Gerin MI, Viding E. Neurocognitive adaptation and mental health vulnerability following maltreatment: The role of social functioning. Child maltreatment. 2019;24(4):435-51.
23. McLaughlin KA, Colich NL, Rodman AM, Weissman DG. Mechanisms linking childhood trauma exposure and psychopathology: A transdiagnostic model of risk and resilience. BMC Med. 2020;18(1):96.
24. Gao S, Assink M, Bi C, Chan KL. Child Maltreatment as a Risk Factor for Rejection Sensitivity: A Three-Level Meta-Analytic Review. Trauma, violence & abuse. 2023:15248380231162979.
25. Copeland WE, Shanahan L, Hinesley J, Chan RF, Aberg KA, Fairbank JA, et al. Association of childhood trauma exposure with adult psychiatric disorders and functional outcomes. JAMA Netw Open. 2018;1(7):e184493.
26. Downey G, Feldman SI. Implications of rejection sensitivity for intimate relationships. Journal of personality and social psychology. 1996;70(6):1327-43.
27. De Paoli T, Fuller-Tyszkiewicz M, Krug I. Insecure attachment and maladaptive schema in disordered eating: The mediating role of rejection sensitivity. Clinical psychology & psychotherapy. 2017;24(6):1273-84.
28. Weissman DG, Nook EC, Dews AA, Miller AB, Lambert HK, Sasse SF, et al. Low Emotional Awareness as a Transdiagnostic Mechanism Underlying Psychopathology in Adolescence. Clin Psychol Sci. 2020;8(6):971-88.
29. Beauchaine TP. Future Directions in Emotion Dysregulation and Youth Psychopathology. Journal of clinical child and adolescent psychology : the official journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53. 2015;44(5):875-96.
30. Gruhn MA, Compas BE. Effects of maltreatment on coping and emotion regulation in childhood and adolescence: A meta-analytic review. Child abuse & neglect. 2020;103:104446.
31. Beauchaine TP, Cicchetti D. Emotion dysregulation and emerging psychopathology: A transdiagnostic, transdisciplinary perspective. Development and psychopathology. 2019;31(3):799-804.
32. Anmella G, De Prisco M, Fico G, Fornaro M, Grande I, Hidalgo-Mazzei D, et al. Emotion dysregulation in bipolar disorder compared to other mental illnesses: a systematic review and meta-analysis. Psychological medicine. 2023;53(16):7484-503.
33. Fleming J, Mullen PE, Sibthorpe B, Bammer G. The long-term impact of childhood sexual abuse in Australian women. Child abuse & neglect. 1999;23(2):145-59.
34. Davis JL, Petretic-Jackson PA. The impact of child sexual abuse on adult interpersonal functioning: A review and synthesis of the empirical literature. Aggression and Violent Behavior. 2000;5(3):291-328.
35. Drapeau M, Perry JC. Childhood trauma and adult interpersonal functioning: a study using the Core Conflictual Relationship Theme Method (CCRT). Child abuse & neglect. 2004;28(10):1049-66.

36. Seitz KI, Bertsch K, Herpertz SC. A Prospective Study of Mental Health During the COVID-19 Pandemic in Childhood Trauma-Exposed Individuals: Social Support Matters. Journal of traumatic stress. 2021;34(3):477-86.
37. Shevlin M, McElroy E, Murphy J. Loneliness mediates the relationship between childhood trauma and adult psychopathology: Evidence from the Adult Psychiatric Morbidity Survey. Social psychiatry and psychiatric epidemiology. 2015;50(4):591-601.
38. Vranceanu AM, Hobfoll SE, Johnson RJ. Child multi-type maltreatment and associated depression and PTSD symptoms: The role of social support and stress. Child abuse & neglect. 2007;31(1):71-84.
39. Levy J, Goldstein A, Feldman R. The neural development of empathy is sensitive to caregiving and early trauma. Nature communications. 2019;10(1):1905.
40. Reinhard MA, Rek SV, Nenov-Matt T, Barton BB, Dewald-Kaufmann J, Merz K, et al. Association of loneliness and social network size in adulthood with childhood maltreatment: Analyses of a population-based and a clinical sample. European psychiatry : the journal of the Association of European Psychiatrists. 2022;65(1):e55.
41. Whisman MA, Sheldon CT, Goering P. Psychiatric disorders and dissatisfaction with social relationships: does type of relationship matter? Journal of abnormal psychology. 2000;109(4):803-8.
42. Fan L, Chen Y, Zhu M, Mao Z, Li N. Correlation between childhood trauma experience and depressive symptoms among young adults: The potential mediating role of loneliness. Child abuse & neglect. 2023;144:106358.
43. Herpertz SC, Schramm E. Modulare Psychotherapie. Ein Mechanismus-basiertes, personalisiertes Vorgehen. Stuttgart: Schattauer; 2022.
44. Elsaesser M, Herpertz S, Piosczyk H, Jenkner C, Hautzinger M, Schramm E. Modular-based psychotherapy (MoBa) versus cognitive-behavioural therapy (CBT) for patients with depression, comorbidities and a history of childhood maltreatment: study protocol for a randomised controlled feasibility trial. BMJ open. 2022;12(7):e057672.
45. David D, Cristea I, Hofmann SG. Why Cognitive Behavioral Therapy Is the Current Gold Standard of Psychotherapy. Frontiers in psychiatry. 2018;9:4.
46. Margraf J, Cwik JC. Mini-DIPS Open Access: Diagnostic Short-Interview for Mental Disorders. [Mini-DIPS Open Access: Diagnostisches Kurzinterview bei psychischen Störungen]. Bochum: Forschungs- und Behandlungszentrum für psychische Gesundheit, Ruhr-Universität; 2017.
47. Beesdo-Baum K, Zaudig M, Wittchen H-U. SCID-5-PD: Strukturiertes Klinisches Interview für DSM-5®-Persönlichkeitsstörungen: Hogrefe; 2019.
48. Beesdo-Baum K, Zaudig M, Wittchen H-U. SCID-5-CV: strukturiertes klinisches Interview für DSM-5-Störungen-Klinische Version: deutsche Bearbeitung des Structured Clinical Interview for DSM-5 Disorders-Clinician version von Michael B. First, Janet BW Williams, Rhonda S. Karg, Robert L. Spitzer: Hogrefe; 2019.
49. Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. The American journal of psychiatry. 1994;151(8):1132-6.
50. Häuser W, Schmutzer G, Brähler E, Glaesmer H. Maltreatment in childhood and adolescence: results from a survey of a representative sample of the German population. Deutsches Arzteblatt international. 2011;108(17):287-94.
51. Allison C, Auyeung B, Baron-Cohen S. Toward brief "Red Flags" for autism screening: The Short Autism Spectrum Quotient and the Short Quantitative Checklist for Autism in toddlers in 1,000 cases and 3,000 controls [corrected]. Journal of the American Academy of Child and Adolescent Psychiatry. 2012;51(2):202-12.e7.
52. Baudson TG, Preckel F. mini-q: Intelligenzscreening in drei Minuten. 2016;62(3):182-97.
53. Elsaesser M, Herpertz S, Piosczyk H, Jenkner C, Hautzinger M, Schramm E. Modular-based psychotherapy (MoBa) versus cognitive–behavioural therapy (CBT) for patients with depression, comorbidities and a history of childhood maltreatment: study protocol for a randomised controlled feasibility trial. BMJ open. 2022;12(7):e057672.

54. Herpertz SC, Schramm E. Modulare psychotherapie: ein mechanismus-basiertes, personalisiertes vorgehen: Klett-Cotta; 2022.
55. Bateman A, Fonagy P. Mentalization-based treatment for personality disorders: A practical guide: OUP Oxford; 2016.
56. Schauer M, Ruf-Leuschner M. Lifeline in der Narrativen Expositionstherapie. Psychotherapeut. 2014;59(3):226-38.
57. Newhill CE, Safran JD, Muran JC. Negotiating the therapeutic alliance: A relational treatment guide: Guilford Press; 2003.
58. Downey G, Feldman SI. Implications of rejection sensitivity for intimate relationships. Journal of personality and social psychology. 1996;70(6):1327.
59. McCullough Jr JP. Treatment for chronic depression: Cognitive behavioral analysis system of psychotherapy (CBASP): Educational Publishing Foundation; 2003.
60. Lavender JM, Tull MT, DiLillo D, Messman-Moore T, Gratz KL. Development and validation of a state-based measure of emotion dysregulation: The State Difficulties in Emotion Regulation Scale (S-DERS). Assessment. 2017;24(2):197-209.
61. Linehan MM. Dialectical behavior therapy for borderline personality disorder: Theory and method. Bulletin of the Menninger Clinic. 1987;51(3):261.
62. Moessner M, Gallas C, Haug S, Kordy H. The clinical psychological diagnostic system (KPD-38): Sensitivity to change and validity of a self-report instrument for outcome monitoring and quality assurance. Clinical Psychology & Psychotherapy. 2011;18(4):331-8.
63. Smith G. Working with trauma: Systemic approaches: Bloomsbury Publishing; 2012.
64. Kim MJ, Knodt AR, Hariri AR. Meta-analytic activation maps can help identify affective processes captured by contrast-based task fMRI: the case of threat-related facial expressions. Social cognitive and affective neuroscience. 2022;17(9):777-87.
65. Breil C, Kanske P, Pittig R, Böckler A. A revised instrument for the assessment of empathy and Theory of Mind in adolescents: Introducing the EmpaToM-Y. Behavior research methods. 2021;53(6):2487-501.
66. Frolichs KM, Rosenblau G, Korn CW. Incorporating social knowledge structures into computational models. Nature communications. 2022;13(1):6205.
67. Korn CW, La Rosée L, Heekeren HR, Roepke S. Social feedback processing in borderline personality disorder. Psychological medicine. 2016;46(3):575-87.
68. Schmidt J, Lamprecht F, Wittmann WW. Zufriedenheit mit der stationären Versorgung. Entwicklung eines Fragebogens und erste Validitätsuntersuchungen. [Satisfaction with inpatient care: Development of a questionnaire and first validity assessments.]. PPmP: Psychotherapie Psychosomatik Medizinische Psychologie. 1989;39(7):248-55.
69. Larsen DL, Attkisson CC, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: development of a general scale. Evaluation and program planning. 1979;2(3):197-207.
70. Weiner BJ, Lewis CC, Stanick C, Powell BJ, Dorsey CN, Clary AS, et al. Psychometric assessment of three newly developed implementation outcome measures. Implementation Science. 2017;12(1):108.
71. Rozental A, Kottorp A, Forsström D, Månsson K, Boettcher J, Andersson G, et al. The Negative Effects Questionnaire: psychometric properties of an instrument for assessing negative effects in psychological treatments. Behavioural and cognitive psychotherapy. 2019;47(5):559-72.
72. Roe D, Dekel R, Harel G, Fennig S. Clients' reasons for terminating psychotherapy: a quantitative and qualitative inquiry. Psychology and psychotherapy. 2006;79(Pt 4):529-38.
73. Franke GH. Brief Symptom Inventory von L. R. Derogatis (Kurzform der SCL-90-R) - Deutsche Version. Manual. [Brief Symptom Inventory by L. R. Derogatis (Short form of the SCL-90-R) - German version. Manual]. Göttingen: Beltz Test; 2000.
74. APA. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) Washington, DC, USA: American Psychiatric Association; 2000.
75. Staebler K, Helbing E, Rosenbach C, Renneberg B. Rejection sensitivity and borderline personality disorder. Clinical psychology & psychotherapy. 2011;18(4):275-83.

76. Lavender JM, Tull MT, DiLillo D, Messman-Moore T, Gratz KL. Development and Validation of a State-Based Measure of Emotion Dysregulation. Assessment. 2017;24(2):197-209.
77. Lambert MJ, Burlingame GM, Umphress V, Hansen NB, Vermeersch DA, Clouse GC, et al. The Reliability and Validity of the Outcome Questionnaire. 1996;3(4):249-58.
78. Puschner B, Cosh SM, Becker TJEJoPA. Patient-Rated Outcome Assessment With the German Version of the Outcome Questionnaire 45 in People With Severe Mental Illness. 2016;32:273-82.
79. Haug S, Puschner B, Lambert MJ, Kordy H. Veränderungsmessung in der Psychotherapie mit dem Ergebnisfragebogen (EB-45). Zeitschrift für Differentielle und Diagnostische Psychologie. 2004;25(3):141-51.
80. Bach B, Kerber A, Aluja A, Bastiaens T, Keeley JW, Claes L, et al. International Assessment of DSM-5 and ICD-11 Personality Disorder Traits: Toward a Common Nosology in DSM-5.1. Psychopathology. 2020;53(3-4):179-88.
81. Spitzer C, Müller S, Kerber A, Hutsebaut J, Brähler E, Zimmermann J. Die deutsche version der level of personality functioning scale-brief form 2.0 (LPFS-BF): faktorenstruktur, konvergente validität und normwerte in der allgemeinbevölkerung. PPmP-Psychotherapie· Psychosomatik· Medizinische Psychologie. 2021;71(07):284-93.
82. Renneberg B, Seehausen A. Fragebogen zu Gedanken und Gefühlen (FGG)—Ein screening instrument für borderline-spezifisches denken. [Questionnaire of Thoughts and Feelings (QTF)—A screening instrument for borderline-specific cognitions.]. Zeitschrift für Klinische Psychologie und Psychotherapie: Forschung und Praxis. 2010;39(3):170-8.
83. Bohus M, Kleindienst N, Limberger MF, Stieglitz RD, Domsalla M, Chapman AL, et al. The short version of the Borderline Symptom List (BSL-23): development and initial data on psychometric properties. Psychopathology. 2009;42(1):32-9.
84. Stiglmayr C, Schmahl C, Bremner JD, Bohus M, Ebner-Priemer U. Development and psychometric characteristics of the DSS-4 as a short instrument to assess dissociative experience during neuropsychological experiments. Psychopathology. 2009;42(6):370-4.
85. Müller S, Wendt LP, Zimmermann J. Development and Validation of the Certainty About Mental States Questionnaire (CAMSQ): A Self-Report Measure of Mentalizing Oneself and Others. Assessment. 2021:10731911211061280.
86. Cordes A, Herrmann-Lingen C, Büchner B, Hessel A. Repräsentative Normierung des ENRICHD Social-Support-Instrument (ESSI) – Deutsche Version [Psychometric properties of the ENRICHD Social Support Instrument (ESSI, German version) in a representative German population sample]. Klinische Diagnostik und Evaluation. 2009;2:16-32.
87. Guy W. ECDEU assessment manual for psychopharmacology: US Department of Health, Education, and Welfare, Public Health Service …; 1976.
88. Patton MQ. Qualitative evaluation and research methods: SAGE Publications, inc; 1990.
89. Krampen G. Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie: STEP: Hogrefe, Verlag für Psychologie; 2002.
90. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working Alliance Inventory-Short Revised (WAI-SR): psychometric properties in outpatients and inpatients. Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice. 2010;17(3):231-9.
91. Lutz W, Tholen S, Schürch E, Berking M. Reliabilität von Kurzformen gängiger psychometrischer Instrumente zur Evaluation des therapeutischen Fortschritts in Psychotherapie und Psychiatrie. . Diagnostica. 2006;52(1):11-25.
92. Clarke A, Putz R, Friede T, Ashdown J, Adi Y, Martin S, et al. Warwick-Edinburgh Mental Well-being Scale (WEMWBS) acceptability and validation in English and Scottish secondary school students (The WAVES Project) Glasgow. 2010.
93. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. Journal of personality and social psychology. 1988;54(6):1063-70.
94. Hariri AR, Bookheimer SY, Mazziotta JC. Modulating emotional responses: effects of a neocortical network on the limbic system. Neuroreport. 2000;11(1):43-8.

95. Breil C, Kanske P, Pittig R, Böckler A. A revised instrument for the assessment of empathy and Theory of Mind in adolescents: Introducing the EmpaToM-Y. Behav Res Methods. 2021;53(6):2487-501.
96. Kanske P, Böckler A, Trautwein FM, Singer T. Dissecting the social brain: Introducing the EmpaToM to reveal distinct neural networks and brain-behavior relations for empathy and Theory of Mind. NeuroImage. 2015;122:6-19.
97. Korn CW, Prehn K, Park SQ, Walter H, Heekeren HR. Positively biased processing of self-relevant social feedback. Journal of Neuroscience. 2012;32(47):16832-44.
98. Cocks K, Torgerson DJ. Sample size calculations for pilot randomized trials: a confidence interval approach. Journal of Clinical Epidemiology. 2013;66(2):197-201.
99. van der Hoeven ML, Assink M, Stams G-JJM, Daams JG, Lindauer RJL, Hein IM. Victims of Child Abuse Dropping Out of Trauma-Focused Treatment: A Meta-Analysis of Risk Factors. Journal of Child & Adolescent Trauma. 2023;16(2):269-83.
100. Wilhelm M, Feldhege J, Bauer S, Moessner M. Einsatz internetbasierter Verlaufsmessung in der Psychotherapieforschung. Psychotherapeut. 2020;65(6):505-11.
101. Cackowski S, Schmahl C. Research Training Group (RTG) / Graduiertenkolleg (GRK) 2350. Impact of adverse childhood experiences on psychosocial and somatic conditions across the lifespan. Neuroforum. 2019;25(4):265-6.
102. Klinitzke G, Romppel M, Häuser W, Brähler E, Glaesmer H. Die deutsche Version des Childhood Trauma Questionnaire (CTQ) - psychometrische Eigenschaften in einer bevölkerungsrepräsentativen Stichprobe [The German version of the Childhood Trauma Questionnaire (CTQ) - psychometric characteristics in a representative sample of the general population]. Psychotherapie Psychosomatik Medizinische Psychologie. 2012;62(2):47-51.
103. Seitz KI, Gerhardt S, von Schroeder C, Panizza A, Thekkumthala D, Bertsch K, et al. Measuring types and timing of childhood maltreatment: The psychometric properties of the KERF-40+. PLoS One. 2022;17(9):e0273931.
104. Teicher MH, Parigger A. The 'Maltreatment and Abuse Chronology of Exposure' (MACE) scale for the retrospective assessment of abuse and neglect during development. PLoS One. 2015;10(2):e0117423.
105. Solmi M, Dragioti E, Croatto G, Radua J, Borgwardt S, Carvalho AF, et al. Risk and protective factors for personality disorders: an umbrella review of published meta-analyses of case–control and cohort studies. Frontiers in Psychiatry. 2021;12:679379.
106. Quenneville AF, Kalogeropoulou E, Küng A-L, Hasler R, Nicastro R, Prada P, et al. Childhood maltreatment, anxiety disorders and outcome in borderline personality disorder. Psychiatry research. 2020;284:112688.
107. Meyer-Lindenberg A, Falkai P, Fallgatter AJ, Hannig R, Lipinski S, Schneider S, et al. The future German Center for Mental Health (Deutsches Zentrum für Psychische Gesundheit): a model for the co-creation of a national translational research structure. Nature Mental Health. 2023;1(3):153-6.

Author's Contributions

KIS together with SCH wrote the original draft of the manuscript and developed the basic idea of the study design with support provided by ES, CS, and HZ. Details of the clinical trial design were forwarded together by all authors from the three sites. KIS, NS, and SF coordinate the study's implementation, JH the MeMoPsy training and supervision. ST and FE designed and introduced the basic module, ES and SCH designed and introduced module 1, FE, RV and KIS module 2, and MH and CAR module 3 of the MeMoPsy intervention. HCF together with SB drafted the design of the process research, TB and ABR the design of the qualitative study. MW is responsible for electronic data assessment and management. CK supported by KIS and EB was responsible for designing the fMRI study, BD for hormonal analyses, SS and LTK for diagnostics, and MF for statistical design and analyses. EV and JB are responsible for the comparator treatment. All authors contributed to and have approved the final manuscript.

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Competing Interests Statement (see also Declaration of interests)

The authors report no potential conflicts of interest.

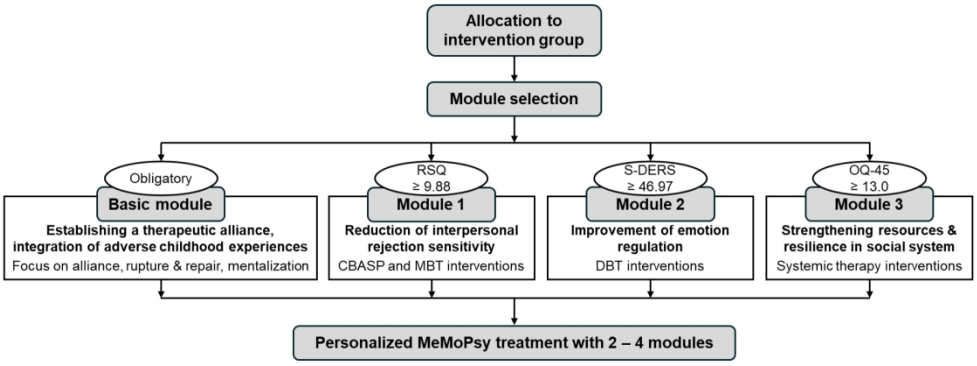

Figure 1. Modular treatment program and selection criteria. CBASP Cognitive Behavioral Analysis System of Psychotherapy; DBT, Dialectical-Behavior Therapy; MBT, Mentalization-Based Psychotherapy; MeMoPsy, mechanism-based modular psychotherapy; OQ-45, 45-item version of the Outcome Questionnaire; RSQ, Rejection Sensitivity Questionnaire; S-DERS, State Difficulties in Emotion Regulation Scale.

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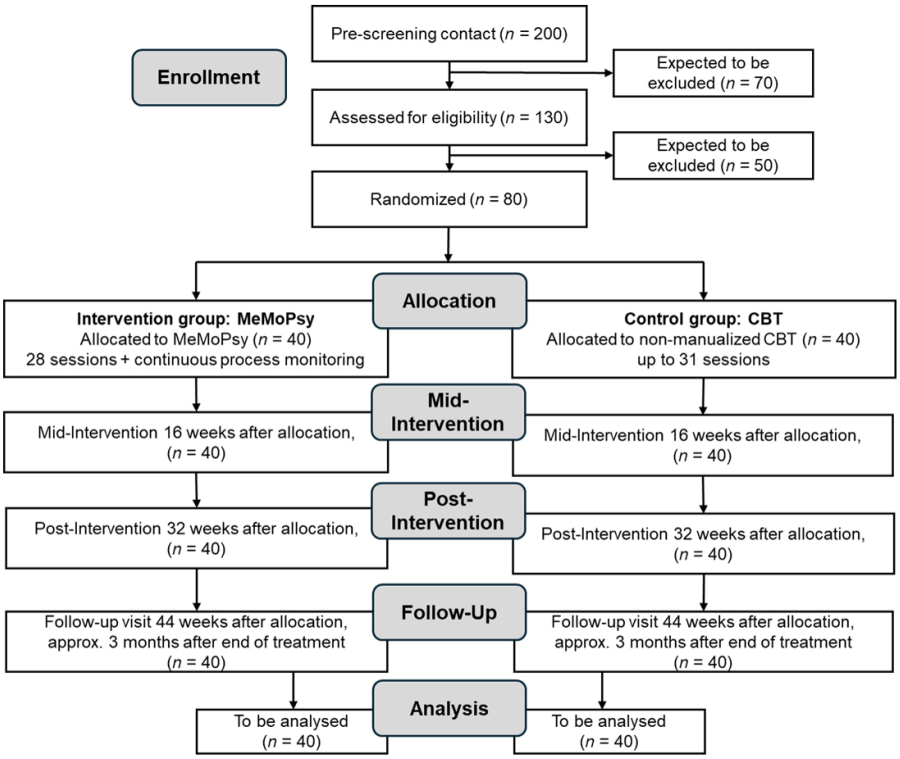

Figure 2. Trial design and flow of patients. CBT, cognitive behavioral therapy; MeMoPsy, mechanism-based modular psychotherapy. Please note that a drop-out estimated to amount to 20% may occur along intervention and follow-up.

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Mechanism-based modular psychotherapy vs. cognitive behavioral therapy for adolescents and young adults with childhood trauma experiences: Study protocol for a feasibility trial within the German Center for Mental Health

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Abstract

Introduction: Patients with mental disorders and a history of childhood trauma show an early onset of psychopathology and often a poor response to standard disorder-specific treatments. They represent a patient group which requires more personalized interventions targeting the transdiagnostic mechanisms related to early trauma and its functional consequences. The mechanism-based, modular psychotherapy (MeMoPsy) approach is conceptualized as an innovative framework for psychotherapy development. It comprises independent, flexibly applicable interventions from various theoretical backgrounds and evidence-based programs within a systematic treatment algorithm, thereby tailoring module selection to the specific needs of traumatized adolescents. *Methods and analysis*: In a randomized controlled feasibility trial (RCT), *N*=80 outpatients between 15 and 25 years of age diagnosed with various mental disorders will receive 28 individual sessions with MeMoPsy or standard cognitive behavioral therapy (CBT). MeMoPsy includes a basic module that addresses trauma history and three additional modules focusing on functional impairments known to be associated with childhood trauma, that is rejection sensitivity, emotion regulation, and relationship difficulties. These modules are selected based on a self-report algorithm. Techniques from Mentalization-Based Psychotherapy (MBT), Cognitive Behavioral Analysis System of Psychotherapy (CBASP), Dialectical Behavior Therapy (DBT), and Systemic Therapy (ST) are integrated in this personalized modular procedure. This proof-of-concept study aims to provide initial evidence for acceptability, feasibility, and changes in self- and diagnostician-rated psychopathology (post-treatment and three months follow-up) of MeMoPsy and to elucidate mechanisms of change, using psychotherapy process research, Ecological Momentary Assessment, and functional magnetic resonance imaging. *Ethics and dissemination:* This RCT obtained approval from independent ethic committees of participating centers and is accompanied by a data and safety monitoring board. Findings will be communicated within the research community as well as with patients and the public by the dissemination strategies of the German Center for Mental Health (DZPG). *Registration*: German Clinical Trials Register DRKS00034058

Strengths and limitations of this study

- This is the first study to investigate the feasibility of a mechanism-based, modular psychotherapy (MeMoPsy) for adolescents and young adults with various, frequently comorbid diagnoses and a history of early trauma, thus, a population known to often show poorer treatment responses to standard psychotherapy compared to non-traumatized patients.
- Besides feasibility, this RCT aims to examine changes in psychopathology following MeMoPsy to generate pilot data for sample size calculation for a subsequent multicenter confirmatory trial.
- Experimental research, Ecological Momentary Assessment (EMA), qualitative interviews as well as regular assessments of the psychotherapy process in patients and therapists will act synergistically to understand the mechanisms of change processes.
- Using cognitive behavioral therapy (CBT) as an active treatment comparator represents a strong comparator for a rigorous evaluation of MeMoPsy with impact for dissemination in mental health care services.
- Since no a priori values are established, the algorithm cut-offs for module selection used here are based on general population means of self-rated questionnaires (according to a pre-study of our group) [1]

Introduction

Background and rationale

Childhood trauma experiences such as abuse and neglect are well-established risk factors for mental health problems [2, 3]. Systematic reviews and meta-analyses consistently indicate robust associations between childhood trauma experiences and a broad range of mental disorders [4, 5], such as depression [6, 7], anxiety disorders [8], eating disorders [9], substance use disorders [10], psychosis [11], and borderline personality disorder [12]. Many of those mental disorders first appear before the age of 24 [13], making adolescence and young adulthood particularly vulnerable periods.

Since “one size fits all”-treatments are not optimal for most patients, innovative approaches focus on more personalized interventions that target the specific functional impairments of patients and associated psychological and neurobiological mechanisms. Patients with mental disorders and childhood trauma experiences are characterized by an earlier onset of psychopathology, more chronic and recurrent symptoms and higher comorbidity rates [14], and – most importantly – they show poorer treatment responses than patients without such trauma experiences [e.g., 14, 15-18]. Thus, the question arises as to why current evidence-based psychotherapeutic treatments appear to be less effective for these patients, as compared to patients without childhood trauma experiences. One possible reason is that the mechanisms linking childhood trauma experiences to mental disorders are not sufficiently understood and are therefore not adequately addressed in current psychotherapeutic treatments [19]. In recent years, numerous mechanisms have been proposed through which childhood trauma experiences could be translated into risk for different mental disorders [e.g., 20, 21, 22]. Some of the most prominent transdiagnostic mechanisms underlying childhood trauma experiences and mental disorders encompass 1.) rejection hypersensitivity [23], 2.) emotion dysregulation [22], as well as 3.) difficulties in (close) interpersonal relationships [24].

First, individuals with childhood trauma experiences exhibit biases in social information processing, specifically a hypersensitivity towards interpersonal rejection [22, 23]. Individuals

with high levels of rejection sensitivity tend to anxiously expect, readily perceive, and overreact to signs of interpersonal rejection [25]. According to a recent meta-analysis including 16 studies and 5335 participants, rejection hypersensitivity is linked to childhood trauma experiences, specifically emotional abuse, regardless of age or sex of those affected [23]. Moreover, rejection hypersensitivity is associated with specific mental disorders, including depression, anxiety disorders, eating disorders, and borderline personality disorder [23, 26].

Second, individuals with childhood trauma experiences are characterized by difficulties in emotion and stress regulation [22]. Childhood trauma experiences are linked to low emotional awareness, i.e. a diminished ability to identify and differentiate one's own emotions [27]. Low emotional awareness may, in turn, contribute to emotion regulation difficulties or emotion dysregulation [22]. Emotion dysregulation has been defined as patterns of emotional experiences and/or expressions interfering with appropriate goal-directed behaviors [28]. Studies suggest that individuals with childhood trauma experiences are more likely to use maladaptive emotion regulation strategies such as rumination, suppression, and impulsive responses [22, 29]. Likewise, individuals with childhood trauma experiences tend to have more difficulties engaging in adaptive emotion regulation strategies such as acceptance and cognitive reappraisal [22, 29]. In addition, emotion regulation difficulties emerge in numerous mental disorders, including mood, anxiety, eating, personality, and schizophrenia spectrum disorders [30, 31].

Finally, and closely associated with rejection hypersensitivity and emotion dysregulation, individuals with childhood trauma experiences tend to have more difficulties in (close) interpersonal relationships [24]. Specifically, individuals with childhood trauma experiences report more dissatisfaction with current relationships [32], less intimacy [33, 34], less social support [35-37], less empathy [38] as well as more loneliness and social isolation [39] than individuals without such experiences. Interestingly, difficulties in (close) interpersonal relationships are not only linked to different mental disorders [40], but could also mediate the relationship between childhood trauma experiences and mental health symptoms [e.g., 41].

Taken together, a growing body of evidence suggests robust associations between childhood trauma experiences, mental disorders and underlying transdiagnostic mechanisms (i.e., rejection hypersensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships). It thus appears promising to target these mechanisms in order to improve current psychotherapeutic treatments for individuals with mental disorders affected by childhood trauma experiences [42].

The Center for Psychosocial Medicine at Heidelberg University together with the Central Institute of Mental Health Mannheim and the Freie Universität Berlin therefore developed a personalized, mechanism-based, modular psychotherapeutic approach (MeMoPsy) for individual outpatient settings. Our MeMoPsy approach builds upon a recent proof-of-concept randomized controlled trial (RCT) conducted in collaboration between our research group and Elisabeth Schramm's research group [43]. In this study, 70 adult outpatients between 18 and 65 years with a primary diagnosis of major depressive disorder, at least one comorbid mental disorder and childhood trauma experiences received 20 sessions of either standard cognitive behavioral therapy alone (CBT) or CBT plus modular-based psychotherapy (MoBa). MoBa is based on psychotherapeutic modules, defined as independent but combinable sets of functional units which target common transdiagnostic mechanisms and teach skills to improve processes such as emotion regulation or theory of mind (ToM). In the MoBa approach, three psychotherapeutic modules focus on transdiagnostic childhood trauma-related dysfunctions, specifically social threat hyperresponsivity and social avoidance behavior, emotion dysregulation as well as lack of empathy, and ToM. To select these modules in the MoBa condition, a personalized treatment algorithm was applied using empirical cut-off values for self-report measures of childhood-trauma related dysfunctions. First encouraging results indicate the feasibility, safety and efficacy of the MoBa approach, with advantages related to patients' and therapists' satisfaction and different clinical outcomes [1].

Building on this recent proof-of-concept RCT (1), we aim to assess the feasibility of MeMoPsy in a multicenter, proof-of-concept RCT. We will compare our MeMoPsy approach with standard, non-manualized CBT, as CBT represents one of the most prominent treatments

as usual in psychotherapeutic health care [44]. While MoBa targeted adult patients aged up to 65 years with depression, comorbid disorders and childhood trauma, MeMoPsy shifts its focus to the needs of a particularly vulnerable patient group, i.e. adolescents and young adults aged 15 to 25 years with various mental disorders and childhood trauma experiences. Similar to MoBa, the psychotherapeutic modules of MeMoPsy focus on mechanisms underlying the association between childhood trauma experiences and mental disorders (i.e., rejection hypersensitivity, emotion dysregulation, difficulties in interpersonal relationships). Further, the personalized treatment algorithm which was used in our previous proof-of-concept study will also be applied in the current study to enable an evidence-based systematic selection of psychotherapeutic modules. We believe that our personalized treatment algorithm represents an advantage as compared to the common clinical practice of intuitively selecting psychotherapeutic interventions according to the clinical judgement, expertise and preferences of the treating therapists. Furthermore, the accompanying process research with regular questionnaires on psychopathology and quality of the therapeutic alliance will enable adaptions to patients´ current needs (within the selected modules) depending on patients´ feedback.

Objectives

The aim of this multicenter, proof-of-concept RCT is to investigate the feasibility of a newly developed mechanism-based, modular psychotherapeutic approach (MeMoPsy) for adolescents and young adults with various mental disorders and childhood trauma experiences as compared to standard non-manualized CBT offered in German mental health care services. Specifically, this study aims to (1) examine the acceptability of the MeMoPsy approach for patients and therapists, (2) determine the feasibility of study-related measurements, (3) investigate changes in psychopathology following MeMoPsy compared to CBT for sample size calculation of a subsequent confirmatory trial, and to elucidate mechanisms of change using psychotherapy process research, Ecological Momentary

Assessment (EMA), and functional magnetic resonance imaging (fMRI). Please refer to Tables 1 and 2 for full details of the specific feasibility and other measures used in our study.

Methods and Analysis

Please note that the current study protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 Checklist [45]. The study protocol's administrative information relating to the SPIRIT 2013 Checklist and the Checklist itself are presented in the Supplement.

Trial design

The study is designed as a randomized, controlled, multicenter feasibility trial with two parallel arms (total *N* = 80), comparing MeMoPsy with routine non-manualized CBT. Randomization will be performed as block randomization stratified by study site (i.e., Heidelberg, Mannheim, Berlin) with a 1:1 allocation.

Study setting

The study will be conducted at three urban German sites, i.e., the Center for Psychosocial Medicine at Heidelberg University, the Central Institute of Mental Health Mannheim, and the Institute of Clinical Child & Adolescence Psychology and Psychotherapy of the Freie Universität Berlin.

Eligibility criteria

Eighty outpatients between 15 and 25 years of age with one or more mental disorder and childhood trauma experiences will be recruited. Patients in the MeMoPsy or CBT condition will be treated by licensed adult and children psychotherapists or psychotherapists in training with at least 2 years of practical experience in treating patients with mental disorders.

Please note that prior psychotherapy experience is not an exclusion criterion; however, prior psychotherapy experience will be assessed in detail in both therapy arms to allow for a comparison regarding familiarity with psychotherapeutic interventions.

Key inclusion and exclusion criteria for patients are:

Inclusion criteria:

1. Age eligibility: 15–25 years
2. One or more mental disorders according to DSM-5 as assessed with the Diagnostic Short-Interview for Mental Disorders (Mini-DIPS) [46], the Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5-PD) [47] for avoidant and borderline personality disorders and the Structured Clinical Interview for DSM-5, Clinical Version (SCID-5-CV) [48] for attention deficit hyperactivity disorder (ADHD).
3. Childhood trauma experiences: at least moderate to severe in one or more of the five subscales of the Childhood Trauma Questionnaire (CTQ; i.e., emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect) [49], as defined by Häuser et al. [50]
4. Meeting the cut-off of at least one mechanism-based treatment module (module 1 to module 3)
5. Statutory health insurance to cover the costs for the psychotherapeutic outpatient treatment
6. Fluent in German
7. Written informed consent

Exclusion criteria:

1. Acute risk of suicide, assessed using the Mini-DIPS (interview) [46]
2. One or more mental disorders requiring diagnosis-specific treatment as assessed by clinical judgement and applying the Mini-DIPS [46] or the 10-item version of the Autism

Spectrum Quotient (AQ-10) [51], including posttraumatic stress disorder; moderate or severe substance use disorder with the exception of cannabis use disorder; acute psychotic or manic symptoms; autism spectrum disorder

3. No ability or willingness to abstain from substance use over the course of treatment
4. Severe cognitive impairment (i.e., IQ < 70) as assessed with the mini-q [52]
5. Other ongoing psychotherapy
6. Serious medical condition that interferes with regularly attending therapy sessions
7. Change in current psychotropic medication or initiation of new psychotropic medication for at least two weeks before inclusion (3 weeks for fluoxetine)

Interventions

The MeMoPsy condition comprises 28 individual psychotherapy sessions over 24 weeks of treatment (twice weekly in weeks 1–4, then once per week in weeks 5–24). Each patient receives a basic module and up to three mechanism-specific therapy modules (Figure 1). The application of the modular interventions is preceded by a diagnostic assessment of the patient's impaired transdiagnostic mechanisms (s. secondary outcomes, Table 2). If the cut-off values of the module-specific questionnaires are exceeded, the respective module will be used for that patient. Building on prior experiences [1, 43, 53], the module-specific cut-off values are based on adult general population samples. While validation of our empirical cut-off values in an adolescent clinical sample is still pending, all three module-specific questionnaires have been tested in adolescent general populations [e.g., 54, 55, 56] and one of them (i.e., Rejection Sensitivity Questionnaire, RSQ) [25] has already been proven to be clinically relevant in a previous trial [1]. Each module comes with a defined series of interventions, some of which are mandatory, while others are optional for the psychotherapist to use during the course of the therapy. MeMoPsy is a personalized treatment in the sense of an algorithm-driven selection of therapy modules. Furthermore, as feedback on therapeutic processes is an integral part of MeMoPsy [42], a routine outcome monitoring (ROM) procedure is established, with study therapists receiving access to their patients' questionnaire scores

(Brief Symptom Inventory, BSI) [57] regarding the therapeutic process and psychopathology throughout the treatment.

The therapy modules are as follows:

- The basic module, which is mandatory for every patient, encompasses a detailed mental health history, psychoeducation and information about the therapy and the therapy focus, the identification and integration of traumatic experiences, and the improvement of mentalization and interpersonal functioning. The therapeutic approach is validating, cooperative, and influenced by the curious and not-knowing stance from mentalization-based therapy (MBT) [58]. Therapists aim to establish a sustainable therapeutic alliance and pay close attention to potential conflicts and ruptures in it. They coregulate the level of emotional arousal where necessary and identify problematic relationship patterns which may arise as a consequence of trauma. Therefore, therapists use interventions such as the lifeline [59], the window of tolerance model, as well as further techniques from the rupture-repair model [60] and MBT [58].
- Module 1 is administered if patients score ≥ 9.88 on the Rejection Sensitivity Questionnaire (RSQ) [25] (cut-off defined as one standard deviation above the general population mean, i.e. the upper 16%, as reported in Schramm et al. [1]) It targets interpersonal rejection sensitivity and avoidance behavior in social situations. It draws on techniques from the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) [61] such as the significant other history, interpersonal discrimination exercises, and situation analyses, and in addition strategies of MBT.
- Module 2 is administered if patients score ≥ 46.97 on the State Difficulties in Emotion Regulation Scale (S-DERS) [62] (cut-off defined as one standard deviation above the general population mean as reported in Lavender et al. [62]). It aims at improving emotional awareness and stress regulation and draws on techniques from Dialectical Behavior Therapy (DBT) [63], such as emotion-specific psychoeducation, anti-

dissociative or distress tolerance skills, mindfulness exercises, and the ability to observe, describe, and regulate aversive emotions.

- Module 3 is administered if patients score ≥ 13 on the German version of the Outcome Questionnaire 45 (OQ-45), Interpersonal Relations subscale [53, 64] (cut-off defined as the 80th percentile of the general population as reported in Lambert et al. [53]). It aims at strengthening resources, resilience, and solution-focus within the social system of close interpersonal relationships, employing basic principles of systemic trauma therapy [65] such as task and goal orientation, resource orientation, and solution-focused interventions, but also genograms or relationship maps. This module may take place in an individual therapy setting, but also in multi-person settings with caregivers or other persons of reference if appropriate.

The modules are not simply added as separate and serial components, but therapists will be trained and supervised to integrate them into the dynamic course of the therapeutic process. Consequently, the amount of time spent with a single module will be reduced if more modules are indicated for an individual patient. The therapists are required to use all defined mandatory interventions within the course of a therapy, but beyond that, they will use their clinical judgement and the aid of their supervisors to choose the most effective interventions from the available modules. Therapists will document the time spent with each module and which interventions they use. Altogether, the treatment procedure is algorithm-driven, but allows for a certain degree of flexibility and further personalization necessary in clinical practice.

The control condition is a treatment-as-usual, non-manualized brief CBT at cooperating psychotherapy training institutes. Patients receive a total of 28 treatment sessions and three preparatory meetings, corresponding to the reimbursement scheme of the German statutory health insurance for psychotherapy. Common CBT elements are, for example, psychoeducation, behavioral activation, cognitive restructuring, and exposition.

All psychotherapists in both study conditions are supervised by board-certified clinical psychologists or physicians with specialization in the respective psychotherapy approach, with supervision taking place on average every fourth therapy session, i.e., there will be in total

seven supervision sessions within a therapy. Psychotherapists in the MeMoPsy condition must complete an intensive training course (four 90-minutes online theory lessons, three days of practical training) held by board-certified clinical psychologists or physicians with specialization in the respective psychotherapy approach, as well as a pilot therapy of at least 15 sessions with at least six additional supervision sessions by the same module experts. In addition, all therapy sessions are recorded on video for the purpose of quality and adherence assurance and can be used as part of supervision.

Outcomes

Please refer to Table 1 for all primary outcomes and corresponding measures, and Table 2 for all secondary outcomes and corresponding measures.

Due to the exploratory nature of this feasibility trial, three primary outcomes were defined: (1) the acceptability of MeMoPsy to patients and therapists, (2) the feasibility of study-related measures, and (3) changes in psychopathology following MeMoPsy compared to standard CBT treatment (see below). Furthermore, a number of secondary outcomes will be explored, including the assumed transdiagnostic mechanisms underlying the link between childhood trauma experiences and mental disorders (i.e., rejection sensitivity, emotion dysregulation, difficulties in interpersonal relationships), psychopathological symptoms and psychotherapeutic processes.

Psychotherapy process research will be used to study the course of transdiagnostic mechanisms of change. On a macroscopic level, we will investigate ongoing change, therapeutic relationship and intersession experiences. On a microscopic level, we will address change events, difficult episodes and therapeutic interventions. Findings will be integrated to analyse the action of therapy modules on the course of general psychopathology and well-being as well as rejection sensitivity, emotion regulation and relationship dynamics.

Furthermore, EMA allows to further operationalize and investigate the assumed mechanisms: First, the dynamics of the mechanisms in everyday life and the connection with the respondents' well-being can be investigated. Second, potential moderators (e.g.,

personality characteristics) that strengthen or weaken this relationship will be investigated. Third, the intervention effects of the three MeMoPsy modules will be examined experimentally (see below) and in everyday life. Saliva sampling of the stress dependent hormone cortisol will be linked to ambulatory assessment. All primary and secondary outcomes and corresponding measures are described in Tables 1 and 2, respectively. Please note that the time points of assessments are given only for the primary outcomes. For a detailed overview of all assessments, please refer to Table S1 in the Supplement.

In addition, neurobiological measurements using fMRI will be performed to elucidate the mechanisms of change initiated by MeMoPsy. Participants complete three tasks in two fMRI testing sessions, one before the start of the treatment and one immediately after the end of treatment. First, the attention bias (i.e., increased sensitivity to rejection) is recorded during fMRI using an emotion classification task, in which emotional faces have to be matched [66]. Second, the assumed interpersonal difficulties will be measured using an fMRI task on empathy and ToM skills (EmpaToM-Y) [67]. Empathy and ToM are considered core competencies of social relationship building. The EmpaToM-Y paradigm consists of videos of young actors and actresses reporting specific social settings. This video set enables independent manipulation and assessment of empathy and ToM. Third, the assumed increased sensitivity to rejection and problems in establishing interpersonal relationships are tested using a task on social information processing. This task represents an adaptation and combination of previous studies in which participants rate themselves on character traits and imagine getting feedback for these traits [68, 69].

Table 1. Primary outcomes and corresponding measures

Primary Outcome	Measure
Acceptability	
Patients' satisfaction	8-item Fragebogen zur Patientenzufriedenheit (ZUF-8) [70], the German adaptation of the 8-item Client Satisfaction Questionnaire (CSQ-8) [71], rated by patients at the end of treatment (T2)
Therapists' satisfaction	Acceptability of Intervention Measure (AIM) and Feasibility of Intervention Measure (FIM) [72], two 5-item scales rated by therapists at the end of treatment (T2)
Negative psychological treatment effects	32-item Negative Effects Questionnaire (NEQ) [73], rated by patients at the end of treatment (T2)
Adherence	Number of therapy sessions attended and number of intervention dropouts, determined by study personnel at the end of treatment (T2)
Feasibility	
Recruitment	Number of patients recruited per month (i.e., recruitment speed) and percentage of suitable patients who agree to participate in the study (i.e., recruitment rate), determined by study personnel at the end of treatment (T2)
Completeness of online data collection	Percentage of online questionnaires completed by patients and therapists before (T0), during (T1) and at the end of treatment (T2), determined by study personnel at T2
Dropout rate	Number of patients terminating their study participation prematurely and their reasons for premature termination as assessed by the self-rated 25-item Reasons for Termination Scale (RTS) [74]
Quality of module-specific cut-off values	Percentage of patients receiving 1, 2 or 3 modules (i.e., module allocation rate), determined by study personnel at the end of treatment (T2)
Changes in psychopathology	
Self-rated severity of psychopathology	53-item Brief Symptom Inventory (BSI) [57], rated by patients at the end of treatment (T2)
Interviewer-rated severity of psychopathology	Global Assessment of Functioning (GAF) [75], a 100-point scale rated by trained and blinded diagnosticians at the end of treatment (T2)

Table 2. Secondary outcomes and corresponding measures

Secondary Outcome	Measure
Transdiagnostic mechanisms of change, targeted by psychotherapeutic modules	
Rejection sensitivity (Module 1)	Module questionnaire: The Rejection Sensitivity Questionnaire (RSQ) [25] assesses the anxious-expectations component of rejection sensitivity. The RSQ encompasses 20 hypothetical interpersonal interactions, characterized by the potential of being rejected by others. For example, patients are asked to imagine asking someone from their workplace out for coffee. Patients rate each interaction on two scales: first, they indicate their concern or anxiety that they will be rejected on a 6-point Likert scale ranging from 1 (very unconcerned) to 6 (very concerned). Then they indicate the likelihood that the other person will engage in non-rejecting behavior toward them on a 6-point Likert scale ranging from 1 (very unlikely) to 6 (very likely). The psychometric properties of the German version have been found to be good [76].
Emotion dysregulation (Module 2)	Module questionnaire: The 21-item State Difficulties in Emotion Regulation Scale (S-DERS) [62] allows to assess different dimensions of emotion dysregulation repeatedly over brief periods of time. The S-DERS consists of four subscales, including Nonacceptance (i.e., non-acceptance of current emotions), Modulate (i.e., momentary difficulties modulating emotional and behavioral reactions), Awareness (i.e., limited awareness of current emotions), and Clarity (i.e., limited clarity about current emotions). Patients rate statements such as “My emotions feel overwhelming” on a 5-point Likert scale ranging from 1 (not at all) to 5 (completely). Preliminary evidence supports the psychometric properties of the measure [62].
Difficulties in (close) interpersonal relationships (Module 3)	Module questionnaire: The 45-item Outcome Questionnaire-45 (OQ-45) [77] is recommended for routine outcome monitoring in a wide range of mental health service settings [78]. The OQ-45 consists of three subscales, including Symptom Distress (25 items), Interpersonal Relations (11 items), and Social Role (9 items). Patients rate statements such as “I am concerned about family troubles” on a 5-point Likert scale ranging from 0 (never) to 4 (almost always). To determine difficulties in (close) interpersonal relationships, only the OQ-45 subscale Interpersonal Relations is used, which refers to the patient’s friendships, family life and romantic relationships. The psychometric properties of the German version have been found to be acceptable to good [64].
Psychopathology	
Severity of personality disorder	36-item Personality Inventory for DSM-5 – Brief Form Plus Modified (PID-5-BF+M) [79] and 12-item German version of the Level of Personality Functioning Scale-Brief Form 2.0 (LPFS-BF) [80], both rated by patients
Severity of borderline personality disorder (BPD) symptomatology	14-item Fragebogen zu Gedanken und Gefühlen (FGG-14, engl.: Questionnaire of Thoughts and Feelings) [81] and 23-item Borderline Symptom List (BSL-23) [82], both rated by patients
Dissociation	4-item Dissoziations-Spannungs-Skala (DSS-4, engl.: 4-item Dissociation Tension Scale) [83], rated by patients
Mentalizing	20-item Certainty about Mental States Questionnaire (CAMSQ) [84], rated by patients
Social support	5-item ENRICHD Social Support Inventory (ESSI) [85], rated by patients
DZPG minimum dataset	Dataset designed by experts of the German Center for Mental Health (Deutsches Zentrum für Psychische Gesundheit, DZPG) to measure core patients’ characteristics. Single items have been selected from existing questionnaires to assess sociodemographics, the exposome, dimensions of the Research Domain Criteria (RDoC), Hierarchical Taxonomy of Psychopathology (HiTOP), and everyday functioning such as mental health and quality of life. Items are rated by patients.
Clinical impression of global functioning	Clinical Global Impressions (CGI) [86], two 7-point scales assessing severity of psychopathology (CGI-Severity, CGI-S) and change since initiation of treatment (CGI-Improvement, CGI-I), rated by therapists

Medication	Self-designed items to assess medication before, during and at the end of treatment, rated by patients, which will allow to calculate a standardized composite psychotropic medication score following established procedures [87]
Psychotherapeutic processes	
Therapeutic homework	Self-designed items to assess compliance with therapeutic homework, rated by patients and therapists
Therapeutic interventions	Self-designed Therapeutic Elements Checklist to assess the use of all therapeutic interventions in the MeMoPsy and CBT condition, including the time spent on those interventions, rated by therapists
Continuous process monitoring	
Therapeutic mechanisms	12-item Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie [88], rated by patients (STEP-P) and therapists (STEP-T)
Therapeutic alliance	12-item Working Alliance Inventory – Short Revised [89], rated by patients (WAI-T) and therapists (WAI-T)
Symptom distress	11-item Symptom Checklist (SCL-K11) [90], rated by patients
Mental wellbeing	7-item Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS) [91], rated by patients
Patients' intersession experiences	Self-designed 16-item Experiences Between Psychotherapy Sessions Questionnaire (EBPSQ), targeting intersession experiences, rated by patients
Course of transdiagnostic mechanisms of change	12 module-specific items, taken from the RSQ, S-DERS, OQ-45 subscale Interpersonal Relations, and Reflective Functioning Questionnaire (RFQ) [92], to assess state aspects of changes in rejection sensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships, and reflective functioning, rated by patients
Therapist-rated severity of psychopathology	Global Assessment of Functioning (GAF) and Global Assessment of Relational Functioning (GARF) [75], two 100-point scales rated by therapists
Additional assessments (optional)	
Ecological Momentary Assessment (EMA)	Daily prompts (29 items) which patients are asked on their smartphone at 8 random times per day over a period of one week before treatment (i.e., seven days after T0) and at the end of treatment (i.e., one day after T2). EMA items assess transdiagnostic mechanisms of change (i.e., rejection sensitivity, emotion dysregulation, difficulties in (close) interpersonal relationships), mental, physical, and social stress, and positive and negative affect. Items are self-designed or taken from the Positive and Negative Affect Schedule (PANAS) [93].
Functional magnetic resonance imaging (fMRI)	Three experimental paradigms performed in the MRI scanner to assess neural changes post (T2) compared to pre-treatment (T0) in interpersonal threat sensitivity [94], empathy and theory of mind [e.g., 95], and social feedback processing [96]
Hormone measurements	Saliva samples to determine cortisol levels in patients. Saliva samples are collected 8 times per day to calculate cortisol awakening responses and diurnal profiles on three consecutive days within the one-week EMA period before and at the end of treatment.
Qualitative interviews	At the end of treatment, qualitative interviews are conducted with the patients and therapists in the MeMoPsy condition in order to explore the experiences made with the therapy and the assessment of its usefulness from the perspective of both. Therapists will be asked about the extent to which they have used the available interventions, their expectations concerning the implementation of tailor-made therapy for clients, and their experiences with the algorithm-driven selection of therapy modules for a population meeting different clinical diagnoses. For the selection of interview partners, either "maximal variation sampling" or "stratified purposeful sampling" [97] is used to consider a wide range of patients and therapists (e.g., age, gender, socio-economic background, previously used therapy methods, professional experience).

Participant timeline

At enrolment, patients will be screened for eligibility, and written informed consent of all eligible patients will be obtained. If the patient is a minor (i.e., 15–17 years old), informed consent must also be given by a parent or legal guardian. Consent forms have been adapted to each type of study participant (i.e., adult, minor, parent or legal guardian to the participating minor, therapists who participate in the qualitative interviews) at each of the three study sites. For a model consent form for an adult participant at the managing site in Heidelberg, please refer to the Supplement. In addition to the participation in the intervention study, patients are asked to participate in one or more further assessments using EMA, fMRI, saliva samples to determine cortisol levels, and qualitative interviews. Patients will be randomized to either MeMoPsy or CBT. Data assessments will take place before the beginning of the intervention (baseline, T0), during the intervention (baseline + 16 weeks, T1), at the end of the intervention (baseline + 32 weeks, T2) and at follow-up (baseline + 44 weeks, T3). A comprehensive overview of the frequency and scope of all core trial visits and the continuous outcome monitoring including all assessments and measures is provided in Table S1 in the Supplement.

Sample size

Due to the exploratory nature of this feasibility trial, no formal sample size calculation was performed. Rather, the current feasibility trial serves to obtain pilot data that can be used for the sample size calculation for a subsequent confirmatory trial. For reasons of feasibility, the number of patients in each group (i.e., MeMoPsy, CBT) was set at $n = 40$, aiming to recruit four patients per month over a recruitment period of ten months. With reference to Cocks and Torgerson [98], a total of 80 patients (assuming 20% dropout) is sufficient to obtain data in order to plan a subsequent confirmatory trial for continuous outcome measures for moderate effect sizes of at least Cohen's $d \geq 0.3$. Significant dropout rates of up to 55% have been reported in clinical trials with children, adolescents, and adults with childhood trauma experiences [99]. In our recent proof-of-concept RCT [1], however, only 5 out of 70 patients (four in MoBa, one in CBT) discontinued treatment prematurely, which corresponds to a

dropout rate of 7%. Building on the latter study, the aim of the current trial is to keep the dropout rate below 20%, which is reasonable given that the MeMoPsy approach focuses on the therapeutic alliance and encompasses regular assessments to keep in contact with the patients.

Recruitment

Patients will be recruited at inpatient and outpatient clinics at three German study sites (i.e., Heidelberg, Mannheim, Berlin). The majority of patients will be recruited at the Center for Psychosocial Medicine at Heidelberg University Hospital, the Central Institute of Mental Health in Mannheim and the psychotherapeutic outpatient clinic of the Department of Clinical Child and Adolescent Psychology and Psychotherapy at Freie Universität Berlin. In addition, patients will be recruited via posts on social media, flyers in private practices and articles in local newspapers to announce the psychotherapeutic treatment offer within the current feasibility trial. Please refer to Figure 2 for the trial design and flow of patients.

Assignment of interventions: Allocation

Randomization will be performed, stratified by study site (i.e., Heidelberg, Mannheim, Berlin), in a 1:1 allocation ratio. The allocation sequence is based on computer-generated random numbers and implemented using the Internet-based software ASMO (*As*sessment and *Mo*nitoring of Mental Health; www.asmo.online), developed and maintained at the Center for Psychotherapy Research at University Hospital Heidelberg [100]. The study staff does not have access to the allocation sequence. Patients will be automatically randomized to either MeMoPsy or CBT after having completed the online baseline assessment. The diagnostician accompanying the baseline assessment will inform another member of the study staff after the patient has finished the online baseline assessment. This person will access the result of the randomized allocation sequence provided by ASMO, and informs the patient about the allocation to either MeMoPsy or CBT. This procedure enables us to keep the diagnostic staff blinded to treatment allocation.

Assignment of interventions: Blinding

Research assistants and diagnosticians involved in recruitment and interview assessments at baseline (T0) and post-intervention (T2) are blinded to treatment allocation. Specifically, blinded diagnosticians will rate severity of psychopathology using the Global Assessment of Functioning Scale (GAF) [75] at T0 and T2. After baseline assessment, patients receive pseudonymized codes which do not contain any information on treatment allocation. Patients and therapists cannot be blinded regarding treatment allocation due to the nature of the psychotherapeutic interventions. Primary outcomes (except changes in psychopathology following MeMoPsy as compared to CBT, see above) and secondary outcomes encompass self-report and therapist-report measures and thus cannot be assessed in a blinded manner. Feedback on psychotherapeutic processes is an integral part of modular psychotherapy [42]. Therefore, therapists in the MeMoPsy condition are not blinded to all of their patients' ratings. Instead, at every 5th session, therapists in the MeMoPsy condition are given access to their patients' ratings of items measuring changes in the assumed transdiagnostic mechanisms linked to the psychotherapeutic modules, the therapeutic alliance, and the psychopathological symptom burden. In addition, at the assessment time points T0, T1, and T2, both the therapists in the MeMoPsy condition and the therapists in the CBT condition are given access to their patients' ratings of the psychopathological symptom burden. This procedure allows for adapting the selection of interventions according to patients´ current needs (within the selected modules). Research assistants involved

- in the additional assessments using EMA, fMRI, and saliva samples to determine cortisol levels will be blinded regarding treatment allocation of the patients.
- in qualitative interviews are not blinded regarding treatment allocation since they are only performed in the MeMoPsy condition.
- in the data analysis will be blinded regarding the treatment allocation with the exception of the data collected using continuous process monitoring which is only done in the MeMoPsy condition.

No circumstances are defined under which unblinding is permissible, as both patients and therapists are not blind to treatment allocation.

Data collection, management, and analysis

Data collection methods

All patients will participate in comprehensive clinical and experimental assessments, including psychometrically validated, widely used measures (see Tables 1 and 2 in the manuscript, and Table S1 in the Supplement).

Screening for initial eligibility (time point T−2) will be performed by trained research assistants using a brief screening questionnaire adapted from a prior large cross-sectional study on childhood trauma experiences [101], including the German version of the CTQ [102]. Screening will be conducted in a conventional paper-and-pencil format. Diagnostic assessments (time point T−1) will be conducted by qualified diagnosticians (i.e., with at least a master's degree in clinical psychology) who will receive standardized diagnostic training before the beginning of the study. Diagnostic assessments include different commonly used measures captured in a paper-and-pencil format: (1) childhood trauma experiences will be assessed with a comprehensive interview, the KERF-40-I [103], which is the brief German interview version of the Maltreatment and Abuse Chronology of Exposure scale [104]; (2) mental disorders will be assessed with an efficient interview, the Mini-DIPS [46]; (3) avoidant and borderline personality disorders will be assessed with the SCID-5-PD [47] to consider frequently occurring personality disorders in adolescent traumatized individuals [105, 106]; (4) ADHD will be assessed with the SCID-5-CV [48] as it cannot be determined by using the Mini-DIPS; (5) symptoms of autism spectrum disorders will be determined with a self-report questionnaire, the AQ-10 [51]; and (6) general cognitive abilities will be measured with a brief screening tool, the mini-q [52]. If no exclusion criteria are identified at screening (T−2) and diagnostics (T−1), the software ASMO is used to register the patient and subsequently administer several online questionnaires to measure patients' and diagnosticians' ratings at baseline (time point T0). ASMO is used both for the core trial visits (i.e., mid-intervention T1,

16 weeks after baseline; post-intervention T2, 32 weeks after baseline; follow-up T3, 44 weeks after baseline) and the continuous process monitoring (i.e., patients' and therapists' ratings collected every session or every 5th session in the MeMoPsy condition). ASMO allows to automatically collect data on primary and secondary outcomes. The scientific staff ensures that patients and therapists continuously fill out the online questionnaires at the designated time points and, if necessary, reminds patients and therapists by email to complete online questionnaires on time.

All patients will be encouraged to take part in additional optional assessments (EMA, fMRI, saliva sampling to determine cortisol levels, and qualitative interviews). All additional assessments will be performed by trained scientific staff under the supervision of experts in the corresponding field.

Once a patient is randomized to one of the two treatment conditions, every reasonable effort will be made to promote patient retention and maximize completeness of data collection. Regular assessments with a maximum interval of 16 weeks will be performed, patients will be reminded to complete the assessments at the designated time points, and patients will be financially reimbursed for their participation in the assessments of primary and secondary outcomes, and additional assessments and research tools (i.e., EMA, fMRI, hormone measurements, qualitative interviews). Data assessment (T1, T2, and T3) will be administered online, allowing patients to complete it from home and thus reducing their burden related to additional on-site visits. All patients will be asked to participate in the core trial assessments (i.e., mid-intervention T1, post-intervention T2, follow-up T3), even if they discontinue treatment prematurely, and thus minimize the number of patients lost to follow-up.

Data management

Data management will be performed using ASMO. The respective servers are located at the University Hospital Heidelberg. Data collected digitally guarantee the highest level of data integrity and quality as risks for missing data and false data entry are minimized. ASMO allows for the monitoring of data collection, the continuous documentation of all access logs,

the traceability of all entered data (i.e., user and timestamp), and for the restoration of previous states. A Distributed Replicated Block Device (DRBD)-based cluster will ensure synchronous replication of all data during data entry on two separate servers and highest availability. In addition, full and incremental backups will be conducted following a predefined plan. Data storage and data transfer will be encrypted. Access to the data will be password-protected and strictly limited to authorized and trained staff members. Data collected in a paper-and-pencil format (i.e., screening for eligibility, diagnostics via interviews at baseline) will be entered electronically by authorized and trained scientific staff using a pseudonymised electronic case report form in ASMO. Data management for the additional assessments will be performed according to standard procedures within the corresponding field.

Statistical methods

Before conducting the final data analysis, a detailed statistical analysis plan will be prepared. Considering the exploratory nature of our feasibility trial, the final data analysis will be performed only descriptively and in accordance with the intention-to-treat principle (i.e., based on the full analysis set, including all patients randomized to one of the two treatment groups). All primary and secondary outcomes will be described by treatment arm and overall using appropriate indices from the empirical distributions (i.e., arithmetic means, standard deviations, minimum, 25% quantile, median, 75% quantile, maximum, relative and absolute frequencies). For the primary and secondary outcomes, effect sizes between the two treatment groups (i.e., MeMoPsy, CBT) will be described in absolute differences and Cohen's *d* with corresponding 95% confidence intervals and will be evaluated by unpaired *t*-tests. For the continuous psychotherapy process research within the intervention group, we follow established standards and employ multilevel modelling to account for the temporal and hierarchical structure of the data. Missing values will be described by relative frequencies and will not be imputed. Patient characteristics between patients with and without missing data in the primary outcomes will be compared in order to identify possible bias. Evaluation of the primary outcomes will be performed blinded to treatment allocation.

For the safety analysis, the frequency of serious adverse events in all randomized patients will be tabulated by treatment group (i.e., MeMoPsy, CBT), presumed association with the intervention, and severity.

All analyses will be performed in R v4.4.0 or higher, available under https://www.r-project.org/

Monitoring

Data monitoring

A Data Safety Monitoring Board (DSMB) has been established, which is independent of the investigators, the sponsor, and of competing interests. The role and reporting structure of the DSMB is detailed in a study-specific DSMB charter, which is available from the corresponding author on request. Briefly, the role of the DSMB is to protect the interests of the trial participants and patients, assess the safety of the interventions during the trial period, and monitor the integrity of the trial. In addition, the role of the DSMB is to support and advise the investigators to protect the validity and credibility of the study without violating the underlying study protocol. To this end, the DSMB will meet in person or online on at least three predefined dates (i.e., after 25%, 50%, 75%, and 100% of the recruitment target has been reached) and as needed (e.g., in case of potential safety concerns, delays in study progress). In the DSMB meetings, the recruitment progress, violations of the study protocol, dropout rates, adverse and serious adverse events, and data quality will be discussed. Serious adverse events, high study dropouts or a high incidence of violations of the study plan may indicate potential safety problems.

The DSMB consists of three German scientists with expertise in psychotherapy research and medical informatics. The DSMB will be supported by individuals with lived experience, who participated in developing the MeMoPsy approach specifically considering the needs of patients (see also the section on Patient and Public Involvement).

No interim analysis will be performed.

Harms

In the current feasibility trial, serious adverse events (SAEs) are defined as death of a patient, child endangerment, acute suicidality, and acute aggressiveness with indication for inpatient treatment (i.e., emergency hospital admission). Adverse events (AEs) are defined as symptom deterioration, occurrence of new symptoms, occurrence of passive suicidal thoughts, problems in the patient-therapist relationship, private problems, occupational problems, or other medical conditions. SAEs and AEs are reported by therapists with deterioration of psychopathology also checked by regular session reports. In a comparable, recently published RCT on modular psychotherapy [1] no SAE occurred. In the current feasibility trial, all study-related measures (i.e., diagnostics, EMA, fMRI, hormone measurements, qualitative interviews) have already been performed in a similar manner in previous studies by the participating investigators without any SAEs on the study participants. Based on our experiences with psychotherapy trials, we do not expect any SAE to occur in connection with our planned feasibility trial. Should a SAE occur, it must be reported within 24 hours of its occurrence to the principal investigator, Sabine C. Herpertz, who will forward this information to the members of the DSMB. Indications of SAEs and AEs will be followed up by the diagnostician or the psychotherapist in charge in accordance with clinical guidelines and good clinical practice (e.g., consulting with an experienced colleague, initiating child and youth welfare measures, initiating emergency hospital admission). If there are any indications that an adult patient is at risk (e.g., recent experience of (serious) abuse or violence), the approach is similar to that for child endangerment, and measures are implemented to ensure safety. Patients with acute suicidal tendencies who require immediate crisis intervention are referred to a suitable specialized facility, but can continue the randomized treatment if the duration of the crisis intervention does not exceed 14 days. Patients who leave treatment due to SAEs will continue to be cared for in accordance with good clinical practice until they are no longer clinically conspicuous.

Auditing

See Data monitoring

In addition, at the request of the study management protocol review, data analysis or similar will be advised. As this is a feasibility study, no external monitoring is planned.

Patient and Public Involvement

The current feasibility trial is part of the German Center for Mental Health (Deutsches Zentrum für Psychische Gesundheit, DZPG). The DZPG pursues the overarching goal of promoting population mental health based on a comprehensive translational research program of national scope (for a concise overview of the DZPG, please see [107]). The DZPG research program is consistently co-created with people with lived experience, and patient and public involvement (PPI) is fostered at all stages of research. In line with this participatory approach, the current feasibility trial has been designed with the support of service users affected by both mental disorders and childhood trauma experiences. Service users have been and will be involved in decision competency in all steps of the research process, which is also reflected by the employment of one service user as an expert by (lived) experience in the current feasibility trial who has checked the study design including outcomes.

Ethics and Dissemination

Research ethics approval

The study protocol, informed consent forms, recruitment materials, participant information on procedures specific to the hormone measurements have been reviewed and approved by the independent Ethics Committees of the Medical Faculty of Heidelberg University (AZ: S-583/2023), and of the Medical Faculty Mannheim of Heidelberg University (AZ:2023-675). The Ethics Committee of Freie Universität Berlin has declared that it will abide by the vote of the Ethics Committee of the managing site in Heidelberg.

Protocol amendments

All relevant modifications have gained approval by the Ethics Committees in Heidelberg, Mannheim and Berlin prior to start of the study and have been implemented in the study registration at the German Clinical Trials Register (Deutsches Register Klinischer Studien, DRKS; DRKS00034058). Each study site is responsible for training their study staff in protocol modifications.

Consent or assent

Informed consent will be obtained by qualified psychologists (at least a master's degree in clinical psychology) trained to ensure adherence to the study protocol. In the informed consent forms approved by the Ethics Committees in Heidelberg, Mannheim and Berlin, patients can consent to the intervention study and the additional measures (i.e., EMA, fMRI, hormone measurements), and qualitative interviews separately.

Confidentiality

All data are subject to medical confidentiality and will be handled in accordance with the European Union General Data Protection Regulation (Datenschutzgrundverordnung, DSGVO) and the German legal regulations concerning data protection and security (Landesdatenschutzgesetz Baden-Wurttemberg, Bundesdatenschutzgesetz). All study-related information will be stored securely at the study sites. All data assessed in a paper-and-pencil format will be stored in locked file cabinets in areas with limited access. All data will be pseudonymised (i.e., identified by a coded identification number) to maintain patient confidentiality. All data assessed electronically using ASMO will be transferred to the ASMO servers located at Heidelberg University Hospital. Data storage and data transfer will be encrypted. Access to the data will be password-protected and strictly limited to authorized and trained staff members. Data will be stored for 10 years.

Declaration of interests

The authors report no potential conflicts of interest.

Access to data

All investigators will have access to the final trial dataset.

Ancillary and post-trial care

Patients can get support from our outpatient and inpatient clinics in case of need.

Dissemination policy

We plan to communicate trial results via publications in peer-reviewed journals and conference contributions. We will use the DZPG newsletter, which addresses people with lived experience (i.e., patients and their families), the DZPG website, press releases, LinkedIn and social media for science communication. We will provide access to the full protocol, participant-level dataset, and statistical code on demand.

References

1. Schramm E, Elsaesser M, Jenkner C, Hautzinger M, Herpertz SC. Algorithm-based modular psychotherapy vs. cognitive-behavioral therapy for patients with depression, psychiatric comorbidities and early trauma: a proof-of-concept randomized controlled trial. World Psychiatry. 2024;23(2):257-66.
2. Baldwin JR, Wang B, Karwatowska L, Schoeler T, Tsaligopoulou A, Munafò MR, et al. Childhood maltreatment and mental health problems: A systematic review and meta-analysis of quasi-experimental studies. Am J Psychiatry. 2023;180(2):117-26.
3. Bellis MA, Hughes K, Ford K, Ramos Rodriguez G, Sethi D, Passmore J. Life course health consequences and associated annual costs of adverse childhood experiences across Europe and North America: A systematic review and meta-analysis. Lancet Public Health. 2019;4(10):e517-e28.
4. Hogg B, Gardoki-Souto I, Valiente-Gómez A, Rosa AR, Fortea L, Radua J, et al. Psychological trauma as a transdiagnostic risk factor for mental disorder: An umbrella meta-analysis. Eur Arch Psychiatry Clin Neurosci. 2023;273(2):397-410.
5. McKay MT, Kilmartin L, Meagher A, Cannon M, Healy C, Clarke MC. A revised and extended systematic review and meta-analysis of the relationship between childhood adversity and adult psychiatric disorder. J Psychiatr Res. 2022;156:268-83.
6. Humphreys KL, LeMoult J, Wear JG, Piersiak HA, Lee A, Gotlib IH. Child maltreatment and depression: A meta-analysis of studies using the Childhood Trauma Questionnaire. Child Abuse Negl. 2020;102:104361.
7. LeMoult J, Humphreys KL, Tracy A, Hoffmeister JA, Ip E, Gotlib IH. Meta-analysis: Exposure to early life stress and risk for depression in childhood and adolescence. J Am Acad Child Adolesc Psychiatry. 2020;59(7):842-55.
8. Li M, D'Arcy C, Meng X. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: Systematic review, meta-analysis, and proportional attributable fractions. Psychol Med. 2016;46(4):717-30.
9. Pignatelli AM, Wampers M, Loriedo C, Biondi M, Vanderlinden J. Childhood neglect in eating disorders: A systematic review and meta-analysis. J Trauma Dissociation. 2017;18(1):100-15.
10. Zhang S, Lin X, Liu J, Pan Y, Zeng X, Chen F, et al. Prevalence of childhood trauma measured by the short form of the Childhood Trauma Questionnaire in people with substance use disorder: A meta-analysis. Psychiatry Res. 2020;294:113524.
11. Bonoldi I, Simeone E, Rocchetti M, Codjoe L, Rossi G, Gambi F, et al. Prevalence of self-reported childhood abuse in psychosis: A meta-analysis of retrospective studies. Psychiatry Res. 2013;210(1):8-15.
12. Porter C, Palmier-Claus J, Branitsky A, Mansell W, Warwick H, Varese F. Childhood adversity and borderline personality disorder: a meta-analysis. Acta Psychiatr Scand. 2020;141(1):6-20.
13. Blakemore SJ. Adolescence and mental health. Lancet. 2019;393(10185):2030-1.
14. Childhood Trauma Meta-Analysis Study Group. Treatment efficacy and effectiveness in adults with major depressive disorder and childhood trauma history: A systematic review and meta-analysis. Lancet Psychiatry. 2022;9(11):860-73.
15. Karatzias T, Murphy P, Cloitre M, Bisson J, Roberts N, Shevlin M, et al. Psychological interventions for ICD-11 complex PTSD symptoms: systematic review and meta-analysis. Psychol Med. 2019;49(11):1761-75.
16. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry. 2012;169(2):141-51.
17. Nelson J, Klumparendt A, Doebler P, Ehring T. Childhood maltreatment and characteristics of adult depression: Meta-analysis. Br J Psychiatry. 2017;210(2):96-104.
18. Shirk SR, Deprince AP, Crisostomo PS, Labus J. Cognitive behavioral therapy for depressed adolescents exposed to interpersonal trauma: An initial effectiveness trial. Psychotherapy. 2014;51(1):167-79.

19. Panagou C, MacBeth A. Deconstructing pathways to resilience: A systematic review of associations between psychosocial mechanisms and transdiagnostic adult mental health outcomes in the context of adverse childhood experiences. Clin Psychol Psychother. 2022;29(5):1626-54.
20. Jaffee SR. Child maltreatment and risk for psychopathology in childhood and adulthood. Annu Rev Clin Psychol. 2017;13:525-51.
21. McCrory E, Ogle JR, Gerin MI, Viding E. Neurocognitive adaptation and mental health vulnerability following maltreatment: The role of social functioning. Child Maltreatment. 2019;24(4):435-51.
22. McLaughlin KA, Colich NL, Rodman AM, Weissman DG. Mechanisms linking childhood trauma exposure and psychopathology: A transdiagnostic model of risk and resilience. BMC Med. 2020;18(1):96.
23. Gao S, Assink M, Bi C, Chan KL. Child Maltreatment as a Risk Factor for Rejection Sensitivity: A Three-Level Meta-Analytic Review. Trauma Violence Abuse. 2023:15248380231162979.
24. Copeland WE, Shanahan L, Hinesley J, Chan RF, Aberg KA, Fairbank JA, et al. Association of childhood trauma exposure with adult psychiatric disorders and functional outcomes. JAMA Netw Open. 2018;1(7):e184493.
25. Downey G, Feldman SI. Implications of rejection sensitivity for intimate relationships. J Pers Soc Psychol. 1996;70(6):1327-43.
26. De Paoli T, Fuller-Tyszkiewicz M, Krug I. Insecure attachment and maladaptive schema in disordered eating: The mediating role of rejection sensitivity. Clin Psychol Psychother. 2017;24(6):1273-84.
27. Weissman DG, Nook EC, Dews AA, Miller AB, Lambert HK, Sasse SF, et al. Low emotional awareness as a transdiagnostic mechanism underlying psychopathology in adolescence. Clin Psychol Sci. 2020;8(6):971-88.
28. Beauchaine TP. Future directions in emotion dysregulation and youth psychopathology. J Clin Child Adolesc Psychol. 2015;44(5):875-96.
29. Gruhn MA, Compas BE. Effects of maltreatment on coping and emotion regulation in childhood and adolescence: A meta-analytic review. Child Abuse Negl. 2020;103:104446.
30. Beauchaine TP, Cicchetti D. Emotion dysregulation and emerging psychopathology: A transdiagnostic, transdisciplinary perspective. Dev Psyhopathol. 2019;31(3):799-804.
31. Anmella G, De Prisco M, Fico G, Fornaro M, Grande I, Hidalgo-Mazzei D, et al. Emotion dysregulation in bipolar disorder compared to other mental illnesses: A systematic review and meta-analysis. Psychol Med. 2023;53(16):7484-503.
32. Fleming J, Mullen PE, Sibthorpe B, Bammer G. The long-term impact of childhood sexual abuse in Australian women. Child Abuse Negl. 1999;23(2):145-59.
33. Davis JL, Petretic-Jackson PA. The impact of child sexual abuse on adult interpersonal functioning: A review and synthesis of the empirical literature. Aggress Violent Behav. 2000;5(3):291-328.
34. Drapeau M, Perry JC. Childhood trauma and adult interpersonal functioning: a study using the Core Conflictual Relationship Theme Method (CCRT). Child Abuse Negl. 2004;28(10):1049-66.
35. Seitz KI, Bertsch K, Herpertz SC. A prospective study of mental health during the COVID-19 pandemic in childhood trauma-exposed individuals: Social support matters. J Trauma Stress. 2021;34(3):477-86.
36. Shevlin M, McElroy E, Murphy J. Loneliness mediates the relationship between childhood trauma and adult psychopathology: Evidence from the Adult Psychiatric Morbidity Survey. Soc Psychiatry Psychiatr Epidemiol. 2015;50(4):591-601.
37. Vranceanu AM, Hobfoll SE, Johnson RJ. Child multi-type maltreatment and associated depression and PTSD symptoms: The role of social support and stress. Child Abuse Negl. 2007;31(1):71-84.
38. Levy J, Goldstein A, Feldman R. The neural development of empathy is sensitive to caregiving and early trauma. Nat Commun. 2019;10(1):1905.

39. Reinhard MA, Rek SV, Nenov-Matt T, Barton BB, Dewald-Kaufmann J, Merz K, et al. Association of loneliness and social network size in adulthood with childhood maltreatment: Analyses of a population-based and a clinical sample. Eur Psychiatry. 2022;65(1):e55.
40. Whisman MA, Sheldon CT, Goering P. Psychiatric disorders and dissatisfaction with social relationships: does type of relationship matter? J Abnorm Psychol. 2000;109(4):803-8.
41. Fan L, Chen Y, Zhu M, Mao Z, Li N. Correlation between childhood trauma experience and depressive symptoms among young adults: The potential mediating role of loneliness. Child Abuse Negl. 2023;144:106358.
42. Herpertz SC, Schramm E. Modulare Psychotherapie. Ein Mechanismus-basiertes, personalisiertes Vorgehen. Stuttgart: Schattauer; 2022.
43. Elsaesser M, Herpertz S, Piosczyk H, Jenkner C, Hautzinger M, Schramm E. Modular-based psychotherapy (MoBa) versus cognitive-behavioural therapy (CBT) for patients with depression, comorbidities and a history of childhood maltreatment: Study protocol for a randomised controlled feasibility trial. BMJ Open. 2022;12(7):e057672.
44. David D, Cristea I, Hofmann SG. Why cognitive behavioral therapy Is the current gold standard of psychotherapy. Front Psychiatry. 2018;9:4.
45. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-7.
46. Margraf J, Cwik JC. Mini-DIPS Open Access: Diagnostic Short-Interview for Mental Disorders. [Mini-DIPS Open Access: Diagnostisches Kurzinterview bei psychischen Störungen]. Bochum: Forschungs- und Behandlungszentrum für psychische Gesundheit, Ruhr-Universität; 2017.
47. Beesdo-Baum K, Zaudig M, Wittchen H-U. SCID-5-PD: Strukturiertes Klinisches Interview für DSM-5®-Persönlichkeitsstörungen: Hogrefe; 2019.
48. Beesdo-Baum K, Zaudig M, Wittchen H-U. SCID-5-CV: strukturiertes klinisches Interview für DSM-5-Störungen-Klinische Version: deutsche Bearbeitung des Structured Clinical Interview for DSM-5 Disorders-Clinician version von Michael B. First, Janet BW Williams, Rhonda S. Karg, Robert L. Spitzer: Hogrefe; 2019.
49. Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am J Psychiatry. 1994;151(8):1132-6.
50. Häuser W, Schmutzer G, Brähler E, Glaesmer H. Maltreatment in childhood and adolescence: results from a survey of a representative sample of the German population. Dtsch Arztebl Int. 2011;108(17):287-94.
51. Allison C, Auyeung B, Baron-Cohen S. Toward brief "Red Flags" for autism screening: The Short Autism Spectrum Quotient and the Short Quantitative Checklist for Autism in toddlers in 1,000 cases and 3,000 controls [corrected]. J Am Acad Child Adolesc Psychiatry. 2012;51(2):202-12.e7.
52. Baudson TG, Preckel F. mini-q: Intelligenzscreening in drei Minuten. 2016;62(3):182-97.
53. Lambert MJ, Hannöver W, Nisslmüller K, Richard M, Kordy H. Fragebogen zum Ergebnis von Psychotherapie. Zur Reliabilität und Validität der deutschen Übersetzung des Outcome Questionnaire 45.2 (OQ-45.2). [Questionnaire on the results of psychotherapy: Reliability and validity of the German translation of the Outcome Questionnaire 45.2 (OQ-45.2).]. Z. Klin. Psychol. Psychother. 2002;31(1):40-6.
54. de Jong K, Nugter M, Polak M, Wagenborg JEA, Spinhoven P, Heiser W. The Outcome Questionnaire (OQ-45) in a Dutch population: A cross-cultural validation. Clin Psychol Psychother. 14, 288 - 301 (2007). 2007;14.
55. Hafen CA, Spilker A, Chango J, Marston ES, Allen JP. To accept or reject? The impact of adolescent rejection sensitivity on early adult romantic relationships. J Res Adolesc. 2014;24(1):55-64.
56. Weinberg A, Klonsky ED. Measurement of emotion dysregulation in adolescents. Psychol Assess. 2009;21(4):616-21.

57. Franke GH. Brief Symptom Inventory von L. R. Derogatis (Kurzform der SCL-90-R) - Deutsche Version. Manual. [Brief Symptom Inventory by L. R. Derogatis (Short form of the SCL-90-R) - German version. Manual]. Göttingen: Beltz Test; 2000.
58. Bateman A, Fonagy P. Mentalization-based treatment for personality disorders: A practical guide: OUP Oxford; 2016.
59. Schauer M, Ruf-Leuschner M. Lifeline in der Narrativen Expositionstherapie. Psychotherapeut. 2014;59(3):226-38.
60. Newhill CE, Safran JD, Muran JC. Negotiating the therapeutic alliance: A relational treatment guide: Guilford Press; 2003.
61. McCullough Jr JP. Treatment for chronic depression: Cognitive Behavioral Analysis System of Psychotherapy (CBASP): Educational Publishing Foundation; 2003.
62. Lavender JM, Tull MT, DiLillo D, Messman-Moore T, Gratz KL. Development and validation of a state-based measure of emotion dysregulation: The State Difficulties in Emotion Regulation Scale (S-DERS). Assessment. 2017;24(2):197-209.
63. Linehan MM. Dialectical behavior therapy for borderline personality disorder: Theory and method. Bull Menn Clin. 1987;51(3):261.
64. Haug S, Puschner B, Lambert MJ, Kordy H. Veränderungsmessung in der Psychotherapie mit dem Ergebnisfragebogen (EB-45). Zeitschrift für Differentielle und Diagnostische Psychologie. 2004;25(3):141-51.
65. Smith G. Working with trauma: Systemic approaches: Bloomsbury Publishing; 2012.
66. Kim MJ, Knodt AR, Hariri AR. Meta-analytic activation maps can help identify affective processes captured by contrast-based task fMRI: the case of threat-related facial expressions. Soc Cogn Affect Neurosci. 2022;17(9):777-87.
67. Breil C, Kanske P, Pittig R, Böckler A. A revised instrument for the assessment of empathy and Theory of Mind in adolescents: Introducing the EmpaToM-Y. Behav Res Methods. 2021;53(6):2487-501.
68. Frolichs KM, Rosenblau G, Korn CW. Incorporating social knowledge structures into computational models. Nat Commun. 2022;13(1):6205.
69. Korn CW, La Rosée L, Heekeren HR, Roepke S. Social feedback processing in borderline personality disorder. Psychol Med. 2016;46(3):575-87.
70. Schmidt J, Lamprecht F, Wittmann WW. Zufriedenheit mit der stationären Versorgung. Entwicklung eines Fragebogens und erste Validitätsuntersuchungen. [Satisfaction with inpatient care: Development of a questionnaire and first validity assessments.]. Psychother Psychosom Med Psychol. 1989;39(7):248-55.
71. Larsen DL, Attkisson CC, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: Development of a general scale. Eval Program Plann. 1979;2(3):197-207.
72. Weiner BJ, Lewis CC, Stanick C, Powell BJ, Dorsey CN, Clary AS, et al. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci. 2017;12(1):108.
73. Rozental A, Kottorp A, Forsström D, Månsson K, Boettcher J, Andersson G, et al. The Negative Effects Questionnaire: psychometric properties of an instrument for assessing negative effects in psychological treatments. Behav Cogn Psychother. 2019;47(5):559-72.
74. Roe D, Dekel R, Harel G, Fennig S. Clients' reasons for terminating psychotherapy: a quantitative and qualitative inquiry. Psychol Psychother. 2006;79(Pt 4):529-38.
75. APA. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) Washington, DC, USA: American Psychiatric Association; 2000.
76. Staebler K, Helbing E, Rosenbach C, Renneberg B. Rejection sensitivity and borderline personality disorder. Clin Psychol Psychother. 2011;18(4):275-83.
77. Lambert MJ, Burlingame GM, Umphress V, Hansen NB, Vermeersch DA, Clouse GC, et al. The reliability and validity of the outcome questionnaire. Clin Psychol Psychother. 1996;3(4):249-58.
78. Puschner B, Cosh SM, Becker TJEJoPA. Patient-rated outcome assessment with the German version of the Outcome Questionnaire 45 in people with severe mental illness. Eur J Psychol Assess. 2016;32:273-82.

79. Bach B, Kerber A, Aluja A, Bastiaens T, Keeley JW, Claes L, et al. International Assessment of DSM-5 and ICD-11 Personality Disorder Traits: Toward a Common Nosology in DSM-5.1. Psychopathology. 2020;53(3-4):179-88.
80. Spitzer C, Müller S, Kerber A, Hutsebaut J, Brähler E, Zimmermann J. Die deutsche Version der Level of Personality Functioning Scale-Brief Form 2.0 (LPFS-BF): Faktorenstruktur, konvergente Validität und Normwerte in der Allgemeinbevölkerung. Psychother Psychosom Med Psychol. 2021;71(07):284-93.
81. Renneberg B, Seehausen A. Fragebogen zu Gedanken und Gefühlen (FGG)—Ein screening instrument für borderline-spezifisches denken. [Questionnaire of Thoughts and Feelings (QTF)—A screening instrument for borderline-specific cognitions.]. Z Kl Psych Psychoth. 2010;39(3):170-8.
82. Bohus M, Kleindienst N, Limberger MF, Stieglitz RD, Domsalla M, Chapman AL, et al. The short version of the Borderline Symptom List (BSL-23): Development and initial data on psychometric properties. Psychopathology. 2009;42(1):32-9.
83. Stiglmayr C, Schmahl C, Bremner JD, Bohus M, Ebner-Priemer U. Development and psychometric characteristics of the DSS-4 as a short instrument to assess dissociative experience during neuropsychological experiments. Psychopathology. 2009;42(6):370-4.
84. Müller S, Wendt LP, Zimmermann J. Development and validation of the Certainty About Mental States Questionnaire (CAMSQ): A self-report measure of mentalizing oneself and others. Assessment. 2021:10731911211061280.
85. Cordes A, Herrmann-Lingen C, Büchner B, Hessel A. Repräsentative Normierung des ENRICHD Social-Support-Instrument (ESSI) – Deutsche Version [Psychometric properties of the ENRICHD Social Support Instrument (ESSI, German version) in a representative German population sample]. Klinische Diagnostik und Evaluation. 2009;2:16-32.
86. Guy W. ECDEU assessment manual for psychopharmacology: US Department of Health, Education, and Welfare, Public Health Service; 1976.
87. Eckstrand KL, Forbes EE, Bertocci MA, Chase HW, Greenberg T, Lockovich J, et al. Anhedonia reduction and the association between left ventral striatal reward response and 6-month improvement in life satisfaction among young adults. JAMA Psychiatry. 2019;76(9):958-65.
88. Krampen G. Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie: STEP: Hogrefe, Verlag für Psychologie; 2002.
89. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working Alliance Inventory-Short Revised (WAI-SR): psychometric properties in outpatients and inpatients. Clin Psychol Psychother. 2010;17(3):231-9.
90. Lutz W, Tholen S, Schürch E, Berking M. Reliabilität von Kurzformen gängiger psychometrischer Instrumente zur Evaluation des therapeutischen Fortschritts in Psychotherapie und Psychiatrie. Diagnostica. 2006;52(1):11-25.
91. Clarke A, Putz R, Friede T, Ashdown J, Adi Y, Martin S, et al. Warwick-Edinburgh Mental Well-being Scale (WEMWBS) acceptability and validation in English and Scottish secondary school students (The WAVES Project) Glasgow. 2010.
92. Fonagy P, Luyten P, Moulton-Perkins A, Lee Y-W, Warren F, Howard S, et al. Development and validation of a self-report measure of mentalizing: The Reflective Functioning Questionnaire. PLoS One. 2016;11(7):e0158678.
93. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol. 1988;54(6):1063-70.
94. Hariri AR, Bookheimer SY, Mazziotta JC. Modulating emotional responses: Effects of a neocortical network on the limbic system. Neuroreport. 2000;11(1):43-8.
95. Kanske P, Böckler A, Trautwein FM, Singer T. Dissecting the social brain: Introducing the EmpaToM to reveal distinct neural networks and brain-behavior relations for empathy and Theory of Mind. NeuroImage. 2015;122:6-19.
96. Korn CW, Prehn K, Park SQ, Walter H, Heekeren HR. Positively biased processing of self-relevant social feedback. J Neurosci. 2012;32(47):16832-44.

97. Patton MQ. Qualitative evaluation and research methods: SAGE Publications, inc; 1990.
98. Cocks K, Torgerson DJ. Sample size calculations for pilot randomized trials: a confidence interval approach. J Clin Epidemio. 2013;66(2):197-201.
99. van der Hoeven ML, Assink M, Stams G-JJM, Daams JG, Lindauer RJL, Hein IM. Victims of child abuse dropping out of trauma-focused treatment: A meta-analysis of risk factors. J Child Adolesc Trauma. 2023;16(2):269-83.
100. Wilhelm M, Feldhege J, Bauer S, Moessner M. Einsatz internetbasierter Verlaufsmessung in der Psychotherapieforschung. Psychotherapeut. 2020;65(6):505-11.
101. Cackowski S, Schmahl C. Research Training Group (RTG) / Graduiertenkolleg (GRK) 2350. Impact of adverse childhood experiences on psychosocial and somatic conditions across the lifespan. Neuroforum. 2019;25(4):265-6.
102. Klinitzke G, Romppel M, Häuser W, Brähler E, Glaesmer H. Die deutsche Version des Childhood Trauma Questionnaire (CTQ) - psychometrische Eigenschaften in einer bevölkerungsrepräsentativen Stichprobe [The German version of the Childhood Trauma Questionnaire (CTQ) - psychometric characteristics in a representative sample of the general population]. Psychother Psychosom Med Psychol. 2012;62(2):47-51.
103. Seitz KI, Gerhardt S, von Schroeder C, Panizza A, Thekkumthala D, Bertsch K, et al. Measuring types and timing of childhood maltreatment: The psychometric properties of the KERF-40+. PLoS One. 2022;17(9):e0273931.
104. Teicher MH, Parigger A. The 'Maltreatment and Abuse Chronology of Exposure' (MACE) scale for the retrospective assessment of abuse and neglect during development. PLoS One. 2015;10(2):e0117423.
105. Solmi M, Dragioti E, Croatto G, Radua J, Borgwardt S, Carvalho AF, et al. Risk and protective factors for personality disorders: an umbrella review of published meta-analyses of case–control and cohort studies. Front Psychiatry. 2021;12:679379.
106. Quenneville AF, Kalogeropoulou E, Küng A-L, Hasler R, Nicastro R, Prada P, et al. Childhood maltreatment, anxiety disorders and outcome in borderline personality disorder. Psychiatry Res. 2020;284:112688.
107. Meyer-Lindenberg A, Falkai P, Fallgatter AJ, Hannig R, Lipinski S, Schneider S, et al. The future German Center for Mental Health (Deutsches Zentrum für Psychische Gesundheit): a model for the co-creation of a national translational research structure. Nat Mental Health. 2023;1(3):153-6.

Author's Contributions

KIS together with SCH wrote the original draft of the manuscript and developed the basic idea of the study design with support provided by ES, CS, and HZ. Details of the clinical trial design were forwarded together by all authors from the three sites. KIS, NS, and SF coordinate the study's implementation, JH the MeMoPsy training and supervision. ST and FE designed and introduced the basic module, ES and SCH designed and introduced module 1, FE, RV and KIS module 2, and MWH and CAR module 3 of the MeMoPsy intervention. HCF together with MW, MWH, NS, and SB drafted the design of the process research, TB and ABR the design of the qualitative study. MW is responsible for electronic data assessment and management. CWK supported by KIS and EB was responsible for designing the fMRI study, BD for hormonal analyses, SvS and LTK for diagnostics, and MF for statistical design and analyses. CC is responsible for the study's implementation at the Berlin study site. EV and JB are responsible for the comparator treatment. All authors contributed to and have approved the final manuscript. SCH is the guarantor.

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Competing Interests Statement (see also Declaration of interests)

The authors report no potential conflicts of interest.

Figure Legends

Figure 1. *Modular treatment program and selection criteria.*

Note. CBASP, Cognitive Behavioral Analysis System of Psychotherapy; DBT, Dialectical Behavior Therapy; MBT, Mentalization-Based Psychotherapy; MeMoPsy, mechanism-based modular psychotherapy; OQ-45, IR, Outcome Questionnaire-45, Interpersonal Relations subscale; RSQ, Rejection Sensitivity Questionnaire; S-DERS, State Difficulties in Emotion Regulation Scale.

Figure 2. *Trial design and flow of patients.*

Note. CBT, cognitive behavioral therapy; MeMoPsy, mechanism-based modular psychotherapy. Please note that a dropout estimated to amount to 20% may occur along intervention and follow-up.

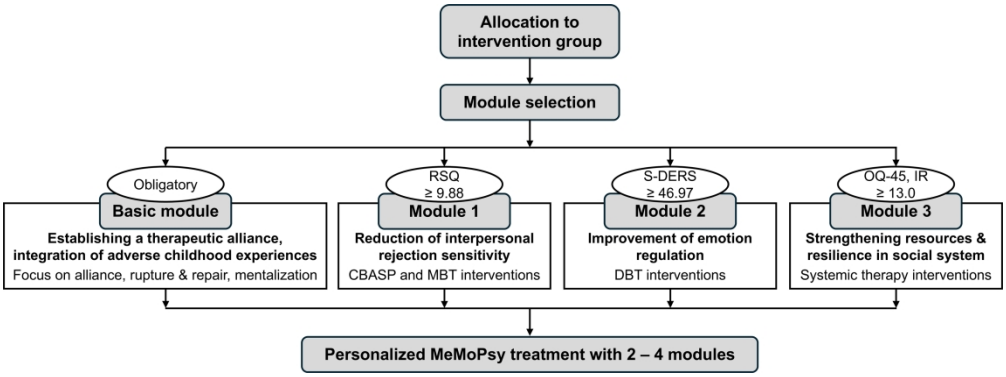

Figure 1. Modular treatment program and selection criteria. CBASP Cognitive Behavioral Analysis System of Psychotherapy; DBT, Dialectical Behavior Therapy; MBT, Mentalization-Based Psychotherapy; MeMoPsy, mechanism-based modular psychotherapy; OQ-45, IR, Outcome Questionnaire-45, Interpersonal Relations subscale; RSQ, Rejection Sensitivity Questionnaire; S-DERS, State Difficulties in Emotion Regulation Scale.

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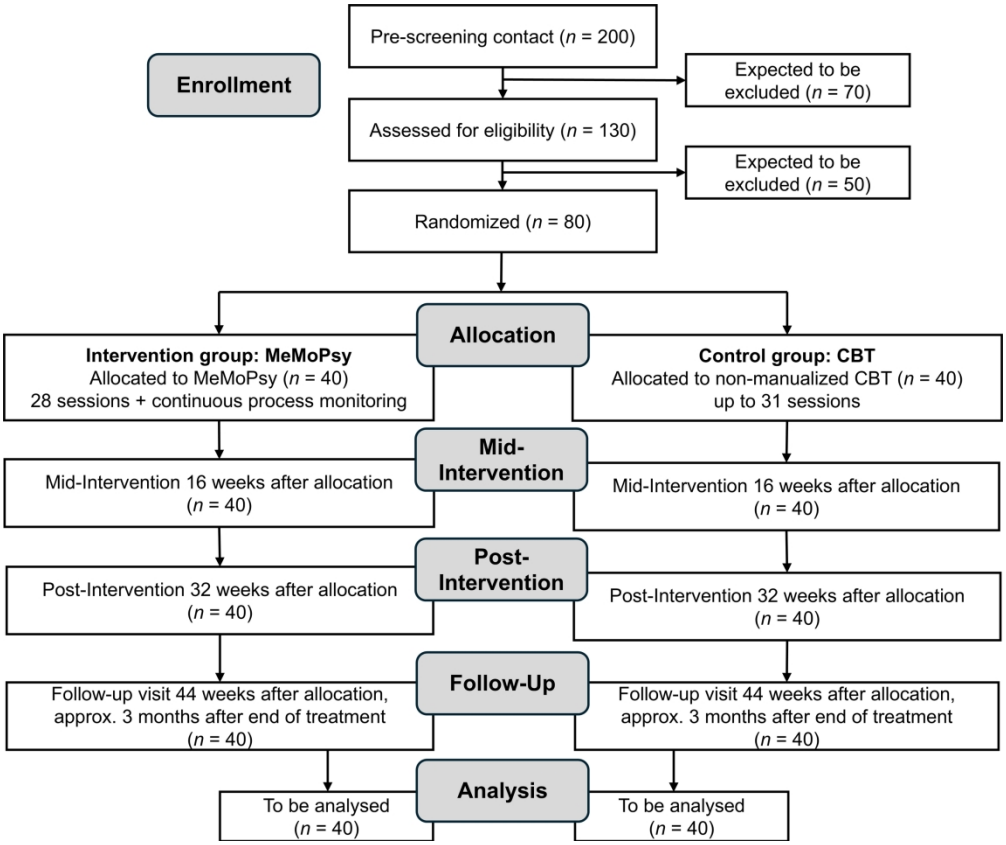

Figure 2. Trial design and flow of patients. CBT, cognitive behavioral therapy; MeMoPsy, mechanism-based modular psychotherapy. Please note that a dropout estimated to amount to 20% may occur along intervention and follow-up.

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S1

Supplement Seitz et al. (under revision)

Mechanism-based modular psychotherapy vs. cognitive behavioral therapy for adolescents and young adults with childhood trauma experiences: Study protocol for a feasibility trial within the German Center for Mental Health

Overview

Supplement Part A: Administrative information

Supplement Part B: Table S1

Supplement Part C: SPIRIT 2013 Checklist

Supplement Part D: Model Consent Form

Supplement Part A: Administrative information

Title: Mechanism-based modular psychotherapy vs. cognitive behavioral therapy for adolescents and young adults with childhood trauma experiences: Study protocol for a feasibility trial within the German Center for Mental Health

Trial registration: Registry: German Clinical Trials Register, Trials Identifier: DRKS00034058

Protocol version: Study Protocol Version 1.4, 28.03.2024

Funding: This study is funded by the Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung [BMBF]) and the ministry of Baden-Württemberg within the initial phase of the German Center for Mental Health (DZPG) (grant: DZPG 01EE2304B).

Names, affiliations, and roles of protocol contributors: Clinical trial protocol: KIS, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University and SCH, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University with support provided by ES, Department of Psychiatry and Psychotherapy, Medical Center, Faculty of Medicine, University of Freiburg, CS, Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health Mannheim, Medical Faculty Mannheim, Heidelberg University, and HZ, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University. Coordination of study's implementation: KIS, NS, Department of General Internal Medicine and Psychosomatics, Center for Psychosocial Medicine, Heidelberg University, and SF, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Heidelberg. Coordination of MeMoPsy training and supervision: JH, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Heidelberg. Design and introduction MeMoPsy basic module: ST, Institute of Psychosocial Prevention, Center for Psychosocial Medicine, Heidelberg University, and FE, Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health Mannheim, Medical Faculty Mannheim, Heidelberg University. Design and introduction MeMoPsy module 1: ES and SCH. Design and introduction MeMoPsy module 2: FE, RV, Department of Psychosomatic Medicine and Psychotherapy, Central Institute of

Mental Health Mannheim, Medical Faculty Mannheim, Heidelberg University, and KIS. Design and introduction MeMoPsy module 3: MWH, Department of General Internal Medicine and Psychosomatics, Center for Psychosocial Medicine, Heidelberg University, and CAR, Faculty of Social Science, Mannheim University. Process research protocol: HCF, Department of General Internal Medicine and Psychosomatics, Center for Psychosocial Medicine, Heidelberg University together with MW, Center for Psychotherapy Research, Institute of Psychosocial Prevention, Center for Psychosocial Medicine, Heidelberg University, MWH, NS, and SB, Center for Psychotherapy Research, Institute of Psychosocial Prevention, Center for Psychosocial Medicine, Heidelberg University. Qualitative research: TB, Heidelberg Institute of Global Health, Heidelberg University and ABR, Heidelberg Institute of Global Health, Heidelberg University. Electronic data assessment and management: MW. fMRI study design: CWK, Department of Social Neuroscience, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, KIS and EB, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Heidelberg. Hormonal analyses: BD, Institute of Medical Psychology, Center for Psychosocial Medicine, University Hospital Heidelberg, Heidelberg University. Diagnostics: SvS, Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Heidelberg, and LTK, Department of General Internal Medicine and Psychosomatics, Center for Psychosocial Medicine, Heidelberg University, Heidelberg. Statistical design and analyses: MF, Institute of Medical Biometry, Heidelberg University. Berlin study site: CC, Department of Education and Psychology, Clinical Child and Adolescence Psychology and Psychotherapy, Freie Universität Berlin. Comparator treatment: EV, Center of Psychological Psychotherapy, Heidelberg University, and JB, Center of Psychological Psychotherapy, Central Institute of Mental Health Mannheim.

Name and contact information for the trial sponsor: Heidelberg University, Center for Psychosocial Medicine, Voßstraße 4, 69115 Heidelberg, Germany.

Role of study sponsor and funders: The sponsor and funders were not involved in the design of the study, the collection, management, analysis, or interpretation of data, writing of the study

protocol or the decision to submit the study protocol for publication. The sponsor and funders do not have any authority over research activities.

S5

Supplement Part B: Table S1

Table S1. Frequency and scope of core trial visits and continuous outcome monitoring

Core trial visits (MeMoPsy and CBT condition)								
Visits			**Screening (T−2)**	**Diagnostics (T−1)**	**Baseline (T0)**	**Mid-Intervention (T1)**	**Post-Interv. (T2)**	**Follow-up (T3)**
Week(s)			**-**	**-**	**0**	**16**	**32**	**44**
	Format	**Measure**						
Diagnostician	I	In-person or telephone screening	●					
		KERF-40-I		●				
		Mini-DIPS		●				
		SCID-5-PD for avoidant and borderline personality disorders		●				
		SCID-5-CV for ADHD		●				
		GAF			●		●	
	Q	CTQ	●					
Patient	Q	AQ-10		●				
		mini-q		●				
		RSQ			●	●	●	●
		S-DERS			●	●	●	●
		OQ-45, subscale IR			●	●	●	●
		ZUF-8				●	●	●
		NEQ				●	●	●
		BSI			●	●	●	●
		PID-5-BF+M			●	●	●	●

		LPFS-BF 2.0			●		●			●		●	
		FGG-14			●								
		BSL-23			●								
		DSS-4			●		●			●		●	
		CAMSQ			●		●			●		●	
		ESSI			●		●			●		●	
		DZPG MDS*			●		●			●		●	
		Homework					●			●			
		WAI-SR					●			●			
		Medication			●		●			●		●	
	Optional	EMA			●					●			
		fMRI			●					●			
		Cortisol			●					●			
		Qual. interviews								●			
Therapist	Q	AIM, FIM			●		●			●			
		CGI			●		●			●			
		Therapeutic Elements Checklist					●			●			
		Homework					●			●			
Continuous outcome monitoring (MeMoPsy condition only)													
						Treatment							
Session(s)						**1**	**6**	**11**	**16**	**21**	**26**		
	Format	**Measure**											
Patient	Q	STEP-P**											
		WAI-P				●	●	●	●	●	●		
		SCL-K11				●	●	●	●	●	●		
		SWEMWBS				●	●	●	●	●	●		
		EBPSQ				●	●	●	●	●	●		

S7

		Module-specific items				•	•	•	•	•	•		
Therapist	Q	STEP-T**											
		WAI-T				•	•	•	•	•	•		
		GAF, GARF				•	•	•	•	•	•		
		Time spent on each module**											

Note. AIM, Acceptability of Intervention Measure; AQ-10, 10-item version of the Autism Spectrum Quotient; BSI, Brief Symptom Inventory; BSL-23, 23-item version of the Borderline Symptom List; CAMSQ, Certainty about Mental States Questionnaire; CGI, Clinical Global Impressions; CTQ, Childhood Trauma Questionnaire; DSS-4, 4-item version of the Dissoziations-Spannungs-Skala; DZPG, Deutsches Zentrum für Psychische Gesundheit (German Center for Mental Health); EBPSQ, Experiences Between Psychotherapy Sessions Questionnaire; ESSI, ENRICHD Social Support Inventory; FGG-14, Fragebogen zu Gedanken und Gefühlen; FIM, Feasibility of Intervention Measure; GAF, Global Assessment of Functioning; GARF, Global Assessment of Relational Functioning; I, interview; IR, Interpersonal Relations; KERF-40-I, brief German interview version of the Maltreatment and Abuse Chronology of Exposure scale; MDS, Minimum Dataset; Mini-DIPS, Diagnostic Short-Interview for Mental Disorders; mini-q, brief screening for cognitive abilities; NEQ, Negative Effects Questionnaire; OQ-45, 45-item version of the Outcome Questionnaire; PD, Personality Disorder; LPFS-BF 2.0 Level of Personality Functioning Scale-Brief Form 2.0; PID-5-BF+M, Personality Inventory for DSM-5 – Brief Form Plus Modified; Q, questionnaire; RSQ, Rejection Sensitivity Questionnaire; SCID-5-PD, Structured Clinical Interview for DSM-5 Personality Disorders; SCID-5-CV, Structured Clinical Interview for DSM-5 Clinical Version; SCL-K11, 11-item version of the Symptom Checklist; S-DERS, State Difficulties in Emotion Regulation Scale; STEP-P/STEP-T, Stundenbogen für die allgemeine und differentielle Einzelpsychotherapie, patient (P) or therapist (T) version; SWEMWBS, Short Warwick-Edinburgh Mental Wellbeing Scale; WAI-P/WAI-T: Working Alliance Inventory, patient (P) or therapist (T) version; ZUF-8, 8-item version of the Fragebogen zur Patientenzufriedenheit.

*: Please note that assessments marked with one asterisk are collected only selectively at T1, T2, and T3 after being collected fully at T0. **: Please note that measures marked with two asterisks are administered after each session in the MeMoPsy condition

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Supplement Part C: SPIRIT 2013 Checklist

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page No in Manuscript or Supplement
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1, S2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	S2
	2b	All items from the World Health Organization Trial Registration Data Set	See German Clinical Trials Register, DRKS00034058
Protocol version	3	Date and version identifier	S2
Funding	4	Sources and types of financial, material, and other support	S2
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	S2-S3
	5b	Name and contact information for the trial sponsor	S3
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	S3-S4

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-8
	6b	Explanation for choice of comparators	8
Objectives	7	Specific objectives or hypotheses	8-9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9-11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-14
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	10-11

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	14
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10-11
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	14-18
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	19, S5-S7
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	19
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	20

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	20
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	20
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	20
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	21-22
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	22
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	22-23

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	23
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	23-24
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	24-25
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	24-25
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	24
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	25
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	25
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	26

Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	27
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	27
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	28
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	28
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	28
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	29
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	29
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	29

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	29
	31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	29
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	S16-S19
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Supplement Part D: Model Consent Form

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Einwilligungserklärung für Patientinnen und Patienten zur Teilnahme an der Studie

Mechanismus-basierte, modulare Psychotherapie für traumatisierte Adoleszente und junge Erwachsene: Eine Machbarkeitsstudie

Version 1.2 – 28.03.2024

Ich habe die Informationsschrift gelesen und wurde zudem mündlich durch Herrn/Frau _____ über das Ziel und den Ablauf der Studie sowie über die Risiken ausführlich und verständlich aufgeklärt. Im Rahmen des Aufklärungsgesprächs hatte ich die Gelegenheit, Fragen zu stellen. Alle meine Fragen wurden zu meiner Zufriedenheit beantwortet. Ich stimme der Teilnahme an der Studie freiwillig zu. Für meine Entscheidung hatte ich ausreichend Zeit. Ein Exemplar der Informationsschrift und der Einwilligungserklärung habe ich erhalten.

Datenschutz

Mir ist bekannt, dass bei dieser Studie personenbezogene Daten verarbeitet werden sollen. Die Verarbeitung der Daten erfolgt nach gesetzlichen Bestimmungen und setzt gemäß Art. 6 Abs. 1 lit. a der Datenschutz-Grundverordnung folgende Einwilligungserklärung voraus:

Ich wurde darüber aufgeklärt und stimme freiwillig zu, dass meine in der Studie erhobenen Daten, insbesondere Angaben über meine Gesundheit[1], zu den in der Informationsschrift beschriebenen Zwecken in pseudonymisierter Form aufgezeichnet, ausgewertet und ggf. auch in pseudonymisierter Form an Universitäten/Kliniken, v.a. Wissenschaftler des Deutschen Zentrums für

[1] Gemäß Art. 9 Abs. 1 DSGVO handelt es sich bei Gesundheitsdaten um personenbezogene Daten besonderer Kategorie in deren Verarbeitung der Studienteilnehmer ausdrücklich einwilligen muss. Gleiches gilt für Daten, aus denen die rassische und ethnische Herkunft, politische Meinungen, religiöse oder weltanschauliche Überzeugungen oder die Gewerkschaftszugehörigkeit hervorgehen, sowie für die Verarbeitung von genetischen Daten, biometrischen Daten zur eindeutigen Identifizierung einer natürlichen Person, Daten zum Sexualleben oder zur sexuellen Orientierung.

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Psychische Gesundheit (DZPG) weitergegeben werden können, u.U. auch in Länder mit geringeren Anforderungen an den Datenschutz als in der Europäischen Union. Im Rahmen dieser Studie erfolgt eine Weitergabe Ihrer pseudonymisierten Daten/Proben u. U. in Drittländer außerhalb der EU und des Europäischen Wirtschaftsraumes ausschließlich zum Zweck der Datenauswertung. Es handelt sich um Länder, für die die Europäische Kommission ein angemessenes gesetzliches Datenschutzniveau festgestellt hat.

Ich stimme zu, dass an der Studie beteiligte Projektmitarbeiter Einblick in meine in der Studie gespeicherten Daten erhalten. Autorisierten und zur Verschwiegenheit verpflichtete Beauftragte (für das Datenmonitoring zuständige Personen) dürfen Einsicht in die bei den Prüfärzt*innen vorhandenen personenbezogenen Daten nehmen soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der Studie notwendig ist. Diese Maßnahme betreffend entbinden Sie die Prüfärzt*innen von der ärztlichen Schweigepflicht. Dritte erhalten jedoch keinen Einblick in personenbezogene Unterlagen. Eine Weitergabe Ihrer Daten erfolgt ggf. nur in pseudonymisierter Form. Den Pseudonymisierungscode erhalten ausschließlich Studienmitarbeitende, die der ärztlichen Schweigepflicht unterliegen. Bei der Veröffentlichung von Ergebnissen der Studie wird Ihr Name ebenfalls nicht genannt. Die personenbezogenen Daten werden anonymisiert, sobald dies nach dem Forschungszweck möglich ist. Die Daten werden bis zum Abschluss der Datenauswertung, mindestens jedoch 10 Jahre aufbewahrt, höchstens aber so lange, wie sie für die in der Einwilligung genannten Forschungszwecke erforderlich sind. Mir ist bekannt, dass diese Einwilligung jederzeit schriftlich oder mündlich ohne Angabe von Gründen widerrufen kann, ohne dass mir dadurch Nachteile entstehen. Die Rechtmäßigkeit der bis zum Widerruf erfolgten Datenverarbeitung wird davon nicht berührt. In diesem Fall kann ich entscheiden, ob die von mir erhobenen Daten gelöscht werden sollen oder weiterhin für die Zwecke der Studie verwendet werden dürfen.

Ich stimme zu, dass meine Kontaktdaten, zwecks Kontaktaufnahme mit mir, an die Ambulanzen weitergeben werden. Ich möchte die Verwendung meiner Daten für andere/künftige Forschungszwecke wie folgt eingrenzen:

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.....

Ich willige ein, dass mich Mitarbeiter*innen des Universitätsklinikums Heidelberg zwecks Teilnahme an zukünftigen Studien anrufen oder anschreiben dürfen. Mit meiner Einwilligung verpflichte ich mich nicht zur Teilnahme an weiteren Studien. Ich habe jederzeit die Gelegenheit diese Einwilligung zu widerrufen, meine Kontaktdaten werden dann unmittelbar gelöscht.

Ja □

Wenn Ja: Handynummer: _____

Wenn Ja: Email-Adresse: _____

Nein □

Ich habe eine Kopie der Patienteninformation und dieser Einwilligungserklärung erhalten. Mit meiner Unterschrift erkläre ich mich bereit, zu den genannten Bedingungen an der Studie *„Mechanismus-basierte, modulare Psychotherapie für traumatisierte Adoleszente und junge Erwachsene: Eine Machbarkeitsstudie“* teilzunehmen.

Wenn Sie an einer oder mehreren der geplanten Untersuchungen **NICHT** teilnehmen möchten, geben Sie dies bitte hier an (Zutreffendes bitte ankreuzen):

□ Ich möchte **NICHT** an den Smartphone-basierten Befragungen (EMA) teilnehmen.

□ Ich möchte **NICHT** an den MRT-Untersuchungen teilnehmen.

□ Ich möchte **NICHT** an den hormonellen Untersuchungen teilnehmen.

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Falls Sie der Teilnahme an der MRT-Untersuchung einwilligen, erfolgt die Aufklärung über die Magnetresonanztomographie (MRT) Sie gesondert. Bitte kreuzen Sie für den Fall Ihrer Einwilligung an der Teilnahme der MRT-Untersuchung im Folgenden das Zutreffende an:

Mit der Mitteilung von Zufallsbefunden bin ich einverstanden:

Ja □

Nein □

Falls Sie auf das Recht des Nichtwissens bestehen und die Antwortmöglichkeit „Nein“ angekreuzt haben, können wir Sie leider nicht in die MRT-Studie einschließen.

Ort, Datum

Name, Vorname des:der Teilnehmer:in
(in Druckbuchstaben)

_____

Unterschrift des:der Teilnehmer:in

Aufklärende Person

Der Patient/Die Patientin wurde von mir im Rahmen eines Gesprächs über das Ziel und den Ablauf der Studie sowie über die Risiken aufgeklärt. Ein Exemplar der Informationsschrift und der Einwilligungserklärung habe ich dem Patienten/der Patientin ausgehändigt.

_____ _____

Ort, Datum

Name, Vorname des:der aufklärenden Person
(in Druckbuchstaben)

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