BMC Complementary Medicine and Therapies

STUDY PROTOCOL

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Study protocol for a randomized controlled trial evaluating the effectiveness of a mother-child intervention model of neurogenic tremor as an add-on to treatment for emotional disorders in adolescents

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Abstract

Background Adolescents exhibit a high prevalence of mental health disorders, with more than half of all cases emerging before the age of 14 years. Since the advent of the COVID-19 pandemic, there has been a marked upsurge in anxiety and depression among adolescents across several nations. Emotional disorders often lead to severe outcomes, including school absenteeism, self-harm, and suicidal tendencies. The suboptimal efficacy of pharmacotherapy, compounded by limited availability and substantial costs associated with individual psychotherapy, underscores the critical need for identifying simple yet efficacious psychotherapeutic interventions suitable for both individual and group settings. Tension and Trauma Release Exercise (TRE) is a mind-body therapeutic approach that efficiently alleviates symptoms of anxiety and depression. This randomized controlled trial (RCT) aims to evaluate the effectiveness of a mother-child intervention model using TRE in enhancing the clinical management of adolescent patients diagnosed with emotional disorders.

Methods This study recruits 140 dyads of adolescents with emotional disorders and their mothers, randomly assigned to intervention or control groups. The intervention arm combines eight weeks of standard pharmacotherapy with an eight-week TRE group therapy, assessing at baseline, post-8-week treatment, and three-month follow-up. Initially, controls receive eight weeks of standard medication with parallel assessments, later transitioning to the same TRE intervention while maintaining continuous evaluation. The study further examines the influence of maternal emotional health on adolescent treatment response and investigates associated neurophysiological and psychological mechanisms.

Discussion This research endeavors to identify a straightforward and potent body-oriented psychological intervention that could improve the clinical outcomes for adolescent patients with emotional disorders. Such findings would carry profound implications not only for the healthy development of teenagers but also for potentially mitigating the burden on families, educational institutions, and society as a whole.

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Trial registration ChiCTR2100044553, Registered March 24, 2021.

Keywords Neurogenic tremor, Adolescents, Emotional disorders, Anxiety, Tension and Trauma Release Exercise (TRE), Randomized controlled trial (RCT), Mind-body therapy, Depression

Reporting standards

The TIDieR checklist in conjunction with The SPIRIT 2013 Checklist were used as to help clarify this protocol's intervention, design, conduct, analysis, and interpretation (see Additional files).

Background

Depression and anxiety disorders are the most common mental health concerns among youth [1]. Teenagers' anxiety and depression can contribute to their fear of going to school, inability to attend school, and even self-harm and suicide [2, 3], causing great pain to both teenagers and parents, and placing a burden on schools and society. Many studies have shown that, compared with the situation before the COVID-19 epidemic, depression and anxiety among adolescents have increased significantly [4, 5]. However, only a minority receives adequate mental health care [6]. This lack of adequate care has been attributed to three main areas. First, major controversies exist regarding the efficacy and safety of antidepressants [7]. Moreover, highly trained therapists and supporters deliver therapeutic content [8]. Nonetheless, traditional one-on-one psychological therapy is expensive. Failing to access treatment at such a critical developmental stage can have serious negative consequences for functioning or even long-term disability [9]. Therefore, identifying safe, simple, and effective psychological treatment methods suitable for individual and group therapies that can be self-learned and used without requiring a high professional background for psychotherapists is crucial.

Tension and Trauma Release Exercise (TRE) is a mind-body therapy based on the neurogenic tremor principle consisting of simple, gentle, and innovative movements. It can safely activate the natural reflex mechanism of human innate tremors to release the tension accumulated in the body owing to stress and trauma, quickly restore the nervous system, and return the body to a balanced state [10, 11]. It is easily taught, learned, and immediately effective, especially for tension and anxiety; it can be used in one-to-one or group therapy settings. Moreover, it can be carried out face-to-face or online. It is a self-help method that can be practiced at home, school, or the office once learned. It does not need to rely on too much language communication and conversation skills; therefore, it applies to adults, teenagers, and children, and this method is not restricted by race or culture [10].

Although this intervention method has been widely used in many countries and plays an important role in trauma treatment and anxiety and depression relief, this method lacks sufficient evidence-based research. Berceli (2009) conducted a randomized controlled trial (RCT) of TRE intervention in a college student population for two weeks (three times per week) and found that TRE reduced the anxiety level of the participants [10]. Additionally, a pilot study on patients with multiple sclerosis found that a 9-week TRE intervention (practiced every day) significantly improved the severity of symptoms (fatigue, difficulty walking, sensory disorders, spasms, muscle weakness, etc.), stress levels, and sleep quality in these patients [12]. However, TRE's exact mechanism of action has not yet been elucidated. Neurogenic tremors are believed to release deep-rooted muscular tension and regulate the nervous system so that the individual returns to a safe, relaxed, and calm state dominated by the parasympathetic nerves [11]. To the best of our knowledge, no studies have explored TRE for the treatment of adolescent emotional disorders.

This study aims to investigate the clinical effectiveness of TRE for adolescent emotional disorders to fill this gap. Considering the close relationship between the occurrence, development, and rehabilitation of adolescent emotional disorders and the family environment, especially maternal mental health status [13–21], this study ultimately intends to utilize the mother-child joint intervention model and clinical RCT to explore the therapeutic effect of TRE intervention on adolescent emotional disorders and the correlated physiological and psychological mechanisms. The research design was structured such that, during the first phase of the study, patients in the intervention cohort are subjected to an eight-week TRE regimen alongside their mothers, serving as an adjunct to the standard pharmacological treatment regimen. In contrast, participants within the control group receive solely the conventional eight-week pharmaceutical therapy. It is imperative for all participants to undertake both baseline assessments and post-intervention evaluations. In the subsequent phase following the initial intervention period, a follow-up evaluation will be executed for every participant three months later. Of particular note, after this follow-up assessment, those initially in the control group will then be offered the identical eight-week TRE intervention previously experienced by the intervention group. Similarly, they will also need to

complete baseline measurements before starting the TRE program and subsequent evaluations post-treatment.

The specific aims and hypotheses are as follows:

Primary aim: To determine the effectiveness of TRE treatment on adolescent emotional disorders.

Hypothesis 1: Patients randomized to TRE with routine medical therapy will show greater improvements in anxiety and depression symptoms than those randomized to the control group. Hypothesis 2: The anxiety and depression levels of mothers in the TRE group significantly improved compared to those of mothers in the control group, and the improvement contributed to the clinical efficacy of the patients through changes in the parent-child relationship or parenting style.

The secondary aim is to explore the neurophysiological and psychological mechanisms through which TRE improves emotional disorders in adolescents.

Hypothesis: Based on animal studies of neurogenic tremors [22–26] and the multiple vagus nerve theory of trauma [27], we hypothesized that TRE can release high-energy charges and protective hormones accumulated in the body's muscle tissue during stress, alter heart rate and respiratory patterns during depression, anxiety, and fear states, and transmit these feedback signals from the body to brain regions through the vagus nerve. The ultimate impact on autonomic nervous function is to regulate the nervous system to be dominated by the ventral vagus nerve of the multiple vagus nervous systems, changing the brain network function and connectivity state related to depression and anxiety emotion processing, thereby restoring the balance of the body's regulation of anxiety, fear, and depressive emotions [28].

The effect of TRE intervention on participants' cortisol rhythm and autonomic nervous system activity in this study will be investigated to verify this hypothesis. Moreover, we will collect Functional Magnetic Resonance Imaging (fMRI) data from the resting-state functional network. We will record the electroencephalogram (EEG) signals in the resting state and during cognitive tasks such as cognitive control, logical reasoning, effort motivation, and emotional regulation flexibility of participants in this study.

Exploratory aim: Since TRE can potentially affect a range of symptoms or various aspects of an individual, an exploratory approach will be used to investigate changes in various outcome measures for an 8-week TRE program.

Hypothesis: Participants randomized to the TRE group will demonstrate a higher degree of outcome improvement. For adolescents, these outcomes encompass rumination, sleep quality, test anxiety, social anxiety, online game disorder, despair, self-injury, suicide, psychological resilience, self-esteem, and alexithymia. For mothers, the improvements involve rumination, sleep quality, despair, psychological resilience, self-esteem, parent-child relationships, and parenting style.

Methods

Study setting and population

This study is being conducted at Beijing Huilongguan Hospital. Participants will be recruited from the hospital's Adolescents Emotional Disorder Clinic. Adolescent patients with emotional disorders and their mothers will be required to participate in this study.

Eligibility criteria

The patient inclusion criteria are as follows: (1) meeting the criteria for a current depressive episode based on the Structured Clinical Interview for DSM-5 [29], with depression and anxiety as the main causes and treatment targets, and the absence of symptoms of command auditory hallucinations or serious suicidal and self-injurious ideas and behaviors; (2) age between 12 and 18 years; (3) no dyslexia in Chinese; (4) no electroconvulsive therapy or transcranial magnetic stimulation was used in the past six months; (5) no plan to participate in any other form of psychological counseling, treatment, or other physical therapy in the next 8 weeks; and (6) voluntarily participating in this study and signing informed consent.

The patient exclusion criteria are as follows: (1) patients with nervous system disease, personality disorder, or alcohol and drug abuse in the past six months; (2) patients with schizophrenia spectrum disorder who were diagnosed or suspected; and (3) patients who were impulsive and excited and unable to cooperate with the study.

The mother inclusion criteria are as follows: 1) mother serves as the principal caregiver, ensuring that she resides with the child for a minimum of half of the week; and 2) willingness to participate in this study with their children, complete all intervention projects and evaluations, and sign informed consent.

Mother exclusion criteria: None.

Interventions

TRE treatment group

Participants assigned to this group will be administered TRE based on routine drug treatment. The intervention is conducted face-to-face in group settings,

with each group comprising 5–8 pairs. Four therapists who have obtained international certification as TRE providers and work in psychiatry with over three years of experience in providing TRE treatment for patients deliver the intervention. The TRE sessions are conducted in the group psychotherapy room at Beijing Huilongguan Hospital. It is essential that the room is clean, level, and free of any tables or chairs. Moreover, an adequate number of yoga mats and blankets must be arranged in the room for each intervention. The intervention encompasses an eight-week duration, characterized by a biweekly schedule wherein one session is allocated on a weekday and the alternate session takes place during the weekend. No one can enter the intervention course except for the therapists, research assistants, and participants.

Before the formal start of treatment, each group has an introduction to the intervention course. The total reaction time is approximately 45 min. The purpose is to familiarize team members with each other and introduce them to the content of the intervention course. The ultimate goal of TRE treatment is to teach participants to use organized progressive exercises to stimulate "self-induced therapeutic tremors. Each treatment activity consists of two parts [30]: 1) guided practice, which consists of six movements. 2) The exercise involving shaking with full excitation and therapeutic significance comprises one action. During the treatment process, the participants can self-regulate their tremor and emotional release levels, which is carried out under safety, comfort, and control abilities. From the beginning of the second TRE activity, before each intervention, participants will be asked to share their physical feelings, emotional changes, sleep, body pain, and gastrointestinal symptoms in the past few days. Before starting the study, the four TRE providers will be trained using the same training program by an expert in the TRE field. Simultaneously, we will record the entire intervention process and seek consent from the participants by signing the informed consent form. We will invite two experts in the TRE field to observe and supervise each recording and to provide feedback to the TRE providers of the trial to ensure strict adherence to the experimental plan throughout the experimental period. This study will evaluate the effectiveness of the interventions based on the actual number of interventions completed by participants. During the 8-week period of TRE treatment, participants are instructed not to undergo any form of psychological or physical therapy, apart from taking prescribed medication. However, after this period, there will no longer be any restrictions on treatment options.

The control group

In the control group, patients initially undergo an eight-week course of pharmacotherapy during which they are mandated to engage in regular monitoring, follow-up, and evaluation of the therapeutic outcomes from the medication regimen (timepoints: enrollment, at eight weeks post-initiation of drug treatment, and subsequently at three months; mothers are also required to complete corresponding assessments concurrently).

Upon the termination of the three-month follow-up phase, these patients are then offered an eight-week TRE group intervention that mirrors the protocol used in the experimental group. It is explained to the patients that the aim of this therapy is to teach them a psychological method designed to consolidate therapeutic benefits and deter relapse occurrences. Mothers are directed to adhere to and finish the eight-week TRE treatment alongside their children, and are further required to collaborate with their children in completing baseline assessments and subsequent evaluations following the eight-week TRE treatment period. This serves a dual purpose. Firstly, it allows all participants in the study to benefit from TRE. Secondly, it contributes additional research evidence regarding the efficacy of TRE. During the 8-week medication administration period at the onset of the study and the subsequent 8-week TRE intervention phase, patients in the control group are required to abstain from any form of non-pharmacological treatments.

Strategies to enhance adherence to intervention protocols

To enhance adherence to the intervention protocols, researchers have implemented several strategies. Firstly, regular weekly phone calls will be conducted with the parents of the patients to gather important information on medication treatment status, recent significant life events, and the utilization of non-pharmacological treatment. This ongoing communication is crucial for ensuring adherence to the study protocol and controlling for potential confounding variables during data analysis. Moreover, monetary compensation (e.g., 500 Chinese Yuan) will be provided to participants in both the TRE intervention group and the control group under specific conditions. For those in the TRE intervention group, the reward is contingent upon their adherence to completing the full 8-week TRE intervention program and successfully finishing the baseline as well as the post-treatment evaluations after 8 weeks of therapy. In parallel, for subjects within the control group, the incentive will be granted if they adhere to an 8-week pharmacological treatment regimen, attend weekly follow-up sessions, and similarly complete the baseline and post-treatment assessments at the 8-week mark.

Participants shedding criteria

(1) participants did not participate in the treatment of the intervention group for three consecutive or cumulative times, and (2) the patient's condition worsened, and they could not continue to participate in the study.

For participants who drop out for various reasons, it is advisable to encourage them to complete all assessments for outcome measures (as indicated in Tables 1, 2 and 3), if possible. Alternatively, a consultation can be conducted to explore the option of online assessments for questionnaire-based outcome measures.

Outcomes

The present study has three outcome categories.

The primary outcomes are a change in anxiety and depression symptoms in adolescents with emotional disorders and an improvement in maternal emotional levels. The measurement tools and evaluation times are listed in Table 1.

Secondary outcomes are changes in overall disease severity and self-assessed anxiety and depression symptoms in adolescents with emotional disorders; stress perception in mothers; and autonomic nervous function, sleep quality, rumination, cognitive function, and brain function in adolescents with emotional disorders and their mothers. The measurement tools and evaluation times are listed in Table 2.

Exploratory outcomes included changes in social anxiety, test anxiety, Internet addiction, hopelessness, self-injury, suicide, resilience, self-esteem, and alexithymia in adolescents with emotional disorders, and changes in self-esteem, psychological resilience, sense of despair, parent-child relationship, and parenting style of mothers. The measurement tools and evaluation times are listed in Table 3.

Sample size

Participants were randomly allocated to either the TRE intervention group or a control group. The effectiveness of the TRE intervention was examined using an independent two-sample t-test, with changes in depressive and anxiety symptoms serving as the independent variables.

A power analysis was conducted utilizing the G*Power software tool [66] to calculate the statistical power for detecting significant differences resulting from the TRE intervention. Based on similar intervention studies that reported a Cohen's d effect size of 0.69 [67], with parameters set at $\alpha = 0.05$ for the significance level and power $(1\text{-}\beta) = 0.95$ for ensuring adequate statistical power, the minimum required sample size was estimated to be 112 participants.

Considering a potential dropout rate of 20% for participants who discontinue before or during the treatment period, the adjusted minimum sample size per group would amount to 70 cases. Consequently, the total combined sample size for both groups comprises 140 pairs of adolescents diagnosed with emotional disorders and their respective mothers.

Table 1 The primary outcome, target, instruments, and evaluation time point

The primary outcome	Target	Instruments	Time Point	Description
depression and anxiety symptoms	patients	HAMD, HAMA	Baseline, 8weeks, 3 months	The Hamilton Depression Scale (HAMD) [31] and Hamilton Anxiety Rating Scale (HAMA) [32] are the most used scales in clinical assessment of depressive and anxiety symptoms, respectively. Doctors evaluate the symptoms of patients based on the content of the scales. Both the scales adopt a 5-level scoring method of 0–4 points. The higher the total scores on the scales, the more severe the individual's emotional symptoms are.
emotional level	mothers	PHQ-9, GAD-7	Baseline, 8weeks, 3 months	The Patient Health Questionnaire-9 (PHQ-9) includes 9 items, mainly evaluating the subjects' decreased interest and mood within the past 2 weeks. Each item is scored on a 0–3 to 4-level scale, with a total score of 0–27 points. The higher the score, the more severe the individual's depressive symptoms are [33]. The Generalized Anxiety Disorder-7 (GAD-7) Scale consists of seven symptom items. This scale is used for screening symptoms of generalized anxiety disorder and evaluating the severity of symptoms. The total score is 0–21 points and a higher total score indicates a more severe symptom [34].

Table 2 The secondary outcome, target, instruments, and evaluation time point

The secondary outcome	Target	Instruments	Time Point	Description
Clinical global impression	patients	CGI-S	Baseline, 8weeks, 3 months	The Clinical Global Impression Scale (CGI-S) is a simple instrument that evaluates the overall severity of mental disorders. This scale can be used to rate the effectiveness of a particular treatment [35].
Self-rated depressive symptoms	patients	SDS	Baseline, 8weeks, 3 months	The self-rating depression scale (SDS) [36] is used to evaluate the participants' depression status and severity according to their feelings for one week. It includes 20 items. It is suitable for people of all ages. The lower the total score obtained by the subjects, the better their situation.
Self-rated anxiety symptoms	patients	SAS	Baseline, 8weeks, 3 months	The self-rating anxiety scale (SAS) [37] evaluates the participants' anxiety status with an interval of one week. It is suitable for people of all ages, and it contains 20 test items and 4 grade scores.
Test anxiety	patients	TAS	Baseline, 8weeks, 3 months	Test anxiety is measured using the Test Anxiety Scale (TAS) [38], which consists of 37 items (0 = no, 1 = yes), where higher scores indicate higher levels of test anxiety (scores range from 0 to 37). The Chinese version of TAS was adapted by Caikang Wang [39], and the reliability and validity were satisfying to high school students [40].
Rumination thinking	Patients mothers	RRS	Baseline, 8weeks, 3 months	The Ruminative Response Scale (RRS) [41] measures the individual's Ruminative thinking, which is a way of thinking that repeatedly focuses on one's own negative emotions and corresponding events. It is a reaction mode of maladaption. The scale consists of 22 items. The items on this scale are scored using a 1–4 level scoring method, and a higher total score indicates a more severe tendency towards rumination.
autonomic nervous system function	Patients mothers	HRV	Baseline, 8weeks, 3 months, before and after a single intervention	The autonomic nervous system is one of the body's major systems for maintaining homeostasis; individuals are sympathetic-predominant when facing change or stress, whereas parasympathetic activity increases during resting and relaxation [42]. Heart rate variability (HRV) is the most used and convenient measuring tool of autonomic function [43, 44]. Several types of HRV indices exist, with respiratory sinus arrhythmia (RSA), High-frequency power (HF), and root mean square of successive differences (RMSSD) being parasympathetic-specific indices [43, 45], especially RSA.
brain function	Patients mothers	EEG, fMRI	Baseline, 8weeks, 3months	The fMRI data of the resting state and the EEG signals in the resting state and during the cognitive tasks such as cognitive control [46], effort motivation [47], logical reasoning (original paradigm), and emotional regulation flexibility [48] of subjects were collected to investigate the impact of TRE on individual brain function.
Cortisol reactivity	Patients mothers	saliva cortisol	Baseline, 8weeks, 3months	Salivary cortisol has been the central factor in psychoneuroendocrinological stress, and changes in neuroendocrine regulation and cortisol reactivity can be used to evaluate the effects of behavioral interventions in real-life circumstances [49].
stress perception	mothers	PSS-10	Baseline, 8weeks, 3 months	The Perceived Stress Scale-10 (PSS-10) measures the degree to which one perceives aspects of one's life as uncontrollable, unpredictable, and overloading [50]. Participants are asked to respond to each item on a 5-point Likert scale ranging from 0 (never) to 4 (very often), indicating how often they have felt or thought a certain way within the past month. Scores can range from 0 to 40, with higher composite scores indicative of greater perceived stress.

Table 2 (continued)

The secondary outcome	Target	Instruments	Time Point	Description
Insomnia symptoms Sleep Quality	patients	PSQI	Baseline, 8weeks, 3 months	Pittsburgh Sleep Quality Index (PSQI) [51] is a self-rated questionnaire that assesses seven components of sleep quality during the previous month: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction. A total of 19 items were rated on a scale scored from 0 (not during the past month) to 3 (≥ 3 times a week). Scores can range from 0–21 and a global score > 5 indicates poor sleep quality. This scale has good reliability and validity in the Chinese adolescent population [52].
	mothers	ISI	Baseline, 8weeks, 3 months	The Insomnia Severity Index (ISI) is mainly used to evaluate the sleep quality, severity of insomnia, and its impact on the daytime function of subjects. The scale consists of 7 items, using the Likert 5-level scoring method, with each item scoring 0–4 points and a total score of 0–28 points. The higher the score, the more severe the insomnia is [53].
somatization symptom	Patients mothers	SESQ	before and after a single intervention	We designed a somatization and emotional symptoms questionnaire (SESQ) with 13 items with reference to the somatization symptom scale [54] to evaluate the improvement of the corresponding parts brought about by a single TRE treatment.

Participant recruitment

To ensure an adequate sample size for this study, a weekly recruitment process is in place involving four physicians from the Adolescents Emotional Disorder Clinic. These doctors will systematically identify and recommend eligible participants during their clinic appointments. Moreover, patients enrolled in this study are entitled to the right of prioritized access to additional appointments at the Adolescent Mood Disorders Outpatient Clinic.

Two dedicated research personnel will conduct meticulous screenings of these referrals to verify their suitability. They will thoroughly explain the research procedures, obtain signed informed consent, and register those who meet the inclusion criteria. The allocation of participants into either the TRE intervention group or the control group will be managed by three graduate students actively participating in this project. They will utilize a random number table to impartially assign participants to groups and subsequently communicate the group assignments. The students will also provide detailed information about the scheduling, location, and procedural aspects pertaining to the baseline measurements, the 8-week treatment endpoint assessment, and the follow-up evaluation at the 3-month mark (refer to Fig. 1). Moreover, these graduate students are responsible for maintaining regular contact with the participants attending each TRE session. They will notify participants about the specific session times and deliver any other pertinent details required for their participation and adherence to the study protocol.

Randomization and allocation

An independent physician unaffiliated with participant enrollment, experimental intervention, data collection, or data analysis will assume the specific responsibility of generating the random allocation sequence through block randomization using SPSS software. This study will systematically produce multiple random number tables as per the advancement of participant recruitment. The generated random number table will be securely stored in three consecutively sealed envelopes managed by three distinct graduate students who have no involvement in any other aspects of the research.

Upon the conclusion of enrolling each batch of participants, the researchers will conduct an unblinding process. To achieve this, it is mandatory that all three envelope custodians jointly and simultaneously unseal their respective envelopes and use an on-site drawing procedure to determine which random number table to apply at each instance. In the event that one or more envelopes exhibit damaged seals, a written explanation must be furnished; otherwise, such a condition would suggest potential leakage of the grouping information.

Participants will be independently and randomly allocated to either the TRE intervention group or the control group, with allocation concealed from the TRE intervention providers, and the experimenters engaged in collecting the experimental data.

A schedule of enrollment, randomization and allocation, interventions, and assessments for the study is found in Table 4.

Table 3 The exploratory outcome, target, instruments, and evaluation time point

The exploratory outcome	Target	Instruments	Time Point	Description
Resilience	Patients	RSCA	Baseline, 8weeks, 3 months	The Resilience Scale for Chinese Adolescents (RSCA) will be administered to assess the resilience of the subjects. RSCA contains 27 items and measures individual resilience from 5 dimensions: emotion regulation, family support, interpersonal assistance, goal concentration, and positive perception. The answer to each item was coded on a 5-point scale from 1 (totally disagree) to 5 (totally agree), giving a combined score between 27 and 135. A higher score represents better resilience in general. This scale has good internal consistency (Cronbach's α = 0.85) [55].
	mothers	CD-RISC-10	Baseline, 8weeks, 3 months	The 10-item Connor-Davidson Resilience Scale (CD-RISC-10) [56] will be administered to assess an individual's metal resilience during the past month. The answer to each item was coded on a 5-point Likert scale from 0 (not true at all) to 4 (true nearly all the time). The item ratings are summed to produce a combined score ranging from 0–40, with higher values implying a greater resilience capability. The Chinese version of the CD-RISC-10 employed in the present study has been confirmed to have good internal consistency (Cronbach's α = 0.851–0.910) and excellent structure validity [57, 58].
Alexithymia	patients	TAS	Baseline, 8weeks, 3 months	The Toronto Alexithymia Scale (TAS) is divided into three dimensions, namely emotional recognition difficulty (7 items), difficulty in emotional expression (5 items), and extroverted thinking (8 items). Emotional recognition difficulty refers to the difficulty an individual has in identifying their own or others' emotions and emotions; emotional expression difficulty refers to an individual's lack of the ability and motivation to accurately describe their emotions through language; and extrovert thinking refers to a decrease in symbolic thinking and imaginative activities, resulting in a lack of attention to the inner world. The scale adopts the Likert 5-level scoring method, and the higher the score, the more severe the individual's alexithymia is [59].
self-esteem	Patients mothers	RSES	Baseline, 8weeks, 3 months	The Ronsenberg self-esteem scale (RSES) consists of 10 questions, using a scoring method of 1 point (very inconsistent) to 4 points (very consistent). Among them, 5 questions (3, 5, 8, 9, 10) are reverse-scoring questions, and a higher score indicates a higher level of self-esteem [60].
Hopelessness	Patients mothers	BHS	Baseline, 8weeks, 3months	The Beck Hopelessness Scale (BHS) consists of 20 items, including three factors: feelings towards the future, loss of motivation, and expectations for the future. This scale uses a score of 1 to 0 (yes/no). The higher the total score, the higher the degree of individual despair [61].
The usage of online games	patients	IGDS	Baseline, 8weeks, 3months	The internet gaming disorder scale (IGDS) measures individuals' addiction to online games, with a total of nine items. Yes = 1 point and No = 0 point. A total score greater than or equal to 5 indicates that an individual may have online gaming barriers [62].
non-suicidal self-injury	patients	FASM	Baseline, 8weeks, 3 months	Functional Assessment of Self-Mutilation (FASM) is used to evaluate whether individuals have engaged in self-injurious behavior without suicidal motivation within the past year, as well as the types and frequency of non-suicidal self-injury (NSSI) behavior occurrences. Asking about any behaviors without suicidal motivation, including intentionally cutting the skin, pulling one's hair, intentionally the wound to hinder healing, etc., and assessing the frequency of self-injury behaviors, any self-injurious behavior with a frequency of ≥ 1 occurrence is considered NSSI behavior [63].

Table 3 (continued)

The exploratory outcome	Target	Instruments	Time Point	Description
Parenting style	mothers	PSDQ	Baseline, 8weeks, 3 months	The Chinese version of the Parenting Styles and Dimensions Questionnaire (PSDQ), with 62 items evaluated using 5 points, was used by a father or mother to evaluate his or her spouse/partner's attitude to the frequency of some children's behaviors, aiming to mainly understand parenting styles. Three parenting styles—authoritative parenting, authoritarian parenting, and permissive parenting—were further divided into 11 factors (dimensions). [64].
Mother-child relationship quality	mothers	NRI	Baseline, 8weeks, 3 months	The Chinese version of the Network of Relationships Inventory (NRI) measures the quality of mother-child relationships and friendships. It consists of 15 items, including five dimensions: companionship, help, emotional support, intimacy, and conflict. The scale was scored at 5 points. The average score of the first four dimensions is used as an indicator of the quality of the parent-child relationship. The higher the score, the higher the quality of the parent-child relationship. After the conversion of the reverse questions, the average score of the 15 items was calculated as the friendship quality score. The higher the score, the higher the friendship quality [65].

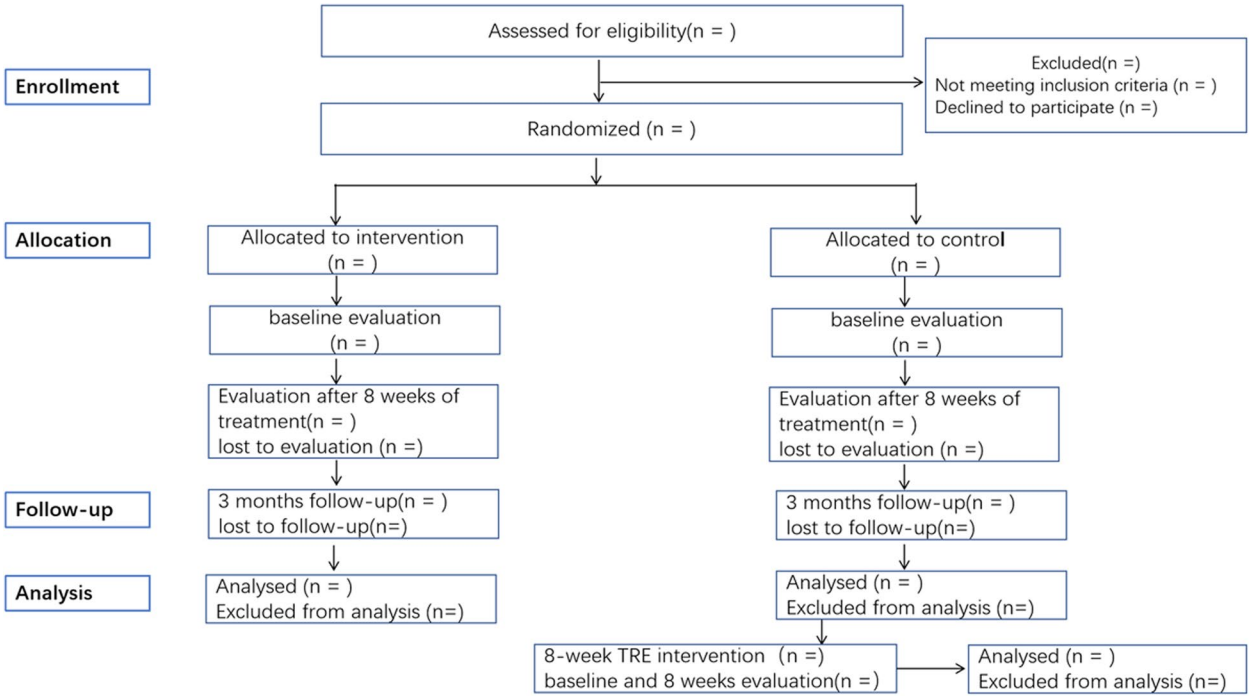

Fig. 1 A Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the study

Data management

To ensure data integrity and confidentiality, the study will implement a web-based data collection system to facilitate and streamline the administration of questionnaires throughout the research process. This system will enforce a comprehensive set of online validation checks coupled with supplementary manual quality control procedures to guarantee accurate and reliable questionnaire data entry. Collected behavioral data, physiological metrics such as heart rate, saliva samples, video documentation, EEG recordings, and MRI data will be securely uploaded to a dedicated, specialized data storage and processing platform managed by the research team. To oversee this process, two dedicated researchers will be appointed to

Table 4 Schedule of enrollment, interventions, and assessments

	Study period[a]							
Time-point	2024 /2025 March-May	2024 /2025 June	2024 /2025 July	2024 /2025 August	2024 /2025 September	2024 /2025 October	2024 /2025 November	2024 /2025 December
Enrollment								
Eligibility screen	×							
Informed consent	×							
Allocation	×							
Intervention								
Control group				×	×	×	×	×
Intervention group	×	×	×					
Assessments								
Baseline	×							
After 8 weeks	×	×	×			×	×	×
3- month follow-up	×	×	×	×	×	×		

[a] We intend to complete the entire research endeavor within a two-year period, with the planned enrollment, intervention, assessment, and follow-up of 70 pairs of participants in each of the years 2024 and 2025

handle the uploading, storage, and verification of the completeness and validity of all collected data. Access to these stored digital records is stringently limited to authorized team members only.

Documents containing participants' personal identification details, including informed consent forms, are secured in locked filing cabinets within a protected environment. In compliance with retention policies, two years following the end of the study, all audio and video recordings will be permanently deleted and destroyed. Conversely, other non-identifiable documentation and data will be retained for archival purposes for at least five years after the trial's completion, adhering to regulatory guidelines and ensuring potential future reanalysis or audits.

Quality control

In this study, all participating researchers are required to undergo comprehensive technical and quality control training prior to the commencement of the project. This training encompasses understanding the study protocol, informed consent procedures, standardized operating guidelines for data collection, and the specific storage protocols applicable to saliva samples. The clinical symptoms of patients are assessed blindly by two uniformly trained postgraduate clinicians using standardized assessment methods. Throughout the course of the study, a minimum of 20% of the patient cohort will have their clinical symptoms evaluated by both assessors to validate the consistency and accuracy of symptom assessments. Researchers responsible for EEG and fMRI data processing must perform preliminary data preprocessing after acquiring data from every batch of at least 10 cases to identify any potential issues within the data acquisition process. Moreover, personnel in charge of collecting and recording heart rate and skin conductance data are mandated to verify the quality of these data each time an intervention is completed to detect any possible equipment malfunctions or errors.

Statistical analysis

In this study, two statistical analysis methods, intention-to-treat (ITT) and per-protocol (PP), will be simultaneously applied. The ITT analysis set will include all patients who have received at least one TRE treatment and at least one post-baseline evaluation of the main efficacy indicators. PP will analyze the main and secondary efficacy indicators for all patients who followed the study protocol and completed all evaluations. Discussing and explaining the differences between the results of the two analyses helps explain the intervention effect of TRE. When the conclusions of the two analytical methods are consistent, they better explain the credibility of the research results. Multiple imputation and chained-equations methods will be adopted to impute the missing values of the outcomes if participants are lost to follow-up at the end of this study. The variables used to impute the missing values of each outcome include the participants' available values, such as baseline values, data at the end of the intervention, and other variables associated with this outcome.

The primary and secondary outcomes will be analyzed using repeated-measures ANOVA in a general linear model. If the age, education level, disease course, etc., of

the participants do not match between the two groups (treatment and control groups) (with significant intergroup differences), variables that may affect the results will be included as control variables in the repeated measures ANOVA. Correlation and logistic regression will be used to analyze the characteristics related to efficacy. A paired sample t-test will be used to verify the effectiveness of the control group receiving 8 weeks of TRE treatment after 3 months of follow-up. We will use R software to analyze the physiological, psychological, and cognitive behavioral data.

Analysis of saliva and heart rate data

Stress hormone cortisol levels will be quantitatively detected in the saliva samples of patients using the internationally widely used Roche Cobas analysis system and its universal reagent, the latest electrochemiluminescence immunoassay (ECLIA), and will then be integrated with other physiological and psychological indicators, and multivariate statistical analysis methods will be performed. Electrocardiogram and respiratory data will be imported into intelligent HRV 3.0.9 (MindWare HRV 3.0.9) to calculate the RSA values and respiratory rate.

Functional and structural data analysis pipeline

Functional brain images will be preprocessed using statistical parametric mapping (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) based on the MATLAB software platform (version 8.1; MathWorks Inc., Natick, MA, USA) or preprocessed with fmriprep. The first five volumes of the functional images will be discarded to ensure signal equilibrium and participant adaptation to the scanning noise. The remaining images will be corrected for slice acquisition timing and realigned for head-motion correction. Subsequently, functional images will be co-registered to each participant's gray matter image, segmented from the corresponding high-resolution T1-weighted image, spatially normalized into a common stereotactic Montreal Neurological Institute (MNI) space, and resampled into 2 mm isotropic voxels. Finally, the images will be smoothed using an isotropic 3D Gaussian kernel with a 6 mm full-width half-maximum (FWHM).

The subsequent network analysis was hypothesis-driven, with predefined regions of interest (ROI) targeting depression and anxiety.

Statistical Parametric Mapping 12 (SPM12, version 7771, https://www.fil.ion.ucl.ac.uk/spm) and Computation Anatomy Toolbox 12 (CAT12, version 1932, https://neuro-jena.github.io/cat) or FreeSurfer will be used to process the T1-weighted images of all participants, reconstruct the central surface of the brain, and estimate the thickness of the cerebral cortex. After obtaining the individual thickness map, the images will be resampled into the common coordinate system (fsaverage) and smoothed with a 12 mm full width at half maximum. Specifically, T1-weighted images will be preprocessed by denoising, spatial registration, bias correction, and skull stripping. The images will be then segmented into gray matter, white matter, and cerebrospinal fluid.

Structural images will be submitted for hypothesis-driven ROI analysis targeting depression and anxiety.

The statistical results will be corrected through multiple comparisons, using either family-wise error correction or false discovery rate correction.

EEG data analysis pipeline

The EEG data will be processed using EEGLAB [68], an open-source toolbox that runs in MATLAB. The specific analysis methods used in this study include spectral, time-frequency, and brain network analyses.

Exploratory analysis

Beyond the primary focus on the ameliorative effects of TRE therapy on adolescent anxiety and depressive symptoms, this study also meticulously investigates the impact of TRE intervention on maternal emotional states. Moreover, it endeavors to explore potential concomitant changes in the dynamics of parent-child relationships and parenting style, and assesses the extent to which such transformations might influence the improvement in adolescents' emotional disorders.

Data monitoring

The Science and Technology Department at Beijing Huilongguan Hospital assumes the responsibility of project governance, implementing rigorous oversight throughout the development phase. The Management Committee carries out a comprehensive progress assessment biannually to evaluate study progression. This encompasses data aggregation, problem identification, strategy formulation, resolution of practical challenges, and ensuring strict adherence to the project's pre-established timeline and protocol.

Participants and the research team are tasked with documenting any adverse events encountered during the study. Notably, severe adverse events are promptly reported to the Ethics Committee of Beijing Huilongguan Hospital. It is essential to highlight that both the Science and Technology Department and the Ethics Committee maintain independence from the investigators and sponsors involved in the study.The Science and Technology Department refrains from disclosing individual analysis results directly to the project team. However, it retains the authority to report these findings to the Ethics Committee should there be concerns regarding patient safety.

In cases where the Ethics Committee identifies potential harm to patients, they reserve the right to recommend termination of the study.

Discussion

This study will be the first RCT to evaluate the effect of the TRE mother-child intervention model on improving the clinical symptoms of adolescent patients with emotional disorders. If successful, we will find a simple, effective, and easily disseminated mind-body therapy to improve the clinical treatment of adolescent emotional disorders.

In all psychotherapy models, taking the body into account can improve cognition, emotion, and behavior, and the body is important for all psychotherapy models as it can improve cognition, emotion, and behavior and shorten the treatment time, which will bring positive effects and changes in all treatment models [69]. As a type of psychosomatic therapy, TRE provides the possibility that it can be used as a separate psychotherapy method and can also be integrated into any other psychotherapy method to improve its treatment efficiency and effect. In the acute phase of anxiety and depression, many psychotherapy methods, such as eye movement desensitization reprocessing (EMDR), are relatively difficult to implement. However, as TRE does not rely on excessive language communication and conversation, it can also play a therapeutic role even in the acute phase of the disease. In addition, because TRE is simple, fast, and easy to learn, it can be used not only as a treatment for conventional adolescent emotional disorders but also as a group or online intervention in large public crisis events, such as large-scale infectious diseases, earthquakes, and floods. In conclusion, TRE has great potential for improving anxiety and depression in adolescents.

Currently, the mechanisms underlying TRE have not been elucidated. TRE was originally designed for stress and post-traumatic stress disorder (PTSD) based on animal studies of neurogenic tremors [22–26]. This study attempts to explore the neuropsychological and physiological mechanisms of TRE in improving adolescent emotional disorders using physiological, EEG, and fMRI techniques based on the theory of multiple vagus nerves [27]. We assume that regardless of whether the participant is in a state of anxiety dominated by the sympathetic nervous system or a state of depression dominated by the dorsal vagus nerve, TRE can induce a state of calm dominated by the ventral vagus nerve. The results of this study will promote our understanding of the mechanisms underlying TRE. Meanwhile, considering the impact of the family environment, especially the role of the mother as an important caregiver, on the child's emotional state [13–21], we adopted the TRE parent-child intervention model to verify the intervention effect and the correlated mechanism.

Limitations

The control group adopted a pure-medication experimental design to ensure the convenient implementation of this trial. Based on this experimental design, we could only explore the synergistic effects of TRE in drug therapy. We could not explore the advantages and disadvantages of TRE compared with other treatment methods. Further validation and discussion of the relevant issues should be conducted in future studies.

Conclusion

In conclusion, this RCT is the inaugural study to scrutinize the clinical effects of TRE in ameliorating emotional disorders among adolescents, concurrently examining the concomitant neurophysiological and psychological underpinnings. The research uniquely incorporates an assessment of the maternal emotional state's influence on their offspring's emotional health, with a focus on elucidating the pertinent mechanisms. The results from this investigation hold substantial promise for significantly influencing adolescent emotional well-being and reshaping conventional healthcare practices.

Trial status

The present investigation has been granted all required regulatory clearances, and the current protocol version in effect is Version 1.3, dated November 1, 2023. Recruitment began on March 15, 2024, with an anticipated completion of subject enrollment by December 31, 2025.

Abbreviations

TRE	Tension and trauma release exercise
RCT	randomized controlled trial
fMRI	Functional Magnetic Resonance Imaging
EEG	electroencephalogram
HAMD	Hamilton Depression Scale
HAMA	the Hamilton Anxiety Rating Scale
PHQ-9	The Patient Health Questionnaire – 9
GAD-7	The Generalized Anxiety Disorder – 7 Scale
CGI-S	The Clinical Global Impression Scale
SDS	Self-rating depression scale
SAS	Self-rating anxiety scale
TAS	the Test Anxiety Scale
RRS	The Ruminative Response Scale
HRV	Heart rate variability
RSA	respiratory sinus arrhythmia
HF	High-frequency power
RMSSD	root mean square of successive differences
PSS-10	The Perceived stress Scale-10
PSQI	Pittsburgh Sleep Quality Index (PSQI)
ISI	The Insomnia Severity Index
SESQ	somatization and emotional symptoms questionnaire
IGDS	The internet gaming disorder scale
RSCA	The Resilience Scale for Chinese Adolescents
CD-RISC-10	The 10-item Connor-Davidson Resilience Scale
TAS	The Toronto Alexithymia Scale
FASM	Functional Assessment of Self-Mutilation

RES	Ronsenberg self-esteem scale
BHS	The Beck Hopelessness Scale
PSDQ	the Chinese version of the Parenting Styles and Dimensions Questionnaire
NRI	the Chinese version of the Network of Relationships Inventory
ANOVA	analysis of variance
ITT	Intention-to-treat (ITT) analysis
PP	Per-protocol analysis
ECLIA	electrochemiluminescence immunoassay
MNI	Montreal Neurological Institute
SPM12	statistical parametric mapping 12
FWHM	full-width half-maximum
ROI	region of interest
CAT12	Computation Anatomy Toolbox 12
EMDR	eye movement desensitization reprocessing
PTSD	post-traumatic stress disorder

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12906-024-04650-8.

Additional file 1. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*.

Acknowledgements
We would like to thank Editage (www.editage.cn) for English language editing.

Authors' contributions
YLZ and JHX drafted the manuscript. YLZ, JHX, JZ, JQS, NY, HZF, ZD, and SPT contributed to research design, protocol development, and approved the final manuscript. SPT and YLZ obtained the funding and made the decision to submit the report for publication.

Funding
This research was supported by Beijing High-Level Public Health Technical Talent Development Project (Discipline Leader – 02–03, Academic Backbones – 02–09), Beijing Natural Science Foundation Grant (No. 7202072), Beijing Municipal Science & Technology Commission Grant (Z191100006619104), and Beijing Hospitals Authority' Ascent Plan (DFL20192001).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The research protocol was approved by the Ethics Committees of Beijing Huilongguan Hospital (approval number: 2019-39-Scientific Research-revised version 2, Date: December 21, 2023). Important protocol modifications of the protocol will be reported to the committee, trial registries, and the journals. This study protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist and the TIDieR checklist. It is pre-registered at the Trial Register under registration number ChiCTR2100044553 (http://www.chictr.org.cn/index.aspx). Informed consent will be obtained from the adolescent participants, their parents and legally authorized representatives in this study. Participants in the project can get feedback reports of all test results and they were compensated for their participation. De-identified data will be used for statistical analysis and the results of this trial will be disseminated through publications in peer-reviewed journals and academic conferences.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 19 March 2024 Accepted: 20 September 2024
Published online: 21 November 2024

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