










# BMJ Open Emotional freedom technique versus written exposure therapy versus waiting list for post-traumatic stress disorder: protocol for a randomised clinical MRI study

Yujin Choi <sup>1</sup>, Yunna Kim <sup>1,2,3</sup>, Sunyoung Choi <sup>1</sup>, Young-Eun Choi <sup>4</sup>,  
Ojin Kwon <sup>1</sup>, Do-Hyung Kwon <sup>2,3,5</sup>, Seung-Ho Lee <sup>2,3,5</sup>,  
Seung-Hun Cho <sup>2,3</sup>, Hyungjun Kim <sup>1</sup>

**To cite:** Choi Y, Kim Y, Choi S, *et al.* Emotional freedom technique versus written exposure therapy versus waiting list for post-traumatic stress disorder: protocol for a randomised clinical MRI study. *BMJ Open* 2023;**13**:e070389. doi:10.1136/bmjopen-2022-070389

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-070389>).

YC and YK contributed equally.

YC and YK are joint first authors.

Received 21 November 2022  
Accepted 31 May 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

**Correspondence to**  
Dr Hyungjun Kim;  
[heyjoon73@kiom.re.kr](mailto:heyjoon73@kiom.re.kr) and  
Prof Seung-Hun Cho;  
[chosh@khmc.or.kr](mailto:chosh@khmc.or.kr)

## ABSTRACT

**Introduction** The emotional freedom technique (EFT) is an acupuncture-based psychotherapy that combines tapping on acupoints with cognitive reframing. EFT has been previously shown to have potential for treating post-traumatic stress disorder (PTSD). However, further clinical evidence and underlying mechanisms of EFT are yet to be fully explored. This proposed clinical trial aims to examine the effect of EFT on patients with PTSD compared with the waitlist (WL) and active controls.

**Methods and analysis** This study was designed as a randomised, assessor-blinded, three-arm clinical MRI study. A total of 120 eligible patients with PTSD will be recruited and randomised into EFT, written exposure therapy (WET) or WL groups. EFT and WET will be applied once a week for 5 weeks. For patients in the WL group, EFT will be performed after 12 weeks. PTSD symptoms, depression, anxiety, somatic symptoms and quality of life will be evaluated. Assessments will be conducted at baseline (week 0), post-treatment (week 6) and follow-up (week 12). Structural and functional brain images and recording videos of facial expressions to emotional stimuli will be obtained before and after treatment. Sixty participants without lifetime traumatic experiences will be enrolled as healthy controls. The primary objective of the study is to compare the change from baseline in the Clinician-Administered PTSD Scale after treatment (week 6) between EFT and WL groups and between EFT and WET groups.

**Ethics and dissemination** Ethical approval was obtained from the Institutional Review Board of the Kyung Hee University Korean Medicine Hospital. The research findings will be shared at national and international conferences and will be published in peer-reviewed journals.

**Trial registration number** Clinical Research Information Service KCT0007360 <https://cris.nih.go.kr/cris/search/detailSearch.do/21974>.

## INTRODUCTION

### Background and rationale

Post-traumatic stress disorder (PTSD) is a disorder that occurs after exposure to traumatic events such as death, serious injury or sexual violence. These symptoms include

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This will be the first randomised controlled trial to evaluate the emotional freedom techniques for patients with post-traumatic stress disorder compared with the waitlist controls and written exposure therapy.
- ⇒ This study will collect a wide range of data, including an assessment of clinical symptoms, questionnaires, recording videos of facial expressions to emotional stimuli and structural and functional MRI, to investigate the underlying neurological mechanisms.
- ⇒ Additionally, baseline characteristics and changes after treatment of patients with post-traumatic stress disorder will be examined in comparison with healthy controls without traumatic experiences.
- ⇒ Because of the nature of psychotherapy interventions, blinding of participants and clinicians is not feasible. Only assessors will be blinded.

repetitive and painful memories of the traumatic event, intrusive symptoms such as dreams, persistent avoidance of stimuli associated with the traumatic event, negative changes in cognition and emotion associated with the traumatic event and pronounced arousal and responsiveness associated with the traumatic event.<sup>1</sup> According to the 2021 National Mental Health Survey conducted in Korea, the lifetime prevalence of PTSD is 1.5% (1.3% for men, 1.6% for women), and the annual prevalence is 0.3% (0.2% for men, 0.3% for women).<sup>2</sup> PTSD often involves depressive, substance use and anxiety disorders simultaneously.<sup>3</sup>

Trauma-focused psychotherapy is the first-line treatment for PTSD.<sup>4 5</sup> Strongly recommended treatments for PTSD include cognitive-behavioural therapy, cognitive processing therapy, cognitive therapy and

prolonged exposure therapy.<sup>6</sup> Among the various psychotherapies for PTSD, exposure therapy is one of the most studied and well-established treatments.<sup>7</sup> However, trauma-focused exposure therapy has a high dropout rate. A meta-analysis reported that 36% of patients who received trauma-specific treatment dropped out in clinical trials, and a dropout rate of 30% in real-world practice in the United States Veterans Health Administration Prolonged Exposure Training Program was similar.<sup>8 9</sup> Two major reasons why veterans dropped out of trauma-focused psychotherapy were a lack of buy-in to treatment and too stressful course, which were mostly related to uncomfortable exposure to the past.<sup>10</sup> Thus, effective therapy with low drop-out rate is required in patients with PTSD.

The emotional freedom technique (EFT) is a acupuncture-based psychotherapy that combines tapping on acupoints and exposure to cognitive reframing.<sup>11</sup> Recently, a systematic review summarised that EFT treatment is effective for psychological and physiological conditions.<sup>12</sup> In reviews on the effect of EFT on patients who experienced traumatic events and were at a high risk of PTSD, 4–10 EFT sessions were effective for PTSD symptoms and were proven to be safe.<sup>13 14</sup> Two randomised controlled trials reported that EFT is potentially effective in improving PTSD symptoms in patients who are diagnosed as PTSD.<sup>15 16</sup> Karatrias *et al* reported that after 8 weeks of EFT treatment, PTSD symptom levels decreased and persisted after a 3-month follow-up, which was not significantly different from those of eye movement desensitisation and reprocessing (EMDR) treatment.<sup>15</sup> In another study, Church *et al* reported that a 4-week EFT treatment reduced PTSD symptom levels and psychological distress compared with the standard care wait list.<sup>16</sup>

According to the assessment by the Korean Medicine Procedure Expert Assessment Committee on 29 April 2021, EFT using acupuncture point tapping was determined as a safe and non-invasive method for symptom improvement in PTSD compared with palliative treatment. However, it was pointed out that there is limited evidence and follow-up data of EFT in PTSD when compared with cognitive-behavioural therapy and EMDR, which are currently recommended as psychotherapies for the treatment of PTSD in textbooks and guidelines.<sup>17</sup> The aforementioned randomised controlled trials have limitations, in which both included a small number of participants (46 and 59, respectively) and used symptom-related parameters to assess efficacy.<sup>15 16</sup> Therefore, further studies with a sufficient number of participants are necessary to examine the effectiveness of EFT in PTSD.

Before planning this trial, we conducted a feasibility trial of a five-session EFT in 30 patients diagnosed with PTSD. In this before-and-after study, PTSD symptoms of participants generally improved after the EFT intervention, compliance with attending EFT sessions was high, and the dropout rate was low. In this trial, we selected WET<sup>18 19</sup> as an active control, as it is a short-term therapy, that is adequate for comparison with five-session of

EFT. In addition, the waiting list (WL) was included as another control group, and this trial will be planned with a three-arm parallel design.

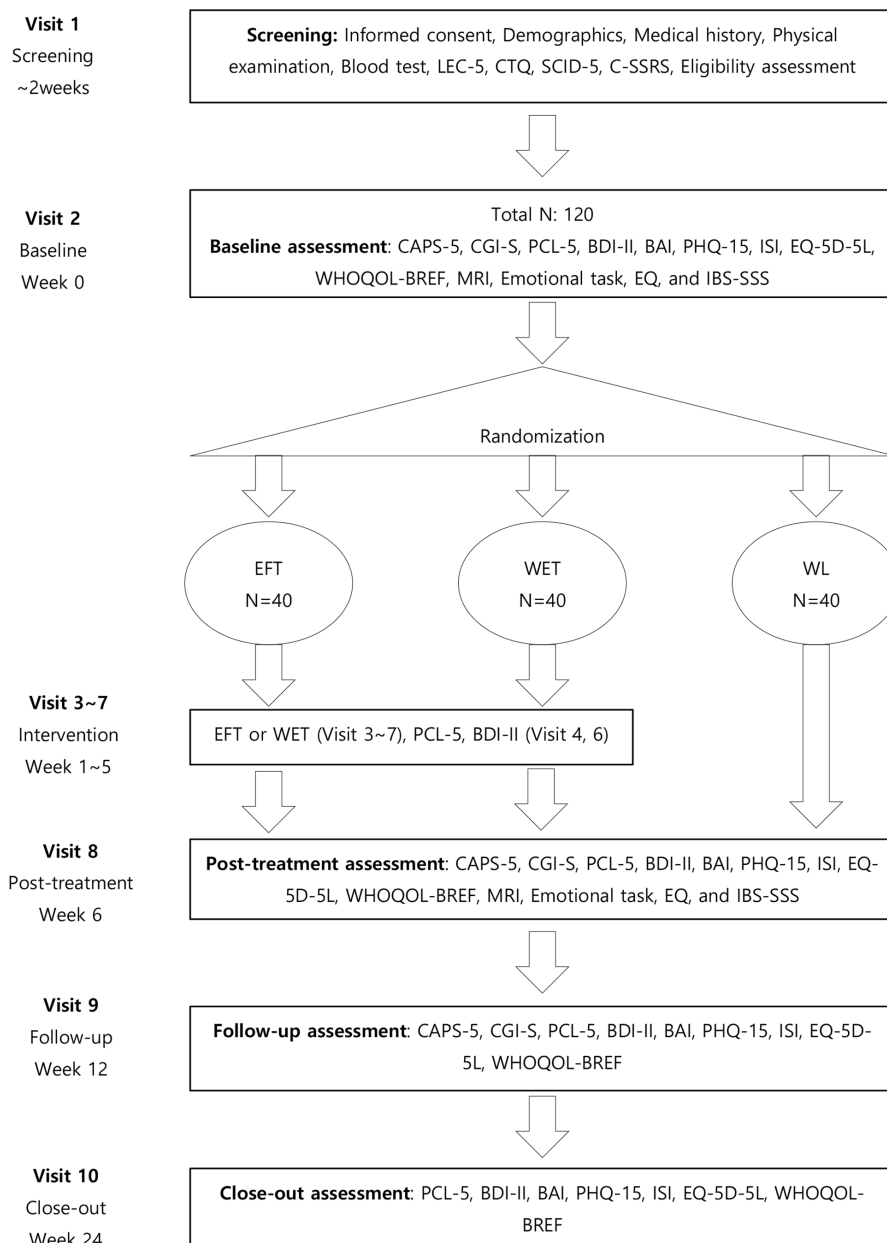
A critical limitation is that there are no well-established biomarkers related to either the diagnosis or prognosis of PTSD.<sup>20</sup> Exploring the underlying mechanisms and seeking predictive factors for the response to PTSD treatments are also important, in addition to simply evaluating the efficacy of the treatment.<sup>21</sup> To meet such demands, attempts have been made to identify biomarkers for PTSD using various methodologies.<sup>22</sup> In comparison with non-trauma controls, patients with PTSD showed left amygdala hyperactivation, and in comparison with non-trauma controls and trauma-exposed controls, patients with PTSD exhibited diminished activation in the medial prefrontal cortex.<sup>23</sup> In a longitudinal functional MRI study, higher dorsal anterior cingulate cortex, insula and amygdala activations in response to negative pictures were predictors of poor response to PTSD treatment.<sup>21</sup> In the present study, structural and functional brain images will be obtained before and after the intervention to explore the underlying mechanisms.

## Objectives

The primary objectives are to evaluate the effect of EFT on PTSD symptoms compared with the WL and to evaluate the non-inferiority of EFT on PTSD symptoms compared with WET. The change from baseline in the Clinician-Administered PTSD Scale (CAPS-5) after the intervention will be compared between the EFT and WL groups and between the EFT and WET groups.

The secondary objectives are to evaluate the effect of EFT compared with WL and WET based on the proportion of participants achieving criteria-based remission of PTSD and symptom-based remission of PTSD after the intervention. Additionally, self-reported PTSD symptoms will be evaluated using the PTSD Checklist-5 (PCL-5), and depression and anxiety will be assessed using the Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI). Somatic symptoms and insomnia will be assessed using the Patient Health Questionnaire (PHQ)-15 and Insomnia Severity Index (ISI). Quality of life will also be evaluated using the EuroQol-5 Dimension-5 Levels (EQ-5D-5L) and WHO quality of life assessment instrument abbreviated version (WHOQOL-BREF). Additionally, the compliance and drop-out rate of each group will be measured. The safety will be assessed through the incidence of adverse events and assessment of suicide risk.

The exploratory objectives are to investigate the biomarkers and other predictors of PTSD diagnosis and prognosis, including (1) the detection of biomarkers for the diagnosis of PTSD at baseline compared with healthy controls, (2) the identification of biomarkers and other predictors for individuals with a better prognosis among patients and (3) understanding the underlying mechanisms of successful treatment. To achieve these objectives, potential biomarkers and other predictors, including



**Figure 1** Flow diagram. BAI, Beck Anxiety Index; BDI-II, Beck Depression Inventory-II; CAPS-5, Clinician-Administered PTSD Scale; CGI-I, Clinical Global Impressions-Improvement scale; CGI-S, Clinical Global Impressions-Severity scale; C-SSRS, Columbia Suicide Severity Rating Scale; CTQ, Childhood Trauma Questionnaire; EFT, Emotional Freedom Techniques; EQ, empathy quotient; EQ-5D-5L, EuroQoL-5 Dimension-5 Levels; IBS-SSS, Irritable Bowel Symptoms Severity Scale; ISI, Insomnia Severity Index; LEC-5, Life Event Checklist for DSM-5; PCL-5, PTSD Checklist-5; PHQ-15, Patient Health Questionnaire-15; SCID-5, Structured Clinical Interview for DSM-5; WET, Written Exposure Therapy; WHOQOL-BREF, WHO QoL assessment instrument abbreviated version; WL, waiting list.

structural and functional MRI, recordings of facial expressions to emotional stimuli, and blood samples, will be collected longitudinally.

### Trial design

This study is designed as a randomised, assessor-blinded, three-arm, parallel-group clinical MRI study. The 120 eligible patients with PTSD will be randomly allocated to the EFT, WET or WL groups in a 1:1:1 ratio (figure 1).

## METHODS AND ANALYSIS

### Study setting

This study will be conducted at a university hospital in Seoul, Korea.

### Eligibility criteria

#### Patients with PTSD

The inclusion criteria will be adults aged between 19 and 65 years; diagnosis of PTSD by Structured Clinical

Interview for DSM-5 (SCID-5); symptoms of PTSD for >3 months, willing to attend weekly visits for 6 weeks and patients who voluntarily agree to participate.

Exclusion criteria will be risk of suicide as assessed by Columbia-Suicide Severity Rating Scale (C-SSRS)<sup>24</sup>; current or past history of schizophrenia or bipolar disorder; alcohol or other substance use disorders within 8 weeks; history of cerebrovascular diseases, brain tumour or traumatic brain injury (participants with mild traumatic brain injury will not be excluded); history of neurological or systemic diseases that may affect the central nervous system; history of acute infectious disease within 2 weeks; history of taking the following medications within 4 weeks; use of systemic steroids, antipsychotics, antidepressants, benzodiazepines, sleep medications (participants taking the medications in stable doses for >2 weeks will not be excluded); history of taking antibiotics within 2 weeks; vaccination within 4 weeks or plans for vaccination during the study period; moderate or higher cognitive impairment; medical conditions requiring inpatient treatment; receipt of medication or other interventions in other clinical trials within 1 month; current active psychotherapy (based on early observation that a significant number of participants with PTSD had recently undergone psychotherapy, making it challenging to enrol participants with the original exclusion criteria of psychotherapy within 6 months, it was modified starting from protocol V.1.7. The characteristics of previously received psychotherapy will be carefully recorded and summarised as part of the baseline characteristics of enrolled participants); pregnant or lactating women; women who do not use medically acceptable contraception (barrier methods, combined oral contraceptives, contraceptive implant, contraceptive injection, intrauterine devices and personal or partner's sterilisation) during the study period; and those determined as unsuitable by the investigators.

### Healthy controls

The inclusion criteria for healthy controls will be adults aged between 19 and 65 years, those without traumatic experiences, those who do not meet the diagnostic criteria of PTSD according to the SCID-5, those who do not have functional/organic disorders and clinically meaningful findings in the history taking and physical examination, PHQ-9 score  $\leq 4$ , Generalised Anxiety Disorder Screener-7 score  $\leq 4$ , PHQ-15 score  $\leq 5$  and those who voluntarily agree to participate.

The exclusion criteria for healthy controls will include a history of major mental disorders. The other exclusion criteria are shown the clinical study registration. The baseline characteristics between PTSD patients and healthy controls will be compared, to explore the biomarkers of PTSD diagnosis. Healthy controls will be recruited in the same site, after the enrolment of patients with PTSD, with balanced sex and age.

### MRI-specific exclusion criteria

These exclusion criteria will be applied to patients with PTSD and the healthy controls: ferrous-containing metal substance within the body and difficulty tolerating enclosed, small spaces because of claustrophobia.

## Interventions

### Emotional freedom techniques

EFT consists of five, 40 min, weekly sessions that include tapping on acupoints and exposure to cognitive reframing.<sup>11</sup> The EFT protocol for patients with PTSD was developed on the basis of previous studies.<sup>13 15 25</sup> In the previous feasibility trial, a developed EFT protocol was applied to 30 patients with PTSD in Korea, and the mean PCL-5 score was decreased to  $-14.33$  (95% CI (CI)  $-19.79$  to  $-8.86$ ) points after the five sessions of EFT. In the first session, the therapist will provide an introduction to EFT. In every session of EFT, therapists will follow the instructions from the EFT Manual (fourth edition).<sup>26</sup> At the beginning of each session, the patient and therapist will define the problem and evaluate the level of emotional distress. They will then create a 'set-up statement', acknowledging the problem and accepting oneself while tapping the SI3 acupoint on the side of the hand. This is one of the essential parts of EFT and includes exposure to trauma with cognitive reframing, where the patient is encouraged to reframe their negative thoughts about the problem in a more positive light. The therapist will then conduct the first sequence of EFT tapping, tapping on various acupoints while repeating a brief phrase of the problem seven times. After this, the 9 Gamut Procedure will be conducted, and the second sequence of EFT tapping will be repeated. The change in emotional distress will be re-evaluated after the sequences.

### Written exposure therapy

WET consists of five, 40 min, weekly sessions that focus on expressive writing about a traumatic event. We will follow the WET protocol developed by Sloan *et al.*<sup>18 19</sup> This WET protocol was applied to patients with PTSD in Korea, and the severity of PTSD symptoms was alleviated with large effect size (partial  $\eta^2$ : 0.524 for PCL-5) after five sessions of WET.<sup>27</sup> In the first session, therapists will introduce WET and select the trauma experience to be covered in this WET session. Before writing, the subjective units of distress (between 0 and 100) will be checked. Instructions for writing will be provided using the WET script developed by Sloan and Marx,<sup>28</sup> which ensure the standard delivery of WET protocol, and participants will write about their trauma in detail for 30 min. From the second to the fifth sessions, specific writing instructions will be provided using the WET script, and 30 min of the writing session will be completed. EFT and WET will be applied by qualified therapists working at the Department of Neuropsychiatry in Korean medicine, who have completed exposure-based treatment and Clinical EFT or WET protocol training. The treatment fidelity will be monitored by the perusal of the therapist written notes

by investigators to ensure that all Clinical EFT and WET standards are met. In addition, to improve adherence to the intervention, participants will be encouraged to visit at predetermined times through regular phone and text messages.

### Waiting list

The participants assigned to WL will not receive any intervention until completion of the follow-up visit. After 12 weeks, the follow-up visit and evaluation will be completed, and EFT will be applied to participants in the WL group. For all participants in the three groups, the use of systemic steroids, antipsychotics, antidepressants, benzodiazepines and sleep medications that were not used at the time of enrolment will be prohibited. If any of these medications are newly administered after enrolment, the participant will be excluded from the per-protocol set. However, other medications that were administered 4 weeks before study enrolment, as well as transient medications for other diseases or symptoms, may be allowed at the clinical discretion of the investigators, provided that those medications are not expected to significantly affect the study results.

### Criteria for discontinuing or modifying allocated interventions

Participants will be considered for treatment cessation and elimination from the study if they meet the following criteria: participants who are found to have not met the inclusion and exclusion criteria at the screening period due to an error; participants who experience serious adverse events (death, life threatening or hospitalisation due to adverse events); participants with adverse events warranting discontinuation of the study intervention; participants whose symptoms worsen and require another treatment; participants who withdraw their consent; participants who are lost to follow-up and participants who are unsuitable for continuing administration by the investigators.

### Outcomes

#### Primary outcome

The primary outcome is the mean change from the baseline CAPS-5 score at week 6 (post-treatment). CAPS-5 is a representative clinician rating scale for PTSD.<sup>29</sup> The CAPS-5 score will be measured at baseline, week 6 (post-treatment) and week 12 (follow-up). The mean change in CAPS-5 scores between baseline and week 6 will be the primary outcome.

#### Secondary outcomes

The mean change from the baseline CAPS-5 score at week 12 (follow-up) as well as the proportions of participants achieving criteria-based and symptom-based remissions of PTSD at week 6 (post-treatment) and week 12 (follow-up) will be secondary outcomes used to assess the severity of PTSD symptoms. Criteria-based and symptom-based remissions of PTSD will be defined based on the results of CAPS-5. Criteria-based remission of PTSD will be defined as no longer meeting the diagnostic criteria

for PTSD, which includes experiencing fewer than the required number of symptoms in each criterion.<sup>30</sup> Meanwhile, a total CAPS-5 score <20 will be defined as the symptom-based remission of PTSD.<sup>30</sup> Additionally, PCL-5 will be used as a self-rating scale to assess the severity of PTSD symptoms.<sup>31 32</sup> BDI-II<sup>33 34</sup> and BAI<sup>35 36</sup> will be used to assess the severity of depression and anxiety symptoms, respectively. Additionally, PHQ-15<sup>37 38</sup> and the ISI<sup>39 40</sup> will be used to assess the severity of somatic symptoms in patients with PTSD. To evaluate the quality of life in patients with PTSD, EQ-5D-5L<sup>41</sup> and WHOQOL-BREF scores<sup>42 43</sup> will be used as secondary outcomes.

#### Safety outcomes

The incidence of adverse events will be presented in three groups based on severity and causality assessment. The occurrence of adverse events will be monitored at every visit. Additionally, the suicide risk will be evaluated by the investigators using C-SSRS at screening, week 6 (post-treatment) and week 12 (follow-up).

#### Exploratory outcomes

Exploratory outcomes will be measured before and after the intervention (weeks 0 and 6). Structural and functional brain images will be obtained using 3T MRI. Emotional tasks<sup>44 45</sup> that induce emotions of joy, anxiety and sadness by watching video clips will be conducted, and the facial expressions of participants during the tasks will be recorded. The facial expression analysis will be conducted using iMotions software. In addition, empathy quotient<sup>46–48</sup> and irritable bowel severity symptom severity scale<sup>49</sup> will be measured as exploratory outcomes. [Figure 2](#) summarises the participant timeline.

#### Sample size

The sample size was computed to detect the mean difference in change from the baseline CAPS-5 score after treatment between the EFT and WL groups. No previous study has compared the CAPS-5 scores between EFT and WL. We estimated that EFT would have an effect size similar to that of EMDR,<sup>15</sup> and in a previous study comparing EMDR with WL, the effect size (Cohen d) of EMDR was 0.65.<sup>50</sup> With a two-sided significance level of 0.05 and a power of 0.8, 38.14 participants are required in each group. Considering a dropout rate of 5%, 40 participants will be recruited per group, and a total of 120 will be investigated. The dropout rate was calculated based on a previous feasibility trial of EFT in patients with PTSD.

Additionally, we calculated the required sample size to evaluate the non-inferiority of EFT compared with WET. Under the assumptions of a significance level of 0.05, power of 0.8, SD of 17, mean difference of 0 and a non-inferiority margin of 10, the estimated sample size per group is 36, without accounting for dropout rates.

#### Recruitment

To achieve adequate participant recruitment, regular advertisements will be conducted through online media, and approved materials will be attached to the bulletin

	Enrolment	Allocation	Intervention					Assessment	Follow-up	Close-out
Time point	~ -14 days	Week 0	Week 1 ~ Week 5					Week 6	Week 12	Week 24
Visit number	Visit 1	Visit 2	Visit 3 ~ Visit 7					Visit 8	Visit 9	Visit 10
<b>ENROLMENT:</b>										
Informed consent	X									
Eligibility screen	X									
C-SSRS	X						X	X		
Allocation		X								
<b>INTERVENTIONS:</b>										
EFT			X	X	X	X	X			
WET			X	X	X	X	X			
WL <sup>1</sup>										
<b>ASSESSMENTS:</b>										
CAPS-5		X						X	X	
CGI-S		X						X	X	
CGI-I								X	X	
PCL-5, BDI-II		X	X	X				X	X	X
BAI		X						X	X	X
PHQ-15, ISI		X						X	X	X
EQ-5D-5L, WHOQOL-BREF		X						X	X	X
MRI		X						X		
Emotional task <sup>2</sup>		X						X		
EQ, IBS-SSS		X						X		

**Figure 2** The schedule of enrolment, intervention and assessment. <sup>1</sup>The participants assigned to WL will not receive any intervention until completion of the follow-up visit. After 12 weeks, EFT will be applied to participants in the WL group. <sup>2</sup>The facial expressions will be recorded during the emotional task. BAI, Beck Anxiety Index; BDI-II, Beck Depression Inventory-II; CAPS-5, Clinician-Administered PTSD Scale; CGI-I, Clinical Global Impressions-Improvement scale; EFT, Emotional Freedom Techniques; EQ, empathy quotient; EQ-5D-5L, EuroQoL-5 Dimension-5 Levels; IBS-SSS, Irritable Bowel Symptoms Severity Scale; ISI, Insomnia Severity Index; PCL-5, PTSD Checklist-5; PHQ-15, Patient Health Questionnaire-15; WET, written exposure therapy; WHOQOL-BREF, WHO QoL assessment instrument abbreviated version; WL, waiting list.

boards inside and outside of the hospital. In the case of delayed recruitment, local advertisement can be implemented. The first participant of the study was enrolled on 8 December 2022, and the date of the last observation is expected to be completed in December 2025.

### Allocation

Random assignment will be performed in compliance with group assignments that are not biased and not exposed to participants and researchers. An independent statistician who is not involved in the performance and evaluation of this clinical trial generated a random assignment sequence in a 1:1:1 ratio for each group using blocked randomisation in SAS (V.9.4, SAS Institute, Cary, North Carolina). The generated random sequence table will be kept by the independent statistician and protected from disclosure.

For each random number, the assignment results will be sealed in an opaque envelope and stored in a locked cabinet. Participants' random numbers will be assigned according to the order in which the participants are enrolled at visit 2 after the screening process. A random number will be given independently of the screening

number. The corresponding envelope will be opened according to the random number, and group assignment will be performed. The date and time of opening and the signature of the researcher who opened it will be written on the open envelope and stored separately.

### Blinding

The participants will be allocated to the EFT, WET or WL groups, and it is impossible to blind therapists and participants during the intervention. Nevertheless, this study is designed as an assessor-blinded trial to control for bias as much as possible. Effectiveness and suicide risk will be evaluated by independent assessors who have not performed the intervention procedure or random assignment. Visits for interventions (3–7) and assessment (2, 8 and 9) will be separated.

### Data collection methods

To assess the severity of PTSD symptoms, the CAPS-5 (clinician-administered tool) and PCL-5 (self-reported instrument) will be used. The CAPS-5 consists of 30 items measuring the severity of PTSD symptoms, and the total score ranges from 0 to 80, with higher scores indicating

more severe symptoms.<sup>29</sup> The validated Korean version of the CAPS-5 will be used.<sup>51</sup> CAPS-5 will be evaluated by qualified investigators. To ensure the consistency of CAPS-5, an investigator meeting was conducted for training before study initiation. The PCL-5 consists of 20 items measuring the severity of PTSD symptoms in the DSM-5, and the total PCL-5 score ranges from 0 to 80, with higher scores indicating severe symptoms.<sup>31</sup> The validated Korean version of the PCL-5 will be used.<sup>32</sup> To assess PTSD and depressive symptoms during the intervention period, the PCL-5 and BDI-II will be measured every 2 weeks. The BDI-II consists of 21 items, and the total score ranges from 0 to 63, with higher scores indicating more severe symptoms.<sup>33</sup> A validated Korean version of the BDI-II will be used.<sup>34</sup> Even if a participant withdraws consent, efforts will be made to schedule an evaluation visit for the CAPS-5.

### Data management

Data in source documents (assessment sheets completed by investigators, questionnaires filled out by participants and electronic medical records) will be entered into the electronic Case Report Form (eCRF). The eCRF was developed using the iCReaT (internet-based Clinical Research and Trial) system provided by the Korea National Institute of Health. A data management plan was prepared before study initiation. Data specifications were defined and source documents for each data point were agreed on. Investigators at the institute were trained for data entry and coding using the eCRF system. The data entered in the eCRF will be checked bimonthly after enrolment of the first participant.

### Statistical methods

#### Analysis sets

The analysis sets will be defined as follows: (1) full analysis (FA) set: population that complies with the intention-to-treat principle, meets major inclusion and exclusion criteria and has obtained at least one primary outcome assessment after the baseline assessment. (2) Per protocol set: population within the FA set who have  $\geq 80\%$  compliance with the interventions, do not take any prohibited medications and do not have major violations to the protocol. (3) Safety analysis set: population consisting of all participants whose safety assessment has been made at least once since the randomised allocation.

#### Statistical methods for analysing the primary outcome

This is a multiarm parallel-group randomised trial,<sup>52</sup> and there are three hypotheses for the primary outcome. The first null hypothesis is that the mean change from baseline at week 6 in the EFT group will be the same as that in the WL group ( $H_0 : \mu_1 = \mu_2$ ,  $H_1 : \mu_1 \neq \mu_2$ ). A mixed-effect model repeated measure (MMRM) will be used, with group and time as fixed factors, and participant as a random factor. The mean difference and 95% CI between two groups and p values will be presented. The first hypothesis aims to assess the effect size of EFT on PTSD symptoms compared with WL.

The second null hypothesis is that the mean change from baseline at week 6 in the WET group will be the same as that in the WL group ( $H_0 : \mu_3 = \mu_2$ ,  $H_1 : \mu_3 \neq \mu_2$ ). MMRM will be used as in the first hypothesis. From the results of the second hypothesis, the non-inferiority margin (M) will be defined. The lower limit of the 95% CI of the mean difference between two groups will be M.

The third null hypothesis is that the mean change from the baseline at week 6 in the WET and EFT group will be greater than M ( $H_0 : \mu_3 - \mu_1 > M$ ,  $H_1 : \mu_3 - \mu_1 \leq M$ ). The third hypothesis assesses the non-inferiority of EFT compared with WET, and M calculated in the second hypothesis will be used. MMRM will be used, similar to the first hypothesis, but the significance level will be set to 2.5% since the non-inferiority test is one sided.

The problem of multiple testing will be solved using the fixed sequence method.<sup>53</sup> If the statistical result for hypothesis 1 is significant, the tests for hypotheses 2 and 3 will be performed. If the first null hypothesis was not rejected, tests for hypotheses 2 and 3 will not be performed. If the first null hypothesis is rejected and the test for hypothesis 2 is performed, in case that the statistical result for hypothesis 2 is significant, the test for hypothesis 3 will be conducted.

#### Statistical methods for analysing the secondary outcomes

Continuous variables (mean changes in CAPS-5, PCL-5, BDI-II, BAI, PHQ-15, ISI, EQ-5D-5L, WHOQOL-BREF and Clinical Global Impression scores) will be tested using the same method as for the primary outcome. Additionally, to compare the difference between before and after the intervention in each group, the Student paired t test or Wilcoxon signed-rank test will be used. Repeated measures analysis of variance will be performed to test the interaction between group and time.

Binary variables (criteria-based remission of PTSD and symptom-based remission of PTSD) will be tested using logistic regression analysis. ORs (95% CI) for the two groups will be presented. Hypothesis setting and multiple-testing problem-solving methods will be the same as those used for the primary outcome.

#### Statistical methods used to handle missing data

The primary outcome will be analysed using MMRM. The MMRM considers missing data using the maximum likelihood and does not require the process of replacing the missing data. In the case of an additional analysis of covariance, missing data will be replaced using the multiple imputation method.

#### Data monitoring

Considering the low risk of interventions and the study purpose, a data monitoring committee is not needed. An interim analysis is not planned. If intervention-related moderate or severe adverse events occur in  $>25\%$  of all participants, the study will be stopped.

## Harms

Adverse events will be carefully recorded at every visit, and the frequency, severity and causality of the adverse events will be assessed in the three groups. Additionally, the suicide risk of the participants will be evaluated using the Columbia Suicide Severity Rating Scale.

## Auditing

Monitoring will be conducted to verify that the clinical study data are accurate and complete, and that the clinical study is performed in accordance with the approved protocol and related regulations. Monitoring of clinical studies will be conducted through regular visits to the institute. The scope of monitoring will include compliance with the clinical study protocol, collection of appropriate and accurate data, obtaining informed consent and recording adverse events. The monitor will check the eCRF, source documents and essential documents during regular visits.

## ETHICS AND DISSEMINATION

### Research ethics approval

This study has been approved by the Institutional Review Board (IRB) of the Kyung Hee University Korean Medicine Hospital (KOMCIRB2021-11-005-001).

### Protocol amendments

Protocol modifications will be determined after sufficient discussion by investigators at the hospital and KIOM and will be applied to the study after obtaining approval for the amendment from the IRB. The current version of protocol is V.1.7 (date: 28 March 2023).

### Consent or assent

Written informed consent will be obtained from all participants prior to screening (online supplemental material S1). The principal investigator and subinvestigators, who are Korean medicine doctors in the hospital and delegated by the principal investigator, will provide information about the clinical study and obtain informed consent from the participants. Informed consent and a description of the study approved by the IRB will be used. Sufficient time and opportunity for the participants to ask questions about the details of the clinical study and to decide whether to participate will be provided. Additional consent will be obtained for the collection and analysis of blood samples.

### Confidentiality

The personal information of each participant will not be entered into eCRF, and the data of each participant will be collected under screening and random numbers.

### Ancillary and post-trial care

Follow-up observation and online follow-up observation will be conducted at weeks 12 and 24. Compensation criteria and plans will be prepared for those who suffer harm from trial participation. The occurrence of adverse events will be

assessed at every visit, and the required treatment and observation will be applied until the symptoms disappear.

## Dissemination policy

The clinical study information and results will be registered with the Clinical Research Information Service. This study's findings will be presented at conferences and published in peer-reviewed journals. The participant-level data set will be uploaded to the Korean Medicine Data Repository ([kmdr.kiom.re.kr](http://kmdr.kiom.re.kr)) after study completion.

## Author affiliations

<sup>1</sup>KM Science Research Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea

<sup>2</sup>Department of Neuropsychiatry, College of Korean Medicine, Kyung Hee University Medical Center, Kyung Hee University, Seoul, Republic of Korea

<sup>3</sup>Research Group of Neuroscience, East-West Medical Research Institute, WHO Collaborating Center, Kyung Hee University, Seoul, Republic of Korea

<sup>4</sup>R&D Strategy Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea

<sup>5</sup>Department of Clinical Korean Medicine, Graduate School, Kyung Hee University, Seoul, Republic of Korea

**Contributors** HK, S-HC, YC, YK and SC conceived the trial. YEC, O-JK, DK and S-HL helped with study implementation. YC and YK completed the initial draft of the manuscript. O-JK generated the randomisation sequence and provided biostatistical advice and information. All authors designed the study and read, edited and approved the final manuscript and supplementary files.

**Funding** This work was supported by the Korea Institute of Oriental Medicine (KIOM) (grant number: KSN2211010). As a government-funded research institute, KIOM is responsible for the study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## ORCID iDs

Yujin Choi <http://orcid.org/0000-0001-5257-2340>

Yunna Kim <http://orcid.org/0000-0003-2286-1242>

Sunyoung Choi <http://orcid.org/0000-0002-7210-4752>

Young-Eun Choi <http://orcid.org/0000-0001-6915-3716>

Ojin Kwon <http://orcid.org/0000-0002-7349-4596>

Do-Hyung Kwon <http://orcid.org/0000-0003-0549-5164>

Seung-Ho Lee <http://orcid.org/0000-0001-8917-8216>

Seung-Hun Cho <http://orcid.org/0000-0002-0627-768X>

Hyunjun Kim <http://orcid.org/0000-0001-7997-7663>



## REFERENCES

- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub, 2013.
- National Center for Mental Health. National mental health survey. 2021. Available: mhs.ncmh.go.kr
- van Minnen A, Zoellner LA, Harned MS, et al. Changes in comorbid conditions after prolonged exposure for PTSD: a literature review. *Curr Psychiatry Rep* 2015;17:17:549..
- Jonas DE, Cusack K, Forneris CA, et al. *Psychological and pharmacological treatments for adults with Posttraumatic stress disorder (PTSD)*. 2013.
- Lee DJ, Schnitzlein CW, Wolf JP, et al. Psychotherapy versus Pharmacotherapy for Posttraumatic stress disorder: systemic review and Meta-Analyses to determine First-Line treatments. *Depress Anxiety* 2016;33:792–806.
- Guideline development panel for the treatment of PTSD in adults APA. summary of the clinical practice guideline for the treatment of Posttraumatic stress disorder (PTSD) in adults. *Am Psychol Jul-Aug* 2019;74:596–607.
- Powers MB, Halpern JM, Ferenschak MP, et al. A meta-analytic review of prolonged exposure for Posttraumatic stress disorder. *Clin Psychol Rev* 2010;30:635–41.
- Imel ZE, Laska K, Jakupcak M, et al. Meta-analysis of dropout in treatments for Posttraumatic stress disorder. *J Consult Clin Psychol* 2013;81:394–404.
- Eftekhari A, Crowley JJ, Mackintosh M-A, et al. Predicting treatment dropout among veterans receiving prolonged exposure therapy. *Psychol Trauma* 2020;12:405–12.
- Hundt NE, Ecker AH, Thompson K, et al. "It didn't fit for me:" A qualitative examination of dropout from prolonged exposure and cognitive processing therapy in veterans. *Psychol Serv* 2020;17:414–21.
- Church D, Stapleton P, Yang A, et al. Is tapping on Acupuncture points an active ingredient in emotional freedom techniques? A systematic review and meta-analysis of comparative studies. *J Nerv Ment Dis* 2018;206:783–93.
- Church D, Stapleton P, Vasudevan A, et al. Clinical EFT as an evidence-based practice for the treatment of psychological and physical conditions: A systematic review. *Front Psychol* 2022;13:951451.
- Church D, Feinstein D. The manual stimulation of Acupuncture points in the treatment of post-traumatic stress disorder: A review of clinical emotional freedom techniques. *Med Acupunct* 2017;29:194–205.
- Sebastian B, Nelms J. The effectiveness of emotional freedom techniques in the treatment of Posttraumatic stress disorder: A meta-analysis. *Explore (NY)* 2017;13:16–25.
- Karatzias T, Power K, Brown K, et al. A controlled comparison of the effectiveness and efficiency of two psychological therapies for Posttraumatic stress disorder: eye movement desensitization and reprocessing vs. emotional freedom techniques. *J Nerv Ment Dis* 2011;199:372–8.
- Church D, Hawk C, Brooks AJ, et al. Psychological trauma symptom improvement in veterans using emotional freedom techniques: a randomized controlled trial. *J Nerv Ment Dis* 2013;201:153–60.
- Korean Medicine Procedure Expert Assessment Committee, Health Insurance Review & Assessment Service. Emotional freedom technique using Acupuncture points tapping. 2022. Available: <https://www.hira.or.kr/bbsDummys.do?pgmid=HIRAA030051000010&brdScnBltNo=4&brdBltno=1&pageIndex=1>
- Sloan DM, Lee DJ, Litwack SD, et al. Written exposure therapy for veterans diagnosed with PTSD: A pilot study. *J Trauma Stress* 2013;26:776–9.
- Sloan DM, Marx BP, Lee DJ, et al. A brief exposure-based treatment vs cognitive processing therapy for Posttraumatic stress disorder: A randomized Noninferiority clinical trial. *JAMA Psychiatry* 2018;75:233–9.
- Yang S, Wynn GH, Ursano RJ. A clinician's guide to PTSD biomarkers and their potential future use. *Focus (Am Psychiatr Publ)* 2018;16:143–52.
- van Rooij SJH, Kennis M, Vink M, et al. Predicting treatment outcome in PTSD: A longitudinal functional MRI study on trauma-unrelated emotional processing. *Neuropsychopharmacology* 2016;41:1156–65.
- Schmidt U, Kaltwasser SF, Wotjak CT. Biomarkers in Posttraumatic stress disorder: overview and implications for future research. *Dis Markers* 2013;35:43–54.
- Patel R, Spreng RN, Shin LM, et al. Neurocircuitry models of Posttraumatic stress disorder and beyond: a meta-analysis of functional neuroimaging studies. *Neurosci Biobehav Rev* 2012;36:2130–42.
- Posner K, Brown GK, Stanley B, et al. The Columbia-suicide severity rating scale: initial validity and internal consistency findings from three Multisite studies with adolescents and adults. *Am J Psychiatry* 2011;168:1266–77.
- Church D, Stapleton P, Mollon P, et al. Guidelines for the treatment of PTSD using clinical EFT (emotional freedom techniques). *Healthcare (Basel)* 2018;6:146.
- Church D. *The EFT Manual*. Hay House, 2018: 398.
- Park J E, Choi K S, Han Y R, et al. An open pilot trial of written exposure therapy for patients with post-traumatic stress disorder in Korea. *Psychiatry Investig* 2021;18:728–35.
- Sloan DM, Marx BP. *Written exposure therapy for PTSD: A brief treatment approach for mental health professionals*. Washington: American Psychological Association, 2019.
- Weathers FW, Blake DD, Schnurr PP, et al. *The clinician-administered PTSD scale for DSM-5 (CAPS-5)*. National Center for PTSD, 2013.
- Weathers FW, Keane TM, Davidson JRT. Clinician-Administered PTSD scale: A review of the first ten years of research. *Depress Anxiety* 2001;13:132–56.
- Weathers FW, Litz BT, Keane TM, et al. *The Ptsd checklist for Dsm-5 (Pcl-5)*. National center for PTSD, 2013: 10. Available: [www.ptsd.va.gov](http://www.ptsd.va.gov)
- Kim JW, Chung HG, Choi JH, et al. Psychometric properties of the Korean version of the PTSD Checklist-5 in elderly Korean veterans of the Vietnam war. *Anxiety and Mood* 2017;13:123–31.
- Beck A, Steer R, Brown G. *Manual for the BDI-II, the psychological corporation*. San Antonio, TX: Psychological Corporation, 1996.
- Sung H, Kim J, Park Y, et al. A study on the Reliability and the validity of Korean version of the Beck depression inventory-II (BDI-II). *J Korean Soc Biol Ther Psychiatry* 2008;14:201–12.
- Beck AT, Steer RA. *Manual for the Beck anxiety inventory*. San Antonio, TX: Psychological Corporation, 1990.
- LeeHK, Lee E-H EH, HwangST, et al. Psychometric properties of the Beck anxiety inventory in the community-dwelling sample of Korean adults. *Korean Journal of Clinical Psychology* 2016;35:822–30.
- Kroenke K, Spitzer RL, Williams JBW. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med* 2002;64:258–66.
- Han C, Pae C-U, Patkar AA, et al. Psychometric properties of the patient health Questionnaire-15 (PHQ-15) for measuring the somatic symptoms of psychiatric outpatients. *Psychosomatics* 2009;50:580–5.
- Bastien CH, Vallières A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med* 2001;2:297–307.
- Cho YW, Song ML, Morin CM. Validation of a Korean version of the insomnia severity index. *J Clin Neurol* 2014;10:210–5.
- Kim SH, Ahn J, Ock M, et al. The EQ-5D-5L valuation study in Korea. *Qual Life Res* 2016;25:1845–52.
- Min SK, Kim KI, Lee CI, et al. Development of the Korean versions of WHO quality of life scale and WHOQOL-BREF. *Qual Life Res* 2002;11:593–600.
- The Whoqol Group. Development of the world health organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998;28:551–8.
- Dimberg U, Thunberg M. Empathy, emotional contagion, and rapid facial reactions to angry and happy facial expressions. *Psych J* 2012;1:118–27.
- Wild B, Erb M, Eyb M, et al. Why are smiles contagious? an fMRI study of the interaction between perception of facial affect and facial movements. *Psychiatry Res* 2003;123:17–36.
- Baron-Cohen S, Wheelwright S. The empathy quotient: an investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. *J Autism Dev Disord* 2004;34:163–75.
- Lawrence EJ, Shaw P, Baker D, et al. Measuring empathy: Reliability and validity of the empathy quotient. *Psychol Med* 2004;34:911–9.
- Heo JH, Lee C-J. Psychometric analysis of the empathy quotient (EQ) scale. *Studies in Humanities* 2010;24:183–200.
- Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther* 1997;11:395–402.
- van den Berg DPG, de Bont P, van der Vleugel BM, et al. Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for Posttraumatic stress disorder in patients with a psychotic disorder: a randomized clinical trial. *JAMA Psychiatry* 2015;72:259–67.
- Kim WH, Jung YE, Roh D, et al. Reliability and validity of the Korean version of clinician-administered Posttraumatic stress disorder scale for DSM-5. *J Korean Med Sci* 2019;34:e219.
- Juszczak E, Altman DG, Hopewell S, et al. Reporting of multi-arm parallel-group randomized trials: extension of the CONSORT 2010 statement. *JAMA* 2019;321:1610–20.
- Wiens BL. A fixed sequence Bonferroni procedure for testing multiple endpoints. *Pharmaceut Statist* 2003;2:211–5.