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Complementary and alternative medicine for post-traumatic stress disorder symptoms: A systematic review

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Abstract

Objectives—To 1) characterize complementary and alternative medicine (CAM) studies for posttraumatic stress disorder symptoms (PTSD), 2) evaluate the quality of these studies, and 3) systematically grade the scientific evidence for individual CAM modalities for PTSD.

Design—Systematic Review. Eight data sources were searched. Selection criteria included any study design assessing PTSD outcomes and any CAM intervention. The body of evidence for each modality was assessed with the Natural Standard evidence-based, validated grading rationale.™

Results and Conclusions—Thirty-three studies (n=1329) were reviewed. Scientific evidence of benefit for PTSD was Strong for repetitive transcranial magnetic stimulation and Good for acupuncture, hypnotherapy, meditation, and visualization. Evidence was Unclear or Conflicting for biofeedback, relaxation, Emotional Freedom and Thought Field therapies, yoga, and natural products. Considerations for clinical applications and future research recommendations are discussed.

Keywords

posttraumatic stress disorder; complementary; alternative medicine

INTRODUCTION

Posttraumatic stress disorder (PTSD) is a serious and growing health issue. Approximately 7.7 million American adults (3.5%) have PTSD in a given year.[1] Not only do people with PTSD experience debilitating symptoms of PTSD, but they also have a higher prevalence of other psychiatric and physical co-morbid conditions such as depression. The annual economic burden of anxiety disorders in the United States is estimated at $42.3–$46.6 billion.[2] The personal and societal costs of PTSD are high due to chronic symptoms, increased co-morbidities, and marked functional impairment.[3–5]

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PTSD may occur when a person has been exposed to a traumatic event that involves actual or threatened death, serious injury, or threat to the physical integrity of self or others. People who acquire PTSD after a traumatic event experience a constellation of symptoms that were not present before the trauma. Symptoms fall into four diagnostic criteria: intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity. People with PTSD persistently re-experience the trauma through recurrent and intrusive distressing recollections of the event, and may experience severe distress when exposed to cues that symbolize or resemble aspects of the trauma. They also avoid thoughts, feelings, conversations, people, places, or activities that are reminiscent of the initial event. People with PTSD can have negative alterations in cognition or mood criteria such as the inability to recall key features of the traumatic event, persistent negative beliefs and expectations about oneself or the world, and markedly diminished interest in significant activities. They also have altered arousal and reactivity symptoms such as hypervigilance, difficulty concentrating, difficulty falling or staying asleep, irritability or outbursts of anger, or exaggerated startle response.[6]

The complex psychopathology and frequency of co-morbid conditions often makes PTSD difficult to treat. Trauma-focused psychotherapy has the strongest evidence for PTSD treatment.[7] Yet, a high percentage of individuals do not engage in or drop-out prematurely from these treatments because of chronic patterns of avoidance and an inability to tolerate the intense emotions often experienced with these approaches.[8] Avoidance behaviors may maintain PTSD symptoms by interfering with the processing of traumatic memories and preventing habituation or relearning to conditioned stimuli.[9] Selective serotonin and serotonin-norepinephrine reuptake inhibitors also have strong evidence for PTSD treatment; however, medication refusal and non-compliance are quite high in this population.[10] Thus, the evaluation of PTSD treatments that could be used in conjunction with or as an alternative to existing therapies is warranted.

Complementary and alternative medicines (CAM) may be beneficial for people with PTSD. The National Institutes of Health, National Center for Complementary and Alternative Medicine (NCCAM) defines CAM as a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine.[11] CAM therapies are attractive because they use an integrative approach to healing and usually do not report side-effects. Most CAM modalities engage the healing process without trauma recall, and are thus, not trauma-focused.

Many people with PTSD currently use CAM for their symptoms despite a lack of definitive evidence for their benefit. Thirty-eight percent of the 23,393 U.S. adults polled in a 2007 National Health Interview Survey used CAM. Of these CAM users, 2.8% reported using CAM for anxiety symptoms or anxiety related conditions including PTSD.[12] The most commonly used modalities were natural products, deep breathing, meditation, chiropractic, massage, yoga, diet-based therapies, progressive relaxation, guided imagery, and homeopathic treatment. Another survey of 1004 adults reported that 43% of respondents used CAM for Generalized Anxiety Disorder, Panic Disorder, Social Anxiety Disorder, or Post-Traumatic Stress Disorder. Acupuncture, meditation/relaxation, biofeedback, chiropractic, massage, prayer, or spiritual practices were the most commonly used

modalities, followed by dietary supplement and/or herbal medicine use.[13] Additionally, nearly 40% people with PTSD surveyed within the Veterans Administration used CAM to address emotional and mental problems.[14]

PTSD is a serious and growing health concern without treatment that is acceptable to all people. CAM therapies may offer complementary and alternative therapies to existing treatments and people with PTSD are already using them for their symptoms. However, the evidence of efficacy of CAM for PTSD is limited. To date, two systematic reviews have assessed the efficacy of CAM for anxiety-related disorders including PTSD. One meta-analysis found that meditative therapies provided significant improvements in anxiety symptoms compared to controls.[15] This study only included one CAM modality and was not specific for PTSD. Another systematic review found very few CAM randomized controlled trials for PTSD using stringent inclusion/exclusion criteria and the authors were unable to make any conclusions about efficacy.[16]

Building upon this previous work, the purpose of this systematic review was to assess the state of the science of CAM for PTSD. The objectives of this systematic review were to: 1) characterize CAM studies where PTSD outcomes were assessed, 2) evaluate the quality of these studies, and 3) systematically evaluate the evidence of CAM for PTSD symptoms. This study adds to the CAM and PTSD field by evaluating the efficacy of CAM modalities for PTSD with broader inclusion/exclusion criteria and therefore, describing a wider view of the research literature than previously done.

METHODS

Literature search methods

Comprehensive searches were conducted by a research librarian using MEDLINE (1950-3/12/2013), PsycINFO (1967-3/12/2013), CINAHL (1982-3/12/2013), Alt HealthWatch (1984-3/12/2012), AMED (1980 - 3/12/2013), Cochrane Library: CENTRAL (3/12/2013), Cochrane Database of Systematic Reviews (3/12/13), Database of Abstracts of Reviews of Effects (3/12/2013), and Health Technology Assessment Database (3/12/13). Search terms included CAM modalities and PTSD terms dependent on the search strategy required for each database (the search strategy for MEDLINE is included as Supplemental Data). All peer-reviewed studies in any language were included.

Study eligibility

Two reviewers independently screened titles and abstracts of all publications retrieved by the search strategies. Studies meeting the following inclusion criteria, and those with insufficient information to determine eligibility from the abstract, were selected for further review:

Study design—Randomized controlled trials (RCTs), non-randomized controlled trials (CTs), cross-over trials, prospective and retrospective observational studies with controls, case-control studies, and uncontrolled pre-post studies where the sample size was greater or equal to five. Studies with intention-to-treat or completer analyses were included.

Types of participants—Adults diagnosed with PTSD and/or adult participants who were administered a measure assessing PTSD symptoms.

Interventions—Any CAM modality as described on the NIH NCCAM website at the time this review was planned (3/1/12)[11] including: Natural Products (herbal medicines, botanical medicine, botanicals, vitamins, minerals, other "natural products", dietary supplements, probiotics, fish oil); Mind-Body Medicine (meditation, yoga, deep-breathing exercises, guided imagery, hypnotherapy, progressive relaxation, qi gong, tai chi, biofeedback); Whole Medical Systems (acupuncture or traditional Chinese medicine, homeopathy, naturopathy, ayurvedic medicine); Manipulative and Body-Based Practices (spinal manipulation, chiropractic, osteopathy, massage); Movement Therapies (Feldenkrais method, Alexander technique, pilates, Rolfing Structural Integration, Trager psychophysical integration); Traditional/Spiritual Healing (shamanic healing, curandero); and Energy medicine (magnet therapy, light therapy, biofields, applied qi gong, Reiki, healing touch, therapeutic touch). The interventions included were based solely on the NCCAM website at the time of study design rather than on the presence of a rationale or mechanism for each included CAM modality and why it may or may not be appropriate for PTSD. Cognitive Behavioral Therapy, Prolonged Exposure Therapy, Eye Movement Desensitization (EMDR) and Reprocessing, Imagery Rehearsal and Restructuring, journaling or expressive writing studies were not included because they are used as evidenced-based standard-care for PTSD treatment. If one of these therapies was compared to a CAM therapy directly, such as EMDR versus Relaxation Therapy, the study was included. If the therapy was multimodal, where it included Cognitive Behavioral Therapy or Prolonged Exposure Therapy in addition to some CAM modalities such as relaxation or creative arts, it was excluded. Repetitive transcranial magnetic stimulation was included as a magnet therapy, and hypnotherapy and biofeedback were included as mind-body medicine therapies.

Outcome measures—Each study had to include at least one measure assessing PTSD symptoms such as intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity. Outcomes from any version of the Diagnostic and Statistical Manual of Mental Disorders were allowed.

Data extraction and management

The following data were collected: study design, number of treatment arms, setting, participant description, inclusion and exclusion criteria, number of subjects, mean age, intervention type and description, attrition rate, home practice details (if any), group or individual practice, outcome, time points at which outcomes were measured, *p*-values for each measure, and adverse events. A single reviewer extracted data and another independent reviewer verified the accuracy and completeness of the data extraction. Any discrepancies were resolved by consensus. All study data were managed with Microsoft Excel and an Access relational database (Microsoft Corporation, Redmond, Washington).

Assessment of methodological quality

Each study was evaluated for risk of bias and methodological quality. RCTs were evaluated with the Cochrane Risk of Bias Tool[17] and the Quality Assessment Tool.[18,17] Non-RCT

studies were assessed for quality with the Quality Assessment Tool only since the Cochrane Risk of Bias Tool is specifically designed for RCTs. Two reviewers assessed the methodological quality of studies independently. A third reviewer resolved any disagreements through consensus.

Instruments used to assess Risk of Bias and Methodological Quality

- The *Cochrane Risk of Bias Tool* evaluates selection, performance, detection, attrition, reporting and other biases and is the current gold standard for assessing bias in RCTs. Each criterion are categorized as High risk of bias, Unclear risk of bias, or Low risk of bias and consider whether the risk of bias is sufficient enough to have a notable impact on the results or conclusions of the trial. A treatment fidelity criterion, which evaluated whether or not the intervention was delivered as designed or that potential intervention deviations were assessed, was added as an "Other Bias."
- The *Quality Assessment Tool* (QAT) used in this study is modeled after the "Aid to the Evaluation of Therapeutic Studies" developed by Reisch et al[18] and was modified as recommended by Deeks.[17,19] It grades study quality on important constructs such as blinding, randomization, adequate reporting, attrition, sample size determination, and control group usage. A quantitative score is calculated that is adjusted for study design by removing questions about randomization, comparisons between groups, and blinding for non-RCT and uncontrolled trials. The result is an adjusted score on a scale of 0–100, 100 being a higher quality study.

Data synthesis and evidence grading

A meta-analysis for this study was not possible because of substantial variation in participant type, interventions, implementation, and outcomes across studies. Therefore, we sought to provide a general understanding of the available evidence for each modality. First, each study was rated as a positive, mixed, negative or neutral study (positive = most PTSD outcomes are positive; mixed = only 1–2 PTSD subscales are positive; negative = no PTSD outcomes are positive; neutral = no difference between intervention and active control) (Table 2). Studies were then grouped by modalities. The level of evidence was then graded for each modality according to the Natural Standard evidence-based grading rationale.™[20] Letter grades of A-F reflect the level of scientific evidence in support of a given therapy for PTSD (A=strong scientific evidence; B=good scientific evidence; C=unclear or conflicting scientific evidence; D = fair negative scientific evidence; F = strong negative scientific evidence; L = lack of evidence). The criteria to designate each grade are described in more detail in Table 1. Grades reflect the level of available scientific data for or against the use of each therapy for a specific medical condition. For example, to receive an A level of evidence a modality had to have statistically significant evidence of benefit from >2 properly conducted RCT's, OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with

supporting evidence in basic science, animal studies, or theory. Natural Standard was founded by healthcare providers and researchers to provide high-quality, evidence-based information about CAM therapies.

RESULTS

Search results

A total of 1596 studies were identified (Figure 1). After removing duplicates, 1337 titles and abstracts were screened for inclusion criteria. Ninety full text articles were assessed for eligibility, and of these, 33 were included in the final review (Table 2).

Description of included studies

All manuscripts were published between 1985 and 2012. Eighteen of the studies were conducted within the last 5 years (2008–2012). There were 17 RCTs, four non-RCTs, nine pre-post designs, and three crossover interventions. The mean sample size was 40 ± 38 (range 5–183). In total, 1329 participants were included. Of the controlled trials, 13 used active control groups (either another intervention or placebo intervention), six used non-active controls (waitlist or treatment as usual), and two used active and non-active controls. Eighteen studies confirmed PTSD diagnosis of participants and 15 did not. PTSD diagnosis was confirmed using clinician assessed diagnostic criteria and/or through structured clinical interviews (DSM-III (2); DSM-IV (6), CAPS (1), M.I.N.I. (1), WHO criteria (1), SCID (4)) for most but not all studies. Three studies did not note criteria for confirming PTSD diagnosis. Participants experienced diverse traumatic events: combat exposure (10 studies), natural disaster (3), sexual assault (3), abuse (2), war (2), fire-fighting (1), mixed traumatic events (11), and one study did not report the trauma type. Seven studies had all male participants and four studies had all female participants. The remaining studies had an average of 45% females ± 38% (range 9–89%). One study did not report gender data. Most studies used mind-body therapies, including biofeedback (4 studies), hypnosis (3), meditation (9), relaxation (4), Emotional Freedom and Thought Field therapies (2), visualization (1), and yogic breath work (1). Other modalities represented were repetitive transcranial magnetic stimulation (rTMS) (5), acupuncture (2), and natural products (inositol and ginkgo biloba) (2). PTSD outcomes varied and included one or more of the following: the PTSD Checklist (PCL, civilian and military versions), Clinician-Administered PTSD Scale (CAPS), Impact of Events Scale (IES), Crime-related PTSD Scale, Posttraumatic Diagnostic Scale, Severity of Symptoms Scale for PTSD (Spanish adaptation of PTSD Symptom Scale by Foa 1993), Treatment Outcome PTSD Scale, and the Clinical Global Impressions (CGI).

Methodological quality of included studies

Methodological quality for all studies as determined by the QAT is presented in Table 2. The mean score was mean 78 ± 9 (median 80, range 54–95). Several criteria were met by the majority of studies (at least 31 out of 33): the purpose of the study was stated, outcomes were validated and adequately described, the intervention was reasonable and appropriate to answer questions posed by researchers, intervention protocols were adequately described, participant demographic information was reported, and descriptive measures were identified

for all important variables. Five studies reported a power calculation to determine adequate sample size. Blinding of participants or outcome assessors was discussed in 11 of the 24 controlled and cross-over design studies. Thirteen studies reported adverse events.

Table 3 summarizes the risk of bias for the 17 RCTs included in this review. Several of the studies failed to provide enough detail for adequate assessment; methods of random sequence generation and allocation concealment were particularly poorly reported. The rTMS studies and the nutraceutical studies used a sham or placebo control group that allowed for participant blinding. One study[21] assessed treatment credibility as it was perceived by the participants (i.e. expectation). Nine of the studies explicitly stated that outcomes assessors were blinded to treatment group. In general, RCT sample sizes were small (7 of the 17 RCTs had n < 33). Three studies performed intention-to-treat analyses.[22–24]

Quality of the body of evidence for each modality

The body of evidence for each modality for PTSD was reviewed. Letter grades were derived for each modality using the Natural Standard evidence-based grading rationale.™ Table 1 describes the criterion for each grade. The individual study outcomes that determined the grades are listed in Table 2.

rTMS—Five trials (3 RCTs, 1 pre-post, and 1 cross-over) were included. The RCTs were of generally high quality (QAT scores ranging from 71 – 88) and all had positive results. Both the pre-post and cross-over trials had lower quality ratings and showed mixed result. **GRADE A**.

Acupuncture—Two RCTs, both of which demonstrated significantly improved symptoms over control conditions were included. Hollifield found that acupuncture was as effective as CBT when compared to a waitlist control,[23] and Zhang found that acupoint stimulation combined with CBT was more effective than CBT alone.[25] Because these are slightly different modalities, further research is warranted. **GRADE B**.

Biofeedback—Four trials (1 RCTs, 1 CT, and 2 pre-post studies) were included. The controlled trials had high QAT quality scores, with either mixed results or no difference from the control group. The other studies had small sample sizes and methodological concerns. **GRADE C**.

Emotional Freedom Technique/Thought Field Therapy—The body of evidence for these mind-body techniques includes one RCT showing no difference between Emotional Freedom Technique and EMDR, and 1 pre-post trial with positive results. While the non-inferiority of Emotional Freedom Technique to EMDR is an intriguing finding, both trials had significant drop out rates (43% and 49%, respectively), bringing into question the validity of results. **GRADE C**.

Hypnotherapy—Three studies (2 RCTs and 1 pre-post) were included. Both RCTs had active control groups. In one study, the hypnotherapy group did just as well as the CBT group at a three-year follow-up.[22] In the other study, the hypnotherapy group had

significantly greater improved outcomes than Zolpidem.[26] The Zolpidem study was targeted at improving insomnia for people with PTSD rather than PTSD symptoms directly and Zopidem as a hypnotic pharmaceutical would not be expected to improve PTSD symptoms. The grade remains the same if this study is excluded. **GRADE B**.

Meditation—Nine studies were included, five RCTs and four pre-posts. Meditation represents the largest number of CAM studies for any modality included in this review. All the pre-post studies showed positive outcomes and high QAT scores (all > 86). While the RCTs were of variable quality and sample size, the majority favored meditation over waitlist controls. Several different types of meditation were assessed and heterogeneity complicated the grading of this modality. **GRADE B**.

Relaxation—Four studies (2 RCTs, 1 pre-post, and 1 cross-over) were included, three of which had significant methodological issues and showed mixed or negative results. **GRADE C**.

Visualization—One large, high quality RCT was included. This study combined healing touch with guided imagery and demonstrated significant improvements in PTSD symptoms compared to treatment as usual. **GRADE B**.

Yoga breath work—One large non-randomized CT was included demonstrating that yoga breath work alone and in combination with exposure therapy is better than wait list for acute trauma survivors. **GRADE C**.

Natural products—Two RCTs were included. One small RCT showed no effect of inositol compared to placebo. Another small RCT showed a positive effect of ginkgo biloba on PTSD outcomes compared to placebo. **GRADE C**.

Grades were reassessed for two sub-groups: 1) studies where PTSD was required and 2) RCTs. These subgroup analyses are important because they reflect more stringent inclusion criteria and lend credibility to the application of these modalities under more specific circumstances. When evaluating only those studies where a PTSD diagnosis was required, all grades remained the same except for three modalities. Meditation was reduced from a B to a C because only one out of the nine meditation studies required a PTSD diagnosis. Guided Imagery and yoga breath work were downgraded to Lack of Evidence because neither of these studies required a PTSD diagnosis. When evaluating only the RCTs, all grades remained the same except, again, yoga breath work was downgraded to Lack of Evidence because it did not include an RCT.

Discussion

The objectives of this review were to systematically characterize and evaluate CAM studies for PTSD. We believe that at this relatively young stage of CAM research it is important to evaluate all the available evidence for a particular modality, and inclusion criteria were deliberately kept broad to capture as many studies as possible. We found 33 CAM studies that used 10 different modalities to assess PTSD outcomes. Scientific evidence of benefit for

PTSD was Strong for rTMS, and Good for acupuncture, hypnotherapy, meditation, and visualization. Evidence was Unclear or Conflicting for biofeedback, relaxation, Emotional Freedom and Thought Field therapies, yoga breath work, and natural products.

Implications for research

Studies included in this review were of variable quality. Important aspects of rigorous research design were often not conducted or not reported. In order to improve the quality of the CAM research field and accurately determine efficacy of CAM modalities, investigators are encouraged to consider the following when designing studies: 1) Choose an appropriate control (i.e. active, non-active or both) depending on the research question;[27] 2) Assess for expectancy and placebo effects because they play a pivotal role in mind-body studies;[28,29] 3) *Blind research staff and participants if possible*; 4) *Randomize participants*; 5) *Clearly define the population being studied*; 6) *Determine an appropriate sample size; and* 7) *Follow standard rigorous clinical design and reporting guidelines*.[30,31] This will help improve the quality of CAM studies and thus the quality of evidence.

Overall completeness and applicability of evidence

Studies in this review recruited from a variety of settings (e.g. Veteran's Administration facilities, outpatient clinics, prison) and countries (North America, Asia, Iran, and Israel). Participants were from the general population, combat veterans, firefighters, and sexual abuse survivors. About one-third of the studies were specific for combat-related trauma and another third enrolled participants with a diverse mix of trauma exposure. Studies varied widely with respect to participant gender. Some studies enrolled only men, other studies only women, and several had a diverse mix of male and female participants. All-male studies most frequently targeted combat-related trauma whereas all-female studies more often addressed sexual abuse, thus reflecting gender differences associated with these trauma exposures. While the grades did not distinguish by trauma type or gender, the results lend preliminary support to the acceptability of CAM for people with a variety of trauma exposures and genders. Additional research and synthesis of evidence is needed to address the efficacy of each modality by trauma exposure and gender.

Implications for clinical practice

There is positive evidence of effectiveness for rTMS, acupuncture, hypnotherapy, meditation, and visualization for the treatment of PTSD symptoms. rTMS had the strongest scientific evidence followed by acupuncture, hypnotherapy, meditation, and visualization. Practitioners may take this evidence into account when considering these CAM modalities for treating patients with PTSD symptoms.

rTMS is a noninvasive and painless technique that directly stimulates cortical neurons and is approved by the Food and Drug administration for the treatment of depression.[32] TMS induces significant changes on monoamine neurotransmitters and cortisol, neuroendocrine factors also affected in PTSD. Future TMS research would clarify dosing relationships to efficacy (i.e. frequency used (low or high), area of brain treated, and timing and duration of sessions). *Acupuncture* is a Chinese medicine energy modality that uses needles inserted into specific points along the body's energetic meridians. Acupuncture may help PTSD

through its effects on the autonomic nervous system and prefrontal and limbic brain structures, systems that are intrinsically involved in PTSD pathophysiology.[23,33]

Meditation also appears to be helpful for PTSD. While there are various meditation styles, all types incorporate self-observation of mental activity, attention training, and cultivating an attitude that highlights process rather than content.[34] Meditation studies show positive benefit for a variety of symptoms related to PTSD such as depressive symptoms or relapse,[35–41] anxiety,[40,42–45] suicidal behavior,[46] and sleep disturbances.[47,48] Meditation may affect PTSD symptoms through attention training, improving prefrontal cortex activity and autonomic nervous system function, changing thought patterns, increasing emotional acceptance and reducing avoidance, and regulating the hypothalamic-pituitary-adrenal axis.[49]

Hypnotherapy, another mind-body medicine, is a psychotherapeutic technique based on the hypnotist providing suggestions for changes in sensation, perception, cognition, affect, mood, or behavior.[50] Hypnotherapy may allow people with PTSD to down-regulate their autonomic nervous system and thus become more receptive to changes in cognition, mood or behavior.

Similarly, *visualization* is designed specifically for the patient's imagination (mind) to have an effect on a physiological system (body). Visualization is a lived experience that is a dynamic, quasi-real, psychophysiological process.[51] Guided imagery is a variation on visualization where another person leads an individual through experiences in the mind to access the physical, emotional and spiritual dimensions that effect physiological change, modulating the individual's response.[52] Both hypnotherapy and visualization/guided imagery could be modified to specifically address the symptoms the person with PTSD is experiencing.

At this point, the evidence is Unclear or Conflicting for biofeedback, Emotional Freedom and Thought Field Therapies, yoga breath work, relaxation, and natural products. Future studies are warranted to clarify results before practitioners should recommend them specifically for PTSD symptoms.

Agreement and disagreements with other studies or reviews

Our work builds on a previous review conducted by Strauss et al. that found inconclusive evidence for all the CAM modalities they assessed using very stringent inclusion and exclusion criteria.[16] Similarly, we found inconclusive evidence for some modalities. However, because we included study designs other than RCTs, participants with PTSD symptoms (and not just a PTSD diagnosis), and used a different grading schema, we were able to present a broader view of the state of CAM research. Our study was also different in that we included rTMS as a CAM modality, evaluated Natural Products, and included non-English papers in our search criteria. While our overall search strategy was not as comprehensive, both reviews highlight the importance of improved CAM clinical trial methods, more rigorous reporting, and the need for more RCTs in CAM research.

Limitations

Various limitations must be considered when reviewing these results. Some modalities included in this review may not be considered CAM modalities (e.g. rTMS because of its psychiatry heritage; biofeedback because of its common use in mainstream academic medicine and clinical psychology; and hypnotherapy as a psychosocial treatment). For this study, we used the CAM definition *a priori* as explained on the NCCAM website[11] at the time of designing the study. Those definitions included magnet therapy under the Energy Medicine category and hypnotherapy under the Mind-Body Medicine category. rTMS, biofeedback, and hypnotherapy could also be included as complementary because they are not evidence-based standard care treatments for PTSD, even though they may be considered conventional for other conditions.

Although we included all languages in our search strategy we only found English papers. We searched only published papers; grey literature resources were not included and hand-searches of relevant bibliographies were not conducted. Publication bias is present when positive trials are more frequently published over negative studies. It is possible that this impacted our review as we found 17 positive trials and five negative trials (7 neutral and four mixed). Another limitation is that we did not take into account outcome measure timing in our grading schema. For example, we were not able to distinguish if each modality had more or less evidence for PTSD symptoms immediately after the treatment versus at a longer-term follow-up. Additional studies with less heterogeneity in methods, participants and outcomes need to be conducted before rigorous meta-analyses can be done. Because of this, the results from this study must be viewed as qualitative trends rather than conclusions.

Conclusions

Several CAM modalities may be helpful for improving PTSD symptoms. rTMS has the strongest evidence for benefit followed by acupuncture, hypnotherapy, meditation, and visualization. There is insufficient evidence to recommend biofeedback, Emotional Freedom and Thought Field Therapies, relaxation, yoga breath work, and natural products at this time. Future research should include larger, properly randomized, controlled trials with appropriately selected control groups and rigorous methodology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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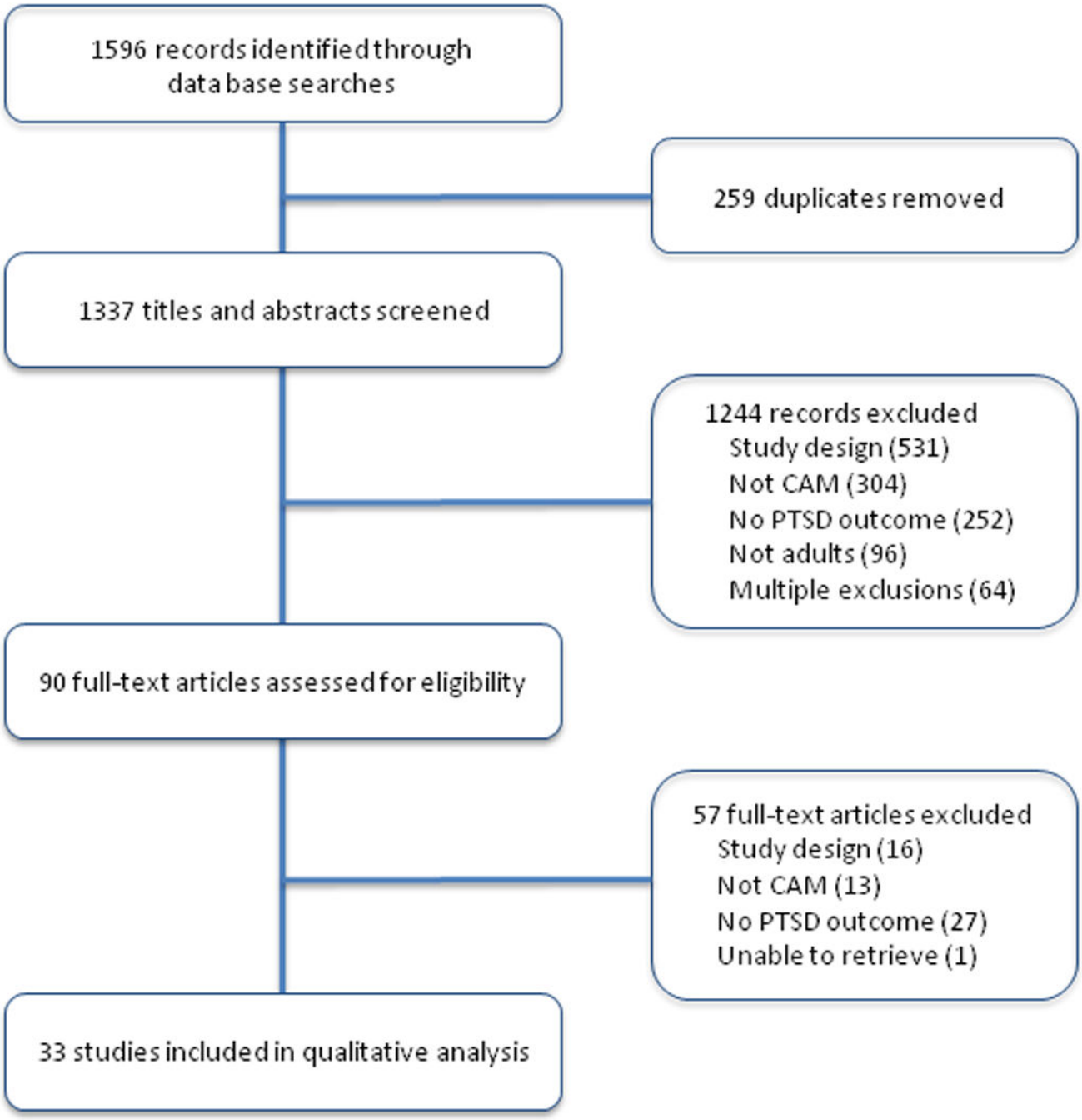

Figure 1.
Study flow diagram.

Table 1

Natural Standard evidence-based validated grading rationale.

Level of evidence grade	Criteria
A (Strong scientific evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.
B (Good scientific evidence)	Statistically significant evidence of benefit from 1–2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND with supporting evidence in basic science, animal studies, or theory.
C (Unclear or conflicting scientific evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria, OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.
D (Fair negative scientific evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/non-randomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit.
F (Strong negative scientific evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.
Lack of evidence	Unable to evaluate efficacy due to lack of adequate available human data.

Table 2

Characteristics of included studies.

Study/ Design	n	% Drop out or missing data	Gender F: M	Mean age yrs ± SD (Range)	Intervention *vs.* Comparator	PTSD dx required	Participant characteristics	Duration of intervention	PTSD outcomes	Results	Overall Study Outcome *	Quality Assessment Score
ENERGY MEDICINE												
Boggio, 2010 RCT	30	13%	21:9	44.5 ± 4.4	rTMS 20Hz to right or left dlPFC *vs.*Sham rTMS	Yes, SCID criteria	Mixed trauma types	5 sessions (1600 pulses per session)/ wk for 2 wks	PCL, TOPS	Right and left rTMS sig dec PTSD outcomes vs sham (PCL p<.001; TOPS p<.001).	Positive[a]	92
Cohen, 2004 RCT	29	17%	7:17*	41.7 ± 11.4 (22–68)	rTMS 10Hz or rTMS 1Hz to right dlPFC *vs.*Sham rTMS	Yes, SCID criteria	Mixed trauma types	Five 20-min sessions/wk for 2 wks	PCL, TOPS, CAPS-Hebrew version	For PCL and TOPS: 10Hz rTMS sig better than sham and 1Hz (p<.002). No diff 1Hz rTMS vs. sham.	Positive[a]	85
Grisaru, 1998 Pre-post	10	0%	3:7	47 (21–53)	rTMS 0.3Hz	Yes, DSM-IV criteria	Mixed trauma types	Single session of 30 pulses at 1 min intervals	IES	No sig change in total IES or IES-I; Sig dec IES-A at 7 day follow up (p=0.033); no sig diff 28 day follow up.	Mixed[c]	71
Osuch, 2009 Cross-over	9	0%	8:1	41.4 ± 12.3 (24–56)	Imaginal exposure therapy plus rTMS 1Hz to right dlPFC *vs.* Imaginal exposure therapy plus sham rTMS	Yes, no criteria specified	Mixed trauma types	Three to five 30-min sessions/wk for a total of 20 sessions	CAPS, IES	No sig diff between exposure + active rTMS vs. exposure + sham rTMS except for moderate dec CAPS hyperarousal subscale (p=0.08).	Mixed[a]	70
Watts, 2012 RCT	20	0%	2:18	Tx: 54 ± 12.3; Ctrl: 57.8 ± 11.8	rTMS 1Hz to right dlPFC *vs.* Sham rTMS	Yes, SCID criteria	Veterans with mostly combat trauma	Five 20-min sessions/wk for 2 wks	CAPS, PCL	rTMS sig reduced CAPS (p=.009) and PCL (p=. 0002) vs sham rTMS.	Positive[a]	80
CHINESE MEDICINE												
Hollifield, 2007 RCT	84	27%	57:27	Acu: 42.3 ± 12.1; CBT: 40.9 ± 13.4; Ctrl: 43.4 ± 13.5	Acupuncture *vs.* 1) CBT; 2) 12-wk waitlist control	Yes, SCID criteria	Mixed trauma types	Acupuncture: two 1-hr sessions/wk for 12 wks; CBT: one 2-hr session/wk for 12 wks	PSS-SR	Both acupuncture and CBT dec PTSD outcomes vs waitlist controls (p<.01). No diff between acup and CBT as both groups improved (p=0.29).	Neutral[a]; Positive[b]	88
Zhang, 2011 RCT	91	1%	55:36	35.0 ± 19.3 (4–89)	Acupoint stimulation (50Hz) + CBT *vs.*CBT	Yes, WHO criteria	Acute PTSD from China's 2008 Zhejiang Province earthquake	Acupoint and CBT: 30 min session every other day over one wk	IES-R Chinese version	Acupoint +CBT more effective reducing IES-R than CBT alone (p<0.01).	Positive[a]	77
MIND-BODY: BIOFEEDBACK												
Lande, 2010 CT	49	20%	6:33 *	mean/range not reported	HRV Biofeedback *vs.* TAU	No	Active duty combat soldiers with self-report PTSD	Two 20-mintue sessions/wk for 3 wks	PCL-M	Both biofeedback and control groups experienced sig dec in PTSD symptoms	Negative[b]	62

Study/ Design	n	% Drop out or missing data	Gender F: M	Mean age yrs ± SD (Range)	Intervention *vs.* Comparator	PTSD dx required	Participant characteristics	Duration of intervention	PTSD outcomes	Results	Overall Study Outcome *	Quality Assessment Score
										over time, no sig diff between groups.		
Muller, 2009 Pre-post	13	15%	8:3 *	35.7 ± 6.1	Pain-focused cognitive behavioral biofeedback	Yes, MINI criteria	Refugees with PTSD, chronic pain, and experience of torture or war	One 90-min session/wk for 10 wks	Post-traumatic Diagnostic Scale	No sig changes in PTSD symptoms over time.	Negative[c]	76
Tan, 2011 RCT	20	5%	0:20	36.0 ± 13.1 (24–62)	HRV Biofeedback *vs.* TAU	Yes, no criteria specified	Veterans with combat-related PTSD	One 30-min session/wk for 8 wks	CAPS, PCL	Biofeedback sig dec CAPS (p<.001) and PCL (p=.035) pre-post; Only CAPS-AN better in biofeedback group vs TAU; no other between group diff but moderate effect sizes for change in overall sx (Cohen's d = 0.52–0.70 for CAPS and PCL respectively).	Mixed[b]	80
Zucker, 2009 RCT	50	24%	17:21 *	(18–60)	RSA Biofeedback *vs.*Progressive muscle relaxation recording	No	Substance use disorder and elevated PTSD sx; mixed trauma types	Personal instruction for portable biofeedback device or PMR recording: 20-mins/day for 4 wks.	PCL, PTS-T	Both groups decreased PTSD scores over time (both groups p<.01). Biofeedback did not improve PCL scores (p=0.32) or PTS-T scores (p=0.73) over control.	Neutral[a]	81
MIND-BODY: THOUGHT FIELD THERAPIES												
Folkes, 2002 Pre-post	61	49%	not reported	27.7 (5–48)	TFT	No	Adult and child refugees from five language groups	One 60 to 90-min session	PCL (adult or child version)	50% dropout rate, analysis completed on 31 individuals with complete data sets. PCL-C scores dropped 40% from pre- to post-intervention (p=0.05).	Positive[c]	62
Karatzias, 2011 RCT	46	43%	26:20	EFT: 39.7 ± 10.9; EMDR: 41.5 ± 10.8	EFT *vs.*EMDR	Yes, DSM-IV criteria	Mixed trauma types	Up to eight 1-hour sessions. EMDR group received 3.7 ± 2.3 hrs, EFT group received 3.8 ± 2.6 hrs.	CAPS, PCL	43.5% dropped out from the EMDR group, and 39.1% dropped out from the EFT group. Both EFT and EMDR improved all outcomes (p<.001). Effect size Cohen's d= 0.80 for both modalities.	Neutral[a]	85
MIND-BODY: HYPNOSIS												
Abramowitz, 2008 RCT	32	0%	0:32	31.7 (21–40)	Hypnosis *vs.*Zolpidem 10mg	Yes, DSM-IV criteria	Chronic combat-related PTSD with insomnia	Hypnosis: Two 1.5-hour sessions/wk for 2 wks; Zolpidem: 10mg nightly for 2 wks	IES-R, PDS	Hypnosis group had sig reductions in PDS (p<.034) and IES scores (p<.0005) compared to Zolpidem over the course of the study.	Positive[a]	77
Abramowitz, 2010 Pre-post	37	3%	0:37	41.2 ± 12.2 (24–64)	Hypnosis paired with olfactory based exposure	Yes, semi-structured interview with DSM-IV criteria	Combat trauma	One 90-min session/wk for 6 wks	IES-R	Hypnosis technique decreased stress reaction after 6 wks (p<.0001).	Positive[c]	81

Study/ Design	n	% Drop out or missing data	Gender F: M	Mean age yrs ± SD (Range)	Intervention *vs.* Comparator	PTSD dx required	Participant characteristics	Duration of intervention	PTSD outcomes	Results	Overall Study Outcome *	Quality Assessment Score
Bryant, 2006 RCT	87	46%	53:34	(17–60)	Hypnosis + CBT *vs.*1) CBT; 2) Supportive counseling	No	Acute stress disorder from motor vehicle accident or sexual assault	CBT and CBT plus hypnosis-Both groups five 90-min sessions	CAPS, IES	No diff in IES scores among groups. CAPS scores for CBT and CBT Hypnosis groups were 43% lower than counseling group at 3 year follow-up (p=0.05).	Neutral[a]	77
MIND-BODY: MEDITATION												
Bormann, 2005 Pre-post	101	39%	6:56 *	61.8 ± 13.2 (33–84)	Mantram Meditation	No	Veterans with combat-related trauma	One 90-min instructional session/wk for 5 wks plus home practice	PCL	PTSD scores (only available for n=30) decreased 13.7% from pre- to post-intervention (p=0.02).	Positive[c]	90
Bormann, 2008 RCT	33	14%	0:33	56 ± 6.6 (40–76)	Mantram Meditation *vs.* Waitlist control	Yes, no criteria specified	Veterans with combat-related PTSD	One 90-min session/wk for 6 wks	PCL, CAPS	Intervention improved CAPS score (effect size −0.33) and PCL score (effect size −0.72), no p values provided.	Positive[b]	85
Brooks, 1985 CT	25	28%	0:18 *	33.3	Transcendental Meditation *vs.*Psychotherapy	No	Vietnam veterans with chronic PTSD	Meditation: One 60-min session/wk for 12 wks; Therapy: One 60-min session/wk for 12 wks	Non-standard PTSD Scale (no reference provided in paper)	Meditation showed positive effect compared to psychotherapy for PTSD and related subscales of emotional numbness, anxiety, depression, alcohol use, insomnia, and family problems (all p<.05).	Positive[a]	54
Harris, 2011 RCT	54	6%	6:48	45.5 ± 13.5	Spiritual prayer and/or meditation *vs.*Waitlist control	No	Veterans with trauma exposure, mixed trauma types	One 2-hour session/wk for 8 wks	PCL	Spiritual prayer/mediation group dec PCL vs waitlist control (p<.02)	Positive[b]	73
Kearney, 2012 Pre-post	92	20%	22:70	51.0 ± 10.6	Mindfulness Based Stress Reduction (MBSR)	No	Veterans, 74% screened positive for PTSD at baseline	One 2.5-hour session/wk for 8 wks	PCL	MBSR decreased PCL total and all subscores (p<.001).	Positive[c]	86
Kimbrough, 2010 Pre-post	27	22%	24:3	45 (23–68)	Mindfulness Based Stress Reduction	No	Adults with history of childhood sexual abuse	One 3-hour session/wk for 8 wks, followed by 3 refresher courses	PCL	MBSR decreased PCL total and all subscores at 8 and 24-wks post-enrollment (p<.0001).	Positive[c]	95
Price, 2005 RCT	25	4%	25:0	41 (median) (26–56)	Mindful Awareness in Body Oriented Therapy *vs.*Massage	No	Adult women currently in therapy for childhood sexual abuse	Two 60-min sessions/wk for 4 wks	Crime-related PTSD Scale	Both body-oriented therapy and regular massage improved PTSD symptoms, no sig diff between the groups (p>.05).	Neutral[a]	81
Price, 2006 RCT	8	0%	8:0	(28–52)	Mindful Awareness in Body Oriented Therapy *vs.*Waitlist control	No	Adult women currently in therapy for childhood sexual abuse	One 60-min session/wk for 8 wks	Crime-related PTSD Scale	Body-oriented therapy group had sig pre-post improvement in PTSD scale (p<0.01), control group did not experience sig improvements.	Positive[b]	72

Study/ Design	n	% Drop out or missing data	Gender F: M	Mean age yrs ± SD (Range)	Intervention *vs.* Comparator	PTSD dx required	Participant characteristics	Duration of intervention	PTSD outcomes	Results	Overall Study Outcome *	Quality Assessment Score
Rosenthal, 2011 Pre-post	6	17%	0:6	(25–40)	Transcendental meditation	PTSD as judged by investigator	OEF/OIF vets with combat-related	3–5 hrs of instruction followed by home practice: 20 mins twice a day for 12 wks	CAPS, PCL-M	Participants showed sig improved CAPS (p=0.02) and PCL-M (p=0.02) scores.	Positive[c]	86
MIND-BODY: RELAXATION												
Colosetti, 2000 Cross-over	5	0%	5:0	38.8 (25–50)	Relaxation (control condition) *vs.*EMDR	Yes, CAPS criteria	Incarcerated women with history of abuse in an intimate relationship	One session relaxation training/wk for 3 to 6 wks followed by one session of EMDR/wk for 3 wks	IES	Neither relaxation training or EMDR exhibited sig changes in PTSD outcomes, no statistics provided due to small sample size.	Negative[a]	65
Echeburua, 1997 CT	20	0%	20:0	20 ± 7.1	PMR (control condition) *vs.*Gradual self-exposure with cognitive restructuring	Yes, ADIS-R DSM-III criteria	Women with history of sexual abuse	1x/wk for 6 wks; home practice 2x/ day.	Scale of Severity of Posttraumatic Stress Disorder Symptoms	Cognitive restructuring lead to the reversal of DSM-III PTSD diagnosis in 100% of participants while relaxation was only 40% by 12 months. PTSD scale score was 4×lower in the cognitive restructuring group.	Negative[a]	60
Mitani, 2006 Pre-post	22	0%	0:22	42.2 ± 9.7	Relaxation	No	Japanese fire fighters in a select fire station	One 60-min instructional session followed by home practice: 2–3 x/wk for 2 months.	IES-R (Japanese version)	Total IES-R scores dec 60% from pre- to post in PTSD stress-related group (p=0.04). Intrusion subscale dec sig in the PTSD stress-related group (p=.038); hyperarousal and avoidance did not change sig. No sig changes in the non-PTSD stress-related group IES scores noted (p=.76 – 1.0).	Mixed[c]	68
Taylor, 2003 RCT	60	25%	45:15	37 ± 10	Relaxation (control condition) *vs.* 1) Exposure therapy; 2) EMDR	Yes, DSM-IV criteria	Mixed trauma types	Eight 90-min individualized session of relaxation, exposure, or EMDR therapy.	CAPS, PTSD Symptom Severity Scale, PTSD dx	Exposure superior to relaxation in reducing # who met PTSD dx (p<.02); no sig diff between EMDR and exposure or EMDR and relaxation for this outcome. CAPS and Symptom Severity Scale dec sig in all groups with no difference between groups.	Neutral[a]	85
MIND-BODY: GUIDED IMAGERY												
Jain, 2012 RCT	123	17%	11:112	Tx: 27.1 (20–42); Ctrl: 27.9 (20–48)	Healing touch plus guided imagery *vs.*TAU	No	Returning combat-exposed active duty military with sig PTSD sx	Two 60-min sessions/wk for 3 wks	PCL-M	Healing touch/guided imagery group had sig dec in PCL score compared to controls (p<0.0005).	Positive[b]	92

Study/ Design	n	% Drop out or missing data	Gender F: M	Mean age yrs ± SD (Range)	Intervention *vs.* Comparator	PTSD dx required	Participant characteristics	Duration of intervention	PTSD outcomes	Results	Overall Study Outcome *	Quality Assessment Score
MIND-BODY: YOGIC BREATH WORK												
Descilo, 2010 CT	183	3%	160:23	Tx 1: 30.8; Tx 2: 35.1; Ctrl: 34.7	Yogic breath work *vs.* 1) Yoga breath work with exposure therapy; 2) 6-wk waitlist control	No	2004 South East Asian tsunami survivors living in refugee camps who scored > 50 on the PCL	Breath work: one 2-hr session/day×4 days. Exposure therapy: as above + 3–5 exposure sessions	PCL	Both treatment groups showed improvement in PCL scores over waitlist control (p<.0001), no diff between active treatments.	Neutral[a]; Positive[b]	83
NUTRACEUTICAL												
Kaplan, 1996 Cross-over	17	24%	5:8 *	39.7 (25–56)	Inositol powder 12g/day *vs.* Placebo (glucose powder) 12g/day	Yes, DSM-III-R criteria	Trauma type not reported	Inositol or placebo daily for 4 wks, 2 wk washout between cross-over	IES-Hebrew version	No sig diff between inositol and placebo for total IES scores or avoidance and intrusion subscales, no p values reported.	Negative[a]	73
Shams,2007 RCT	40	0%	34:6	Tx: 38.2 ± 11.2; Ctrl: 38.5 ± 13.7	Gingko Biloba 200mg vs. Placebo	Yes, DSM-IV	Earthquake survivors	12 wks	Watson's PTSD Scale	Sig improvement in gingko group over control (p<.01)	Positive[a]	73

Acu: acupuncture; ADIS-R: Anxiety Disorders Interview schedule Revised; CAPS: Clinician-Administered PTSD Scale; CAPS-AN: Clinician-Administered PTSD Scale Avoidance/Numbing Subscale; CBT: cognitive behavioral therapy; CGI-I: Clinical Global Impression-Improvement; CGI-S: Clinical Global Impression-Severity; Ctrl: Control group; Dec: decreased; Diff: difference; dlPFC: dorsolateral prefrontal cortex; DSM: Diagnostic and Statistical Manual of Mental Disorders; EFT: Emotional Freedom Technique; EMDR: Eye Movement Desensitization and Reprocessing; Hr: Hour; IES: Impact of Event Scale; IES-R: Impact of Event Scale-Revised; IES-I: Impact of Event Scale Intrusion Subscale; IES-A: Impact of Event Scale Avoidance Subscale; MBSR: Mindfulness Based Stress Reduction; Min: Minute; MINI: Mini International Neuropsychiatric Interview with DSM-IV criteria; OEF: Operation Enduring Freedom; OIF: Operation Iraqi Freedom; PCL: PTSD Checklist Civilian Version; PCLM: PTSD Checklist Military Version; PDS: Posttraumatic Diagnostic Scale; PMR: Progressive muscle relaxation; PSS-SR: Posttraumatic Stress Disorder Symptom Scale Self Report; PTS-T: Posttraumatic Stress-Total scale of the Detailed Assessment of Posttraumatic States; RSA: Respiratory sinus arrhythmia; rTMS: repetitive transcranial stimulation; SCID: Structured Clinical Interview DSM-IV; Sig: Significant; Sx: Symptom; TAU: Treatment as usual; TFT: Thought field therapy; TOPS: Treatment Outcomes for PTSD Scale; Tx: Treatment; WHO: World Health Organization; Wk: Week

*These studies only provided gender characteristics for those who completed the trial.

**Criteria for determining overall study outcome: Positive = most PTSD outcomes showed statistically significant improvements, Mixed = only 1–2 PTSD subscales are significantly improved, Negative = no PTSD outcomes significantly improved, Neutral = both intervention and active control showed significant improvements, no difference between the groups, Two studies have two grades to account for comparisons between the active control and non-active control groups. For example, Hollifield had a positive results compared to the waitlist (Positiveb) but a Neutral results compared to the active control because both active control groups had improvements from before to after the intervention.

[a]= active control comparison

[b]= non-active control comparison

[c]= no control

Table 3

Summary of risk of bias for randomized controlled CAM trials for PTSD.

Study	Intervention	Random sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Fidelity of intervention assessed
Energy modalities								
Boggio, 2010	rTMS	+	?	+	+	+	+	N/A
Cohen, 2004	rTMS	?	?	+	+	?	+	N/A
Watts, 2012	rTMS	?	?	+	+	+	+	N/A
Chinese medicine								
Hollifield, 2007	Acupuncture	+	+	-	+	+	+	+
Zhang, 2011	Acupoint stimulation	?	?	-	-	+	+	-
Nutraceutical								
Shams, 2007	Ginkgo Biloba	?	?	+	?	+	+	?
Mind-body modalities								
Tan, 2011	Biofeedback	?	?	-	?	+	+	+
Zucker, 2009	Biofeedback	+	?	-	?	+	+	?
Karatzias, 2011	EFT	+	?	-	+	+	+	?
Abramowitz, 2008	Hypnosis	?	?	-	?	+	+	?
Bryant, 2006	Hypnosis	+	-	-	+	-	+	+
Bormann, 2008	Meditation	+	?	-	+	+	+	+
Harris, 2011	Meditation	+	?	-	?	+	+	+
Price, 2005	Meditation	?	?	-	?	+	+	+

Study	Intervention	Random sequence generation	Allocation concealment	Blinding of participants/ personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Fidelity of intervention assessed
Price, 2006	Meditation	?	?	-	?	+	+	+
Taylor, 2003	Relaxation	?	?	+	+	-	+	+
Jain, 2012	Guided imagery	+	+	-	+	?	+	?

EFT: emotional freedom technique; rTMS: repetitive transcranial magnetic stimulation

(+) Low risk of bias

(-) High risk of bias

(?) Unclear risk of bias