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To cite this article: Jonathan I. Bisson, Marieke van Gelderen, Neil P. Roberts & Catrin Lewis (2020) Non-pharmacological and non-psychological approaches to the treatment of PTSD: results of a systematic review and meta-analyses, European Journal of Psychotraumatology, 11:1, 1795361, DOI: 10.1080/20008198.2020.1795361

To link to this article: https://doi.org/10.1080/20008198.2020.1795361

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Published online: 24 Aug 2020.

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Non-pharmacological and non-psychological approaches to the treatment of PTSD: results of a systematic review and meta-analyses

Jonathan I. Bisson a, Marieke van Gelderen b,c, Neil P. Roberts a,d and Catrin Lewis a

*National Centre for Mental Health (NCMH), Division of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Cardiff, UK; *Department of Psychology, ARQ Centrum 45, Diemen, Netherlands; *Department of Psychiatry, Leiden University Medical Center, Leiden, Netherlands; *Psychology and Psychological Therapies, Cardiff & Vale University Health Board, Cardiff, UK

ABSTRACT
Background: Non-pharmacological and non-psychological approaches to the treatment of post-traumatic stress disorder (PTSD) have often been excluded from systematic reviews and meta-analyses. Consequently, we know little regarding their efficacy.

Objective: To determine the effect sizes of non-pharmacological and non-psychological treatment approaches for PTSD.

Method: We undertook a systematic review and meta-analyses following Cochrane Collaboration guidelines. A pre-determined definition of clinical importance was applied to the results and the quality of evidence was appraised using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.

Results: 30 randomised controlled trials (RCTs) of a range of heterogeneous non-psychological and non-pharmacological interventions (28 in adults, two in children and adolescents) were included. There was emerging evidence for six different approaches (acupuncture, neurofeedback, saikokeishikankyoto (a herbal preparation), somatic experiencing, transcranial magnetic stimulation, and yoga).

Conclusions: Given the level of evidence available, it would be premature to offer non-pharmacological and non-psychological interventions routinely, but those with evidence of efficacy provide alternatives for people who do not respond to, do not tolerate or do not want more conventional evidence-based interventions. This review should stimulate further research in this area.

Enfoques no farmacológicos y no psicológicos para el tratamiento del tept: Resultados de una revisión sistemática y metanálisis

Antecedentes: Los enfoques no farmacológicos y no psicológicos para el tratamiento del trastorno de estrés postraumático (TEPT) han sido frecuentemente excluidos de las revisiones sistemáticas y los metaanálisis. Consecuentemente, poco sabemos acerca de su eficacia.

Objetivo: Determinar los tamaños de efecto de los enfoques de tratamiento no farmacológicos y no psicológicos para el TEPT.

Método: Realizamos una revisión sistemática siguiendo las guías de la Colaboración Cochrane. Se aplicó una definición predeterminada de la importancia clínica a los resultados y se evaluó la calidad de la evidencia usando el enfoque de Calificación del Análisis, Desarrollo y Evaluación de las Recomendaciones (GRADE) por sus siglas en inglés de Grading of Recommendations Assessment, Development and Evaluation.

Resultados: Se incluyeron 30 estudios controlados aleatorizados (RCTs) de un rango de intervenciones heterogéneas no psicológicas y no farmacológicas (28 en adultos, dos en niños y adolescentes). Hubo evidencia emergente para 6 diferentes enfoques (acupuntura, neurofeedback, saikokeishikankyoto (una preparación a base de hierbas), experiencia somática, estimulación magnética transcranial y yoga).

Conclusiones: Dado el nivel de evidencia disponible, sería prematuro ofrecer intervenciones no farmacológicas y no psicológicas de forma rutinaria, pero aquellas con evidencia de eficacia brindan alternativas para las personas que no responden, no toleran o no quieren intervenciones convencionales basadas en la evidencia. Esta revisión debería estimular mayor investigación en esta área.

ARTICLE HISTORY
Received 21 April 2020
Revised 18 June 2020
Accepted 2 July 2020

KEYWORDS
Non-pharmacological; non-psychological; systematic review; PTSD treatment

PALABRAS CLAVE
No farmacológica; No psicológica; Revisión sistemática; Tratamiento para el TEPT

HIGHLIGHTS
• There is emerging evidence of effect for acupuncture, neurofeedback, saikokeishikankyoto (a herbal preparation), somatic experiencing, transcranial magnetic stimulation, and yoga for the treatment of post-traumatic stress disorder (PTSD).

CONTACT
Jonathan I. Bisson, BissonJI@Cardiff.ac.uk
Division of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Cardiff CF24 4HQ

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Although a number of psychological and pharmacological treatments have been shown to be effective for the treatment of post-traumatic stress disorder (PTSD) (Hoskins et al., in review; Lewis, Roberts, Andrew, Starling, & Bisson, 2020), treatment resistance is common (Blanchard et al., 2003) and people with PTSD can find some interventions difficult to tolerate (Lewis, Roberts, Gibson, & Bisson, 2020). There is, therefore, a strong imperative to establish more effective and better-tolerated treatments for PTSD, including alternative management approaches to increase choice and address the preference of some people not to take medication or engage in psychological therapy. Anecdotal/proof of concept reports of their success have led to an increasing interest in alternative approaches and an increasingly robust evidence base being developed. This overview paper considers the 2018 ISTSS Prevention and Treatment Guidelines’ recommendations (International Society of Traumatic Stress Studies [ISTSS] [Online], 2018) regarding non-pharmacological and non-psychological interventions for PTSD and their implications for practice and future research.

The development process for the ISTSS Guidelines adhered to a strong methodology whereby PICO (Population, Intervention, Comparator, Outcomes) scoping questions were generated before any reviews or analyses were conducted (International Society of Traumatic Stress Studies [ISTSS] [Online], 2018). A key consideration was how to deal with interventions that were not pharmacological or psychological treatments. Such interventions include techniques commonly labelled as complementary or alternative therapies, for example, yoga and meditation, but also physical therapies such as transcranial magnetic stimulation (TMS) and neurofeedback.

The ISTSS Treatment Guidelines Committee included scoping questions that considered:

For adults with PTSD (and for children and adolescents with clinically relevant post-traumatic stress symptoms), do non-psychological and non-pharmacological treatments/interventions when compared to other treatments, treatment as usual, waiting list or no treatment, result in a reduction of symptoms, improved functioning/quality of life, presence of disorder, or adverse effects?

This paper presents the results of the systematic review and meta-analysis results pertaining to this scoping question as a short communication. The methodological process for addressing this question followed the same procedure as that outlined for the other ISTSS Guidelines scoping questions (Bisson et al., 2019) and is described in detail elsewhere (Hoskins et al., in review; Lewis et al., 2020). The methodology included risk of bias evaluations and data extraction procedures based on Cochrane Review guidelines (Higgins & Green, 2011) and an evaluation of the quality of findings using GRADE (Guyatt, Oxman, Schünemann, & Tugwell, 2011).

1. The evidence

Of the 327 randomised controlled trials (RCTs) included in the meta-analyses for the ISTSS Guidelines, 30 (9.2%) related to non-psychological and non-pharmacological interventions (28 in adults, two in children and adolescents). The individual studies, that covered a range of heterogeneous interventions, and risk of bias ratings are shown in Table 1.

Table 2 summarises the results of the meta-analyses undertaken with respect to specific interventions versus treatment as usual or wait list control.

In addition to RCTs that compared active interventions with TAU or WL, a number of studies compared one intervention with another. There was no evidence of a difference in four of these comparisons: acupuncture versus CBT with a trauma focus [k = 1; N = 48; SMD −0.35, CI −0.92 to 0.22]; hypnotherapy versus CBT with a trauma focus [k = 1; N = 56; SMD 0.34, CI −0.19 to 0.86]; electroacupuncture versus paroxetine [k = 1; N = 127; SMD −0.21, CI −0.56 to 0.14]; and mindfulness-based stress reduction versus present-centred therapy [k = 3; N = 324; SMD −0.07, CI −0.29 to 0.15]. One active treatment was superior to another in two comparisons: mantram repetition over...
| Study | Intervention | N   | Trauma          | Control          | Random sequence | Allocation | Blinding of outcome | Incomplete outcome data assessment | Selective reporting | Other sources of bias |
|-------|--------------|-----|-----------------|------------------|-----------------|------------|--------------------|----------------------------------|-------------------|---------------------|
| Ahmadizadeh and Rezaei (2018) | TMS | 58  | Military veterans | Sham TMS         | Unclear         | Low        | Low                | Low                              | Unclear           | Low                 |
| Bormann, Thorp, Wetherell, Golshan, and Lang (2013) | Mantram repetition | 29  | Military veterans | WL/TAU           | Unclear         | Low        | Low                | Low                              | Unclear           | Low                 |
| Bormann, Thorp, Wetherell, and Golshan (2008) | Mantram repetition | 146 | Military veterans | WL/TAU           | Low             | Unclear    | Unclear            | High                             | Unclear           | Low                 |
| Bormann et al. (2018) | Mantram repetition | 173 | Military veterans | Present-centred therapy | Low            | Low        | Low                | Low                              | Low               | Low                 |
| Bremner et al. (2017) | MBSR | 17  | Military veterans | Present-centred therapy | Unclear        | High       | Low                | Unclear                          | High              | High                |
| Brom, Kleber, and Defares (1989) | Hypnotherapy | 29  | Various          | WL/CBT-TF        | Unclear         | High       | Low                | Low                              | Unclear           | Low                 |
| Brom et al. (2017) | Somatic experiencing | 60  | Various          | WL               | Low             | High       | Low                | Low                              | Unclear           | High                |
| Carr et al. (2012) | Group music therapy | 16  | Various          | WL               | Low             | Low        | Low                | Low                              | Low               | High                |
| Carter, Gerbarg, Brown, Ware, and D’Ambrosio (2013) | Yoga | 25  | Military veterans | TAU              | Low           | Low        | High               | High                             | Unclear           | High                |
| Cohen et al. (2004) | TMS | 16  | Various          | Sham TMS         | Unclear         | Low        | Low                | High                             | Unclear           | Low                 |
| Davis et al. (2019) | MBSR | 191 | Military veterans | PCT              | Low            | Unclear    | Low                | Unclear                          | Low               | Unclear             |
| Gelkopf, Hasson-Ohayon, Bikman, and Kravetz (2013) | Nature adventure therapy | 42  | Military         | WL               | Low           | Unclear    | Unclear            | High                             | Unclear           | High                |
| Goldstein et al. (2017) | Group physical exercise | 47  | Military         | WL               | Unclear        | Unclear    | Low                | Low                              | Low               | Low                 |
| Hollifield, Sinclair-Lian, Warner, and Hammerschlag (2007) | Acupuncture | 72  | Various          | WL/CBT-TF        | Unclear         | High       | Low                | Low                              | Unclear           | Low                 |
| Keehan, McDermott, Malte, Martinez, and Simpson (2013) | Group MBSR | 47  | Military         | WL/TAU           | Unclear        | Unclear    | Low                | Unclear                          | High              | Low                 |
| Mitchell et al. (2014) | Yoga | 38  | Various, females only | WL/TAU       | Low            | Unclear    | Unclear            | Low                              | Unclear           | High                |
| Niles et al. (2012) | MBSR | 26  | Military         | Psychoeducation  | Unclear         | High       | High               | High                             | Unclear           | High                |
| Noohi, Miraghaie, and Arabi (2017) | Neurofeedback | 30  | Various          | WL/TAU           | Unlear         | Unclear    | Unclear            | Low                              | Unclear           | Low                 |
| Numata et al. (2014) | Sailokeishikanyakoto (Japanese herbal formula) | 43  | Earthquake      | WL/TAU           | Low            | Low        | High               | High                             | Unclear           | Low                 |
| Polusny et al. (2015) | MBSR | 116 | Military         | PCT              | Low            | Unclear    | Low                | Low                              | High              | High                |
| Reinhardt et al. (2018) | Yoga | 15  | Military         | WL/TAU           | Low            | Unclear    | Unclear            | High                             | Unclear           | High                |
| Rosenbaum, Sherrington, and Tiedemann (2015) | Physical exercise | 58  | Various          | WL/TAU           | Low            | Low        | Low                | Low                              | Low               | Low                 |
| School, Putman, and Van Der Does (2013) | Attentional bias modification | 102 | Various          | WL/TAU           | Low            | Low        | Low                | Low                              | Low               | Low                 |
| Seppälä et al. (2014) | Yoga | 20  | Military         | WL/TAU           | Low            | Unclear    | Low                | High                             | Unclear           | High                |
| van der Kolk et al. (2014) | Yoga | 64  | Women            | WL/TAU           | Low            | Unclear    | Low                | High                             | Unclear           | High                |
| van der Kolk et al. (2016) | Neurofeedback | 44  | Various          | WL/TAU           | Low            | Unclear    | Low                | Low                              | Low               | Low                 |
| Wang, Hu, Wang, Pang, and Zhang (2012) | Acupuncture | 127 | Earthquake      | Paroxetine       | Unclear        | Unclear    | Unclear            | Low                              | Unclear           | Low                 |
| Watts, Landon, Groft, and Young-Xu (2012) | TMS | 20  | Various          | Sham TMS         | Unclear        | Unclear    | Low                | Unclear                          | Low               | High                |
| Gordon, Staples, Blyta, Bytyqi, and Wilson (2008) | Mind-body skills group | 77  | Children post-war | WL/TAU          | Unclear        | High       | Unclear            | Low                              | Low               | Low                 |
| Lysiak-Stelzer, Singer, Patricia, and Chemtob (2007) | Trauma-focused expressive art therapy | 29  | Children various | WL/TAU           | Unclear        | Unclear    | Low                | High                             | Unclear           | High                |

CBT-TF: cognitive-behavioural therapy with a trauma focus; MBSR: mindfulness-based stress reduction; PCT: present-centred therapy; TMS: transcranial magnetic stimulation; WL/TAU: wait list/treatment as usual.
present-centred therapy \( [k = 1; N = 173; \text{SMD} \ -0.37, \ CI \ -0.68 \text{ to } -0.07] \); and mindfulness-based stress reduction over psychoeducation \( [k = 1; N = 27; \text{SMD} \ -1.23, \ CI \ -2.07 \text{ to } -0.40] \).

### 2. Quality of evidence

As illustrated in Table 2, the quality of evidence was judged as very low for all the interventions considered except yoga for which it was considered low, leading to significant uncertainty about the estimates generated. The quality of evidence was lower than found for pharmacological and psychological treatments (Hoskins et al., in review; Lewis et al., 2020). It is noteworthy, however, that the quality of some individual studies was high, as demonstrated by low risk of bias ratings in Table 1.

### 3. Recommendations

As a result of the evidence described above, six non-pharmacological and non-psychological interventions were recommended in the ISTSS Guidelines as interventions with emerging evidence for the treatment of PTSD in adults (see Table 3). There was insufficient

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**Table 2. Results of included interventions versus treatment as usual or wait list.**

| Intervention | Description of intervention | Number of studies; number of participants; standardised mean difference; and 95% confidence intervals | GRADE judgement for quality of evidence |
|--------------|-----------------------------|-------------------------------------------------------------------------------------------------|---------------------------------------|
| Transcranial magnetic stimulation (TMS) | Magnetic fields used repetitively to stimulate nerve cells in targeted areas of the brain. | \( k = 3; N = 94; \text{SMD} \ -1.53, \ CI \ -2.76 \text{ to } -0.30 \) | Very uncertain about the estimate. |
| Mantram repetition | Repeating a holy word(s) or phrase(s). | \( k = 2; N = 175; \text{SMD} \ -0.27, \ CI \ -0.57 \text{ to } 0.02 \) | Very uncertain about the estimate. |
| Acupuncture | Insertion of fine needles at specific points on the body (acupressure points). | \( k = 1; N = 48; \text{SMD} \ -0.92, \ CI \ -1.51 \text{ to } -0.32 \) | Very uncertain about the estimate. |
| Hypnotherapy | Hypnosis used to induce an altered state of consciousness before undertaking therapeutic work. | \( k = 1; N = 52; \text{SMD} \ -0.04, \ CI \ -0.58 \text{ to } 0.51 \) | Very uncertain about the estimate. |
| Somatic experiencing | Focuses on perceived body sensations and how to regulate these. | \( k = 1; N = 60; \text{SMD} \ -0.75, \ CI \ -1.28 \text{ to } -0.22 \) | Very uncertain about the estimate. |
| Group music therapy | Improvisation with musical instruments, with therapists providing improvised instrumental support and interaction. | \( k = 1; N = 16; \text{SMD} \ -2.12, \ CI \ -3.41 \text{ to } -0.83 \) | Very uncertain about the estimate. |
| Yoga | An integrative practice of body postures, breathing, and meditation. | \( k = 5; N = 162; \text{SMD} \ -0.37, \ CI \ -0.68 \text{ to } -0.05 \) | Further research likely to have an important impact on confidence in the estimate of effect and likely to change the estimate. |
| Nature adventure therapy | Engaging in outdoor group activities to support recovery. | \( k = 1; N = 42; \text{SMD} \ -0.40, \ CI \ -1.01 \text{ to } 0.22 \) | Very uncertain about the estimate. |
| Mindfulness-based stress reduction | Includes meditation practice, mindful awareness practice, and its application to real-life situations and to facilitate acceptance of traumatic memories. | \( k = 1; N = 47; \text{SMD} \ -0.49, \ CI \ -1.07 \text{ to } 0.09 \) | Very uncertain about the estimate. |
| Neurofeedback | Real-time displays of brain activity used to help individuals train (self-regulate) their brain activity. | \( k = 2; N = 74; \text{SMD} \ -2.14, \ CI \ -4.20 \text{ to } -0.08 \) | Very uncertain about the estimate. |
| Saikokeishikankyoto | Traditional Japanese herbal medicine. | \( k = 1; N = 43; \text{SMD} \ -0.91, \ CI \ -1.55 \text{ to } -0.28 \) | Very uncertain about the estimate. |
| Physical exercise | Usually a programme of aerobic exercise. | \( k = 2; N = 105; \text{SMD} \ -0.36, \ CI \ -0.75 \text{ to } 0.03 \) | Very uncertain about the estimate. |
| Attentional bias modification | Computer-based training to keep attention away from threatening information. | \( k = 1; N = 102; \text{SMD} \ -0.23, \ CI \ -0.62 \text{ to } 0.16 \) | Very uncertain about the estimate. |
| Mind–body skills in children | Using the mind to impact physical functioning. | \( k = 1; N = 77; \text{SMD} \ -0.37, \ CI \ -0.82 \text{ to } 0.08 \) | Very uncertain about the estimate. |
| Trauma-focused art therapy in children | Using art as a medium for trauma-focused work. | \( k = 1; N = 30; \text{SMD} \ -1.46, \ CI \ -2.30 \text{ to } -0.63 \) | Very uncertain about the estimate. |

**Table 3. ISTSS guideline interventions with emerging evidence for the treatment of PTSD.**

- Acupuncture
- Neurofeedback
- Saikokeishikankyoto
- Somatic experiencing
- Transcranial magnetic stimulation (TMS)
- Yoga

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\( ^a \)Control condition for TMS was sham TMS.
evidence to recommend any non-pharmacological or non-psychological intervention for children.

4. Discussion

The inclusion of emerging evidence recommendations for six different non-pharmacological and non-psychological interventions for the treatment of PTSD in the 2018 ISTSS Guidelines heralds a step change in the evidence-base available. Although more evidence is required before these interventions can be routinely recommended to people with PTSD, they offer alternative choices for people who may not have responded to or been able to tolerate interventions with better evidence or who would prefer an alternative approach. Several of the recommended interventions are already in widespread use and have an evidence-base for the treatment of other conditions.

Complementary therapies such as acupuncture and yoga have a developed evidence base for other health conditions (Bridges & Sharma, 2017; Smith, Armour, Lee, Wang, & Hay, 2018) but it is perhaps surprising that these are recommended above other established alternative approaches such as meditation. This may, however, reflect the dearth of RCTs in this area. Indeed, since the ISTSS Guidelines were completed, a large RCT of transcendental meditation (Nidich et al., 2018) in veterans with PTSD found it non-inferior to prolonged exposure and superior to health education.

Somatic experiencing has long been advocated as an effective approach to the management of PTSD with many practitioners and people with PTSD arguing for body-based interventions. Saikokeishikankyoto is not well known outside Japan but in Japan is a widely available herbal preparation and used for various ailments.

Neurofeedback has been used to treat PTSD since the 1980s (Peniston & Kulkosky, 1991) and the advent of MRI-assisted neurofeedback, as opposed to EEG-assisted neurofeedback, appears to have stimulated new interest in its use. Transcranial magnetic stimulation is now an approved treatment in many countries for treatment-resistant depression (NICE, 2015).

4.1. Limitations

Although the systematic review, meta-analysis and guideline development methodology adopted for the ISTSS Guidelines was of a very high standard, there are significant limitations with respect to the design of the primary trials included, many have high risks of bias and there is significant uncertainty with respect to the reliability of their findings. This is compounded in some instances by heterogeneous delivery of specific interventions across included studies, for example, for TMS and neurofeedback. There are also issues with respect to basing recommendations on comparisons with TAU/WL controls as opposed to other controls. For example, mantram repetition and mindfulness-based stress reduction were not recommended despite having shown superior over present-centred therapy and psychoeducation, respectively. A challenge to the evaluation of all non-pharmacological interventions is the difficulty/impossibility of designing and conducting rigorous placebo-controlled, double-blind RCTs of them. The interventions considered were reported to be well tolerated, but there was limited measurement of tolerance and this was not formally assessed as part of the review.

4.2. Clinical implications

Given the level of evidence available, it would be premature to offer the recommended non-pharmacological and non-psychological interventions routinely, but they provide alternatives for people who do not respond to, do not tolerate or do not want more conventional evidence-based interventions. Some, e.g. yoga, are likely to be much more readily available and have been associated with less adverse effects than others. That said, even more invasive interventions such as transcranial magnetic stimulation have been well tolerated in the trials reported to date.

4.3. Research implications

A clear message is that people with PTSD can be helped by novel, alternative approaches, and this should stimulate further research to refine and standardise specific interventions (e.g. the TMS studies used different dosing regimens, complicating direct comparison) and also to subject the interventions with the most promise to more rigorous RCTs with larger samples to determine their true place in the treatment of PTSD. There is also a need for more mechanistic research to determine how specific interventions work, and for whom, to enable informed choices and a more personalised approach to the delivery of treatment to people with PTSD.

Acknowledgments

We would like to acknowledge the input and support of the Cochrane Collaboration and the International Society for Traumatic Stress Studies (ISTSS).

Author contribution

All authors were responsible for the original study design. The search was conducted by the Cochrane Collaboration.
Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was unfunded.

ORCID

Jonathan I. Bisson http://orcid.org/0000-0001-5170-1243
Marieke van Gelderen http://orcid.org/0000-0003-4574-8226
Neil P. Roberts http://orcid.org/0000-0002-6277-0102
Catrin Lewis http://orcid.org/0000-0002-3818-9377

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