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SHORT COMMUNICATION

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

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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.

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关键词
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Enfoques no farmacologicos y no psicologicos para el tratamiento del tept: Resultados de una revision sistematica y metanalisis

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 metanálisis. 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 ingles 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 transcraneal 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.

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PTSD 的非药物和非心理学方法治疗：来自系统综述和元分析的结果

背景:治疗创伤后应激障碍 (PTSD) 的非药物学和非心理学方法常常被系统综述和元分析排除。因此, 我们对其疗效知之甚少。
目的:确定PTSD的非药物和非心理治疗方法的效应量。
方法:我们根据Cochrane协作指南进行了系统综述。将临床重要性的预定义应用于结果, 并使用'建议, 评估, 发展和评估' (GRADE) 方法评估证据的质量。
结果:纳入了30项各种异质的非心理和非药物干预措施的随机对照试验 (RCT) (成人28例, 儿童和青少年2例) 。有六种不同方法的新证据 (针灸, 神经反馈, saikokeishikankyoto (一种草药制剂), 躯体体验, 经颅磁刺激和瑜伽) 。
结论:鉴于可获得的证据水平, 定期提供非药物和非心理干预为时过早, 但有疗效的证据为那些不响应, 不容忍或不愿接受更多传统循证干预的人提供了替代方案。这项综述应促进这一领域的进一步研究。

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

Table 1. Studies included in meta-analyses and risk of bias ratings.

Study	Intervention	*N*	Trauma	Control	Random sequence generation	Allocation concealment	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	Unclear	Low	Low	Low	High
Bormann, Thorp, Wetherell, and Golshan (2008)	Mantram repetition	146	Military veterans	WL/TAU	Low	Unclear	Unclear	High	Unclear	High
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	Low	High	Unclear	High	High
Brom, Kleber, and Defares (1989)	Hypnotherapy	79	Various	WL/CBT-TF	Unclear	Unclear	High	Unclear	Unclear	High
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	High	Low	Unclear	High
Carter, Gerbarg, Brown, Ware, and D'Ambrosio (2013)	Yoga	25	Military veterans	TAU	Low	High	Low	High	Unclear	High
Cohen et al. (2004)	TMS	16	Various	Sham TMS	Unclear	Unclear	Low	High	Unclear	High
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	Low	Low	Low	Low	Unclear	Low
Kearney, McDermott, Malte, Martinez, and Simpson (2013)	Group MBSR	47	Military	WL/TAU	Unclear	Unclear	Low	Unclear	Unclear	High
Mitchell et al. (2014)	Yoga	38	Various, females only	WL/TAU	Low	Unclear	Unclear	Low	Unclear	High
Niles et al. (2012)	MBSR	27	Military	Psychoeducation	Unclear	High	High	Unclear	Unclear	High
Noohi, Miraghaie, and Arabi (2017)	Neurofeedback	30	Various	WL/TAU	Unclear	Unclear	Unclear	Unclear	Unclear	High
Numata et al. (2014)	Saikokeishikankyoto (Japanese herbal formula)	43	Earthquake	WL/TAU	Low	Low	High	Unclear	Low	Unclear
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
Schoorl, 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 interpersonal violence	WL/TAU	Unclear	Unclear	Low	Low	Low	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	Unclear
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
Lyshak-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.

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

Intervention	Description of intervention	Summary result versus TAU/WL (number of studies; number of participants; standardised mean difference; and 95% confidence intervals)	GRADE judgement for quality of evidence
Transcranial magnetic stimulation (TMS)[a]	Magnetic fields used repetitively to stimulate nerve cells in targeted areas of the brain.	k = 3; N = 94; SMD −1.53, CI −2.76 to −0.30	Very uncertain about the estimate.
Mantram repetition	Repeating a holy word(s) or phrase(s).	k = 2; N = 175; SMD −0.27, CI −0.57 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; SMD −0.92, CI −1.51 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; SMD −0.04, CI −0.58 to 0.51	Very uncertain about the estimate.
Somatic experiencing	Focuses on perceived body sensations and how to regulate these.	k = 1; N = 60; SMD −0.75, CI −1.28 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; SMD −2.12, CI −3.41 to −0.83	Very uncertain about the estimate.
Yoga	An integrative practice of body postures, breathing, and meditation.	k = 5; N = 162; SMD −0.37, CI −0.68 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; SMD −0.40, CI −1.01 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; SMD −0.49, CI −1.07 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; SMD −2.14, CI −4.20 to −0.08	Very uncertain about the estimate.
Saikokeishikankyoto	Traditional Japanese herbal medicine.	k = 1; N = 43; SMD −0.91, CI −1.55 to −0.28	Very uncertain about the estimate.
Physical exercise	Usually a programme of aerobic exercise	k = 2; N = 105; SMD −0.36, CI −0.75 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; SMD −0.23, CI −0.62 to 0.16	Very uncertain about the estimate.
Mind–body skills in children	Using the mind to impact physical functioning	k = 1; N = 77; SMD −0.37, CI −0.82 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; SMD −1.46, CI −2.30 to −0.63	Very uncertain about the estimate.

[a]Control condition for TMS was sham TMS.

present-centred therapy [k = 1; N = 173; SMD −0.37, CI −0.68 to −0.07]; and mindfulness-based stress reduction over psychoeducation [k = 1; N = 27; SMD −1.23, CI −2.07 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

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

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

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 superiority 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.

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Author contribution

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

CL and MvG were responsible for data extraction, risk of bias assessments and data analysis. All authors were responsible for the interpretation of the analyses. All authors were involved in writing the report.

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