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Effects of mindfulness-based interventions on symptoms and interoception in trauma-related disorders and exposure to traumatic events: Systematic review and meta-analysis

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ABSTRACT

Interoception is defined as the sense of the internal state of the body. Dysfunctions in interoception are found in several mental disorders, including trauma-related conditions. Mindfulness-Based Interventions (MBIs) have been shown to influence interoceptive processes. Randomised controlled trials (RCTs) have investigated whether MBIs impact symptoms and interoception in patients with trauma-related disorders. We undertook a systematic review and meta-analysis to synthesize these data. We included RCTs with an MBI arm which enrolled adult patients with trauma related-disorders or exposure to a traumatic experience, and addressed changes in interoception and trauma-related symptoms. A random-effects multivariate meta-analytic model was performed to quantify group differences in score change from baseline to follow-up. Twelve studies were included in the systematic review, and eleven in the meta-analysis. Overall, MBIs showed small to moderate positive effects on both interoception and symptoms. Despite a high heterogeneity in results, sensitivity analyses confirmed the robustness of the findings. We conclude that the efficacy of MBIs on trauma-related symptoms and interoception is supported by randomised evidence. However, further research is needed to understand whether changes in interoception might underpin the effectiveness of MBIs in trauma-related disorders.

1. Introduction

The term *interoception* refers to the process by which the nervous system interprets signals emerging within the body to build a moment-to-moment scan of the internal state across both conscious and unconscious levels (Critchley, 2004; Farb et al., 2015; Khalsa et al., 2018).

The brain is believed to build a model of sensations that arise from within the body by combining the moment-to-moment scan of the body with prior information, including beliefs and expectations, which can strongly shape the current interoceptive perception (Craig, 2002; Seth, 2013). After integrating interoceptive information, brain activity leads to behaviours to attain desired physiological states, through regulatory reflexes and feedback control on humoral secretions (Craig, 2002, 2009; Critchley and Harrison, 2013; Damasio and Carvalho, 2013). However, extensive research in recent decades has shown that dysfunction in interoceptive pathways can result in maladaptive behaviours and may

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be linked to mental and physical illnesses, including trauma-related disorders (Lanius, 2015).

There is evidence that improved interoceptive accuracy is associated with reduced post-traumatic symptomatic burden. In a recent study assessing interoceptive accuracy and sensitivity in a sample of sexual trauma survivors affected by symptoms of post-traumatic stress disorder (PTSD), Reinhardt and colleagues found that as interoceptive accuracy increased, PTSD symptom severity decreased (Reinhardt et al., 2020). At the same time, there is evidence that childhood trauma is negatively associated with interoceptive accuracy (IAc) after the stressor (Schaan et al., 2019) and that bodily dissociation and emotion regulation may have significant effects on post-traumatic symptoms in women with substance abuse disorders and high prevalence of reported trauma and symptoms of post-traumatic stress (PTS) (Price and Herting, 2013). Dissociative reactions are a key feature of trauma-related disorders or can be a reaction to traumatic exposure, as well as marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event and avoidance of specific situations (American Psychiatric Association, 2023). When involving body awareness, these symptoms can be considered as a disruption in interoceptive pathways: indeed, dissociation from triggers related to traumatic events might result from a state in which an individual suppresses bodily signals (Farb et al., 2015). Moreover, inhibition of interoceptive signals may lead to other dissociative phenomena, such as 'clouding' or the absence of important and desirable sensations, as well as dysfunctional beliefs about the world and personal relation to it (Paulus and Stein, 2010).

Mindfulness-Based Interventions (MBIs) are therapies that incorporate mindfulness techniques in a secular, manualized way to either improve wellbeing or to treat specific psychiatric conditions (Shapero et al., 2018). 'Mindfulness' can be defined as the act of "paying attention in a particular way, on purpose, in the present moment, and non-judgmentally" (Kabat-Zinn, 2003). If awareness of thought patterns is a cognitive mechanism that requires the ability to comprehend an individual's thought process, the act of cultivating attention might be achieved by anchoring the mind to interoceptive signals such as the breath or other body sensations (Mehling et al., 2011). When considering PTSD, MBIs are known to be efficacious as adjuncts or alternative therapies (Kim et al., 2013), acting for example by reducing somatic dissociation among sexual trauma survivors (Price et al., 2007). There are different types of MBIs. Some (including yoga, meditation, and Mindfulness-Based Stress Reduction) use solely bodily or meditative practices to increase mindfulness skills, whereas others (including Dialectical Behavioural Therapy and Acceptance and Commitment Therapy) incorporate mindfulness practices and employ a range of non–meditation-based techniques to promote mindfulness skills (Shapero et al. 2018). MBIs have been shown to increase interoception, possibly as a result of neuroplastic changes within the insula (Gibson, 2019). A recent study investigating neural plasticity in interoceptive networks following a course of Mindful Awareness in Body-oriented Therapy (MABT) in a group of healthy individuals found that MABT was associated with insula deactivation, increased functional connectivity between the dorsal attention network and the somatomotor cortex, and positive changes in subjective interoception (Price et al., 2023).

An improvement in interoception might be linked to the ability to be present to the moment-to-moment experience without judgement or without being influenced by emotional reactivity, which is considered to be one of the main benefits of meditation practices (Brandmeyer et al., 2019; Kabat-Zinn, 2003). A recent study found that mindfulness meditation may lead to an improvement in interoceptive awareness and to a reduction in dissociative tendencies (D'Antoni et al., 2022). On this basis, D'Antoni et al. hypothesized that cultivating mindful skills could increase mindful responses to triggering life events, in contrast with other reactive and defensive responses such as dissociation, therefore leading to a reduction in the sensitivity towards triggers that could potentially cause post-traumatic symptoms (D'Antoni et al., 2022).

Dysfunction of interoceptive pathways could be an important component of trauma exposure and trauma-related disorders that might manifest in post-traumatic symptoms, and MBIs have been shown to increase interoception (Lanius et al., 2015; Gibson et al., 2019). However, little is still known about the effect of MBIs on trauma-related symptomatology and on interoception in patients affected by these disorders or who have been exposed to traumatic events. Moreover, there is no consensus as to whether changes in interoception could be a potential mechanism of action of MBIs. If MBIs appear to be beneficial in patients with trauma-related conditions or symptoms, understanding their mechanisms of action could extend understanding about trauma mechanisms, and lead to development of novel therapies.

On this premise, the aim of this study was to systematically review the literature and quantitatively pool relevant studies to assess whether MBIs improves trauma-related symptoms and interoception and evaluate if changes in interoception could be a mechanism of action for these interventions. We carried out a systematic review of the literature with meta-analysis with the aim of answering three questions: (1) do MBIs significantly improve symptoms in patients with trauma-related disorders or that have been exposed to traumatic events?; (2) is there a significant change in interoceptive measures in individuals with trauma-related disorders or that have been exposed to traumatic events treated with MBIs?; (3) is there a correlation between the two?

2. Methods

This study was carried out and reported according to PRISMA guidelines (Page et al., 2021) and was prospectively registered on PROSPERO (CRD42022318577). All analyses were conducted on previously published studies. Therefore, no specific ethical approvals were required.

2.1. Literature search

We searched PubMed, PsycINFO, Embase + Embase classic, OVID MEDLINE, CINAHL, Web of Science and Google Scholar from inception to 16.03.2022 without restrictions on dates, language, or type of record (e.g., abstract, conference proceedings/ theses). We ran an updated search from 17.03.2022 to 29.02.2024. The search strategy is reported in the Supplementary Materials.

2.2. Selection procedure and eligibility criteria

Inclusion criteria were as follows: (1) randomized controlled trials (RCTs) with participants aged 18 years or older with a diagnosis of trauma-related disorder defined by DSM or ICD criteria or following exposure to traumatic events; (2) interventions of interest: MBIs including meditation, Mindfulness-Based Stress Reduction (MBSR), Mindfulness-Based Cognitive Therapy (MBCT), Dialectical Behaviour Therapy (DBT), Acceptance and Commitment Therapy (ACT), Body-Oriented Therapy, yoga, *Pranayama*, contemplative practices, *Qigong, Tai Chi*; (3) comparison: medication, placebo, psychological treatment other than mindfulness-based, or waitlist; (4) outcomes: changes in trauma-related symptoms (including dissociative symptoms, hyperarousal and avoidance) measured through validated questionnaires; changes in interoceptive awareness, in interoceptive accuracy measures, interoceptive metacognition measures, and self-report measures including validated questionnaires on interoception. We excluded studies on minors (<18 years old). No limitations on race, religion, or gender of the study population were imposed.

On first screening all titles were assessed against the inclusion criteria. Afterwards, all potentially eligible abstracts were screened against the inclusion criteria. We then obtained the full texts for potentially eligible articles for a third screening. Screening was done by two reviewers independently (LM and HF or JH). Discrepancies were resolved by consensus, or when not possible, by a third reviewer (NH).

2.3. Data extraction and quality assessment

Data were extracted and checked by two independent reviewers (LM and HF or JH) using a piloted form. Discrepancies were resolved by consensus, or if not possible the opinion of a third reviewer was sought (NH).

The following data were obtained: citation information (authors, date, type of publication); patient population information (diagnosis, diagnostic criteria, age and sex); active intervention(s), intervention(s) serving as control, study design, duration of study, method of randomization, nature and method of blinding, primary and secondary outcome measures of study; results (sample size, missing data, mean and standard deviation for change in score of trauma-related disorders symptoms in both treatment and control groups); sample size, mean, and standard deviation for change in interoception measures in both treatment and control groups.

When studies involved multiple treatment arms, we extracted data from all arms and performed analyses comparing each MBI treatment to each control intervention.

Risk of bias (RoB) assessment was based on the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB2) (Sterne et al., 2019). Risk of bias due to randomization, deviations from the intended intervention, missing data, outcome measurement, and selective reporting were assessed.

2.4. Outcome measures

For measures of trauma-related symptoms, we considered studies that used validated questionnaires addressing PTSD symptoms, such as the PTSD Checklist (PCL), the Clinicians Administered PTSD Scale (CAPS), the Harvard Trauma Questionnaire (HTQ), the Crime-Related Post-Traumatic Stress Disorder (CR-PTSD) (Price, 2005) and the PTSD Symptoms Scale - Self Report (PSS-SR).

For measures of interoception, we considered studies that used validated questionnaires aimed at evaluating interoceptive sensitivity, such as the Scale of Body Connection (SBC) and the Multidimensional Assessment of Interoceptive Awareness (MAIA) questionnaire. Although mindfulness and interoception are different constructs, several studies have reported significant correlations between the two in populations such as the one we wanted to explore (Price et al., 2018a; Gibson, 2019). On this premise, and given the overlap and significant correlations between the MAIA questionnaire and the Five Facets Mindfulness Questionnaire (FFMQ) (Hanley et al., 2017), we decided to include papers that used this questionnaire. We also considered studies that used tests to evaluate interoceptive awareness, such as the Heartbeat-Evoked Brain Response (HEBR).

When studies involved more than one measure evaluating the constructs of interest, we extracted data for all measurements.

2.5. Statistical analysis

All statistical analyses were performed in the R environment. We conducted two meta-analyses: (1) about changes in interoception measured by questionnaires before and after MBIs; and (2) about changes trauma-related symptoms before and after MBIs. Bias-corrected Standardized Mean Differences (SMDs, i.e., Hedges' g) and 95 % Confidence Intervals (95 % CI) were estimated to quantify differences between groups change from baseline to follow-up in trauma-related symptoms and interoception. Effect size estimations were performed using the metaConvert R package (Gosling et al., 2024). In one study (Nakamura et al., 2017), the group means were available but not the standard deviation: to enable the inclusion of this study, we imputed standard deviation using the approach proposed by Furukawa et al. (Furukawa et al., 2006).

Importantly, several studies generated multiple effect sizes, either because (i) they had multiple measurements of the same outcome (e.g., both the MAIA and FFMQ to measure interoception), (ii) they had one measure for each outcome (i.e., one measure for interoception and one measure for PTSD symptoms), (iii) or both. Running a standard meta-analytic model without accounting for this dependency between effect size estimates could produce biased results. Therefore, we conducted a random-effects multivariate meta-analysis using the approach described by Pustejovsky and Tipton (2021). We assumed a correlation between dependent effect sizes of $r = 0.8$ (we additionally tested the consequences of this assumption in a sensitivity analysis). A restricted likelihood maximum estimator was used.

We performed the following sensitivity analyses: (1) using the standard Statistical Robust Variance Estimation (RVE) model (Fisher and Tipton, 2015); (2) using only post-test SMDs; (3) assuming a correlation between dependent effect sizes of $r = 0.2$; (4) restricting to studies with low and moderate RoB; (5) restricting to studies with non-imputed SD; (6) restricting to studies that pre-defined changes in interoception and changes in symptoms as primary outcomes; (7) restricting to studies that did not use a waiting-list control group; (8) addressing possible differences in results when using different interoception measurements. We also performed a Jackknife leave-one-out analysis to determine whether a particular study was heavily contributing to the observed results. Finally, we explored the presence of small-study effects using the Nakagawa et al. (2023) and PET-PEESE (Stanley and Doucouliagos, 2014) methods, and using Egger's funnel plot asymmetry test (Egger et al., 1997) independently for each outcome, using the metaumbrella R package (Gosling, et al., 2023).

3. Results

Our original search initially identified 2564 records. After removal of duplicates, 2449 titles and abstracts were screened, 85 full-text articles were obtained, and 11 records met the inclusion criteria. In our updated search, which included studies published between 17.03.2022 and 29.02.2024, we identified 104 new records. No new eligible study was identified after the updated search. Fig. 1 shows the complete study selection flow diagram with numbers from the updated search showed in red (Fig. 1).

3.1. Description of included studies

We report here the key details of the included studies. Further information about each study is summarized in Table 1.

3.1.1. Population

The total number of participants in included studies was $n = 1194$, with sample sizes ranging from $n = 14$ to $n = 209$ patients: half of the studies had samples of less than 100 patients. Mean age ranged between 35 years and 58.6 years. Three of 11 studies enrolled only female patients (Classen et al., 2021; Price, 2005; Price et al., 2019) and two studies included a higher proportion of females compared to males (Davis et al., 2020; Nordbrandt et al., 2020). In the remaining six studies, most participants were males (Colgan et al., 2016; Kang et al., 2021; Mehling et al., 2018; Nakamura et al., 2011, 2017; Polusny et al., 2015).

3.1.2. Diagnoses

Six studies were conducted with patients with a diagnosis of PTSD or subthreshold PTSD (Colgan et al., 2016; Davis et al., 2020; Kang et al., 2021; Mehling et al., 2017; Nordbrandt et al., 2020; Polusny et al., 2015), one study with patients with PTSD and self-reported sleep disturbance (Nakamura et al., 2011), one study with patients with complex PTSD or subthreshold complex PTSD (Classen et al., 2021), one with patients with Substance Use Disorder (SUD) and exposure to trauma (Price et al., 2019), one with individuals with an exposure to childhood sexual abuse (Price, 2005), and one with individuals with an exposure to combat trauma who presented with symptoms of sleep

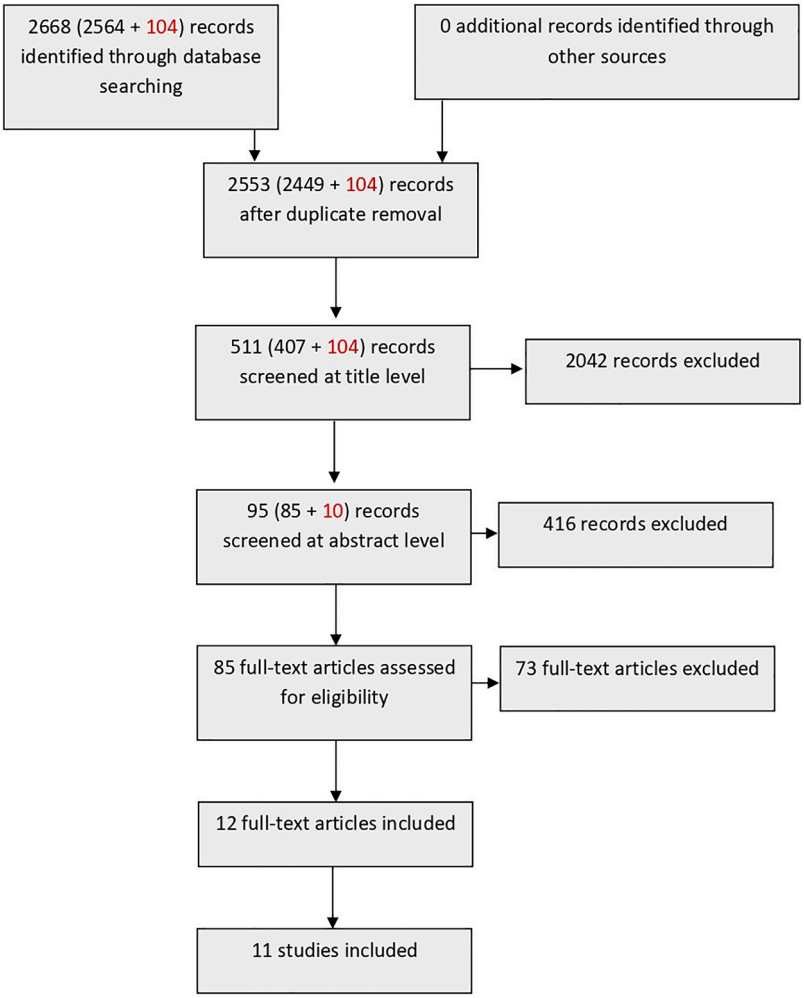

Fig. 1. Study selection flow diagram. In brackets, black numbers refer to the original literature search results, red numbers refer to the updated literature search results.

disturbance (Nakamura et al., 2017). Overall, mean scores for PTSD related scales were high at baseline throughout the whole sample and all included studies showed high percentages of PTSD symptoms and dissociation throughout samples.

3.1.3. *Interventions*

Included studies investigated a range of MBIs and control interventions. Two studies compared Mindfulness Based Stress Reduction (MBSR) with Present-Centered Group Therapy, an active control intervention which was shown to be effective for patients with PTSD (Kang et al., 2021; Polusny et al., 2015). One study compared two MBSR interventions (body scan and mindful breathing) with two control interventions (sitting quietly and slow breathing) (Colgan et al., 2016). Two studies compared a mind–body intervention focused on sleep disturbance, mind–body bridging (MBB), with a sleep hygiene program (Nakamura et al., 2011, 2017). One study compared a holistic hatha yoga program with a wellness lifestyle program (Davis et al., 2020). Four studies compared body-awareness interventions, namely Body-Oriented Therapy, Trauma and the Body Group and Basic Body-Awareness Therapy, with various control interventions (Classen et al., 2021; Nordbrandt et al., 2020; Price, 2005; Price et al., 2019). Finally, one study compared an integrative exercise program using aerobic and resistance exercise that included mindfulness-based principles and yoga with a waitlist control (Mehling et al., 2018).

3.1.4. *Outcome measures*

In all included studies, interoception was measured with specific questionnaires, apart from Kang et al., which evaluated interoceptive awareness with the Heartbeat-Evoked Brain Response (HEBR), a brain-based electroencephalographic (EEG) measurement of interoceptive attention, emotion, and self-related neural processes (Kang et al., 2021). Two studies used the Scale of Body Connection (SBC) (Classen et al., 2021; Price, 2005), three studies the Multidimensional Assessment of Interoceptive Awareness (MAIA) questionnaire (Davis et al., 2020; Nordbrandt et al., 2020; Price et al., 2019), four studies the Five Facets of Mindfulness Questionnaire (FFMQ) (Colgan et al., 2016; Nakamura et al., 2011, 2017; Polusny et al., 2015), and one study used both MAIA and FFMQ (Mehling et al., 2018).

Considering PTSD symptoms, all included studies measured symptoms through validated PTSD questionnaires. Four studies used the PTSD Checklist (PCL) (Classen et al., 2021; Colgan et al., 2016; Nakamura et al., 2011, 2017). One study used the Clinicians Administered PTSD Scale (CAPS) (Mehling et al., 2018). Another study used the Harvard Trauma Questionnaire (HTQ) (Nordbrandt et al., 2020), one the Crime-Related Posttraumatic Stress Disorder (CR-PTSD) (Price, 2005) and one the PTSD Symptoms Scale - Self Report (PSS-SR) (Price et al., 2019). Three studies used both PCL and CAPS (Davis et al., 2020; Kang et al., 2021; Polusny et al., 2015).

3.1.5. *Results from Kang et al. (2021)*

One of the 12 studies included in this systematic review was not

Table 1
Summary of papers examining the impact of MBIs on symptoms and interoception in patients affected by Trauma-Related Disorders. Abbreviations: CAPS, Clinicians Administered PTSD Scale; CR-PTSD, Cancer-Related Posttraumatic Stress Disorder; FFMQ, Five Facet Mindfulness Questionnaire; HEBR, Heartbeat-Evoked Brain Response; HTQ, Harvard Trauma Questionnaire; MAIA, Multidimensional Assessment of Interoceptive Awareness; PCL, PTSD Checklist; PSS-SR, PTSD Symptoms Scale - Self Report; PTSD, Post Traumatic Stress Disorder; SBC, Scale of Body Connection; TAU, Treatment as Usual.

Reference	N	% Females	Mean Age (SD)	Diagnosis (diagnostic criteria) or type of trauma exposure	Intervention		Study Duration	Symptoms Outcome Measure	Interoception Outcome Measure	Effects on PTSD symptoms s	Effects on interoception	Overall risk of Bias
					MBI	Control						
Classen et al., 2021	37	100 %	Not reported	Full or subthreshold complex PTDS (ICD-11 criteria)	Trauma and the Body Group (TBG)	Waitlist Control	20 sessions (no given frequency)	PCL	SBC	No significant differences between groups	Treatment showed significant increase in body awareness	High
Davis et al., 2020	209	71 %	49,9 (12,6)	PTSD (DSM 5)	Holistic Yoga Program (HYP)	Wellness Lifestyle Program (WLP)	16 weeks (twice weekly)	PCL, CAPS	MAIA	Significant improvement in treatment group	Significant improvement in 5 of 8 subscales measuring Interoceptive Awareness in treatment group	High
Colgan et al., 2016	102	5,8 %	52 (12)	PTSD (DSM 4)	Body Scan (BS) or Mindful Breathing (MB)	Sitting Quietly (SQ) or Slow Breathing (SB)	6 weeks (once weekly)	PCL	FFMQ	Significantly decreased in both treatment groups and in the SQ group. At post-treatment, scores in the MB group were marginally significantly lower than the SB group. There were no significant differences between BS, SB, and SQ, groups. In the BS group, 30% of participants experienced a reliable decrease and 11 % of participants experienced a substantial decrease in PCL-C score. In the MB group, 24% of participants reported reliable decreases and additional 10 % reported sustainable decreases in PCL-C score	The time (pre, post) × treatment group interaction for FFMQ was not significant; however, in the BS group, pre- to post-treatment total FFMQ scores increased significantly, as did the mindfulness facet acting with awareness. In the MB group, total FFMQ scores did not significantly increase; however, scores in nonjudgmental acceptance increased. At post-treatment, the MB group had significantly higher FFMQ scores than the SB group, and the SQ group, and the BS group had statistically significantly higher scores than the SQ group. In the BS group, 38% of participants experienced a reliable increase in FFMQ. Additional 12% of participants experienced substantial change in FFMQ. In the MB intervention, 28% of participants endorsed reliable increases in FFMQ, with additional 16% endorsing substantial increases	Some Concerns
Kang et al., 2021	98	14,3 %	58,6 (10,4) for MBI group	PTSD (DSM 5)	Mindfulness-Based Stress Reduction (MBSR)	Present-Centered Group Therapy (PCGT)	8-weeks (once weekly + *a* daylong)	PCL, CAPS	HEBR	Greater improvement in PTSD symptoms in treatment group than in control group	Only treatment group had significant increase in the theta HEBR in the frontal lectrode cluster. The group differences n the intervention-related theta HEBR changes were significant n the similar frontal electrode cluster.	Low

(*continued on next page*)

Table 1 (*continued*)

Reference	N	% Females	Mean Age (SD)	Diagnosis (diagnostic criteria) or type of trauma exposure	Intervention		Study Duration	Symptoms Outcome Measure	Interoception Outcome Measure	Effects on PTSD symptoms s	Effects on interoception	Overall risk of Bias
					MBI	Control						
	116	16 %	58,5 (9,8)	Full or subthreshold PTSD (DSM 4)	Mindfulness-Based Stress Reduction (MBSR)	Present-Centered Group Therapy (PCGT)	8-weeks (once weekly + *a* daylong)	PCL, CAPS	FFMQ	PCL-C scores in the MB group were marginally significantly lower than the SB group	Treatment reported greater mprovement in FFMQ	Some concerns
Mehling et al., 2017	47	19,15 %	47,42 (15,94) for MBI group	PTSD (DSM 4)	Integrative Exercise (IE)	Waitlist Control (WC)	12-weeks (once weekly)	CAPS	MAIA, FFMQ	Treatment group demonstrated a significantly greater reduction in PTSD symptom severity compared ith WL. When evaluating CAPS ubscales, there was differential improvement in symptoms of hyperarousal avoring the IE group. Though not statistically significant, there as a moderate effect of differential improvement in symptoms of reexperiencing and avoidance/numbing in treatment group vs WL.	There were positive effect sizes for IE n scores of FFMQ Non-Reactivity and the MAIA subscales for Body Listening and Self-Regulation. Moderate effect sizes were found for FFMQ subscales for Observing, the MAIA subscale for Emotional Awareness, as well as Focused Attention and Restful Repose as specific positive states of mind.	Some concerns
Nakamura et al., 2017	60	10 %	50,7 (7,3)	Exposure to combat trauma	Mind–body bridging (MBB)	Sleep Hygiene Program (SED)	3-weeks (once weekly)	PCL	FFMQ	Treatment showed PCL-M mean score improvements, whereas SED showed no significant difference.	Treatment FFMQ total core increased without any significant change.	Some concerns
Nakamura et al., 2011	63	4,76 %	53,8 (10,4) for MBI group	PTSD (criteria not reported)	Mind Body Bridging (MBB)	Sleep Education Control (SED)	2-weeks (once weekly)	PCL	FFMQ	PTSD symptoms severity was significantly lessened in treatment vs control.	Treatment showed a greater increase in mindfulness scores than co	Some concerns
Nordbrandt et al., 2020	318	52,8 %	44,6 (10,3)	PTSD (ICD 10)	Basic Body Awareness Therapy (BBAT) + TAU	Mixed Physical Activity (MPA) + TAU	20-weeks (once weekly)	HTQ	MAIA	No post-treatment group differences in scores. However, there was a significant decline n HTQ scores for intervention groups between pre- and post-treatment ratings. No significant group differences n change over time.	No significant pre- or post-treatment group differences for MAIA score.	Some concerns
Price, 2005	24	100 %	41 (15)	Exposure to childhood trauma	Body-Oriented Therapy (BOT)	Massage Group (MG)	8-weeks (once weekly)	CR-PTSD	SBC	No significant differences between groups	No significant differences between groups	Some concerns
Price et al., 2019	120	100 %	35 (not reported)	Primary Diagnosis SUD, exposure to trauma (100 %)	Mindfulness Awareness in Body Oriented Therapy (MABT) + TAU	Women's Health Education (WHE) + TAU	8–10 weeks (8 weekly sessions)	PSS-SR	MAIA	No significant differences between groups.	Significant overall longitudinal effect between groups was observed across time. Between-group focal comparisons showed that MABT improved significantly compared to WHE from baseline.	Some concerns

included in the meta-analysis for changes in interoception as the outcome measure was a biological marker of interoception (electroencephalogram, EEG) as opposed to questionnaire measures (Kang et al., 2021). In this study, the authors investigated the impact of MBSR vs an active control intervention and assessed PTSD symptoms and EEG measures of neural outcomes, including an interoceptive brain response (heartbeat-evoked brain responses). Further information about methods and outcomes is summarized in Table 1. Results showed that mindfulness meditation may improve attentional control and resting brain states, in particular frontal theta heartbeat evoked brain response, which is considered to be correlated with bodily self-consciousness and is mostly activated during the resting state in the somatosensory cortex and insula (Kem et al., 2013; Gentsch et al., 2019). Therefore, MBSR-related increase in the frontal theta HEBR might represent enhanced cerebral interoceptive functions that promote bodily awareness. This could be the primary cerebral mechanism that improves symptoms of PTSD in patients treated with MBSR (Kang et al., 2021).

3.2. Risk of bias assessment

The findings of our risk of bias assessment for each included study are displayed in Table 1 and in Fig. 2. Most studies ($n = 9$, 75 %) were rated as "some concerns". For most of these studies, this was due to potential selective reporting of results, i.e. due to the absence or lack of a pre-registered analysis plan or of publicly available official repositories of pre-registered analysis plan (Classen et al., 2021; Colgan et al., 2016; Davis et al., 2020; Mehling et al., 2018; Nakamura et al., 2011, 2017; Nordbrandt et al., 2020; Polusny et al., 2015; Price, 2005; Price et al., 2019). In addition, two studies were judged to be potentially biased due to the randomisation process: the first for uncertainties around the randomisation process with possible baseline imbalances (Nordbrandt et al., 2020); the second for modifying the randomization balance after the study had started (Price et al., 2019). One study showed concerns because it was unclear how missing data were handled (Mehling et al., 2018). Two studies were rated as "high" risk of bias, one because of missing outcome data, with data available for only 142 of 212 participants and greater attribution to treatment group vs control group (Davis et al., 2020); the second for missing outcome data and deviation from intended treatment because data provided by the control group was included in both the treatment estimate and the non-treatment estimate of change over time after the trial had already started (Classen et al., 2021). Only one study was rated as "low" risk of bias (Kang et al., 2021).

3.3. Meta-analytic findings

When extracting data from the selected studies, one study assessed trauma-related symptoms with a specific questionnaire, but assessed interoception through EEG (Kang et al., 2021). Therefore, the quantitative analysis was conducted on all 11 studies for trauma-related symptoms, and on 10 out of 11 studies for interoception.

3.3.1. Effects of MBIs on trauma-related symptoms

This analysis was conducted on data from 11 studies (Classen et al., 2021; Colgan et al., 2016; Davis et al., 2020; Kang et al., 2021; Mehling et al., 2018; Nakamura et al., 2011, 2017; Nordbrandt et al., 2020; Polusny et al., 2015; Price, 2005; Price et al., 2019). The analysis included 957 participants - 498 in the intervention group and 459 in the control group. Fig. 3 shows the forest plot for intervention effects on symptoms. There was a significant effect of MBIs on symptoms compared with control interventions ($g = 0.323$, 95 %CI: 0.116–0.531, $p = 0.007$), but we found evidence of substantial heterogeneity (tau = 0.0497, $I^2 = 77$ %).

3.3.2. Effects of MBIs on interoception

This analysis was conducted on data from 10 studies (Classen et al., 2021; Colgan et al., 2016; Davis et al., 2020; Mehling et al., 2018;

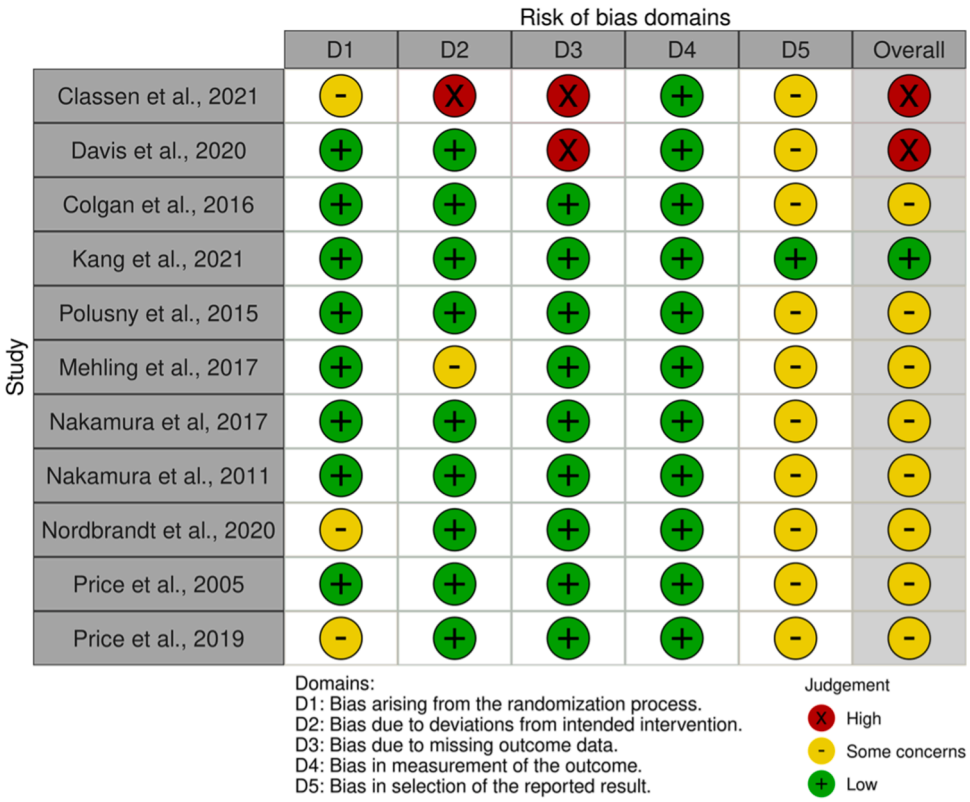

Fig. 2. Traffic light plot summarizing authors' judgements regarding risk of bias for each included study - figure provided by RoBvis (https://www.riskofbias.info/welcome/robvis-visualization-tool).

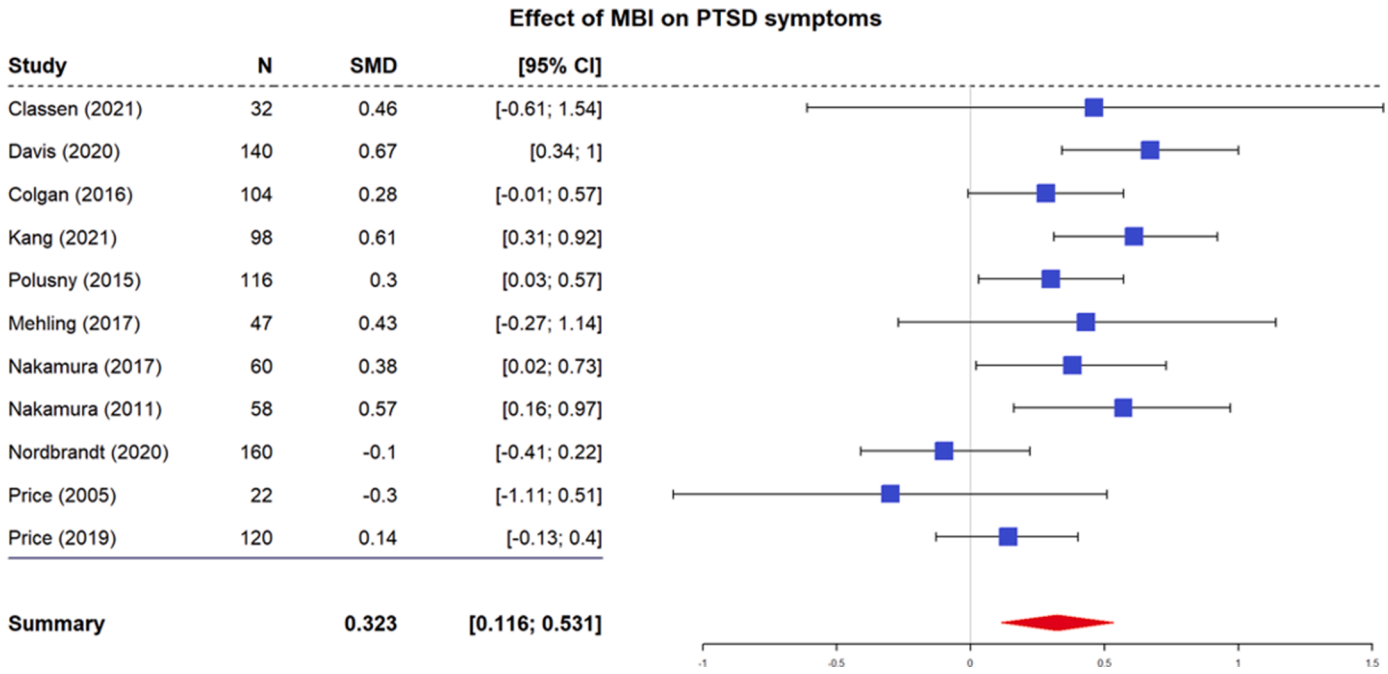

Fig. 3. Forest plot for intervention effects on trauma-related symptoms with SMDs and 95 % CI.

Nakamura et al., 2011, 2017; Nordbrandt et al., 2020; Polusny et al., 2015; Price, 2005; Price et al., 2019). The analysis included 1009 participants - 528 in the intervention group and 481 in the control group. Fig. 4 shows the forest plot for the effects of MBIs on interoception. The overall effect size of MBIs on interoception was $g = 0.253$, 95 %CI: 0.058–0.448. The difference between intervention and control groups was statistically significant ($p = 0.017$). Again, we found important heterogeneity (tau=0.0424, I^2=84 %).

It was not possible to statistically assess whether changes in interoception may represent a mechanism of action for MBIs on symptoms in this cohort of patients, as correlations between the two outcomes were not reported in any of the included studies. However, one of the included studies' populations (Price et al., 2019) was assessed at baseline to evaluate possible correlations between post-traumatic symptoms and interoception (Price et al., 2018).

3.3.3. *Sensitivity analyses*

To assess the robustness of our findings and to identify potential sources of heterogeneity, we conducted a wide range of sensitivity analyses. As shown in Fig. 5, results from these sensitivity analyses were similar to those of the main analysis, thus confirming the robustness of the main findings.

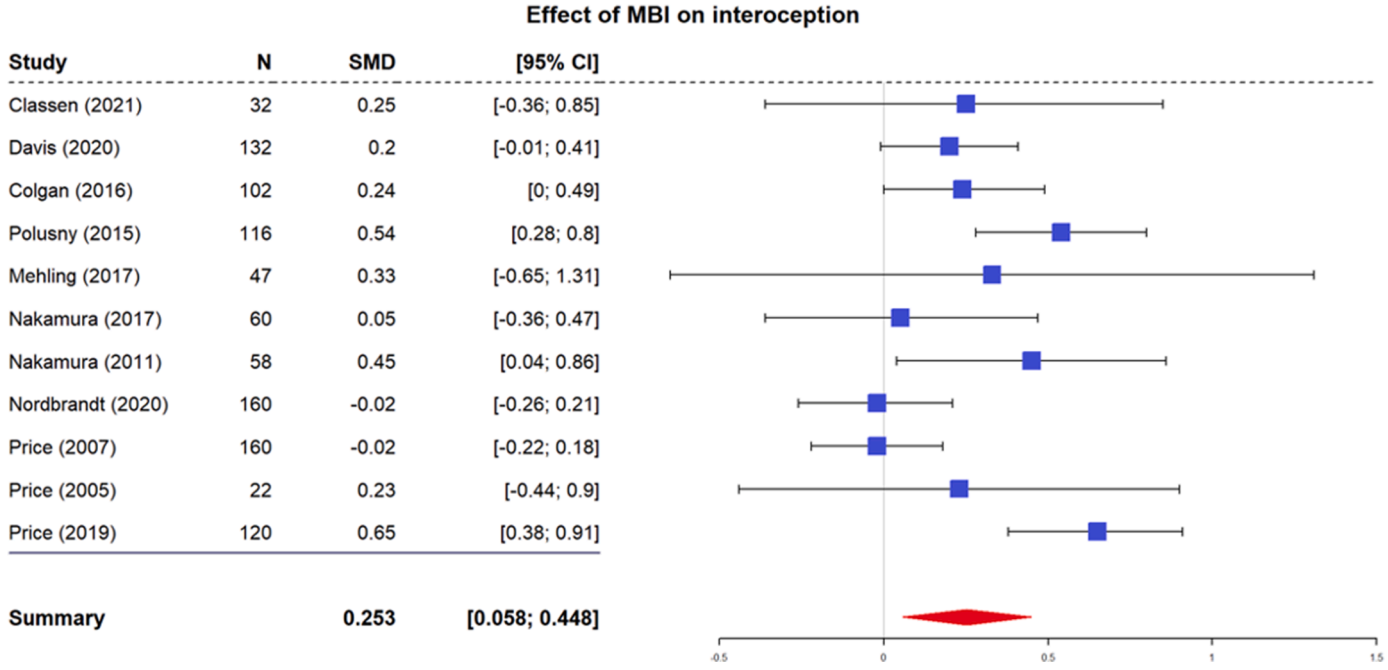

Fig. 4. Forest plot for intervention effects on interoception with SMDs and 95 % CI.

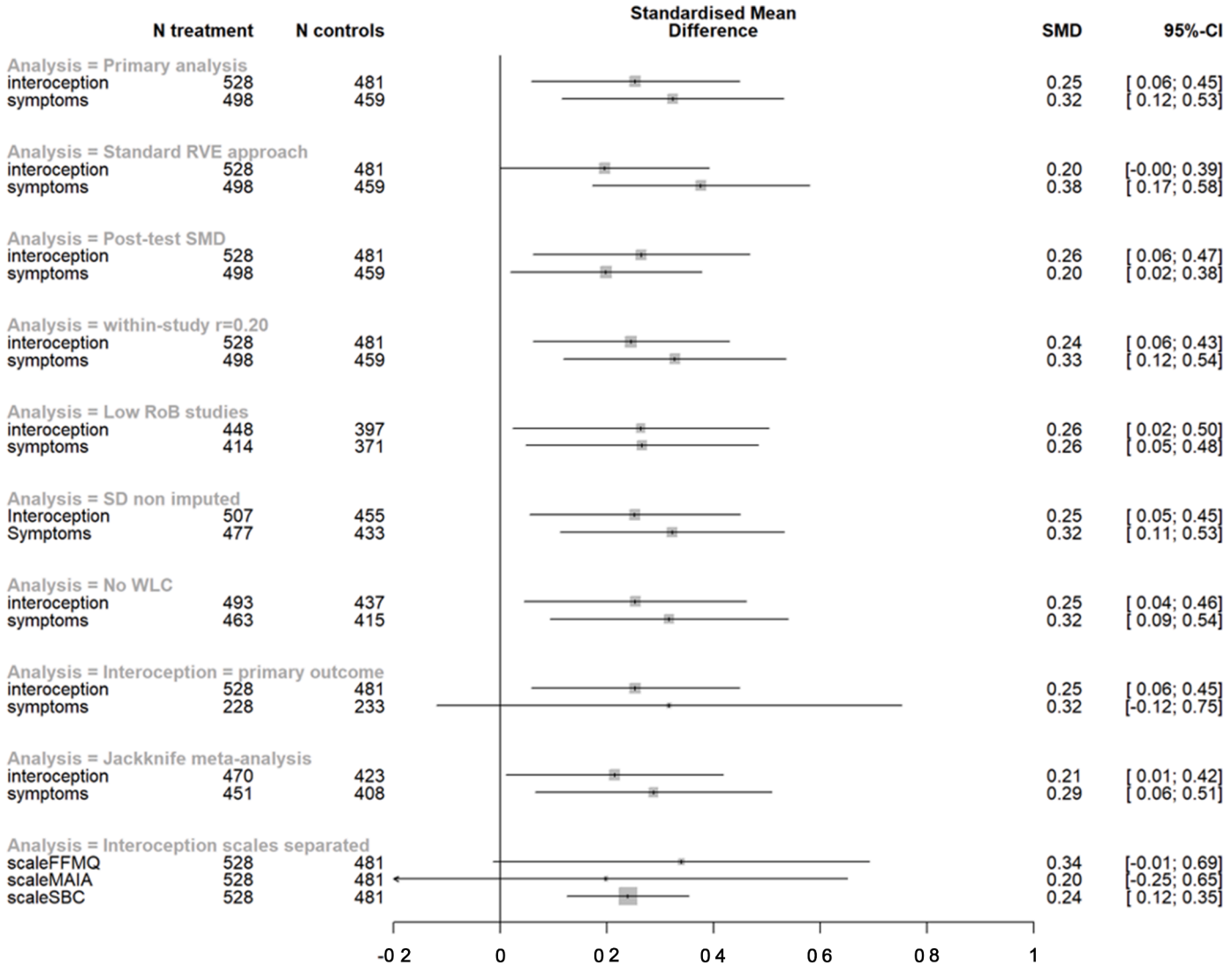

Fig. 5. Summary of results for main and sensitivity analyses.

3.3.4. *Small study-effects*

Lastly, we explored the presence of small study effects. With all three methods (Nakaragawa and PET-PEESE methods across outcomes, and the Egger's test performed independently for each outcome) we found no evidence of substantial small-study effects (all p-values > 0.10).

4. Discussion

The aim of this systematic review and meta-analysis was to provide, for the first time, meta-analytic evidence of the effect of MBIs on symptoms and interoception in patients affected by trauma-related disorders or those exposed to traumatic events. Eleven studies were included in the qualitative synthesis and in the quantitative meta-analysis. Results showed small to moderate effects of MBIs on both trauma-related symptoms and interoception.

Overall, for most included studies, quality of evidence was judged to be low to moderate. This finding is similar to other systematic reviews and meta-analyses on this topic (Hilton et al., 2017; Liu et al., 2022).

The total number of participants in our study was 1194. This sample size is similar to other systematic reviews and meta-analyses of MBIs for specific psychiatric disorders, for example Social Anxiety Disorder (Liu et al., 2021). However, sample sizes were larger in studies that synthesized results for the effect of MBIs in non-psychiatric conditions, such as cancer (Xunlin et al., 2020).

4.1. *Effect on symptoms*

There was a moderate positive effect of MBIs on symptoms in patients affected by trauma-related disorders or exposed to traumatic events. Although the effect of MBIs on symptoms compared with control groups was statistically significant, an effect size of 0.35 could represent less than the Minimal Clinically Important Difference (MCID) for PTSD in the most frequently used scales, namely the CAPS and PCL. The MCID represents the minimum reduction in symptom severity that would be considered clinically relevant (Copay et al., 2007; Hays and Woolley, 2000). Considering PTSD symptoms, a recent study found that the MCID for CAPS and PCL, on both severity and change measures, should be higher than an effect size of 0.5 (Stefanovics et al., 2018). Therefore, the effect of MBIs on post-trauma symptoms could be clinically irrelevant, although still statistically significant when compared with control interventions. It should also be noted that many studies included patients without clinical diagnoses or with subthreshold symptoms: hence the full efficacy of MBIs could be masked by a floor effect in this current analysis, this being an area which needs further investigation.

The findings from our main analysis accord with other meta-analyses that have evaluated the efficacy of MBIs in patients affected by PTSD. Hopwood and Schutte found that MBIs significantly reduced PTSD symptoms with a positive effect compared with control conditions ($g = 0.44$) (Hopwood and Schutte, 2017). Another meta-analysis showed that

mindfulness meditation moderately positively reduced PTSD symptoms in patients with military-related PTSD ($g = 0.33$) (Sun et al., 2021).

Considering other treatments, meta-analyses indicate that psychotherapies including cognitive therapy, exposure therapy, and eye movement desensitization and reprocessing (EMDR) have high efficacy for PTSD symptoms, with effect sizes higher than 0.80, while pharmacotherapies including paroxetine, sertraline, fluoxetine, risperidone, topiramate, and venlafaxine exhibit moderate to large effects ($g = 0.74$, 0.41, 0.43, 0.41, 1.20, and 0.48, respectively) (Watts et al., 2013). Our findings, as well as those of other researchers in this field, show that MBIs could provide effects within the 95 % confidence intervals of those of pharmacotherapy on PTSD symptomatology. However, this impact may not be as robust as those of specific forms of psychotherapy, although blinding in psychotherapy studies tends to be rarely sufficiently documented (Juul et al., 2021).

4.2. Effect on interoception

Our findings suggest that MBIs were moderately efficacious in improving interoception when compared with control interventions. These findings were robust to choices made during the analysis: sensitivity analyses showed broadly similar results. The use of different interoception assessment scales (FFMQ, MAIA or SBC) did not account for materially different results.

Data extracted from the studies included in this synthesis were not suited to address whether changes in interoception could directly cause changes in symptoms or vice versa. However, several of the included studies showed larger changes in interoception in at least one of the interoception scales or subscales, with effect sizes higher than 0.5 (Classen et al., 2021; Mehling et al. 2017; Polusny et al. 2015; Nakamura et al., 2011; Price et al., 2018; Davis et al., 2020). These studies were also those which found greater changes in symptoms (Classen et at., 2021; Davis et al., 2020; Polusny et al., 2015; Mehling et al., 2017; Nakamura et al., 2011), with one exception (Price et al. 2018) where the impact on symptoms was minimal. For two of these studies (Classen et al., 2021; Davis et al., 2020) the quality of evidence was low. For all other studies (Polusny et al., 2015; Mehling et al., 2017; Nakamura et al., 2011), quality of evidence was moderate, with some concerns on possible selection of reported results. On these premises, although these findings should be interpreted with caution, this provides weight to the hypothesis that changes in interoception are linked with changes in symptoms. This is in line with other literature, including a meta-analysis that compared physical activity vs control interventions on PTSD symptoms and found a positive effect ($g = 0.35$), with two of the four included studies utilizing a yoga intervention (Rosenbaum et al., 2015). Although Rosenbaum's synthesis did not focus on interoception, the positive effect of physical activity on PTSD suggests the importance of enhancing knowledge about the potential role of mind-body connections on PTSD symptoms and their treatment.

4.3. Limitations

Our findings should be interpreted in the context of some possible limitations. The number of included studies was relatively small, and the population selective, with most studies evaluating patients affected by PTSD without considering other trauma-related diagnoses, and we found important heterogeneity in our results. Since we included MBIs without a distinction between treatments, there was substantial variability in study duration. Moreover, the present review focused solely on end-of-intervention results, without including follow-ups. Further, many of the included studies were found to be at medium to high risk of bias, with only one study assessed as low risk of bias. Another consideration is the heterogeneity of outcome measures, especially the FFMQ scale, which is not specifically designed to address interoception only. Moreover, we included interventions such as Body-Oriented Therapy that combine talk therapy with mindfulness interventions. This heterogeneity is an important confounder. Finally, due to the small sample, we have not been able to assess whether different types of MBIs could lead to different impacts on symptomatology or interoception.

4.4. Future directions

These findings support the need for future research exploring the impact of mindfulness and other MBIs in patients with trauma-related disorders.

Most RCTs included in this review included a low number of participants, had imprecise protocols, and undefined statistical analyses, which can affect the interpretation of results. The relatively small number of participants included in our meta-analysis emphasizes the need for further research into the potential benefit of these interventions in patients affected by psychiatric illnesses. Moreover, the low to moderate quality of evidence of the included studies supports the need for rigorous RCTs in this field.

Differentiating cohorts based on specific traumas and/or on specific MBIs could enhance understanding of underlying mechanisms by which MBIs may be effective on trauma-related disorders, as well as addressing which symptoms may be most impacted by these interventions. Future research should focus on designing RCTs with "low" risk of bias to understand whether MBIs may be truly effective.

Considering populations, no study included in this paper evaluated the impact of MBIs on patients diagnosed with personality disorders, although the role of trauma in the aetiology of these conditions is well known (Goodman et al., 2004). Finally, further studies, especially RCTs, may be necessary to understand the role of interoception in the mechanism of action of MBIs on traumatic symptoms. There is also a need to evaluate interoception with more specific questionnaires and/or with specific tasks, to understand which specific facets may impact symptomatology the most.

CRediT authorship contribution statement

L. Molteni: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **C.J. Gosling:** Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision. **H.A. Fagan:** Methodology, Investigation, Data curation. **J. Hyde:** Methodology, Investigation, Data curation. **B. Benatti:** Supervision. **B. Dell'Osso:** Supervision. **S. Cortese:** Conceptualization, Methodology, Writing – review & editing, Supervision. **D.S. Baldwin:** Conceptualization, Methodology, Writing – review & editing, Supervision. **N.T.M. Huneke:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Prof. Baldwin is a Medical Patron of Anxiety UK, and a co-applicant in an NIHR-funded study of EMDR for post-traumatic symptoms following intensive care unit admissions.

Prof. Dell'Osso has received Grant /Research Support from LivaNova, Inc., Angelini, and Lundbeck, and Lecture Honoraria from Angelini, Janssen, Otzuka, and Lundbeck, outside the present work.

Dr. Benatti has received consultant fee for Lundbeck.

Dr Huneke is an NIHR Academic Clinical Lecturer. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR, NHS or the UK Department of Health and Social Care.

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Supplementary materials

The supplementary material for statical analyses can be found at https://corentinjgosling.github.io/MOLTENI_2022/#Supplementary_3_Additional_analyses.

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2024.115897.

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