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CLINICAL RESEARCH ARTICLE



# Targeting hyperarousal: Mantram Repetition Program for PTSD in US veterans

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## ABSTRACT

**Background**: Hyperarousal appears to play an important role in the development and maintenance of posttraumatic stress disorder (PTSD) symptoms, but current evidence-based treatments appear to address this symptom type less effectively than the other symptom clusters. The Mantram Repetition Program (MRP) is a meditation-based intervention that has previously been shown to improve symptoms of posttraumatic stress disorder (PTSD) and may be especially helpful for hyperarousal. If MRP is an effective tool for decreasing this often treatment-resistant symptom cluster, it may become an important clinical tool.

**Objective**: The goal of this secondary analysis was to examine the effect of the MRP on hyperarousal and other PTSD symptom clusters and to examine hyperarousal as a mediator of treatment response.

**Method**: Secondary analyses were conducted on data from a randomized controlled trial in which Veterans with PTSD ($n$ = 173) were assigned to the MRP or a non-specific psychotherapy control and assessed pre-treatment, post-treatment and 8 weeks after treatment completion. The impact of the interventions on PTSD symptom clusters was examined, and time-lagged hierarchical linear modelling was applied to examine alternative mediation models.

**Results**: All PTSD symptom clusters improved in both treatments. MRP led to greater reductions in hyperarousal at post-treatment (Hedge's $g$ = 0.57) and follow-up (Hedge's $g$ = 0.52), and in numbing at post-treatment (Hedge's $g$ = 0.47). Hyperarousal mediated reductions in the composite of the other PTSD symptom clusters. Although the reverse model was significant as well, the effect was weaker in this direction.

**Conclusion**: Interventions focused on the management of hyperarousal may play an important role in recovery from PTSD. The MRP appears efficacious in reducing hyperarousal, and thereby impacting other PTSD symptom clusters, as one pathway to facilitating recovery.

## Abordando la hipervigilancia: El Programa de Repetición de Mantras para el TEPT en veteranos estadounidenses

**Antecedentes**: La hipervigilancia parece desempeñar un papel importante tanto en el desarrollo como en la mantención de los síntomas del trastorno de estrés postraumático (TEPT), pero los tratamientos basados en la evidencia actuales parecen abordar esta sintomatología de una manera menos efectiva que otras constelaciones de síntomas. El Programa de Repetición de Mantras (MRP por sus siglas en inglés) es una intervención basada en la meditación que previamente ha demostrado que puede mejorar los síntomas del TEPT y que pudiese ser beneficiosa específicamente en la hipervigilancia Si el MRP fuese una técnica efectiva para disminuir este síntoma que frecuentemente es resistente al tratamiento, se podría convertir en una herramienta clínica importante.

**Objetivo**: El objetivo de este análisis secundario fue el evaluar el efecto del MRP sobre la hipervigilancia y otras constelaciones sintomáticas del TEPT, y el de evaluar cómo la hipervigilancia media la respuesta al tratamiento.

**Método**: Se realizaron análisis secundarios sobre la base de datos de un ensayo clínico controlado aleatorizado en el cual un grupo de veteranos con TEPT (n = 173) fueron asignados al programa MRP o a un grupo control de psicoterapia inespecífica. Se evaluaron antes del tratamiento, inmediatamente luego del tratamiento, y a las ocho semanas posteriores de concluir el tratamiento. Se evaluó el impacto de las intervenciones sobre las constelaciones de síntomas del TEPT, y se aplicó un modelo linear jerárquico de temporalidad retrasada para evaluar modelos alternativos de mediación.

**Resultados**: Todas las constelaciones sintomáticas del TEPT mejoraron con ambos tratamientos. El MRP condujo a mayores reducciones en la hipervigilancia inmediatamente luego del tratamiento (g de Hedge = 0,57) y en el seguimiento (g de Hedge = 0,52), así como en la insensibilidad inmediatamente luego del tratamiento (g de Hedge = 0,47). La hipervigilancia medió las reducciones en la integración de otras constelaciones sintomáticas del TEPT.

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## PALABRAS CLAVE

Tratamientos complementarios e integrantes; Mediación (nf); Meditación (nf); Trastorno de estrés postraumático; Veteranos

## 关键词

辅助及综合治疗; 中介; 冥想; 创伤后应激障碍; 退伍军人

## HIGHLIGHTS

- We examined effects of the Mantram Repetition Program (MRP) on PTSD symptoms.
- MRP demonstrated significantly greater reductions in hyperarousal at post-treatment and 8-week follow-up.
- Hyperarousal also mediated reductions in the other PTSD symptom clusters.

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A pesar de que el modelo de regresión también fue significativo, el efecto fue más débil en esta dirección.
**Conclusión**: Las intervenciones enfocadas en el manejo de la hipervigilancia podrían desempeñar un papel importante en la recuperación del TEPT. El MRP impresiona ser eficaz en reducir la hipervigilancia, generando de esta manera un impacto sobre otras constelaciones sintomáticas del TEPT, constituyéndose en un camino para facilitar la recuperación.

## 以高唤起为靶点：针对美国退伍军人创伤后应激障碍的念诵疗法

**背景**：高唤起似乎在创伤后应激障碍（PTSD）症状的发展和维持中呈现出了重要作用，但目前针对这一症状的循证治疗似乎不如其他症状簇那么有效。 念诵疗法（Mantram Repetition Program, MRP）是一种基于冥想的干预措施，此前已被证明可改善创伤后应激障碍（PTSD）的症状，且可能尤其对高唤起有用。如果MRP可有效降低这种经常治疗无效的症状簇水平，那么它就可能成为一个重要的临床工具。
**目的**：此二次分析的目的是考查MRP对高唤起和其他PTSD症状簇的效果，并考查高唤起是否是治疗反应的一个中介变量。
**方法**：对来自一个随机对照试验的数据进行了二次分析，这个试验将173名患有PTSD的退伍军人分为MRP组或非特异性心理治疗对照组，并分别在治疗前、治疗后和治疗完成后8周进行评估。考查了对创伤后应激障碍症状簇进行干预的影响，并应用时滞性多层线性模型来检验备择中介模型。
**结果**：所有PTSD症状簇在两种治疗中都有所改善。 在MRP组的治疗中，高唤起症状在治疗后（Hedge's g= 0.57）和随访中（Hedge's g= 0.52）大幅降低，麻木水平在治疗后（Hedge's g= 0.47）明显下降。高唤起中介了其他PTSD症状簇水平的降低。虽然逆向模型也显著，但效应更弱。
**结论**：聚焦于高唤起治疗的干预措施可能在创伤后应激障碍的恢复中发挥重要作用。 MRP可有效降低高唤起水平，从而影响到其他PTSD症状簇，可作为促进康复的一种途径。

More than half (56.6%) of USA (US) veterans returning from Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) endorse exposure to traumatic events and more than a third (36.9%) meet criteria for posttraumatic stress disorder (PTSD; Baker et al., 2009), creating tremendous additional demand for effective PTSD treatment strategies to meet the needs of this newest cohort of combat veterans. Although well-established, efficacious psychotherapies for PTSD exist, 30–51% of veterans do not make clinically meaningful improvement, and 28–40% do not experience remission under current best practice (Steenkamp, Litz, Hoge, & Marmar, 2015). PTSD is a multi-faceted disorder, and any given treatment may not address all aspects of the disorder. For example, Prolonged Exposure (PE) most consistently impacts re-experiencing and avoidance (Schnurr & Lunney, 2015), and Cognitive Processing Therapy (CPT) has been observed to impact re-experiencing and emotional numbing to a greater extent than avoidance or hyperarousal (Monson et al., 2006). Similarly, Zayfert and DeViva (2004) found that, despite large decreases in clinician-rated symptoms, 41% of patients completing cognitive behavioural therapy (CBT) for PTSD continued to manifest clinically significant insomnia, anger and irritability, which may be explained by the persistence of hyperarousal. Thus, there is a clinical need for treatments that effectively reduce hyperarousal.

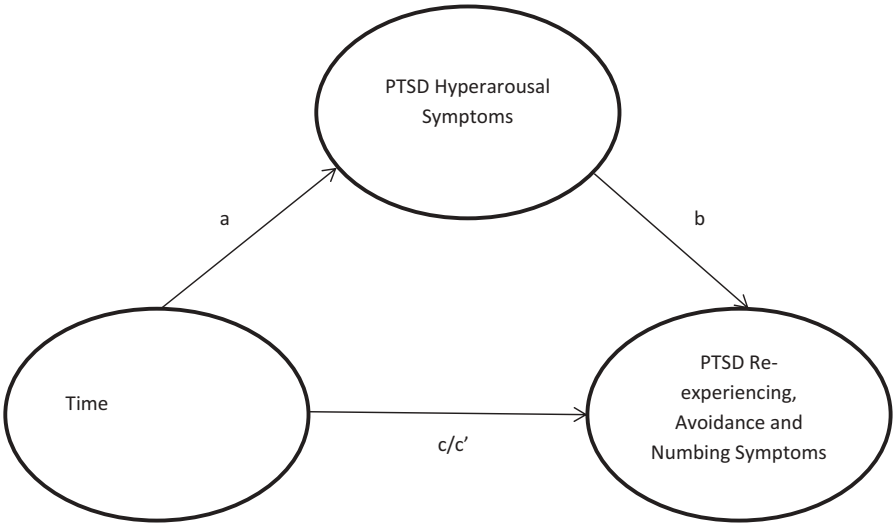


**Figure 1.** Proposed mediation model. *a* = effect of predictor on proposed mediator; *b* = effect of proposed mediator on outcome when controlling for predictor; *c'* = direct effect of predictor when controlling for proposed mediator. The indirect path of the predictor on the outcome via the proposed mediator occurs via the product of paths *a* and *b*.

Hyperarousal is of clinical importance; for example, those who report hyperarousal to be their most bothersome symptom at baseline improve less in overall distress over time than other trauma-exposed individuals (Schell, Marshall, & Jaycox, 2004). Further, several models of PTSD underscore the importance of hyperarousal in the maintenance of the disorder. Consistent with a cognitive conceptualization of the disorder, individuals with PTSD are more likely to interpret symptoms of physiological arousal as threatening (Lang, Kennedy, & Stein, 2002), forming a vicious cycle of reactivity to one's fear response (Marshall, Miles, & Stewart, 2010). Extinction models, on the other hand, posit that fear-related physiological arousal may act as a conditioned response that maintains reactivity to conditioned stimuli (i.e., trauma-related cues; Careaga, Girardi, & Suchecki, 2016). PTSD, therefore, may result from the failure to extinguish these contingencies (Blechert, Michael, Vriends, Margraf, & Wilhelm, 2007; Rothbaum & Davis, 2003).

Extant literature suggests the need for novel interventions, particularly those to hyperarousal symptoms. A growing number of veterans pursue complementary (i.e. in combination with other approaches, also referred to as adjunctive), alternative (i.e. in place of other treatments) and integrative (i.e. as part of a holistic recovery plan that focuses on restoring well-being) therapies to address their clinical needs (Goertz et al., 2013). The Mantram Repetition Program (MRP) is comprised of a set of portable, meditation-based tools (mantram repetition, one-pointed attention and slowing down) to help participants train attention and regulate emotions (Wadlinger & Isaacowitz, 2011). A key component of the MRP is the mantram, a short spiritual phrase or prayer to be repeated frequently to initiate the relaxation response. With practice, it is suggested, participants develop the ability to manage distressing thoughts and emotions. In an initial randomized controlled trial, MRP was evaluated as a complement to treatment-as-usual consisting of the case and medication management (MRP+TAU) as compared to or TAU alone. MRP+TAU led to significant improvements in PTSD symptoms; the strongest observed effects were on symptoms of hyperarousal (Bormann, Thorp, Wetherell, Golshan, & Lang, 2013). The MRP also has been associated with moderate-to-large reductions in insomnia with concurrent reductions in PTSD symptoms in veterans (Beck et al., 2017; Bormann et al., 2018). These findings are consistent with previous work that suggests that mantra-based meditation practices are associated with reduced physiological arousal (Lang et al., 2012).

The data used herein were drawn from a randomized, controlled trial of MRP as compared to Present-Centred Therapy, a non-specific psychotherapy control; the purpose of the trial was an evaluation of the efficacy of MRP (refer to Bormann et al., 2018). MRP resulted in significantly greater improvements in overall PTSD severity at post-treatment and 2-month follow-up (Bormann et al., 2018), but did not examine cluster-specific changes. The current secondary analysis aimed to explore whether MRP particularly targets hyperarousal (Bormann et al., 2013). An additional aim was to examine hyperarousal as a mediator of improvement in the other PTSD symptom clusters. The implication of this work would be the identification of a viable strategy for addressing hyperarousal, a hard-to-treat symptom, and potentially advancing care for PTSD.

## 1. Method

### 1.1. Participants

This study involved secondary analysis of data previously collected from 173 veterans enrolled in a multisite randomized controlled trial comparing individually delivered MRP to individually delivered Present-Centred Therapy (PCT) (NCT-01506323). Results of primary outcomes and subject flow in this trial have been reported previously (Bormann et al., 2018). Inclusion criteria were being age 18 or older, diagnosed with PTSD secondary to a military-related trauma, stabilized on psychotropic medications for at least 2 months prior to enrolment, and not concurrently participating in other PTSD-related therapies. Exclusion criteria were active substance abuse, having severe suicidal ideation, psychosis, dementia, or untreated bipolar disorder, and having engaged in any complementary therapies in the past 6 months.

The average age in this sample was 48.90 years ($SD$ = 14.54) and more than a third ($n$ = 61, 35.3%) reported an income of less than $20,000 annually. More than two-thirds of this sample ($n$ = 119, 68.8%) identified their race as White, 13 (7.5%) identified as an American Indian or Alaskan Native, 7 (4.0%) as Asian or Asian American, 28 (16.2%) as Black or African American, and 10 (5.8%) as Native Hawaiian or a Pacific Islander (participants could identify with more than one racial or ethnic group). Further, 30 (17.3%) described themselves as Hispanic or Latino(a). Most of the sample identified as male ($n$ = 147, 85.0%). Approximately one third ($n$ = 58, 33.5%) reported they were currently married or in a relationship with a partner. Nearly two-thirds of the sample ($n$ = 113, 65.3%) reported current use of psychiatric medications for PTSD.

### 1.2. Measures

#### 1.2.1. Clinician-administered PTSD scale for DSM-IV (CAPS)

The CAPS (Blake et al., 1995) is a structured clinician-administered interview to assess for the presence and severity of PTSD; it is considered the gold-standard diagnostic interview for PTSD. CAPS assessment items assess the frequency and severity of DSM-IV-TR PTSD symptoms. The CAPS demonstrates good internal consistency interrater reliability, and excellent convergent validity (Weathers, Keane, & Davidson, 2001). Cronbach's α was 0.91 in this sample. Participants were assessed using the CAPS at baseline, following completion of treatment, and at 8-week follow-up. CAPS subscale scores are presented herein because of our interest in differentiating among clusters; for results related to the CAPS total score, the reader is referred to Bormann et al. (2018), which reports the main study outcomes.

#### 1.2.2. Posttraumatic checklist-military version (PCL-M)

The PCL-M (Weathers, Litz, Herman, Huska, & Keane, 1993) is a 17-item self-report inventory assessing DSM-IV PTSD symptoms. Respondents rate each item from 1 ('not at all') to 5 ('extremely') to describe a combination of the frequency and severity of each symptom, with higher scores indicating worse symptoms. The military version phrases items specifically in relation to military-related experiences. It demonstrates good internal consistency and convergent validity (Wilkins, Lang, & Norman, 2011). Cronbach's α was 0.92 in this sample. For mediation analyses, re-experiencing, avoidance, and numbing were summed to create a composite score. Participants completed the PCL-M at baseline, weekly during the intervention, at post-treatment, and at 8-week follow-up.

PTSD symptom clusters used in this study were those recommended by King, Leskin, King, and Weathers (1998) and were used to more closely approximate DSM 5th Version (DSM-5) criteria for the disorder as this study was conducted before its release; re-experiencing and hyperarousal are unchanged from the DSM-IV scores. Four symptom clusters were used: (1) reexperiencing (CAPS, α = .78, .77, .77 for pre-treatment, post-treatment, and 8-week follow-up, respectively; PCL-M, α = .89, .82, .90); (2) avoidance (CAPS, α = .60, .56, .54; PCL-M, α = .83, .84, .91); (3) emotional numbing (CAPS, α = .63, .61, .65; PCL-M, α = .79, .79, .79); and (4) hyperarousal (CAPS, α = .61, .63, .60; PCL-M, α = .79, .79, .79).

### 1.3. Procedures

Approval was obtained from the VA Human Research Protection Programmes at the two participating institutions, the Bedford VA Medical Centre and the VA San Diego Healthcare System. Veterans were recruited using flyers and provider referrals. Consenting participants were assessed using a structured interview administered by a blind assessor and self-report measures. Following the completion of the initial assessment, participants were randomly assigned into either the experimental condition (MRP) or the control (PCT). Assessments occurred again at the end of treatment and 2 months after treatment completion. Methodology, including randomization procedures, is described in detail in the parent manuscript (Bormann et al., 2018). After randomization, the two groups did not differ in terms of age, gender, race, income, years of education, nor PTSD medication use.

### 1.4. Interventions

All participants received individual therapy delivered by a trained clinician. The interventions were manualized and delivered in eight weekly, 60-min sessions. MRP teaches how to redirect attention, regulate emotion, and elicit relaxation by silently and intermittently repeating a self-selected, sacred word or phrase. Present-Centred Therapy (PCT) is a non-specific psychotherapy control. In each session, the therapist helps participants to identify challenges they are facing and to draw on their personal wisdom and resources to address those problems. All sessions were recorded, and 15% were randomly selected for review by an expert clinician; both conditions were delivered with a high level of fidelity.

### 1.5. Data analytic plan

The data used in these analyses formed a multilevel, hierarchical structure with repeated measures (baseline, weekly during treatment, follow-ups) nested within participants. For each model we tested, Level 1 data included the measures of PTSD collected at each time point. Individual participants were the Level 2 units. Thus, these data were appropriate for hierarchical linear modelling. This approach is robust against missing data and variable numbers of observations between participants (Raudenbush, 2001). Missing data in our data set, because it is the final analysed data set from the parent trial, were limited to participants who did not have data for an entire time point; our analytic plan allows us to use available data at each time point, even when another time point is missing for a given individual. In the parent RCT (Bormann et al., 2018), item-level missingness was minimal, so multiple imputation was used to estimate missing item responses in these rare cases. Data were analysed with an intent-to-treat approach in a multilevel modelling framework to aid a more conservative estimation of treatment efficacy (Heritier, Gebski, & Keech, 2003) while recognizing the pragmatic challenges of longitudinal treatment research with a clinical population of Veterans.

To evaluate effects of treatment and condition on PTSD symptom clusters, we used linear mixed-effects modelling to analyse the effects of time, condition, and their interaction; models included random intercepts and slopes of time. Differences in outcomes were evaluated using the between-groups Hedge's *g* effect size. CAPS, the gold-standard for PTSD assessment, was used for these analyses. The PCL-M was used in mediation analyses, however, because this measure was collected weekly and allowed for demonstration of temporal precedence. We tested for mediation by examining if the presence of the proposed mediator, PCL hyperarousal, attenuated the effect of the predictor (time) on the criterion variable, a composite of re-experiencing, avoidance, and numbing (see Figure 1). We used the methodology established by Bauer, Preacher, and Gil (2006) and Kenny, Korchmaros, and Bolger (2003). We evaluated models using the composite of the non-hyperarousal symptoms as the outcome in each of the treatment conditions. Using repeated measures, we 'lagged' our proposed mediators to examine whether changes in the mediator at time *t* predicted the outcome variable at *t* + 1 (for example, see Aderka, Foa, Applebaum, Shafran, & Gilboa-Schechtman, 2011; Bomyea et al., 2015; Donegan & Dugas, 2012). We used the indirect effect, *ab*, as the effect size in these analyses. Per Preacher and Kelley (2011), the indirect effect can communicate both practical importance and effect size.

## 2. Results

### 2.1. Descriptive statistics

Descriptive statistics are displayed in Table 1. The intervention groups did not differ with respect to attrition. At posttreatment, 22% had discontinued from MRP, whereas 14% dropped PCT ($\chi^2$ = 1.92, p = 0.16). At follow-up, 26% were lost from the MRP group as compared with 15% in PCT ($\chi^2$ = 3.93, p = 0.07) (Bormann et al., 2018). The parent RCT's attrition analysis found that only age differed between those who completed (mean age = 50, SD = 14.59) and those who dropped out of treatment (mean age = 43.88, SD = 13.41), F (1,171) = 4.78, p < 0.05. Because age was not differentially related to the treatment group, however, we conclude that it is unlikely to affect the pattern of symptom change associated with MRP vs PCT.

Total scores on the CAPS and PCL-M in this sample have previously been reported (Bormann et al., 2018). The omnibus between-group difference on CAPS PTSD symptom measures was not significant (Pillai's Trace $F(8, 149) = 0.05$, $p = 0.483$). Also, there were no baseline (i.e., prior to randomization, prior to start of treatment), differences in PTSD cluster scores on the CAPS and PCL-M (see Table 1).

### 2.2. Treatment effects on hyperarousal and other symptom clusters

Results of linear mixed-effects models are presented in Table 2. The fixed effect of time was significant for all four symptom clusters as measured by the CAPS ($p$s < 0.001) and the effect of condition was not significant in any of the four models ($0.067 \leq p$s $\leq 0.958$). The time x condition interaction was significant for numbing ($t(1,118.45) = -3.15$, $p = 0.002$) and hyperarousal ($t(1,88.53) = -4.03$, $p < 0.001$) but not for re-experiencing ($t(1,118.22) = -1.01$, $p = 0.316$) nor avoidance ($t(1,124.22) = -1.02$, $p = 0.312$).

To understand these interactions, we examined between-group effect sizes, Hedges' *g* (see Table 3). Differences between MRP and PCT (i.e., the 95% confidence interval did not contain 0) emerged for numbing at post-treatment, $g = 0.47$, and for hyperarousal at post-treatment, $g = 0.57$, and 8-week follow-up, $g = 0.52$.

### 2.3. Mediational models

#### 2.3.1. Hyperarousal as a mediator

We first examined whether change in hyperarousal mediated change in the composite of the other three symptom clusters (see Table 4). Within the MRP group, time had significant effects on both the composite of re-experiencing, avoidance and numbing (path c: $B = -0.60$, SE = 0.08, $p < 0.001$) and hyperarousal (path a: $B = -0.29$,

**Table 1.** Descriptive statistics for PTSD symptoms.

| | | Mantram Repetition Program | | | | | | Present-Centred Therapy | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | BL CAPS ($n$ = 89) PCL ($n$ = 85) | | Post CAPS ($n$ = 69) PCL ($n$ = 68) | | 8WFU CAPS ($n$ = 65) PCL ($n$ = 61) | | BL CAPS ($n$ = 84) PCL ($n$ = 79) | | Post CAPS ($n$ = 72) PCL ($n$ = 70) | | 8WFU CAPS ($n$ = 71) PCL ($n$ = 66) | |
| | | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* |
| CAPS | Re-experiencing | 21.90 | 7.65 | 14.58 | 8.74 | 13.27 | 8.89 | 21.36 | 6.90 | 16.46 | 9.10 | 15.26 | 10.35 |
| | Avoidance | 10.66 | 3.74 | 7.19 | 4.22 | 6.76 | 4.36 | 10.05 | 3.40 | 8.22 | 4.69 | 6.61 | 5.47 |
| | Numbing | 19.68 | 6.92 | 12.82 | 7.73 | 12.17 | 8.49 | 18.95 | 7.58 | 16.52 | 7.77 | 15.70 | 8.96 |
| | Hyperarousal | 25.51 | 5.58 | 17.75 | 8.75 | 16.80 | 8.89 | 24.38 | 6.02 | 22.16 | 6.65 | 21.12 | 7.48 |
| PCL | Re-experiencing | 16.56 | 4.43 | 12.69 | 4.91 | 12.77 | 4.90 | 15.80 | 4.34 | 13.67 | 4.51 | 13.14 | 5.24 |
| | Avoidance | 7.59 | 2.07 | 5.72 | 2.43 | 5.77 | 2.43 | 7.15 | 2.12 | 6.59 | 2.60 | 5.97 | 2.68 |
| | Numbing | 16.55 | 4.48 | 12.60 | 5.05 | 12.15 | 4.71 | 15.84 | 4.30 | 13.90 | 4.81 | 13.52 | 5.13 |
| | Hyperarousal | 18.56 | 4.13 | 14.38 | 5.26 | 14.01 | 5.05 | 18.78 | 3.55 | 16.19 | 4.50 | 15.80 | 4.67 |

CAPS = Clinician-Administered PTSD Scale; PCL = Posttraumatic Checklist – Military Version; BL = Baseline; Post = Post-treatment; 8WFU = 8-week Follow-up.

**Table 2.** Linear mixed-effects models.

| Predictor | B | SE | df | t | p | LLCI | ULCI |
|---|---|---|---|---|---|---|---|
| Outcome: CAPS–Re-experiencing | | | | | | | |
| Time | −0.48 | 0.06 | 118.22 | −8.6 | <0.001 | −0.59 | −0.37 |
| Group | −0.32 | 1.06 | 169.07 | −0.31 | 0.761 | −2.41 | 1.76 |
| Time x Group | −0.11 | 0.11 | 118.22 | −1.01 | 0.316 | −0.34 | 0.11 |
| Outcome: CAPS–Avoidance | | | | | | | |
| Time | −0.25 | 0.03 | 124.22 | −7.93 | <0.001 | −0.31 | −0.19 |
| Group | −0.03 | 0.5 | 173.43 | −0.05 | 0.958 | −1.01 | 0.96 |
| Time x Group | −0.06 | 0.06 | 124.22 | −1.02 | 0.312 | −0.19 | 0.06 |
| Outcome: CAPS–Numbing | | | | | | | |
| Time | −0.42 | 0.05 | 118.45 | −9.10 | <0.001 | −0.51 | −0.33 |
| Group | −1.36 | 1.04 | 168.08 | −1.31 | 0.192 | −3.4 | 0.69 |
| Time x Group | −0.29 | 0.09 | 118.45 | −3.15 | 0.002 | −0.46 | −0.11 |
| Outcome: CAPS–Hyperarousal | | | | | | | |
| Time | −0.42 | 0.05 | 88.53 | −8.22 | <0.001 | −0.52 | −0.32 |
| Group | −1.64 | 0.89 | 161.29 | −1.84 | 0.067 | −3.41 | 0.12 |
| Time x Group | −0.41 | 0.1 | 88.53 | −4.03 | <0.001 | −0.61 | −0.21 |

LLCI = lower limit of the 95% confidence interval; ULCI = upper limit of the 95% confidence interval. CAPS = Clinician-Administered PTSD Scale.

SE = 0.04, $p < 0.001$). When the composite was regressed onto time and hyperarousal simultaneously, the effects of both time (path c': $B = -0.40$, SE = 0.11, $p < 0.001$) and hyperarousal (path b: $B = 1.43$, SE = 0.16, $p < 0.001$) were significant. Based on these data, hyperarousal significantly mediated improvements in the composite of the other clusters (ab: $B = -0.41$; 95% CI [−0.56, −0.28]) in the MRP group.

The Level 1 model regressing the composite score on time in the PCT group indicated that symptoms significantly decreased following PCT (path c: $B = -0.40$, SE = 0.08, $p < 0.001$). Regressing hyperarousal on time revealed significant improvements in hyperarousal (path a: $B = -0.19$, SE = 0.03, $p < 0.001$). When modelled simultaneously to predict the composite, the effect of hyperarousal remained significant (path b: $B = 1.53$, SE = 0.15, $p < 0.001$), but the effect of time did not (path c': $B = -0.12$, SE = 0.13, $p = 0.375$). These results indicate that hyperarousal significantly mediated change in the composite of the other three symptom clusters (ab: $B = -0.29$; 95% CI [−0.40, −0.19]) in the PCT group as well. Although the effect observed in the MRP condition is numerically greater than the effect in the PCT condition, the 95% confidence intervals overlap indicating they do not differ significantly in this sample.

### 2.3.2. Reverse models

Results of the reverse models for both treatment arms are in Table 5. Within the MRP group, time had significant effects on both hyperarousal (path c: $B = -0.29$, SE = 0.04, $p < 0.001$) and the composite of the other clusters (path a: $B = -0.60$, SE = 0.08, $p < 0.001$). When regressing hyperarousal onto time and the composite simultaneously, time (path c': $B = -0.17$, SE = 0.05, $p = 0.001$) and the composite (path b: $B = 0.28$, SE = 0.05, $p < 0.001$) both had significant effects. Based on these data, the sum of the non-hyperarousal symptoms significantly mediated improvements in hyperarousal (path ab: $B = -0.17$; 95% CI [−0.23, −0.11]). This confidence interval did not overlap between the original and reverse models, indicating that the mediation effect of hyperarousal on the other symptom types was greater than the reverse in the MRP condition.

In the PCT condition, the Level 1 model regressing hyperarousal on time indicated that hyperarousal significantly decreased following PCT (path c: $B = -0.19$, SE = 0.03, $p < 0.001$). Regressing the composite of the other symptom clusters on time revealed significant improvements in these symptoms (path a: $B = -0.40$, SE = 0.08, $p < 0.001$). Modelled concurrently to predict hyperarousal, the effect of the composite remained significant (path b: $B = 0.28$, SE = 0.05, $p < 0.001$) as did the effect of time (path c': $B = -0.17$, SE = 0.06, $p = 0.007$). These results suggested the non-hyperarousal symptoms significantly mediated change in hyperarousal (path ab: $B = -0.17$; 95% CI [−0.18, −0.05]). However, like the results observed in the MRP condition, this 95% confidence interval does not overlap with the confidence interval observed in the hypothesized original model suggesting the mediation effect of hyperarousal on the composite is greater than the reverse.

## 3. Discussion

This study evaluated the effect of a meditation-based intervention, MRP, as compared to an active control condition, PCT, on hyperarousal, a subset of PTSD

**Table 4.** Multilevel mediation.

| Path | Predictor | Outcome | Estimate | *SE* | *df* | *t* | *p* |
|---|---|---|---|---|---|---|---|
| Present-Centred Therapy | | | | | | | |
| c | Time | PCL-RAN | −0.40** | 0.08 | 68.24 | −4.90 | <0.001 |
| a | Time | PCL-H | −0.19** | 0.03 | 53.44 | −5.51 | <0.001 |
| b | PCL-H | PCL-RAN | 1.53** | 0.15 | 27.37 | 9.98 | <0.001 |
| c' | Time | PCL-RAN | −0.12 | 0.13 | 49.52 | −0.90 | 0.375 |
| Mantram Repetition Program | | | | | | | |
| c | Time | PCL-RAN | −0.60** | 0.08 | 64.66 | −7.29 | <0.001 |
| a | Time | PCL-H | −0.29** | 0.04 | 64.40 | −7.15 | <0.001 |
| b | PCL-H | PCL-RAN | 1.43** | 0.16 | 55.76 | 9.14 | <0.001 |
| c' | Time | PCL-RAN | −0.40 | 0.11 | 80.41 | −3.70 | <0.001 |

*$p \leq 0.05$, **$p \leq 0.05$. PCL-RAN = Posttraumatic Checklist–Military Version (PCL-M) composite of re-experiencing, avoidance, and numbing factors; PCL-H = PCL, Hyperarousal Subscale.

**Table 3.** Between-groups effect sizes.

| | Pre-treatment | Post-treatment | 8-week follow-up |
|---|---|---|---|
| CAPS–Re-experiencing | −0.07 (−0.38, 0.23) | 0.24 (−0.09, 0.58) | 0.20 (−0.22, 0.63) |
| CAPS–Avoidance | −0.71 (−0.47, 0.13) | 0.23 (−0.11, 0.57) | −0.02 (−0.46, 0.40) |
| CAPS–Numbing | −0.10 (−0.40, 0.20) | 0.47* (0.14, 0.82) | 0.40 (−0.02, 0.84) |
| CAPS–Hyperarousal | −0.19 (−0.50, 0.11) | 0.57* (0.22, 0.91) | 0.52* (0.09, 0.96) |

*$p \leq 0.05$ as demonstrated by the absence of 0 from the 95% confidence interval. Effect sizes are Hedge's *g*. CAPS = Clinician-Administered PTSD Scale.

**Table 5.** Reverse multilevel mediation.

| Path | Predictor | Outcome | Estimate | *SE* | *df* | *t* | *p* |
|---|---|---|---|---|---|---|---|
| Mantram Repetition Program | | | | | | | |
| c | Time | PCL-H | −0.60 | 0.04 | 64.40 | −7.15 | <0.001 |
| a | Time | PCL-RAN | −0.60 | 0.08 | 64.66 | −7.29 | <0.001 |
| b | PCL-H | PCL-H | 0.29 | 0.03 | 142.65 | 10.54 | <0.001 |
| c′ | Time | PCL-H | −0.17 | 0.06 | 46.08 | −2.84 | 0.007 |
| Present-Centred Therapy | | | | | | | |
| c | Time | PCL-H | −0.19 | 0.03 | 53.44 | −5.51 | <0.001 |
| a | Time | PCL-RAN | −0.40 | 0.08 | 68.24 | −4.90 | <0.001 |
| b | PCL-H | PCL-H | 0.28 | 0.05 | 107.44 | 5.10 | <0.001 |
| c′ | Time | PCL-H | −0.12 | 0.07 | 21.56 | −1.70 | 0.105 |

PCL-RAN = Posttraumatic Checklist–Military Version (PCL-M), composite of re-experiencing, avoidance, and numbing factors; PCL-H = PCL, Hyperarousal Subscale.

symptoms that is not well addressed by existing empirically supported PTSD treatments. Consistent with our prior findings (Bormann et al., 2013), MRP was associated with significantly greater change in hyperarousal than PCT. MRP also resulted in more change in numbing symptoms at post-treatment, but this effect was not sustained. MRP did not outperform the control condition in relation to re-experiencing or avoidance. It should be noted, however, that all symptom clusters significantly improved for both treatments, which is consistent with past studies that have demonstrated that PCT is efficacious for the treatment of PTSD (Frost, Laska, & Wampold, 2014). Further, mediational models were applied to evaluate hyperarousal as a driver of change in PTSD symptoms. As predicted, change in hyperarousal mediated change in the aggregate of the remaining PTSD symptom clusters. While the reverse model was significant as well, the hyperarousal model was stronger.

Although there is insufficient evidence to recommend any complementary or alternative practice as a first-line treatment for PTSD (Lang & Niles, 2019), these results support the clinical application of MRP to target hyperarousal, which may be a useful complement to current evidence-based approaches. Further, the mediation analysis suggests that improvements in hyperarousal may spill over to target the disorder more broadly if MRP is applied as an alternative approach. As with any emerging intervention, however, providers should utilize appropriate strategies to monitor clinical response and adjust the treatment approach based on patient needs.

This work highlights the need for additional research. Although this is the second study to show that MRP targets hyperarousal, the mechanisms by which this occurs are not well understood. Assessing other indices of hyperarousal such as physiology or biomarkers could allow us to better tease apart the contributions of actual and perceived arousal. Further, the similarities to and differences from other meditation-based approaches for PTSD should be better elucidated. A recent PTSD study showed that transcendental meditation, another mantra-based practice, was not inferior to Prolonged Exposure (PE) and outperformed health education (Nidich et al., 2018). Although theory predicts that it too might support a reduction in physiological arousal (Lang et al., 2012), such data are not yet available. Change in hyperarousal has also been observed with yoga (Wells, Lang, Schmalzl, Groessl, & Strauss, 2016) and compassion meditation (Lang et al., 2019); investigators should be encouraged to report data on symptom clusters to further our understanding of potential complementary uses of meditation. Finally, MRP can be combined with other approaches in several ways (e.g., sequential, parallel, integrated), but data are lacking on the outcomes associated with various approaches. Given the number of possible combinations, it will be a methodological challenge to examine the various programmes of care. This project included all patients with PTSD, so the targeted application of MRP to patients who have prominent or intractable symptoms of hyperarousal has yet to be evaluated. Given that hyperarousal has previously demonstrated temporal precedence naturalistically among civilians (Marshall, Schell, Glynn, & Shetty, 2006), the possibility of early application of MRP to prevent the development of PTSD could be considered as well.

Results of this study should be interpreted within the context of several limitations. This study used a sample of US veterans diagnosed with military-related PTSD, and these results may not generalize to other populations. Further, Dr Bormann has been the first to apply MRP to PTSD, so allegiance effects are possible. We also do not have data regarding the time since the occurrence of the index traumatic event. Age moderates the relationship between coping and distress, possibly due to increased vulnerability to stressors following trauma (Littleton, Horsley, John, & Nelson, 2007), so including time since trauma as a covariate may have affected our results. Additionally, the parent RCT from which this secondary analysis is drawn used a conservative power estimation (i.e., 80% power to detect medium effect on CAPS, using one time point instead of two resulting in a needed sample size of 150 per treatment arm); however, it did not reach its initial recruitment goal and therefore the current analysis may be underpowered. In spite of this, we have replicated past results (Bormann et al., 2013), although it is possible that group differences in the other clusters may have been detected with a larger sample. Additionally, this secondary analysis did not include a sensitivity analysis to account for possible confounding variables such as past treatment history; a larger sample size and a priori identification of possible confounders are encouraged in future studies. Finally, the study was implemented before the release of DSM-5, so it is possible that these results would not generalize to the current diagnostic system.

Consistent with trends towards personalized medicine, optimal psychotherapeutic treatments may need to vary based on an individual's unique presentation (Friedman, 2014). This may be especially true for veterans with hyperarousal or related symptoms (e.g., irritability, sleep difficulties) that remain even

after significant improvements in other PTSD symptoms or when hyperarousal-related symptoms prevent engagement in trauma treatment. Indeed, our study is consistent with others that have noted the potential for improving overall PTSD treatment outcomes by reducing hyperarousal symptoms (Doron-LaMarca et al., 2015). MRP appears to be a useful strategy for reducing PTSD-related hyperarousal and would have reasonable application as an alternative or complementary treatment for PTSD in veterans.

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