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EMDR vs. other psychological therapies for PTSD: A systematic review and individual participant data meta-analysis.

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Background

Eye Movement Desensitisation and Reprocessing (EMDR) is a recommended treatment for posttraumatic stress disorder (PTSD). For the first time using individual participant data, this systematic review and individual participant data meta-analysis (IPDMA) examined the overall effectiveness of EMDR in reducing PTSD symptoms, achieving response and remission, and reducing treatment dropout among adults with PTSD symptoms, compared to other psychological treatments. Additionally, we examined available sociodemographic, clinical, and intervention-related moderators of the efficacy of EMDR treatment for PTSD.

Methods

This study included primary data of randomized controlled trials (RCTs) comparing EMDR with other psychological treatments. Eligible studies were identified by a systematic search in PubMed, Embase, PsyclNFO, PTSDpubs and CENTRAL up till the 11th of January 2021. The target population was adults with above-threshold baseline PTSD symptoms on any standardised self-report measure. Trials were eligible if at least 70% of study participants had been diagnosed with PTSD using a structured clinical interview. Primary outcomes included PTSD symptom severity, treatment response, and PTSD remission. Treatment dropout was a secondary outcome. Subsequent analyses focused on examining the effect of moderators on treatment outcomes.

Results

The systematic search retrieved 8 of 15 eligible RCTs in this IPDMA (346 patients). Within each study, EMDR significantly reduced PTSD severity at post-test. Comparator treatments included relaxation therapy, emotional freedom technique, trauma-focused cognitive behavioural psychotherapies, and REM-Desensitization. One-stage IPDMA found no significant difference between EMDR and other psychological treatments in reducing PTSD symptom severity (β = −0.24), achieving response (β = 0.86), attaining remission (β = 1.05), or reducing treatment dropout rates (β = -0.25). Employment status and gender were found to moderate EMDR effects. More specifically, unemployed participants receiving EMDR had higher PTSD symptom severity at the post-test, and males were more likely to drop out of EMDR treatment than females. In the total sample, higher baseline PTSD symptom severity was found to be associated with higher post-test PTSD severity in the total sample (EMDR and other psychological treatments for PTSD).

Conclusion

In line with past research, the current study found no significant difference between EMDR and other psychological treatments on PTSD outcomes. We found some indication of the moderating effects of gender and employment status. Systematic examination of individual factors that influence the effectiveness of EMDR therapy in adults with PTSD allows for the personalisation of PTSD treatment with enhanced precision.

INTRODUCTION

Eye movement desensitization and reprocessing (EMDR) is a relatively new trauma-focused (TF) psychotherapy developed for treating posttraumatic stress disorder (PTSD) that was first introduced in the 1980s (Shapiro, 1989). This treatment involves the patient focusing on the most distressing mental images of the event while performing bilateral stimulation. After bringing up their most distressing mental images (exposure to the traumatic event), the patient's emotional arousal is interrupted by employing another stimulus (bilateral stimulation and interruption of attention) which is assumed to lead to a reduction in arousal and distress (Jeffries & Davis, 2013; Rothbaum et al., 2005).

Since EMDR's introduction, several mechanistic hypotheses have been proposed to explain the effects of bilateral stimulation in EMDR (Landin-Romero et al., 2018). One of them is the adaptive information processing (AIP) model (Shapiro & Laliotis, 2011). During stressful situations, a person's AIP system has the innate ability to process and store the event. However, the AIP system may be hindered or blocked by trauma leading to long-term distress associated with an event (Hase et al., 2008). It is suggested that during EMDR, there is a re-setting of the AIP system with a reduction in distress and negative emotions that are encoded because of the traumatic experience, leading to the integration of upsetting information into a more adaptive, positive state (Shapiro, 2001, 2006).

Another theory to explain the effects of bilateral stimulation is the working memory theory. The working memory theory proposes that EMDR reduces the vividness and emotionality of traumatic memories by taxing working memory during memory retrieval. This renders the image less vivid and emotional upon which it is reconsolidated as such in the long-term memory (van den Hout & Engelhard, 2012). The additive benefits of eye movements to traumatic memory retrieval have been mainly supported by laboratory studies in healthy individuals (Houben et al., 2020). A recent meta-analysis has confirmed that working memory tasks such as eye movements do have an emotional deregulation effect (de Voogd & Hermans, 2022) probably through a deactivation of the amygdala (de Voogd et al., 2018).

Other theories include the orientating response model suggesting that bilateral stimulation activate an investigatory reflex which causes an alert response (Barrowcliff et al., 2004). When no threat appears, the patient relaxes which reduces the negative emotions associated with the memories related to the traumatic event. Additionally, this investigatory reflex heightens awareness and facilitates exploratory behaviour which can lead to improved cognitive processes (Lee & Cuijpers, 2013). However, a recent meta-analysis that included dismantling studies comparing EMDR with and without eye movements, found no benefit of eye movements casting doubt about the superiority of EMDR to trauma-focused treatments without eye movements, such as exposure therapy, or trauma-focused CBT (Cuijpers et al., 2020).

Most international guidelines for the treatment of PTSD recommend the use of either trauma-focused cognitive behaviour therapies (CBT-TF) or EMDR as first-line treatments for PTSD (Departments of Veterans Affairs and Defense, 2017; International Society for Traumatic Stress Studies, 2019; National Institute for Health and Care Excellence, 2018; Phoenix Australia-Centre for Posttraumatic Mental Health, 2013). These guidelines are based on evidence-based research and provide recommendations to optimize patient treatment. Past meta-analyses (MA) have found EMDR to significantly improve PTSD symptom severity at post-test assessment (Bisson & Olff, 2021; Cuijpers et al., 2020; Cusack et al., 2016; Lewis et al., 2020). Consistent with other disorders (Papola et al.,2022), large effect sizes have been reported when comparing EMDR for PTSD to wait-list-control (WLC) groups, and smaller effects when compared to treatment-as-usual groups and other active treatment groups.

Currently, very little is known about moderators and predictors of EMDR treatment outcomes. Age, gender, baseline severity of PTSD, depression, and anxiety were not significantly associated with PTSD symptoms after EMDR treatment (Capezzani et al., 2013). Similarly, gender did not significantly influence treatment effects in a later study (Ter Heide et al., 2016). In the same study, participants who did not have refugee status had a greater reduction in PTSD symptoms compared to those with refugee status (Ter Heide et al., 2016). There is literature suggesting that veterans with PTSD

respond less to trauma-focused treatments in general, and to EMDR specifically (Haagen et al., 2015). However, methodological quality of the studies may play a role in these comparisons. There is also a great deal of inconsistency in the literature concerning the influence of specific moderators and predictors of psychotherapy outcomes in PTSD in general. No significant associations with treatment outcomes have been found for factors such as age (Ivarsson et al., 2014; Karatzias et al., 2007; Lewis et al., 2017), gender (Karatzias et al., 2007; Lewis et al., 2017; Blanchard et al., 2003; Galovski et al., 2012; Haagen et al., 2017), marital status (Karatzias et al., 2007), employment status (Ivarsson et al., 2014; Karatzias et al., 2007), therapy type (Karatzias et al., 2007), time since trauma (Ehlers et al., 2003; Karatzias et al., 2007), type of trauma (Karatzias et al., 2007), and psychiatric comorbidity (Cloitre et al., 2002; Rizvi et al., 2009). Some individual psychotherapy studies have found that higher education (Lewis et al., 2017), higher levels of guilt (Rizvi et al., 2009), and therapeutic alliance (Cloitre et al., 2002) were associated with a better PTSD treatment response. Additionally, there is some evidence suggesting that comorbid psychiatric disorders reduce the beneficial effects of treatment on PTSD outcomes (Hagenaars et al., 2010; van Minnen et al., 2002). A long-standing issue in the field is that randomized controlled trials (RCT) and study-level (also known as aggregate or traditional) MA often lack sufficient statistical power to identify significant moderators of treatment effect (Gurung et al., 2015). This may be the reason for the gap in the current literature when it comes to moderators and predictors of EMDR. An individual participant data meta-analysis (IPDMA) synthesizes raw participant-level data from multiple related studies to answer a specific set of research questions. This can be done using a one-stage or two-stage approach (Riley et al., 2021). The simpler and more utilized two-stage approach uses the participant-level data to calculate aggregate data in each trial separately, and then combines the aggregate data in a univariate MA model. This is similar to a study-level MA. On the other hand, the one-stage approach analyses participant-level data from all the trials in a single step using a generalised linear mixed model that accounts for the clustering of participants within trials. These two approaches tend to give very similar results when the same assumptions and estimation methods are used.

However, when the number of trials included in the IPDMA is small then a one-stage approach is more exact (Riley et al., 2021). Using an IPDMA approach, we can maximize statistical power to detect more precise effects and explore participant-level characteristics as moderators of treatment outcomes.

By gaining insight into potential moderators and predictors of the effectiveness of EMDR, we may have better precision to identify patients who would benefit the most from EMDR. This is important since EMDR is highly protocolized, relatively straightforward to administer, and requires shorter episodes of imaginal trauma exposure (Nijdam et al., 2012; Schubert & Lee, 2009) in comparison to CBT-TF psychotherapies. The aims of this study were to (1) investigate the effectiveness of EMDR in reducing PTSD symptom severity, achieving treatment response, attaining PTSD remission, and reducing treatment dropout rates in comparison to another psychological treatment, and (2) explore potential sociodemographic, clinical, and intervention-related moderators of EMDR treatment effects in PTSD.

METHODS

This IPDMA was reported in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) IPD Statement (Stewart et al., 2015). We registered the study on PROSPERO (CRD42020138638). Additional information can also be found in the protocol paper (Wright et al., 2022). This study was reviewed and granted ethical approval by the South African National Health Research Ethics Committee (S19/10/218).

Eligibility Criteria

Study inclusion was limited to RCTs comparing EMDR to active treatments. Active treatments included other psychological treatments (e.g., relaxation therapy, emotional freedom technique, and trauma-focused cognitive behavioural psychotherapies). We excluded studies comparing EMDR to WLC and treatment-as-usual groups. Studies were included if participants were adults (18 years or older) with above-threshold PTSD symptoms based on any established self-report scale or a clinical diagnosis of PTSD. Within each study, at least 70% of the participants were required to have a clinical

diagnosis of PTSD according to any version of the DSM or ICD criteria. Only studies published in English were included.

Study Identification and Selection Process

We used an existing database of psychological treatments for PTSD that was created by the Cardiff University Traumatic Stress Research Group (CUTSRG) to perform a systematic review and MA for the treatment guidelines of the International Society for Traumatic Stress Studies (ISTSS). A search was conducted by the Cochrane Collaboration Cochrane with the same inclusion criteria including all studies published until May 2018 (Bisson et al., 2013; Bisson et al., 2019; Lewis et al., 2020). We updated the search using the same search strategy (see Appendix 1). The search strategy included the screening of major bibliographic databases such as PubMED, Embase, PsycINFO, PTSDpubs, and CENTRAL. We also screened past systematic reviews for additional articles. Our updated searches included studies published between the 1st of May 2018 and the 11th of January 2021 (see Appendix 2).

Two researchers (SLW and DP) independently screened the titles and abstracts for the initial update (1st of May 2018 till the 13th of May 2019). Titles and abstracts for the second update (1st of January 2019 till the 11th of January 2021) were also screened by two researchers (SLW and ABW).

The same researchers screened the full text of studies that possibly met the inclusion criteria. Senior members of the review team (MS and GS) resolved any uncertainties regarding study inclusion.

Data Collection

Authors of eligible trials were contacted to request the use of their participant-level datasets. At least six additional reminder emails were sent at intervals of two to three weeks if no response was received. If a response had not been received at this point, an additional two authors were contacted (when possible). If after this no response was received, we attempted to reach out to the corresponding authors on ResearchGate and LinkedIn. If a response was still not received, the dataset was considered unavailable along with those where the corresponding author declined to share data. In cases where the author was able to provide their participant-level dataset, data

collection and storage were conducted in alignment with the European General Data Protection Regulation (Regulation (EU) 2016/679). Participant-level datasets were anonymised before sharing and were stored in an existing encrypted, password-protected folder at VU University Amsterdam. For data protection purposes, we sent the link for the encrypted folder to a different email address than the one we used for the password. Our data collection commenced at the start of 2019 as planned, however it was extended to two and a half years because an insufficient number of datasets had been collected by the end of 2019.

Primary and secondary outcomes

The primary outcome data included PTSD symptom severity, treatment response, and PTSD remission. The secondary outcome was treatment dropout. PTSD symptom severity scores were measured using PTSD measures and clinical interviews. Studies included in this IPDMA used self-report measures like the Impact of Event Scale-Revised (IES-R; Weiss & Marmar, 1997), PTSD Checklist (PCL; Blanchard et al., 1996), and the Mississippi Scale for PTSD (MPTSD; Keane et al., 1984). We used self-report measures because we wanted to use the same type of assessment across studies. All available studies provided self-report PTSD severity outcomes but not all studies provided PTSD severity outcome data based on clinical interviews. Treatment response was defined as a 50% reduction in baseline PTSD symptom scores (Karyotaki et al., 2017). Participants were considered in PTSD remission if they no longer had a formal diagnosis of PTSD at the post-test. In line with the definition used by CUTSRG for ISTSS' treatment guidelines, we considered a participant who left the study before the post-test assessment as a treatment dropout (Lewis et al., 2020). Assessment time points included baseline and post-test. In addition, we requested available baseline sociodemographic, clinical, and intervention-related variables in order to investigate their effect on treatment outcomes (when there was sufficient data to do so). Moderators included gender; age; relationship status; partner or no partner (married/ cohabitating or divorced/ widowed/ separated/ single); marital status (yes or no); tertiary education (yes or no); employed (yes or no); using psychotropic medication (yes/no); above threshold depression (yes/no); anxiety threshold (yes or

no); chronic (duration of PTSD symptoms > 3 months; yes or no), and comorbid psychiatric disorder (yes or no).

Risk of bias assessment

Studies were assessed for risk of bias using Cochrane Risk of Bias 2 Tool (RoB 2; Higgins et al., 2022). Each study was assessed independently by two researchers (SW and SS) to determine whether there was a risk for bias related to bias arising from the following domains: randomisation process (D1), deviations from intended intervention (D2), missing outcome data (D3), measurement of the outcome (D4), and bias in the selection of the reported result (D5). Each domain comprises signalling questions which lead to a domain-level judgement on the risk of bias. Based on domain-level judgements, an overall risk-of-bias judgement for each outcome in each study was then reached. Any uncertainty was resolved by a third member of the review team.

DATA ANALYSIS

Data analysis was conducted in Stata 17 (StataCorp, 2021). We combined all individual data sets into a merged data set, using a generic standardized protocol for integrating participant-level datasets (Stewart et al., 2015). Study-level variables were included for both the available and unavailable participant-level datasets, which were extracted from the studies' available documentation, such as publications and trial registries.

Study-Level MA

We conducted a study-level MA to examine the differences across the 8 studies that provided participant-level data and the seven studies for which data were unavailable. The difference between the studies that did and did not provide data was compared in a subgroup analysis. Heterogeneity was examined by calculating I^2 indicating heterogeneity as a percentage with 25% as low, 50% as moderate, and 75% as high (Higgins & Thompson, 2002). The 95% confidence intervals (CI) around I^2 were calculated using the non-central chi-squared-based approach in the heterogi module of Stata (Ioannidis et al., 2007; Orsini et al.,2005). We examined publication bias by visually

inspecting the funnel plot, using the trim and fill procedure and Egger's test of funnel plot asymmetry (Duval & Tweedie, 2000; Egger et al., 1997)

IPDMA

PTSD total scores were standardized by transformation into z scores across the pool of the studies before conducting the main analysis. Missing outcome data for PTSD symptom severity at post-test were estimated using multiple imputation under the missing-at-random assumption (miimputemvnin STATAsoftware, version 17; StataCorp, 2021). This method generated 20 imputed data sets using data on baseline PTSD symptom severity scores. These newly imputed datasets included the observed and the imputed standardized PTSD symptom scores for missing values. They were analysed separately using the selected model, and the results were averaged according to Rubin's rules (Riley et al., 2010).

One-stage IPDMA

In a one-stage IPDMA, we merged all participant-level data from all studies with participants clustered within studies. One-stage IPDMA yields more precise and less biased estimates of effect, maximizes the statistical power, and accounts for parameter correlation (Debray et al., 2013; Stewart & Parmar, 1993). We calculated the standardized β coefficient for the examined comparisons. This estimate indicates how many SDs the dependent variable changes per SD increase in the predictor variable. Thus, the higher the β the greater the effect of the predictor variable on the dependent variable, although there is no association among the variables if the β is 0. Using a one-stage approach, we analysed the effect of the interventions on PTSD symptom severity at the end of treatment with a multilevel mixed-effects linear regression using a random intercepts model with a random effect for each trial and fixed effects for the intervention and symptom severity, using STATA's mixed command. Post-test PTSD scores were used as the dependent variable and trial arm condition (EMDR vs control) as the independent variable while controlling for baseline PTSD symptom severity. We analysed the effect of the interventions on treatment response at post-test using a multilevel mixed-effects logistic regression (using a random intercepts model with a random

effect for each trial and fixed effects for the intervention and PTSD symptom severity, using STATA's melogit command). Response (yes or no) was the dependent variable, and treatment condition was the independent variable. This was repeated for PTSD remission and dropout.

Two-stage IPDMA

The two-stage approach uses participant-level data to derive aggregate data (such as treatment effect estimates) in each trial separately, and then combines the aggregate data in a study-level MA model. We ran a two-stage IPDMA using STATA's ipdmetan command.

Moderator analysis

We tested whether available demographic and clinical characteristics (gender, age, relationship status, marital status, completed some form of tertiary education, employment status, chronic PTSD status, use of psychotropics, above threshold depression, and presence of comorbidity) moderated the effect of EMDR on PTSD outcomes. Not all included studies reported data on the selected moderators. We included moderator analyses when the variables were reported by 3 or more studies. To examine moderators, we added the interaction between each potential moderator and treatment outcome on PTSD severity into a multilevel mixed-effects linear regression model. We similarly added the interaction between each potential moderator and treatment response into a multilevel mixed-effects logistic regression model. Each potential moderator was included in a separate model as the main effect.

RESULTS

Study Selection and Participant-Level Data Obtained

The systematic literature search resulted in 15 eligible articles. We were able to obtain participant-level data from 8 studies, comprising 346 participants (Ahmadi et al., 2015; Capezzani et al., 2013; Carletto et al., 2016; Devilly & Spence, 1999; Karatzias et al., 2011; Laugharne et al., 2016; Lee et al., 2002; Nijdam et al., 2012) and these were included in the analyses reported herein. Seven eligible datasets were unavailable and could not be included in this IPDMA (Boterhoven-De Haan et al., 2020; Carlson et al., 2016; Power et al., 2002; Rothbaum et al., 2005; Taylor et al., 2003; Ter Heide et

al., 2016; Vaughan et al., 1994). Of the unavailable studies, corresponding authors reported that two were lost, three did not respond to the study invitations, one indicated that consent issues precluded data sharing, and one study was still in progress.

Study and Participant Characteristics

The eight studies evaluated EMDR against the following treatments: one relaxation therapy (Carletto et al., 2016), one REM-Desensitization (Ahmadi et al., 2015), one emotional freedom technique (Karatzias et al., 2011), one Prolonged Exposure (CBT-TF(PE)) (Laugharne et al., 2016), one Prolonged exposure (CBT-TF(BEP)) (Nijdam et al., 2012), and three CBT-TF (Unspecified) (Capezzani et al., 2013; Lee et al., 2002; Devilly et al., 1999). Both the EMDR and comparator treatments had significant improvements in overall PTSD symptom severity at the post-test assessment in comparison to their group baseline scores.

All eight EMDR studies used the standard EMDR protocol (Shapiro, 1989). The included studies were conducted in the following countries: Iran (1), Netherlands (1), Australia (3), Italy (2), and Scotland (1). All the included EMDR interventions were conducted in person and in a one-on-one format (see Appendix 3). Additionally, all participants had a diagnosis of PTSD at the baseline assessment. The mean (SD) age of participants was 38.61 (11.90) years. 204 (59.13%) of 345 were female, 125 (51.02%) of 245 were married or cohabitating, and 101 (41.22%) were single. 109 (53.17%) of 205 had completed some form of tertiary education, 133 (53.63%) of 248 had no comorbid diagnosis at the baseline assessment, 95 (41.67%) of 228 were stable on psychotropic medication, and 261 (95.96%) of 272 had chronic PTSD at the baseline assessment (see Appendix 4). The mean (SD) baseline PTSD symptom score was 53.78 (10.63) on the Impact of Event Scale (Horowitz et al., 1979), 68.88 (20.28) on the Impact of Event Scale-Revised (IES-R; Weiss et al., 1997); 57.61 (10.76) on the PCL (Blanchard et al., 1996), and 114.44 (34.02) on Keane's Post-Traumatic Stress Disorder Scale from the Minnesota Multiphasic Personality Inventory (MMPI-K; Keane, Malloy, & Fairbank, 1984) in the respective studies. Finally, 94 (33.22%) out of the 283 participants dropped out of treatment before the post-test assessment.

Risk of Bias Assessment

Appendix 5 presents the RoB2 ratings for the studies included in this IPDMA. The overall risk of bias was scored *some concerns* for seven of the eight studies which can be attributed to *some concerns* scores on domain one and domain five. Four of the eight studies scored *some concerns* on domain one, risk of bias arising from the randomization process because the information about the randomization methods was limited to a statement that the study was randomized. Additionally, masking participants is difficult to achieve in psychotherapy research. Seven of the eight studies were scored with *some concerns* on domain five, risk of bias in selection of the reported result, because no protocol and registration information was available.

Results of study-level MA

15 studies compared EMDR with another psychological treatment. The results of the study-level MA of all 15 included studies revealed no significant difference in PTSD symptom severity between EMDR and the comparator interventions at the post-test assessment (g = -0.091; 95% CI [-0.33, 0.15]; p = .462). Heterogeneity was moderate (I^2 = 55.79%). There was no significant difference between the outcome findings of studies included in the present IPDMA and studies with unavailable data (p = .87) (see Appendix 6). Based on a visual inspection of the funnel plot of standard error Hedges' g, it is unlikely publication bias is present in this MA (see Appendix 7).

Primary outcomes

IPDMA: PTSD Symptom Severity

Appendix 8 presents the main and moderator results of a one-stage IPDMA on *PTSD symptom severity* at the post-test. A one-stage IPDMA found no significant difference between EMDR and comparator interventions on *PTSD symptom severity* (β = −0.24; 95% CI [-0.62, 0.14]; p = .210; n (studies) = 270 (8)). The full sample one-stage IPDMA analysis based on imputed PTSD severity outcome data (β = - 0.20; 95% CI [-0.52, 0.12]; p = .217; n (studies) = 339 (8)), and the two-stage (g = – .20; 95% CI [-0.55, 0.14]; p = .251) yielded a similar result to the one-stage IPDMA completer analysis. Baseline PTSD symptom severity was found to be a significant predictor of post-test PTSD

severity in the one-stage completer analysis (β = 0.43; p = .000), and the imputed analysis (β = 0.43; p = .000). More specifically, higher baseline PTSD symptom severity was associated with higher post-test PTSD severity.

In the completer analysis, employment status significantly moderated the relationship between therapy type and post-test PTSD symptom severity. More specifically, unemployed participants who received EMDR reported significantly higher PTSD symptom severity at the post-test than employed participants who received EMDR (β = 0.80, p = .019). None of the other participant-level variables (sociodemographic, clinical, and intervention-related characteristics) significantly moderated PTSD symptom severity after EMDR treatment in the completer or imputed datasets (see Appendix 8).

IPDMA: Treatment Response

In one-stage analysis, no significant difference in the effect of EMDR compared with other psychological treatments was found for *PTSD treatment response* (β = 0.86; 95% CI [-.03, 1.74]; p = .057; n (studies) = 270(8)) (see Appendix 9). The OR was 2.36. The two-stage analysis MA also found no significant difference in effect between EMDR and other psychological treatments for *PTSD treatment response* (β = 0.52; 95% CI [-0.42, 1.46]; p = .278). The OR was 1.68. Employment status significantly moderated the relationship between therapy type and PTSD treatment response. More specifically, unemployed participants who received EMDR were significantly less likely to have responded to treatment at post-test than the employed participants who received EMDR (β = -.63, p = .005). None of the other sociodemographic, clinical, and intervention-related characteristics of participants was significantly associated with treatment response (see Appendix 10).

IPDMA: PTSD remission

In a one-stage IPDMA, no significant difference in effect between EMDR and other psychological treatments for *PTSD remission* at post-test were found (β = 1.05; 95% CI [-0.11, 2.22]; p = .075; n (studies) =199(5)) (see Appendix 10). The OR was 2.87. The two-stage analysis found a significant effect of EMDR compared with other psychological treatments for *PTSD remission* at post-test (g =

1.00; 95% CI [0.14; 1.87]; p = .023. The OR was 2.73. There was insufficient data to run a moderator analysis.

Secondary outcome

IPDMA: treatment dropout

One-stage IPDMA on *treatment dropout* found no significant difference in effect between EMDR and other psychological treatments at post-test (β = -0.25; 95% CI [-0.79; 0.29]; p = 0.369; OR =0.78; n (studies) = 283 (6)) (see Appendix 11). The two-stage analysis found no significant difference in the effect of EMDR over controls for *PTSD treatment dropout* at post-test (β = - 0.19; 95% CI [-0.83, 0.45]; p = .553). The OR was 0.82. Gender significantly moderated the relationship between therapy type and PTSD dropout. More specifically, male participants in EMDR groups were significantly more likely to drop out of EMDR treatment than female participants in EMDR groups (β = 0.23, p = .028). None of the other sociodemographic, clinical, and intervention-related characteristics of participants was significantly associated with treatment dropout (see Appendix 12).

DISCUSSION

In this study, we compared the effects of EMDR on PTSD severity, treatment response, treatment remission and treatment dropout to that of other psychological treatments. We aimed to identify moderators of these EMDR treatment outcomes of which there is currently very limited literature available. While past MAs have repeatedly found significant improvements in PTSD outcomes compared to baseline assessments, the uncertainty is centred around what participant-level variables moderate EMDR treatment effects in PTSD.

In line with past research, the current study found no significant difference between EMDR and other psychological treatments on PTSD severity, treatment response, or treatment dropout in either the one- or two-stage IPDMA (Lewis et al., 2020). It is important to note that all the psychological comparator treatment groups were found to be effective in treating PTSD when interpreting these findings. We found no significant difference between EMDR and the psychological treatment control groups on PTSD remission at post-test in the one-stage analysis. However, a

significant main effect in favour of EMDR was found in the two-stage analysis on PTSD remission. Considering the small sample sizes of the included trials, the one-stage IPDMA result is most likely the more accurate reflection of the "true effect". In line with previous research, baseline PTSD was a significant predictor of post-test PTSD symptom severity (Taylor et al., 2003). Specifically, higher baseline PTSD symptom severity was associated with higher post-test PTSD symptom severity. An earlier study found that higher PTSD baseline scores on PTSD self-report measures were associated with better treatment outcomes on self-report PTSD questionnaires (Karatzias et al., 2007). Overall, this was not the case in this aggregated set of trials. While there are distinct differences between EMDR and the other TF therapies, our finding suggests they are equally efficacious at treating PTSD symptoms. These findings are in line with past study-level MA (Lewis et al., 2020).

Our moderator analysis was exploratory in nature and based on available sociodemographic, clinical, and intervention-related variables available in the obtained databases. Results from our completer moderator analysis found unemployed participants who received EMDR reported significantly higher PTSD symptom severity at post-test than employed participants who received EMDR. Similarly, we found unemployed participants who received EMDR were significantly less likely to respond to treatment by post-test than the participants who received EMDR and were employed. Past research supports our current findings. Unemployed participants were found to be more likely to suffer from higher levels of mental health problems including PTSD (Bosman & van der Velden, 2018; McKee-Ryan et al., 2005; Paul & Moser, 2009). In a longitudinal study among employed and unemployed trauma-exposed participants, unemployed participants continued to experience higher levels of mental health problems even years after exposure (Bosman & van der Velden,2018). Research has attributed the benefits of employment as income, status, relationships, and esteem (Chen, Westman, & Hobfoll, 2015; Paul & Batinic, 2010). Unemployed participants might be more socially isolated in comparison to their employed counterparts or have more severe or further advanced symptoms (Nijdam, et al., 2023) resulting in less beneficial PTSD outcomes at post-test.

Furthermore, it is possible that financial concerns and associated psychological distress could distract or hinder the recovery process in unemployed participants.

We also found that male participants who received EMDR were significantly more likely to drop out of treatment than female participants who received EMDR. Both brain and behaviour differences in men and women may explain why men were found to be more likely to drop out of EMDR treatment in comparison to female participants (Olff et al., 2017). In a recent survey among Australian males who attended mental health services, various reasons for drop-out were self-reported, among which was a lack of connection with the therapist, the sense that therapy lacked progress and the cost/ inconvenience related with attending therapy sessions (Seidler et al., 2021). Thus, it is crucial that studies examine strategies to make interventions more attractive and acceptable for males, in order to prevent drop-out.

To our knowledge, this study is the first MA to use individual participant-level data to examine moderators of EMDR for adults with PTSD. Among the strengths of the present study was its higher power to detect statistically significant moderators compared with study-level MA or any of the current RCTs aimed at investigating the efficacy of EMDR for adults with PTSD. The use of an IPDMA made it possible to investigate participant-level moderators (such as employment status and gender). Based on a visual inspection of the funnel plot of standard error Hedges' g, it is unlikely publication bias is present in this MA.

Several limitations of our IPDMA should be mentioned. First, the small sample sizes of the included studies, and consequently the total number of participants included in this IPDMA, limited our ability to detect certain moderators. Second, our findings are at risk of availability bias because we could not access data from seven eligible studies. However, the results of the study-level MA indicated no significant difference between the studies included in the present IPDMA and studies with unavailable data. 6 of the 15 studies were published more than 20 years ago (<= 2003). Only two of these 6 older studies were available for this IPDMA (Devilly et al., 1999; Lee et al., 2002).

Additionally, we could not examine several variables that could potentially influence EMDR treatment response, such as symptom duration or the number of treatment sessions attended because we did not have sufficient studies reporting these variables to conduct these analyses. Furthermore, most of the participants had chronic PTSD. Therefore, the current findings can only be generalized to patients with chronic PTSD.

Considering that EMDR is highly protocolized, and is relatively straightforward to administer, it may be a more cost and resource-effective treatment option to implement in areas with limited human resources. In the only systematic review to compare the relative cost-effectiveness of different PTSD treatments, EMDR was found to be the most cost-effective (Mavranezouli et al., 2020). However, further studies are needed in this area, in particular, large international RCTs. With the increased use of secondary analyses and IPDMA, researchers are strongly urged to anonymise and store their data (in a usable format) for long-term use. In terms of the FAIR data principles, this not only improves scientific integrity but also prevents us from overlooking important discoveries. Data sharing, compiling and storage have become much faster and easier. By increasing the sample sizes in the EMDR effectiveness trials, reducing risk of bias, and increasing the number of RCTs statistical power can be increased which could improve our precision in detecting clinically relevant moderators of treatment outcomes. An update of this IPDMA in the future may have greater statistical power to provide further insight into moderating effects of participant-level factors on PTSD treatment response.

In sum, this is the first IPDMA to have examined the effect of EMDR in comparison to other psychological treatments and explore what individual-level characteristics moderate PTSD treatment outcomes. Overall, no significant difference was found between EMDR and other psychological treatments in terms of PTSD outcomes. Findings from this IPDMA suggest that unemployed participants are less likely to respond to the EMDR treatment and have significantly higher PTSD symptom severity at post-test in comparison to employed participants receiving EMDR.

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