The Effectiveness of EMDR for Medically Unexplained Symptoms: A Systematic Literature Review

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Introduction: It has been hypothesized that certain persistent physical symptoms (PPS) may be linked to unresolved traumatic or distressing somatic-symptom related memories. EMDR intervention targets and reintegrates distressing memories, thus reducing the re-experiencing of physical sensations. The primary aim of this review was to examine effectiveness of EMDR for PPS. Secondary aims were to investigate effectiveness of EMDR on secondary outcomes (post-traumatic stress, anxiety, and depression), and to evaluate the acceptability of EMDR for this client group. **Method:** Six electronic databases (PsycInfo, PsycArticles, CINAHL, MEDLINE, Web of Science and SCOPUS) were searched for peer-reviewed literature, with no restrictions on publication dates. Twenty-eight studies met inclusion criteria. Studies were included if the primary aim of EMDR intervention was to reduce intensity, frequency or reported distress associated with PPS. Studies were quality appraised using the MMAT tool prior to narrative synthesis of key findings. **Results:** Studies varied in design and included RCT, UCT, case study and case series. EMDR treatment length varied between studies; 1–20 sessions. All studies reported significant improvement in PPS at post-test. Effect sizes were available to report in five studies and ranged from moderate to large. Improvement in secondary outcomes were reported in all repeated measure studies. Where available, large effect sizes were reported for reduction in anxiety and depression. Overall drop-out rates in studies with representative samples was low (10.6%). Quality of research varied; low (42.8%), medium (21.4%), and high (35.7%). **Conclusions:** There is promising emerging evidence for effectiveness and acceptability of EMDR for a range of PPS. However, firm conclusions on efficacy cannot be made. While comparisons between PPS presentations cannot be drawn due to methodological differences, the findings for pain and tinnitus are the most compelling due to methodological quality. High-quality sufficiently powered RCTs are recommended to determine efficacy.

Keywords: EMDR; eye movement desensitization and reprocessing; persistent physical symptoms; medically unexplained symptoms; systematic review

Persistent physical symptoms (PPS), previously referred to as medically unexplained symptoms (MUS) is considered an umbrella term that encompasses "persistent bodily complaints for which adequate examination does not reveal sufficiently explanatory structural or other specified pathology" (Henningsen et al., 2007). PPS encompasses several different presentations affecting different systems of the body (e.g., perception, sensation, movement) (Gupta, 2013; Wessely et al., 1999). There is a current paradigm shift in this area of research following revision in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5; American Psychiatric Association [APA], 2013). Most notably, medically explained and medically unexplained somatic symptoms are no longer differentiated, instead focus is given to the level of associated distress. While this change occurred with the aim to destigmatize medically unexplained presentations, there is no scientific consensus on whether the mechanisms

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that underpin biomedical conditions are the same in symptoms in which there is no known medical cause (Rief & Martin, 2014). This has potential implications on research and clinical practice. Biopsychosocial models of MUS/PPS highlight a complex interaction between multiple biological and psychosocial etiological factors (Brown, 2007). More recent models have proposed multi-factorial mechanisms of symptom perception and propose that clinical intervention should focus on targeting inferential processes (Van den Bergh et al., 2017).

While true prevalence is unknown, a meta-analysis estimated that 45% of primary care appointments may be attributed to medically unexplained presentations (Nimnuan et al., 2001). Comparably, an epidemiological study found that approximately 50% of patient presentations in secondary care settings were deemed medically unexplained (Haller et al., 2015). For presentations indicative of functional neurological disorder, estimations stand between 4 and 12 per 100,000 (Carson et al., 2012). PPS can be disabling for individuals, resulting in unemployment, sickness absences, frequent healthcare appointments and invasive medical investigations (Bermingham et al., 2010; Burton et al., 2011). UK estimates of the annual cost of MUS are around £18 billion (Bermingham et al., 2010).

Treatment outcomes for individuals with PPS are generally poor with insignificant effects for reduction of symptoms (Van Dessel et al., 2014) and frequent healthcare use (Jones & Williams, 2019). Lack of guidelines and the limited evidence base for this client group are considered barriers to improving long-term outcomes (Rommelfanger et al., 2017). In England, there are limited NHS National Institute for Health and Care Excellence (NICE) guidelines regarding evidence-based psychological interventions for PPS (e.g., tinnitus, irritable bowel syndrome, functional neurological disorder, non-epileptic attack), with the exception of chronic pain (NICE, 2019). In addition, clients with PPS report poor experiences of healthcare professionals and clinical intervention (Burke, 2019; Robson & Lian, 2017). While there have been attempts to determine effective psychological interventions for this client group, confirmatory conclusions have not been drawn due to the paucity of research.

Cognitive behavioral therapy (CBT) for PPS focuses on challenging maladaptive cognitions and "unhelpful illness behaviors" such as avoidance (Gutkin et al., 2021), whereas psychodynamic therapy (PDT) aims to resolve intrapsychic conflict and maladaptive defence mechanisms (e.g., emotional avoidance and somatization) (McCullough et al., 2001). Meta-analysis (Kleinstäuber et al., 2011) of CBT for PPS found magnitude of treatment effect to be small (d = 0.25). These findings are consistent with more recent meta-analysis that reported small and moderate effect size for CBT (d = 0.49) and PDT (d = 0.69) respectively (Gutkin et al., 2021). In the chronic pain literature, meta-analysis on the effectiveness of Acceptance and Commitment Therapy (ACT) highlighted significant medium to large effect sizes on self-reported pain acceptance but insignificant effect on measures of pain intensity and quality of life (Hughes et al., 2017). However, these findings should be interpreted with caution due to lack of active control groups, small sample sizes, and low-quality data.

Within the wider literature, psychological trauma and stress are considered relevant in terms of PPS in which etiology and maintenance are not better explained by biomedical factors. In presentations consistent with functional neurological disorder (FND), meta-analysis found that adverse life events were reported eight times more commonly in individuals with FND than non-clinical controls and two times more commonly than other clinical populations (Lehn et al., 2016). Similarly, individuals presenting with functional non-epileptic seizures were found to have significantly higher rates of PTSD than individuals with epilepsy (Marchetti et al., 2007). These findings are consistent with a range of PPS presentations. Trauma and emotional neglect are considered risk factors to developing psychogenic seizures (Marchetti et al., 2007), chronic fatigue (Crawley et al., 2012; Heim et al., 2006, 2009), and chronic pain (Fishbain et al., 2017). In addition, trauma and complex and ongoing life stressors have been hypothesized to trigger and maintain episodes of phantom pain (Fuchs et al., 2018; Otis et al., 2010), general somatic complaints (Afari et al., 2014), tinnitus (Fagelson, 2007, 2016; Gupta, 2013), and dermatologic symptoms (Bilkis, 1998). While causal mechanisms are complex and widely debated, recent meta-analysis findings suggest that chronic exposure to psychological trauma is associated with autonomic nervous system dysfunction, as measured by heart-rate variability (Schneider & Schwerdtfeger, 2020). Compared to "healthy" controls, patients with MUS have been found to show a reduction in heart-rate variability, indicating reduced parasympathetic activity (Ruschil et al., 2021). Eye-movement desensitization and reprocessing (EMDR) therapy has been found to reduce arousal by engaging the parasympathetic nervous system (Vojtova & Hasto, 2009), highlighting its potential usefulness for individuals presenting with PPS.

EMDR is an eight-phased protocol that aims to sequentially target and reintegrate distressing

memories using bilateral eye movements (Shapiro, 2001). EMDR is underpinned by the Adaptive Information Processing model (AIP) which postulates that "symptoms" may be the result of unprocessed traumatic or somatic-symptom related memories (Shapiro, 2001). When triggered, these memories result in the re-experiencing of associated emotions, cognitions, and physical sensations (Shapiro, 2014). By focusing on the reprocessing of specific memories, somatic and emotional arousal is decreased and thus the re-experiencing of physical sensations is reduced (Shapiro, 2001). In the context of PPS, it is hypothesized that symptoms are a physical re-experience (Van der Kolk & Fisler, 1995, as cited in Van Rood & De Roos, 2009) that can be maintained through cognitive and emotional re-experience (Van Rood & Visser, 2008, as cited in Van Rood & De Roos, 2009). For example, the sound of a car may trigger myoclonic limb movements in an individual who had previously survived a car accident (e.g., physical re-experience). Additionally, associated cognitions (e.g., "I'm weak") and physiological arousal (e.g., anxiety) may also re-activate unprocessed memories and trigger physical symptoms (e.g., emotional and cognitive re-experiencing). Van Rood and De Roos (2009) hypothesized that "both the post-traumatic stress that is the result of the triggering of the traumatic memory and the way the patient copes with this stressful situation may maintain the physical complaint and hinder recovery" (p. 250).

The evidence base for EMDR and PTSD is generally well established, with meta-analysis finding EMDR as efficacious as trauma-focused CBT (TF-CBT; Bisson et al., 2013; Seidler & Wagner, 2006). However, the evidence base for EMDR and PPS is still emerging. Van Rood and De Roos (2009) conducted a systematic review of EMDR in the treatment of MUS, although conclusions on direction of effect could not be made due to methodological limitations of studies. Furthermore, the review included body dysmorphic disorder and olfactory reference syndrome, which are no longer considered somatic presentations. While narrative accounts of the literature in this area have been published (Matthijssen et al., 2020; Shapiro, 2014; Tefft & Jordan, 2016), these were not systematic in nature. Other systematic reviews published in the literature have been broader in context, synthesizing findings of all RCTs of EMDR. In one such review, only one RCT of MUS (chronic pain) was included and therefore conclusions on effectiveness could not be established (Gomez et al., 2017). The chronic pain literature has been systematically reviewed in 2014 and 2019 (Tesarz et al., 2014, 2019) concluding that consistent findings on the efficacy of EMDR were promising, however interpretations of these results should be considered in light of varying intervention protocols and methodological limitations. In 2018, a systematic review of the effectiveness of EMDR for FND was conducted and concluded that emerging evidence was promising but further research was needed. However, this review only included three papers in total (case series/studies) published before 2008 (Cope et al., 2018).

At present, the overall literature regarding effectiveness of EMDR for PPS has not been systematically reviewed and quality appraised since 2009. The purpose of this review was to provide on update on Van Rood and De Roos systematic review and examine all available studies using EMDR in the treatment of PPS, regardless of study design or publication date. The primary aim of this review was to examine the effectiveness of EMDR for reducing frequency, intensity, and associated distress of PPS in adult populations. Secondary aims were to investigate effectiveness of EMDR on secondary outcomes (post-traumatic stress, anxiety, and depression), and to evaluate the acceptability of EMDR for this client group.

Methods

Registration

This systematic literature review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) CRD42021268332.

Search Strategy

The search strategy was completed in adherence to PRISMA guidelines (Page et al., 2021). Six electronic databases (PsycINFO, PsycArticles, CINAHL, MEDLINE, Web of Science and SCOPUS) were searched for peer-reviewed literature, with no restrictions on publication dates. The last search was conducted on 27/02/2022.

Database	Coverage
PsycINFO	1806 to present
PsycArticles	1935 to present
CINAHL	1982 to present
MEDLINE	1946 to present
Web of Science	1900 to present
SCOPUS	1788 to present

The search terms included: ("eye movement desensitisation and reprocessing" OR "eye movement desensitization and reprocessing" OR "eye movement

desensiti?ation therap*" OR EMDR) AND ("medically unexplained" OR "medically unexplained symptoms" OR "persistent physical symptom" OR somatic OR "somatic symptom" OR "conversion disorder" OR somatoform OR "functional neurological disorder" OR functional neurological symptom OR "phantom pain" OR "pain" OR "non-epileptic attack" OR "non-epileptic seizure" OR "idiopathic drop attack" OR "chronic fatigue" OR "tinnitus" OR psychogenic OR psychosomatic). Terms were applied to titles, abstracts, and keywords. Search syntax were adapted, and controlled vocabulary indices were used for each database, where possible.

Ancestry searches were completed on relevant meta-analyses (Kleinstäuber et al., 2011), systematic reviews (Cope et al., 2018; Tesarz et al., 2014, 2019; Valiente-Gómez et al., 2017; Van Rood & De Roos, 2009), and literature reviews (Matthijssen et al., 2020; Shapiro, 2014; Tefft & Jordan, 2016). The reference lists of studies identified for inclusion in this review were also searched. Conference abstract searches were completed in SCOPUS, and authors were contacted requesting full texts.

Study Selection

The referencing software EndNote was used to manage citations. After duplicates were removed, all studies were reviewed using the inclusion criteria (see Appendix A). Two of the three authors worked independently in the screening of each record with any disagreements resolved by referral to third author.

Inclusion criterion	Rationale
All empirical studies	Due to limited studies published in this area, inclusion of all studies widens the scope of the review
Primary aim of EMDR intervention to reduce intensity, frequency, or reported distress associated with "medically unexplained symptom"	Primary focus of review
Adult participant sample characterized by persistent physical symptoms in which onset or maintenance is not better explained by biological factors	Primary focus of review and theoretically consistent with adaptive information processing (AIP) model that underpins hypothesized mechanisms of EMDR
Peer-reviewed	To provide a measure of quality control
All studies available in English language	Translation resources not available

The inclusion of studies solely adhering to full EMDR protocol (Shapiro, 2001) without adaptations (e.g., integrated therapies) was initially considered to answer the review question. However, much of the research in this area are case studies from clinical settings where adaptations or pharmacological intervention may be used in conjunction. Due to limited studies published in this area, it was deemed important to broaden the scope of the review. PPS in which onset or maintenance is not better explained by biological factors were included (e.g., psychogenic seizures, myoclonic movements, chronic fatigue). Studies in which it was hypothesized that distressing memories underpinned the onset or maintenance of symptoms were also included (e.g., tinnitus, migraine, dermatologic complaints).

Articles examining the effects of EMDR on physical symptoms in which onset or maintenance of symptoms was predominantly explained by biomedical factors; post-surgery pain (Maroufi et al., 2016), arthritis (Höfel et al., 2018, Nia et al., 2018), cancer-related pain (Gielkens et al., 2018) were excluded. Research including child participants were also excluded (Dautovic et al., 2016; Demirci & Sagaltici, 2021; Gauvry et al., 2013). Grey literature (not peer-reviewed) was excluded to provide a measure of quality control (Estergard, 2008; Kavakci et al., 2012). Studies that used EMDR-related protocols (e.g., EMD or bilateral stimulation [BLS]) or experimentally induced symptoms were excluded (Friedberg, 2004).

In cases in which studies were considered appropriate based on abstract but full texts were not available in English, enquiries were made to authors regarding translated versions. One response was received, resulting in inclusion of an additional study (Rostaminejad et al., 2017). Due to lack of translator resources, five papers were unable to be considered in this review (Brennstuhl et al., 2016; Flik & De Roos, 2010; Gündoğmuş et al., 2019; Kavakci et al., 2014; Sinici, 2016). Twenty-eight studies met the outlined eligibility criteria.

Data Abstraction

To reduce bias in reporting, data extraction was completed prior to quality appraisal. The data extracted included characteristics of studies (author(s), date, location, study design, sample, medically unexplained symptom, comorbidities, intervention length, outcome measures, follow-up), and a summary of key findings. All measures of PPS symptoms (frequency, intensity, distress) and secondary outcomes (post-traumatic stress, anxiety and depression) were included if a minimum of pre- and post-test scores were reported.

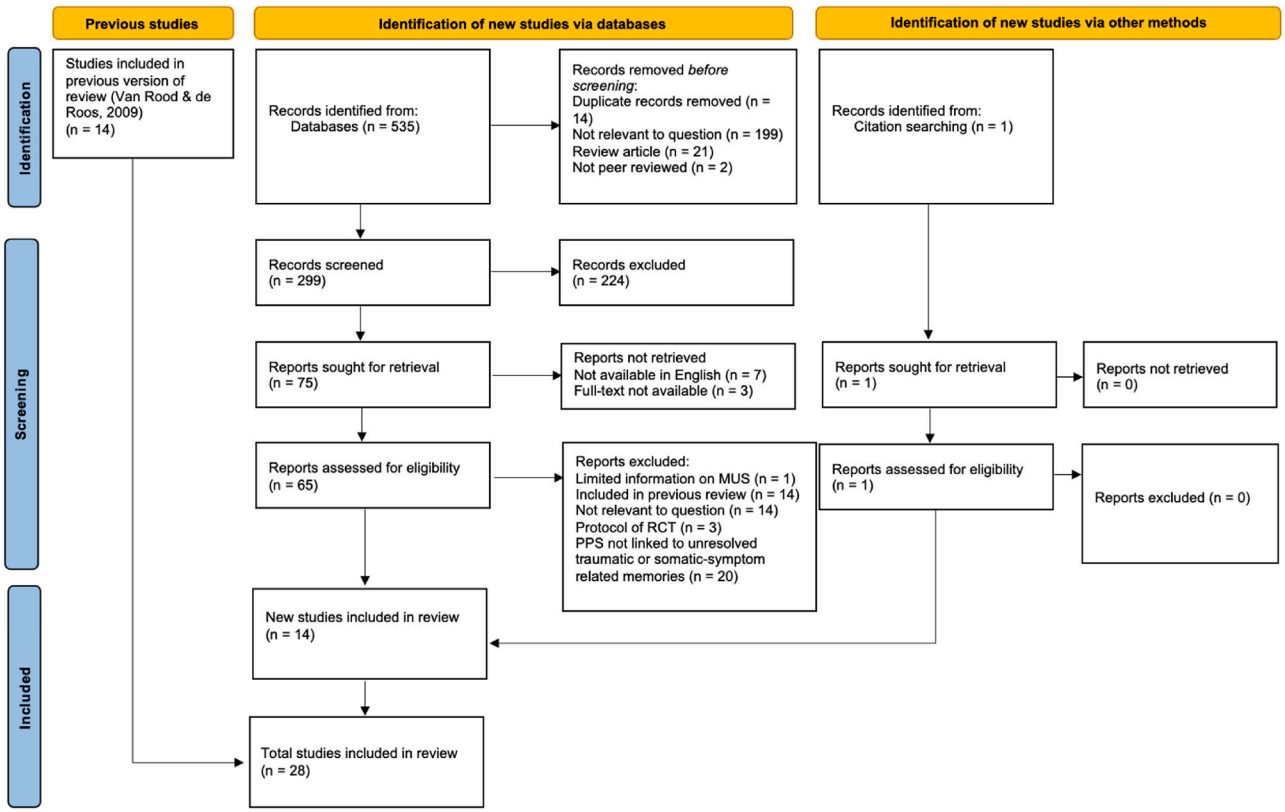

Figure 1. PRISMA flowchart of study selection process.

There were no other restrictions on number of data points collected, however length of follow-up was considered when interpreting findings. Clinically significant change (CSC) and reliable change index (RCI) analysis was completed for studies that did not include analysis of data (e.g., case reports/series). Effect sizes were calculated where possible. One reviewer collected data from each study and this was checked by the remaining two reviewers. Any discrepancies were resolved by consensus.

Quality Appraisal

Quality appraisal was completed using the Mixed Methods Appraisal Tool (Hong et al., 2018). The MMAT tool was developed for systematic reviews that include studies with heterogeneous designs. Mixed reviews are often required when aiming to evaluate interventions relevant to clinical practice in which the evidence base is still emerging (Pluye & Hong, 2014). While the updated version of this tool includes two screening questions (regarding coherence of research question and data collection), these were not used as part of appraisal due to the large number of retrospective case studies included in the review. The MMAT requires researchers to select the appropriate methodological category for each study, apply the five separate criteria, and assign a rating ("Yes," "No," "Can't tell"). Conversion of ratings into metrics and presenting an overall score of each study without rationale is discouraged, as this is unlikely to provide sufficient information (Hong et al., 2018). While there are no cut-off values outlined in the MMAT, each study was rated "low," "moderate," or "high" quality based on the number of criteria met. Exclusion of "low" quality studies may limit the breadth of review (Verhage & Boels, 2017) thus no studies were excluded due to methodological quality. However, quality of study was taken into account when synthesizing data. All three authors rated quality of studies independently. Interrater reliability was 94.3%, with any discrepancies discussed and agreed upon.

Data Synthesis

Due to the paucity of research in this area, the search strategy was not restricted to randomized controlled trials (RCTs) and therefore meta-analysis was not appropriate. The studies included were heterogeneous in design and thus findings were organized and summarized through narrative synthesis. This allowed for the exploration of similarities and differences between studies, and identification of relationships within the data relevant to the focus of the review. Narrative synthesis was conducted in line with established framework and guidance (Popay et al., 2006).

Where available, standardized mean differences were used to determine effectiveness. Magnitude of treatment effect was reported using different effect size measurements across studies. Interpretations were made in line with relevant benchmarks described in the literature (Cohen, 1988). Clinically significant change (CSC) and reliable change index (RCI) analysis was completed for studies that did not include analysis of data (e.g., case reports/series) (Jacobson & Truax, 1992). RCI analysis was calculated by dividing the standard error with the difference between pre-post treatment scores (Jacobson & Truax, 1992). CSC was defined by meeting one of three criteria; 1) a pre-and-post change of >2 standard deviations from baseline mean, 2) post-test scores within 2 standard deviations of reported normative sample mean, 3) post-test scores fall within sub-clinical or non-clinical ranges (as defined by benchmarks reported in psychometric manual; Jacobson & Truax, 1992). These calculations can only be used for outcome measures for which normative values are available and therefore cannot be applied to frequency or intensity of physical symptoms.

Client self-report and relevant health information was used to contextualize the findings. Drop-out rates and follow-up data were used to measure acceptability and long-term effectiveness of intervention.

Results

Characteristics of Studies

As displayed in Appendix B, each study was allocated a number for reference purposes. The twenty-eight peer-reviewed studies were published between 2000 and 2020. Thirteen studies were conducted in Europe, seven in North America, one in South America, three in Australia, and four in Asia. Studies were published in the English language, with the exception of one in which a translated version was provided following a request to the first author. Regarding methodology, case reports/studies were the most common design, followed by case series. Of the sixteen case reports/series, 10 used pre-post measures and six provided a qualitative account of a clinical case. The remaining studies were seven randomized controlled studies, four uncontrolled clinical trials and a within-groups design.

The gender of participants was reported in all studies except one; however, gender ratio of participants in said study was later clarified by the author for the purpose of a review (Van Rood & De Roos, 2009). Of the total sample who received EMDR, 253 were female (70.2%) and 107 were male (29.8%). The same participant was reported in both Grant (2000) and Grant and Threlfo (2002) paper. Ethnicity and nationality of participants was explicitly reported in only five studies: Caucasian ($n = 51$), Asian ($n = 12$), Hispanic ($n = 9$) and African American ($n = 1$). Subsequently, 80% of the review sample's ethnicity is unknown.

All participants experienced a range of persistent physical symptoms. Presentation indicative of Functional Neurological Disorder and Pain (chronic, migraine, complex regional) was the most common amongst participants, followed by Phantom Pain, Tinnitus, Chronic Fatigue, and Dermatologic Disorders. Unresolved traumatic or somatic-symptom related memories were linked to onset or maintenance of PPS. In six studies, participants met diagnostic criteria for PTSD. In the remaining studies, it was unclear whether participants had or would meet criteria for formal diagnosis of PTSD. A range of comorbidities were reported amongst participants: Complex trauma, borderline personality disorder, dissociation, health anxiety, substance use, obsessive compulsive disorder, depression, psychosis, anxiety, fatigue, insomnia, and traumatic brain injury.

All twenty-eight studies used EMDR (Shapiro, 2001) to target PPS. Six studies used pain protocols, one study used elements of the pain protocol and another developed a headache protocol for the purposes of their study. Treatment length varied across studies, ranging from 1 to 20 sessions. In three of the RCTs, EMDR was delivered as the sole intervention and compared to treatment-as-usual (TAU) control group (Demirci et al., 2017; Gerhardt et al. 2016; Rostaminejad et al., 2017). Three RCTs delivered an integrated EMDR; tinnitus retraining therapy plus EMDR (Luyten et al., 2020), cranial pressure plus EMDR (Marcus, 2008) and hypnosis plus EMDR (Ray & Page, 2002). In several other studies, EMDR was delivered in conjunction with other interventions; pharmacological (Chemali & Meadows, 2004; De Roos et al., 2010; Konuk et al., 2011; Marcus, 2008; Mazzola et al., 2009; Schneider et al., 2008), counselling sessions (Kelley & Benbadis, 2007), solution-focused and cognitive-behavioral therapies (Proudlock, 2015).

PPS were measured via self-report of frequency, severity, and associated distress (e.g., number of episodes, pain rating scales). Secondary outcome measures were most frequently measured by standardized psychometrics; Impact of Events Scale (IES), Beck's Anxiety/Depression Inventory (BAI; BDI). See Appendix B, for all included outcome measures.

Pre-test and post-test measurements were included in twenty-one of the twenty-eight studies. Follow-up

was completed for all studies except four (D'Andréa et al., 2021; Demirci et al., 2017; Grant, 2000; Mazzola et al., 2009). Follow-up periods ranged from 1 day to 40 months. Of the total 523 participants, 360 received EMDR, and 163 received treatment as usual (control group).

Quality Appraisal

An overview of the quality appraisal process is outlined in Appendix A. In line with MMAT scoring guidance (Pluye et al., 2011), quality ratings were assigned to each study based on the number of criteria met within their study category. A study was deemed "high" quality if four or more criteria were clearly met; "medium" quality if three criteria were clearly met, and "low" quality for two or less (Pluye et al., 2011). The methodological quality of studies impacts the risk of bias and subsequently the reliability of the conclusions drawn from the data. Following quality appraisal, eleven studies were found to be high quality (Brennstuhl et al., 2015; D'Andrea et al., 2021; De Roos et al., 2010; Gerhardt et al., 2016; Luyten et al., 2020; Marcus et al., 2008; Mazzola et al., 2009; Phillips et al., 2019; Rikkert et al., 2018; Rostaminejad et al., 2017; Suárez et al., 2020); six studies moderate quality (Demirci et al., 2017; Konuk et al., 2011; Schneider et al., 2008; Silver et al., 2008; Wilensky, 2006), and eleven studies low quality (Altunbaş, 2018; Chemali & Meadows, 2004; Cope, 2020; Grant, 2000; Grant & Threlfo, 2002; Gupta & Gupta, 2002; Kelley & Benbadis, 2007; Proudlock, 2015; Ray & Page, 2002; Royle, 2008; Russell, 2008).

Four of the six included RCTs were judged to be high quality (Gerhardt et al., 2016; Luyten et al., 2020; Rostaminejad et al., 2017; Suárez et al., 2020). Strengths of these studies included comparable group baselines at pre-test, detailed description of randomization strategy and researcher blinding. While effect sizes were reported in six RCTs, they were not reported in one (Rostaminejad et al., 2017) and were therefore calculated for purpose of this review. None of the RCTs were sufficiently powered to provide confirmatory evidence of efficacy, this was appropriately acknowledged and reflected in interpretation of findings. The other three RCTs were found to be moderate (Demirci et al., 2017) and low quality (Marcus, 2008) due to it being unclear whether randomization was appropriately performed, lack of assessor blinding, and non-representative samples. In the moderate quality RCT (Marcus et al., 2008) it was unclear whether appropriate randomization had been performed and outcome assessors were not blinded to the intervention. In all RCTs, intervention adherence was judged to be high.

The remaining high quality studies were uncontrolled clinical trials (D'Andréa et al., 2021; De Roos et al., 2010; Mazzola et al., 2009; Phillips et al., 2019; Rikkert et al., 2018) and a case study (Brennstuhl et al., 2015). While the uncontrolled studies included a sample representative of the target population, appropriate measures, and complete outcome data, it was unclear whether confounders were controlled for in the analysis. The high quality case study included a representative sample and appropriate measures, however it was unclear whether appropriate statistical analysis was used. The moderate quality case reports and case series lacked control groups making it difficult to determine whether reported outcomes were related to impact of EMDR or other confounding variables. It was unclear whether appropriate methods to account for confounders were implemented. Similarly, in studies that used EMDR in conjunction with another intervention, it was difficult to isolate benefits of the independent variable.

A large percentage of included studies (42.8%) were judged to be low in quality. The qualitative case studies (Grant, 2000; Gupta & Gupta 2002; Kelley & Benbadis, 2007; Proudlock, 2015; Royle, 2008) provided a narrative account of a clinical case, and it was unclear whether findings were adequately substantiated by data. In multiple studies vague statements such as "improvement in symptoms" or "fewer symptoms" were not adequately derived from reported data, and it was unclear whether this was clinical judgement or client self-report. In two studies (Chemali & Meadows, 2004; Proudlock, 2015), psychometrics (IES, BDI, BAI) were completed at pre-test but were not repeated at post-test, resulting in incomplete outcome data. Further limitations were highlighted in the analysis and interpretation of findings. In several case studies/series, statistical analysis of data was not reported and was therefore completed for purpose of this review. In the non-randomized quantitative study (Ray & Page, 2002), it was unclear whether a representative sample had been sought or whether confounders had been accounted for in the design and analysis.

Due to heterogeneity of presentation, representation within this population is difficult. In several studies the sampling strategy was unclear and there were no indicators that a representative sample that been sought (e.g., characteristics of population, inclusion/exclusion criteria). These studies appeared to be

retrospective accounts of clinical cases, and likely utilized convenience sampling.

Overall, studies used standardized outcome measures for secondary outcomes (IES, BDI, BAI). In the chronic pain and phantom pain studies, standardized pain measures were commonly used (NRS; MPI-D) alongside general health measures (SF-36). However, due to lack of standardized outcome measures for other medically unexplained presentations, remaining quantitative studies measured change via frequency, intensity, or associated distress. In one study (Silver et al., 2008), this numerical data was contextualized with client and family self-report, clinical judgement, and medical records.

Across all studies, except one (Marcus, 2008), it was unclear whether attempts were made to assess fidelity of intervention. In addition, no assessments of proposed mechanisms of action were included.

Effectiveness of EMDR for Persistent Physical Symptoms

The key findings from each study are summarized in Appendix B. Due to heterogeneity of study design, this preliminary synthesis aimed to synthesize findings regarding the direction of effects. Where possible, results were summarized using magnitude of treatment effect sizes. Effect sizes were calculated for the purpose of this review in studies that reported the relevant raw data (standardized mean difference and standard deviation). All twenty-eight studies reported an improvement in primary and secondary outcomes following EMDR intervention. However, definitive conclusions on effectiveness cannot be made due to methodological differences and quality of data.

The six included RCTs reported significant reduction in PPS at post-test compared to control group (TAU). Demirci et al. (2017) reported a significant improvement in somatic symptoms and pain following EMDR ($\eta^2 = 0.94$; $\eta^2 = 0.89$) versus Duloxetine control group ($\eta^2 = 0.68$; $\eta^2 = 0.48$). However, caution should be made when interpreting eta-squared effect sizes as this is considered a biased measure of population variance that increases likelihood of overestimations. Gerhardt et al. (2016) found that 45% of participants who received EMDR experienced significant reduction in pain intensity at post-test versus 0% in TAU control group ($d = 0.79$). In addition, 50% of participants who received EMDR rated their condition as "much improved" or "very much improved" compared to 0% in control group ($d = 1.69$). Similarly, large effect sizes were reported in Rostaminejad et al. (2017) with statistically significant reduction in pain intensity and associated distress at post-test ($d = 3.23$), superior to TAU ($d = 0.8$). These findings were consistent with other included pain RCTs with significant reduction in pain intensity at post-test compared to TAU (Suárez et al., 2020) and significantly greater improvement in rapidity of pain reduction compared to TAU (Marcus, 2008). Five of the six RCTs reported follow up data with EMDR being superior to TAU with moderate to large effect; Marcus (2008) ($f = 0.247$) Gerhardt et al. (2016) ($d = 0.50$), Rostaminejad et al. (2017) ($d = 3.9$). These results were maintained at follow-up. While RCTs reported moderate to large effect sizes, study samples were small and spontaneous remission was not controlled for as waiting list control groups were not included. None of the RCTs were sufficiently powered to provide confirmatory evidence of efficacy, this was appropriately acknowledged and reflected in interpretation of findings.

Findings from the uncontrolled clinical trials were consistent with those reported in the RCTs. De Roos et al. (2010) outlined that 80% of patients reported clinically significant reduction in pain at post-test with medium effect sizes indicated ($\eta^2 = 0.63$). In addition, 40% of participants reported themselves to be "pain free" following EMDR and discontinued their pain medication. Similarly, statistically significant reductions were reported in pain levels and subsequent reduction of medication (Mazzola et al., 2009). These findings were consistent with the tinnitus uncontrolled clinical trials, with statistically significant reduction in symptoms in the "majority" of participants (D'Andrea et al., 2021; Phillips et al., 2019) with moderate effect sizes observed ($d = .72$; Rikkert et al., 2018). These results were maintained at follow-up.

Effect sizes were not reported in the case series/studies and relevant data needed for these calculations were not included for primary outcomes. In the case studies/series, all participants experienced marked improvement in their persistent physical symptoms (e.g., reduction in frequency, severity, or distress). Altunbaş (2018) reported improvement in vision clarity compared to pre-treatment. However, it was unclear whether this finding was substantiated in the data, as there was no quantitative measure repeated over time to assess impact of EMDR. Improvement in primary outcomes were also observed in the remaining case reports; complete elimination of seizures, reduction in pain (chronic, complex, phantom), improvement in dermatologic symptoms, decrease in fatigue, reduction in somatic symptoms, and complete elimination of myoclonic movements. In several studies (Chemali & Meadows, 2004; Grant, 2000; Gupta & Gupta, 2002; Kelley & Benbadis, 2007; Proudlock, 2015; Royle,

2008) it was unclear whether findings were derived from client self-report or clinical judgement. These improvements were reported to be maintained at follow-up, except for Grant (2000) which did not report follow up data and Proudlock (2015) which reported additional EMDR sessions delivered at 6-month follow-up. However, due to lack of extended baseline or data collected over multiple time points, it is difficult to conclude at what point these changes occurred. The absence of a control group makes it difficult to assess whether these changes occurred directly as a result of EMDR intervention. These findings should be interpreted with caution due to the limitations in methodology and quality of data.

Comparisons between PPS cannot be drawn due to paucity of studies and differences in methodological quality.

Effectiveness of EMDR for Secondary Outcomes

Improvement in secondary outcomes were reported in all repeated measure studies. With regard to studies that measured post-traumatic stress symptoms, clinically significant and reliable change was observed in IES scores in several studies with clients scoring within sub-clinical (Cope et al., 2020; De Roos et al., 2010; Schneider et al., 2008), or non-clinical ranges at post-test (Russell, 2008; Silver et al., 2008; Wilensky, 2006).

Three studies used the BAI to measure anxiety symptoms, two of which reported clinically significant and reliable change at post-test (Altunbaş, 2018; Demirci et al., 2017). Effect sizes were calculated for Demirci et al. (2017) ($d = 4.1$) which indicated larger magnitude of effect in comparison to the Duloxetine control group ($d = 0.7$).

Seven studies used the BDI to measure depressive symptoms and reported clinically significant and reliable change (Altunbaş, 2018; Demirci et al., 2017; Phillips et al., 2019; Russell, 2008; Silver et al., 2008; Wilensky, 2006), and sub-clinical scores at post-test (Schneider et al., 2008). Where effect sizes were reported (Demirci et al., 2017) magnitude of treatment calculations indicated a larger effect size ($d = 2.6$) in comparison to the Duloxetine control group ($d = 0.6$).

Acceptability of EMDR for Medically Unexplained Symptoms

Drop-out rates can be useful in determining acceptability of intervention. Due to the convenience sampling utilized in several studies included in the review (e.g., case studies/series), results on drop-out rates are limited to studies with a representative sample. Of the 262 participants in studies with representative samples, 28 dropped out during intervention (10.6%). Reasons for drop-out during intervention were cited as physical and mental health difficulties, no change in symptoms, travel, work commitments, and reduction of pain to acceptable level for client as reasoning. In several studies no explanations were given by participants who dropped out during intervention. Rikkert et al. (2018) reported that one participant experienced painful childhood memories which they did not wish to explore and therefore chose to withdraw from the study. In the RCTs that included data on drop-out, rates in the EMDR arm were less than or equal to control groups. Kelley and Benbadis (2007) outlined that 50% of clients declined EMDR following consultation, with limited information on reasoning provided. However, it was unclear whether participants declined to participate in research or EMDR specifically. In the remaining studies, data regarding clients who declined to engage in EMDR was not reported.

In all studies but two (Kelley & Bendadis, 2007; Konuk et al., 2011) no iatrogenic effects associated with the intervention were reported. One client experienced a dissociative episode during the EMDR protocol (Kelley & Benbadis, 2007) and was later diagnosed with a pre-existing dissociative disorder. The authors acknowledged that had this information been known prior, extensive stabilization and preparation work would have been included in the treatment plan. In addition, Konuk et al. (2011) reported that while frequency and duration of migraines had significantly decreased at post-test, these had been observed to increase during the intervention phase.

No other studies collected data on client experience of intervention and therefore firm conclusions on acceptability of EMDR for this client group cannot be drawn.

Discussion

The aims of this review were to 1) examine the effectiveness of EMDR for persistent physical symptoms, 2) examine effectiveness of EMDR for secondary outcomes (post-traumatic stress, anxiety, and depression) and 3) evaluate the acceptability of EMDR for this client group. All 28 included studies reported reduction in severity or frequency of medically unexplained symptoms and improvement in secondary outcomes. Treatment outcomes were maintained in all studies, except one (Proudlock, 2015) which required delivery of additional EMDR sessions due to rebound of pain. Where reported, effect sizes for PPS were moderate

to very large, with EMDR outperforming TAU control groups. None of the studies were sufficiently powered to provide confirmatory evidence of efficacy and therefore firm conclusions cannot be made. TAU controls were primarily psychopharmacological and thus future RCTs should aim to compare EMDR with other trauma-focused therapies (e.g., narrative exposure therapy [NET] TF-CBT) while including a waiting list comparator to control for spontaneous remission.

In studies measuring secondary outcomes, clinically significant and reliable change was reported for post-traumatic stress symptoms (IES), depression (BDI), and anxiety (BAI). While effect sizes for post-traumatic stress were not reported, the direction of effect is consistent with meta-analysis findings in the literature (Chen et al., 2014; Wilson et al., 2018). Magnitude of treatment effect for anxiety and depression were large, and superior to TAU control groups. These positive findings are consistent with RCTs examining the effectiveness of EMDR for anxiety (Meentken et al., 2020; Triscari et al., 2015) and depression (Hase et al., 2015; Meentken et al., 2020).

Overall drop-out rates were low (10.6%) in studies with representative samples suggesting that EMDR is generally tolerated by this client group. Iatrogenic effects were reported in two studies. In one study, this appeared to be due to a pre-existing dissociative disorder (Kelley & Bendadis, 2007). In another study, frequency of migraines was observed to increase during intervention and decrease in frequency and duration at post-test (Konuk et al., 2011). Despite this, there is evidence to suggest EMDR is a potentially acceptable and clinically safe intervention for MUS. However, attrition rates alone are not adequate in examining acceptability and future qualitative research is needed to explore this. For case study research, the inclusion of change interviews (Elliott et al., 2001) following intervention is recommended to assess acceptability and feasibility.

When considering strengths of the reviewed evidence, EMDR was evaluated with diverse samples in terms of age, medically unexplained presentation, psychological comorbidity, and cultural background. This suggests tentative evidence for its use with a variety of populations. However, the limitations of the included studies must be considered. While demographic data was generally well reported, the details of intervention format and delivery was significantly lacking in several studies. Number of EMDR sessions varied considerably between 1 and 20 sessions. In addition to these inconsistencies, the selection process of participants was unclear in several studies. This was most notably the studies that utilized a case study/series design, in which inclusion and exclusion criteria were not reported and it was likely that these were retrospective accounts of a clinical case. The possibility of publication bias must be considered, as case studies are significantly more likely to be published in cases with positive outcomes (Nissen et al., 2014). Findings from these studies cannot be generalized, however they provide insight and direction for further research. To increase quality of evidence of case studies/series, multiple baseline designs are recommended to assess whether changes occur due to intervention.

The results of the studies must be considered in the context of the quality of evidence and methodology. Ten studies included in this review were high quality, three of which were RCTs examining the effectiveness of EMDR for pain and one RCT examining effectiveness for chronic subjective tinnitus. The remaining six high-quality studies were also examining effectiveness of EMDR for pain or tinnitus. While comparisons between persistent physical symptoms cannot be drawn due to paucity of studies and differences in methodological quality, the evidence for pain and tinnitus is most compelling. Despite these promising findings, further research with sufficiently powered samples is needed. For other types of persistent physical symptoms (e.g., functional neurological disorder, chronic fatigue), quality of evidence was generally low (42.8%) and it was unclear whether some case study findings were substantiated in the data. High-quality RCTs examining efficacy are recommended. The lack of validated measures for PPS is also highlighted in this review. Reliability and validity of current measures of PPS have not been established, although outcome measures specific to FND presentations are in development (Pick et al., 2020).

A strength of this review process was that scoping searches were not restricted to one study design, and all quantitative and qualitative studies were considered. This was deemed necessary due to the paucity of research in this area and allowed for a broad examination of the evidence. Quality appraisal was conducted prior to synthesis to reduce bias in data extraction, and no studies were excluded on this basis. However, quality of data was taken into account when reporting findings. Despite this, there are several limitations of this review. Firstly, due to the restricted scope of this review, PPS in which causal and maintaining mechanisms are considered to be largely biological were excluded. However, the authors acknowledge that there is an ongoing paradigm shift in this area of research with current debate

on the differentiation between medically explained and unexplained symptoms. As a result of this, the breadth of this review is limited to symptoms in which etiology or maintenance is considered "medically unexplained" and is not better explained by biological factors. In addition, this review was restricted to studies written in the English language with adult samples only and therefore other relevant studies may have been excluded. Although six databases were searched, the authors acknowledge that other relevant databases were not accessed and therefore other relevant studies may have been missed. The limitations of the review methodology must also be highlighted. Due to the heterogeneity of the studies in this area, meta-analysis was not appropriate and thus data was organized using narrative synthesis. While this method allows for identification of relationships within the data, it does not provide a precise estimate of treatment effect.

In conclusion, there is promising emerging evidence for the effectiveness and acceptability of EMDR for a range of PPS. However, findings for pain and tinnitus are the most compelling due to methodological quality. Firm conclusions on efficacy cannot be made and further high-quality empirical research is warranted.

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Appendix A

Critical Appraisal of the Included Studies Based on the MMAT Tool

Study	Qualitative MMAT item				
	1.1. Is the qualitative approach appropriate to answer the research question?	1.2. Are the qualitative data collection methods adequate to address the research question?	1.3. Are the findings adequately derived from the data?	1.4. Is the interpretation of results sufficiently substantiated by data?	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?
Kelley and Benbadis (2007)	Unclear	No	Unclear	Unclear	No
Gupta and Gupta (2002)	Unclear	No	Unclear	Unclear	No
Grant (2000)	Unclear	No	Unclear	Unclear	No
Hughes (2014)	Unclear	No	Unclear	Unclear	No
Proudlock (2015)	Unclear	No	Unclear	Unclear	No
Royle (2008)					

Study	Quantitative randomized controlled MMAT item				
	2.1. Is randomization appropriately performed?	2.2. Are the groups comparable at baseline?	2.3. Are there complete outcome data?	2.4. Are outcome assessors blinded to the intervention provided?	2.5 Did the participants adhere to the assigned intervention?
Demirci et al. (2017)	Unclear	Yes	Unclear	Unclear	Yes
Gerhardt et al. (2016)	Yes	Yes	Yes	Yes	Yes
Luyten et al. (2020)	Yes	Yes	Yes	Yes	Yes
Marcus (2008)	Unclear	Yes	Yes	No	Yes
Rostaminejad et al. (2017)	Yes	Yes	Yes	Unclear	Yes
Suárez et al. (2020)	Yes	Yes	Yes	Unclear	Yes

Critical Appraisal of the Included Studies Based on the MMAT Tool (*Continued*)

Study	Quantitative non-randomised MMAT item				
	3.1. Are the participants representative of the target population?	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	3.3. Are there complete outcome data?	3.4. Are the confounders accounted for in the design and analysis?	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?
De Roos et al. (2010)	Yes	Yes	Yes	Unclear	Yes
Konuk et al. (2011)	No	Yes	Yes	No	Yes
Phillips et al. (2019)	Yes	Yes	Yes	Unclear	Yes
Mazzola et al. (2009)	Yes	Yes	Yes	Unclear	Yes
Ray and Page (2002)	Unclear	Unclear	Yes	Unclear	Yes
Rikkert et al. (2018)	Yes	Yes	Yes	Unclear	Yes

Study	Quantitative descriptive MMAT item				
	4.1. Is the sampling strategy relevant to address the research question?	4.2. Is the sample representative of the target population?	4.3. Are the measurements appropriate?	4.4. Is the data complete?	4.5. Is the statistical analysis appropriate to answer the research question?
Altunbaş (2018)	Unclear	Unclear	Yes	Unclear	Unclear
Brennstuhl et al. (2015)	Yes	Yes	Yes	Yes	Unclear
Chemali and Meadows (2004)	Unclear	Unclear	Yes	No	Unclear
Cope (2020)	Unclear	Unclear	Yes	Yes	Unclear
Grant and Threlfo (2002)	No	No	Yes	Unclear	Yes
Russell (2008)	Unclear	Yes	Yes	Yes	No
Schneider et al. (2008)	Unclear	Unclear	Yes	Yes	Yes
Silver et al. (2008)	Unclear	Unclear	Yes	Yes	No
Wilensky (2006)	Yes	Unclear	Yes	No	Unclear

Appendix B

Characteristics and Key Findings of Studies

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
1	Altunbaş (2018), Turkey	Case report Peer-reviewed	*N* = 1 Age: 35 Gender: Female White Turkish	Daytime blindness (hemeralopia)	PTSD	EMDR, 9 sessions	BAI; BDI; CAPS, IES-R	3-month	• Client reported improvement in vision clarity compared to pre-treatment. • Clinically significant and reliable change measured in IES-R, BAI, BDI at post-test. • Maintained at 3-month follow up.	Low
2	D'Andrea et al. (2021), France	Uncontrolled Clinical Trial	*N* = 38 Age: Not reported Gender: Female (*n* = 17), Male (*n* = 21)	Tinnitus	Not reported	5 sessions	THI, VAS	No follow up	• Statistically significant reduction in tinnitus symptoms in 78.9% patients. • Significant improvement in reported quality of life and daily functioning. • 86.8% participant completed EMDR.	High
3	Brennstuhl et al. (2015), France	Case study	*N* = 2 Age range: 48–56 Gender: Female	Phantom Breast Syndrome	Chronic pain	9–12 sessions (standard and pain protocol)	STAI, CES-D, Pain and Sensation Intensity	3–6 months	• Significant decrease in phantom breast sensation and pain at post-test and maintained at follow-up. • Significant decrease in depression and anxiety scores at post-test and maintained at follow up.	High

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
4	Chemali and Meadows (2004) North America	Case report Peer-reviewed	*N* = 1 Age: 48 Gender: Female Not specified	Psychogenic seizures	PTSD, Borderline Personality Disorder	EMDR, 18 months (session number not specified)	*N* of seizures, DES, BDI, QUOLIE-31	3-month	• Client seizure free following 18 months of EMDR. • Clonazepam (prescribed for seizures) reduced (dosage information not provided). • Maintained at 3-month follow up.	Low
5	Cope (2020) UK	Case report Peer-reviewed	*N* = 2 Age range: 20–50 Gender: Female (n = 1), Male (n = 1) Not specified	Functional non-epileptic attack Functional sensory symptoms	Complex trauma Health Anxiety	EMDR, 20 sessions	BES, BIPQ, GAD-7, HAI, IES-R, MDI, PHQ-9	3-month	• Reduction in frequency of FNEA and dissociative episodes. • Reduction in severity of functional sensory symptoms and associated distress. • Post-treatment scores in subclinical range for PHQ-9, GAD-7, IES-R. • Post treatment scores in subclinical range for all subtypes of dissociation (n = 1 remained in clinical range for "emotional constriction" subtype).	Low

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
6	Demirci et al. (2017), Turkey	Randomized Clinical Trial Peer-reviewed	$N = 31$ (EMDR arm) Mean age: 27.65 Gender: Female ($n = 31$) Not specified	Somatic Symptom Disorder General pain	Psychological Trauma	EMDR, 6 sessions (90 mins each)	SCL-90, BAI, BDI, SF-36	No follow up	• Significant improvement in somatic symptoms at post-test ($n^2 = 0.94$). • Both EMDR and TAU (Duloxetine) resulted in significant decreases in SF-36, BAI, BDI at post-test. • EMDR group reported larger effect size ($n^2 = 0.94$) compared to TAU ($n^2 = 0.68$).	Moderate
7	De Roos et al. (2010), Netherlands	Uncontrolled clinical trial (pre-test/post-test design) Peer-reviewed	$N = 10$ Mean age: 50.1 Gender: Female ($n = 4$), Male ($n = 6$) Not specified	Phantom limb pain	Psychological trauma, Obsessive Compulsive Disorder, Substance Use	EMDR, 3–10 sessions (90 mins each)	Pain rating, SCL-90, CIS-20R, IES, SIL, SF-36	26–40 month	• 80% of patients reported clinically significant reduction in pain at post-test (medium effect size; $n^2 = 0.63$). Maintained at follow up. • Four participants reported to be "pain free" at post-test and discontinued pain medication. • Significant reduction in trauma measures (IES, SIL) to subclinical range at post-test.	High

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
8	Gerhardt et al. (2016), Germany	Randomized controlled pilot study Peer-reviewed	$N = 20$ (EMDR arm) Mean age: 56.6 Gender: Female ($n = 14$), Male ($n = 6$) White German	Non-specific chronic back pain	"Experience of psychological trauma" (assessed by Structured Clinical Interview DSM-5)	EMDR standard procedure and pain protocols, 10 sessions (90 mins each)	*N* days with pain, NRS pain intensity, MPI-D, PGIC	6-month	• 45% of participants who received EMDR experienced significant reduction in pain intensity ($d = 0.79$) and disability (0.39) versus 0% in TAU control group. Follow up ($d = 0.50$). • 50% of participants who received EMDR rated their condition as "much improved" ($n = 8$) or "very much improved" ($n = 2$) compared to 0% in control group ($d = 1.69$).	High
9	Grant (2000), Australia	Case series	$N = 2$ Age range: 28–40 Gender: Female	Chronic pain	Depression, PTSD	Chronic pain protocol—no. sessions not specified	Qualitative self-report	Not specified	• Both clients reported marked improvement in pain symptoms, functioning and associated distress.	Low
10	Grant and Threlfo (2002), Australia	Case series	$N = 3$* Age range: 27–54 Gender: Female	Chronic pain	Depression, Fatigue	Chronic pain protocol—9 weekly sessions	SFMPQ, CSQ, VOC, Qualitative self-report	2 months	• Significant decrease in pain and distress for all participants. • Marked increase in perceived ability to cope with pain and reported daily functioning.	Low

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
11	Gupta & Gupta (2002), Canada	Case series	$N = 4$ Age range: 22–43 Gender: Female ($n = 3$), Male ($n = 1$)	Dermatologic Disorders	Anxiety, Complex Trauma	3–6 sessions	VOC, Qualitative self-report	6–12 months	• All patients reported significant improvement in symptoms. Maintained at follow-up.	Low
12	Hughes (2014), Canada	Case study	$N = 1$ Age: 35 years Gender: Female	Complex regional pain	Depression, Fatigue, Trauma	16 sessions	Qualitative Self-Report	8 months	• Client reported decreased pain, decreased substance use and improved mood at post-test. Maintained at follow up. • Client reported improvement in daily functioning and perceived ability to cope with chronic pain.	Low

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
13	Kelley and Benbadis (2007) North America	Case series Peer-reviewed	*N* = 8 Mean age: 37.1 Gender: Female (*n* = 4), Male (*n* = 4) White American	Psychogenic non-epileptic seizures	PTSD, Complex Trauma, Depression, Obsessive Compulsive Disorder, Dissociative Disorder, Anxiety, Substance Use, Psychosis, Traumatic Brain Injury	Counselling sessions followed by EMDR, 0–7 sessions EMDR protocol	VOC, *N* of psychogenic seizures	18-month	• Two out of three participants who received EMDR were seizure free following 6–7 sessions of intervention. Maintained at follow up. • 12.5% reported being seizure free after consult only (*n* = 1) • 12.5% declined treatment after consult (*n* = 1) • 25% dropped out after 2–3 counselling sessions prior to receiving EMDR (*n* = 2)	Low
14	Konuk et al. (2011), Turkey	Uncontrolled clinical trial	*N* = 11 Age range: 18–50 Gender: Female (*n* = 9), Male (*n* = 2)	Migraines	Trauma related to headaches	8 sessions	NRS, SA-45, WHQ	3 months	• Statistically significant decreases in frequency and duration of headaches. Frequency of headaches increased during intervention but decreased post-treatment. • No reductions in reported pain intensity. • Significant decrease in pain medication and number of medical visits. • Maintained at follow up.	Moderate

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
15	Luyten et al. (2020), Belgium	RCT	$N = 46$ (EMDR arm) Mean age: 47.87 Gender: Female ($n = 26$), Male ($n = 63$)	Chronic Subjective Tinnitus	Anxiety, Depression	5 sessions EMDR (plus Tinnitus Retraining Therapy)	TFI, VAS, TQ, HADS, HQ	3 months	• TRT/EMDR showed clinically significant reduction in tinnitus symptoms compared to TRT/CBT. • Both TRT/EMDR and TRT/CBT showed significant decrease in tinnitus complaints, hyperacusis, anxiety and depression. • Maintained at follow up.	High
16	Marcus (2008), North America	RCT	$N = 21$ (Integrated EMDR arm) Mean age: 38.33 Gender: Female ($n = 41$), Male ($n = 2$)	Migraine	Not reported	1 session (60 minutes) EMDR with diaphragmatic breathing and cranial compression	SPL, MIDAS, HDI	1, 2, 7 days	• Both the integrated EMDR and TAU (pain medication) groups reported reduced migraine pain posttreatment. Integrated EMDR group showed significantly greater improvements in rapidity of pain reduction. • Maintained at follow up.	Moderate

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
17	Mazzola et al (2009), Argentina	Uncontrolled clinical trial	*N* = 38 Age: Not specified Gender: Female (*n* = 32), Male (*n* = 6)	Chronic pain 30 (79%) headaches; 4 (10.5%) fibromyalgia; 4 (10.5%) neuropathic pain	Personality disorder, Depression, Anxiety	12 weekly sessions	SF-36, STAI, BDI, SCID-II, VAS	No follow-up	• Significant reduction in pain levels resulting in reduction of medication (e.g., benzodiazepines, opioids). • EMDR resulted in significant decrease in BDI and STAI at post-test. • Statistically significant positive change in perceptions of quality of life (SF-36).	High
18	Phillips et al. (2019), UK	Uncontrolled clinical trial	*N* = 14 Mean age: 57.2 Gender: Female (*n* = 7), Male (*n* = 7)	Tinnitus	Anxiety, Depression	3–10 sessions	THI, BDI, BAI	6 months	• Statistically significant improvement in tinnitus symptoms in "majority of participants." • Marked decrease in depression and anxiety at post-test. • Results maintained at 6 month follow up.	High

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
19	Proudlock (2015) England	Case report, Peer-reviewed	*N* = 1 Age: "Late 50s" Gender: Male White British	Abdomen pain	Psychological trauma, Anxiety	EMDR plus "principles of SLT and CBT," 20 sessions	IES	6-month	• Client reported reduction in frequency and severity of pain. • Client reported improvement in depressed mood. • At 6 month follow up, client required 6 additional sessions to manage pain associated with recurrent bladder infections.	Low
20	Ray and Page (2002), Australia	Non-randomized Trial	*N* = 17 Mean age: 36.8 Gender: Female (*n* = 7), Male (*n* = 10)	Chronic pain	PTSD, Depression	1 session of EMDR followed by 1 session hypnosis or 1 session hypnosis followed by EMDR (randomly assigned)	MPQ	<1 month	• Non-significant reduction in self-reported pain in EMDR condition. • Statistically significant pain reduction reported in hypnosis condition. • 86.7% reported preference for hypnosis over EMDR post-treatment.	Low

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
21	Rikkert et al. (2018), Netherlands	Within-groups design	*N* = 35 Mean age: 49.2 Gender: Female (*n* = 16), Male (*n* = 19)	Tinnitus	Sleeping difficulties, pain, trauma, other somatic complaint not otherwise specified	6 sessions	TFI, Mini TQ, SCL-90, SRIP	3 months	• Significant reduction in tinnitus distress at post-test compared to passive control condition. Medium effect size observed (d = .72). • Almost 1 in 2 participants reported benefiting from EMDR. • Results maintained at follow up.	High
22	Rostaminejad et al. (2017) Iran	Randomized controlled trial, Peer-reviewed	*N* = 30 (EMDR arm) Mean age: 42.8 Gender: Female (*n* = 9), Male (*n* = 21) Not specified	Phantom limb pain	Psychological trauma related to amputation	EMDR, 12 sessions (60 mins each)	VOC, Pain rating scale	24-month	• At post-test, 86% of participants who had received EMDR reported being "almost or completely pain free." Maintained at follow up. • Statistically significant reduction in pain intensity and associated distress at post-test (P < .001). Effect size calculated for purpose of review (d = 3.23). • In comparison, 96.3% of control group (allocated to routine care) reported no reduction in pain in same period.	High

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
23	Royle (2008), UK	Case report, Peer reviewed	*N* = 1 Age: 49 Gender: Male Not specified	Chronic fatigue	Anxiety, depression, work related stress	EMDR, 9 sessions	VOC, Qualitative self-report	6, 12-month	• Significant decrease in fatigue which allowed client to return to employment and other daily activities. • Reduction in symptom-perpetuating maladaptive cognitions. • Maintained at 12 month follow up.	Low
24	Russell (2008), Japan	Case report, Peer-reviewed	*N* = 1 Age: 40 Gender: Male Not specified	Exaggerated startle response, chronic pain, somatic symptoms	Combat related trauma	EMDR, 5 sessions	IES, BDI, Health Status	1, 3, 6-month	• Marked improvement in health status self-report at post-test. Maintained at 6 month follow up. • Clinically significant and reliable change in IES and BDI scores at post-test. Scores in non-clinical range. Maintained at follow up.	Low

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
25	Schneider et al., (2008), Germany	Case series, Peer-reviewed	$N = 5$ Mean age: 49.2 Gender: Female ($n = 1$), Male ($n = 4$) Not specified	Phantom limb pain	PTSD	EMDR, 3–15 sessions	IES, BDI, Faces pain scale	12–24 month	• Complete elimination of phantom limb pain in two cases. Maintained at follow up. • Reduction in pain in three cases. At follow up, one case (who did not complete full protocol due to relocation) reported "rebound in pain frequency." • At post-test and follow up, two clients reduced pain medication (e.g., morphine) and discontinued Diazepam. • Average IES and BDI scores in subclinical range at post-test and follow up.	Moderate

(*continued*)

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
26	Silver et al. (2008), North America & Japan	Case report, Peer-reviewed	*N* = 1 Age: 73 Gender: Male Not specified	Myoclonic movements (upper body shaking & jerking)	Combat related PTSD	EMDR, 2 sessions	IES, BDI, BHS	1, 6-month	• Clinically significant and reliable change in IES, BDI and BHS scores at post-test. No longer in clinical ranges. Maintained at follow up. • Client reported complete elimination of myoclonic movements. Maintained at 6 month follow up.	Moderate
27	Suárez et al. (2020), Spain	RCT Pilot	*N* = 14 (EMDR arm) Age range: 49–60 Gender: Female (*n* = 22), Male (*n* = 6)	Chronic Pain	Depression, Anxiety	12 sessions	VAS, PDI, EDQ-5D-5L, HADS	3 months	• EMDR+TAU group reported significant improvement in pain intensity, anxiety and depression scores at post-test when compared to TAU. • Results from EMDR maintained at follow up.	High

Characteristics and Key Findings of Studies (*Continued*)

N	Author (year), country	Design	Sample	Medically unexplained symptom	Comorbidities	Treatment (protocol, number of sessions)	Outcome measures (primary and secondary)	Follow up	Key findings	MMAT quality rating
28	Wilensky (2006), Canada	Case series, Peer-reviewed	$N = 5$ Mean age: 45.6 Gender: Female ($n = 1$), Male ($n = 4$) Not specified	Phantom limb pain	Psychological trauma	EMDR, 3–9 sessions	IES, BDI, PDI, TSI	1, 3-year (two clients only)	• Four of the five clients completed planned protocol and reported complete elimination or marked reduction in pain. • One client stopped treatment after reducing reported pain by 50%. • Significant reduction in BDI and PDI scores at post-test. • Significant reduction in IES scores at post-test. One client no longer scoring in clinical range. • Three clients lost to follow up.	Moderate

BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CAPS = Clinician-Administered Post-traumatic stress disorder Scale; IES-R = Impact of Events Scale Revised; BES = Beliefs About Emotions Scale; BIPQ = Brief Illness Perception Questionnaire; GAD-7 = Generalized Anxiety Disorder Scale; HAI = Health Anxiety Inventory; IMDI = Multiscale Dissociation Inventory; PHQ-9 = Patient Health Questionnaire; CIS-R = Checklist Individual Strength Revised; SCL-90 = Symptom Checklist; SIL = Self-Inventory List; SF-36 = Short Form Health Survey; NRS Pain = Numeric Pain Rating Scale; MPI-D = Multi-dimensional Pain Inventory (Dutch Version); PGIC = Patient Global Impressions of Change; VOC = Validity of Cognition; BHS = Beck's Hopelessness Scale; PDI = Peters' Delusions Inventory; TSI = Trauma Symptom Inventory; SFMPQ = Short-Form McGill Melzack Pain Questionnaire; CSQ = Coping Skills Questionnaire; VAS = Visual Analog Score; WHQ = Weekly Headache Questionnaire; SA-45 = Symptom Assessment 45 Questionnaire; SCID = Structured Clinical Interview for DSM; STAI = State Trait Anxiety Inventory; CES-D = Centre for Epidemiologic Studies—Depression; EQ-5D-5L = EuroQol 5 Dimensions Quality of Life; TFI = Tinnitus Functional Index; Mini TQ = Mini Tinnitus Questionnaire; SRIP = Self-Rating Inventory List for Post-Traumatic Stress Disorder; THI = Tinnitus Handicap Inventory; HQ—Hyperacusis Questionnaire; CTQ = Childhood Trauma Questionnaire; ADES = Adolescent Dissociative Experiences Scale; SPL = Subjective Pain Level; HDI = Headache Disability Inventory; MDAS = Migraine Disability Assessment Scale.