EMDR for Depression: A Meta-Analysis and Systematic Review

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The literature on the efficacy of eye movement desensitization and reprocessing (EMDR) for treating depression is heterogeneous due to research design, quality issues, and trials methodology. The current meta-analysis seeks to examine EMDR for depression with the aim of answering the aforementioned limitations. Thirty-nine studies were included for analysis after a review of the relevant literature. Univariate meta-regressions were run to examine dose-response and the effect of moderating variables. Subanalysis for primary and secondary depression showed a large, significant, and heterogeneous effect-size estimates, where EMDR significantly improved symptoms of depression in contrast to all control types. At post hoc, data were reexamined and a significant and large, yet heterogeneous, effect-size estimate emerged between the EMDR and control arm after the removal of two outliers [Hedges' g = 0.70, 95% CI = 0.50–0.89, p-value < .01, I^2 = 70%, K = 37]. This is the first meta-analysis examining for the effect of EMDR comparing to various control modalities on depression with dose-response. We found (a) that studies were balanced at onset in terms of depression severity, and (b) a large and significant effect of EMDR on depression at the end of trials. Additionally, the significance of the aggregate effect-size estimate at the end of trials was unchanged by the intake of psychotropic medications, reported demographic variables, or EMDR methodology.

Keywords: depression; eye movement desensitization and reprocessing (EMDR) therapy; meta-analysis; psychotherapy

Eye movement desensitization and reprocessing (EMDR) therapy was developed in 1989 by the late Francine Shapiro (Shapiro, 1989) and aimed to treat traumatic memories and associated symptoms. This psychotherapeutic approach involves a standard eight-phase protocol that consists of bilateral stimulation to reprocess and integrate traumatic memories (Landin-Romero et al., 2018; Shapiro, 2018). The treatment targets memories of adverse life experiences, which produce negative symptoms when activated by sensory cues. Following EMDR treatment, neurobiological research has found recovery of brain structural organization, with successful processing of traumatic memories and related symptom reduction (Bossini et al., 2017; Boukezzi et al., 2017). Evidence emerging from several meta-analyses (Benish et al., 2008; Bradley et al., 2005; Chen et al., 2015; Chen et al., 2014; Davidson & Parker, 2001; Jonas et al., 2013; Seidler & Wagner, 2006; Van Etten & Taylor, 1998) shows that EMDR is an evidence-based treatment for posttraumatic stress disorder (PTSD).

Literature Review

Depression may be triggered and sustained by stressful life events and traumatic experiences, and research

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has indicated that chronic and acute stressors can trigger depressive episodes (Heim & Nemeroff, 2001; McFarlane, 2010). Risch et al. (2009) found that "stressful life events are the only risk factor to be significantly correlated with the onset of depression" (p. 2). Several studies have shown how events like physical and emotional abuse are significant psychosocial risk factors for the development of major depressive disorder, and have been linked with a poorer response and remission outcome for standard antidepressant treatment and higher severity of symptoms (Bahk et al., 2017; Dias de Mattos Souza et al., 2016; Tunnard et al., 2014; Vitriol et al., 2017; Wiersma et al., 2009; Williams et al., 2016). Therefore, it seems reasonable that a therapy that has been very successful in treating trauma can also help treat depression (if the patient has experienced any traumatic events over their lifetime).

Several studies have tested EMDR therapy as either the main treatment or adjunctive treatment for primary depression and depressive symptoms, and have garnered favorable, yet heterogeneous, results. For example, a systematic review of EMDR studies for the treatment of PTSD or pain (Wood & Ricketts, 2013), which considered depression as a comorbid diagnosis, concluded that comorbid depression along with PTSD symptoms could be significantly reduced with EMDR therapy. Carletto et al. (2017) later updated the systematic review by Wood and Ricketts (2013) and focused on controlled studies that examined the efficacy of EMDR therapy for primary depression and reported benefits of EMDR in treating depression. The authors concluded that the body of research is still in its infancy and that further studies are needed to support the validity of EMDR in being considered as an effective intervention in depression.

Some studies with limited neurobiological basis have posited that EMDR can be a viable alternative treatment approach, or a second option to failed primary treatment for depression (Minelli et al., 2019; Ostacoli et al., 2018). Ostacoli et al. (2018) recently published a quantitative Randomized Controlled Trial (RCT), which compared the efficacy of EMDR and cognitive behavioral therapy (CBT) as adjunctive treatments (to antidepressants) in patients with recurrent depressive disorder. EMDR therapy treatment was shown as effective as CBT in the reduction of depressive symptoms, both at the end of treatment and 6 months later. Minelli et al. (2019) conducted an RCT to compare the efficacy of EMDR and trauma-focused CBT in treatment-resistant depression (TRD). The findings indicated a decrease in depression symptoms in both treatment groups, with EMDR treatment showing greater efficacy. At the follow-up assessment, only EMDR maintained clinical improvements. These studies are encouraging in their application of these two interventions in different populations and settings, yet they come with design heterogeneity that encompasses various EMDR trial durations and assessment approaches. Similarly, other studies, for instance, differently examined this effect via an EMDR Integrative Group Protocol with a crossover research design (Passoni et al., 2018).

A recent quantitative meta-analysis of RCTs that examined EMDR versus CBT in patients with PTSD to compare the efficacy of both in alleviating PTSD-related symptoms, anxiety, and depression was conducted by Khan et al. (2018). The results of the meta-analysis showed no significant difference between the two treatment modalities in reducing depression; however, EMDR was better than CBT in reducing anxiety and PTSD symptoms (Khan et al., 2018).

The review of the literature on the efficacy of EMDR in treating depression has shown very promising results. However, there have been several limitations, mainly consisting of methodological variations (e.g., using different depression rating scales), which render generalizability of results difficult. Additionally, the effect of psychotropic medication and other factors, such as study designs (randomized or not), primary versus secondary depression, or that comorbid depression was accompanying a psychiatric or medical condition (e.g., PTSD vs. cancer), has not been taken into consideration.

Aim of the Current Meta-Analysis

The literature on the efficacy of EMDR in treating depression is heterogeneous due to research design and quality, and treatment methodology. Thus, we intend meta-analytically to examine the effect of EMDR on depression with the aim of answering some of the underscored limitations.

Method

Search and Coding Strategy

Initial search of the electronic literature (PsycINFO & PubMed) was carried on April 15, 2019. Two assessors (KL and AAS) individually examined the retrieved studies by *a priori* set selection criteria. Search terms were as follows. For PubMed: ((“depressive disorder“[MeSH Terms] OR (“depressive“[All Fields] AND “disorder“[All Fields]) OR “depressive

disorder"[All Fields] OR "depression"[All Fields] OR "depression"[MeSH Terms]) OR ("consciousness disorders"[MeSH Terms] OR ("consciousness"[All Fields] AND "disorders"[All Fields]) OR "consciousness disorders"[All Fields] OR "depressed"[All Fields]) OR depressive[All Fields] OR ("affect"[MeSH Terms] OR "affect"[All Fields] OR "mood"[All Fields]) OR ("affect"[MeSH Terms] OR "affect"[All Fields])) AND ("eye movement desensitization reprocessing"[Mesh] OR "EMDR"[All Fields]). For PsycINFO: Boolean/Phrase [depressive disorder* OR Depressive OR depression OR depressed OR consciousness disorder* OR affect OR mood] AND [eye movement desensitization reprocessing OR EMDR].

Studies were included if they were (a) providing either cross-sectional or observational data on studies of EMDR versus other treatment, (b) adult patients, (c) assessed primary or secondary depression, and (d) English language abstracts. See e-supplement 1 for the list of included studies with demographic presentation.

Studies were excluded if: (a) literature review, letter to editor, conference abstract, thesis/dissertation abstract, meta-analysis (pooled data studies, individual patient meta-analysis), single case experimental design, case report, case series (<5 person), book chapters, and reporting study protocol; (b) non-English language papers; (c) no data on depression assessment endpoint was reported; and (d) hybrid psychotherapy treatment as a treatment arm was also excluded. Also, we have excluded studies if their validity was questionable, as confirmed with the original publishing journal. See e-supplement 2 for the list of excluded studies.

The PRISMA flow diagram (Moher et al., 2009) was used to exhibit our data selection process (see Figure 1). We examined for study quality and statistical heterogeneity, and source of bias as necessary. Univariate meta-regression analyses, with method of moments, were run to examine dose-response and the effect of moderating variables [e.g., demographics (age, sex, country of data), depression variables (assessment scales, depression type, medication/psychotropic intake, medical-psychiatric comorbidity), EMDR-related variables (duration of trials, duration, and number of sessions), and study level variables (randomized, type of control group)]. Forest plot was used to present the estimated results per studies and an aggregate result. The study was submitted to PROSPERO for transparency (registration identification number: CRD42019138815). We used the STROBE checklist (Vandenbroucke et al., 2007) for the quality assessment of the studies to keep a consistent quantitative scoring across studies, and given the lack of consensus among authors on quality assessment (Moskalewicz & Oremus, 2020). Subsequently, we have also examined the quality of the studies with well-recognized qualitative tools including version 2 of the Cochrane risk-of-bias (ROB 2) tool for randomized trials (Sterne et al., 2019) and the Newcastle-Ottawa Scale (NOS) for observational studies (Wells et al., 2019). See e-supplement 3, e-supplement 4, and e-supplement 5, for quality assessment tables.

Data Analysis Strategy

We retrieved mean, standard deviation (*SD*), and the sample size for each arm of each study comparing EMDR to controls. In the absence of *SD*, we used the reported standard error values ($SD = SE \times SQRT\ N$), the 95% confidence interval (CI) [$SD = SQRT\ N \times (CI\ upper\ level - CI\ lower\ level)/\ 3.92$; where 3.92 is 2×1.96] to estimate the *SD* values needed for analysis, or used the reported *p*-values and effect-size in the absence of all other data. Additionally, we retrieved categorical and continuous-type data specific to moderating factors as needed.

We calculated an effect-size estimate under the random effect model, with associated 95% CI for each study, and subsequently run an aggregate effect-size estimate (Hedges' *g*) using the mean, *SD*, and the sample size for each arm of the studies (both at baseline and end point). We have used the random effect model at onset, since the result of the in-house feasibility assessment of a dozen papers was heterogeneous in terms of the mean difference between the EMDR and control arms of the studies.

We referred to the Cochran Q and I^2 tests in the evaluation of heterogeneity, where a significant Q test indicates that the variation among studies may be attributed to heterogeneity rather than chance, and larger I^2 values indicate increasing heterogeneity (Babikian et al., 1990). For the assessment of publication bias, we referred to both graphical examination of data via a funnel plot and statistical evaluations using Begg and Mazumdar's (1994) rank correlation (the Kendall's tau with continuity correlation), Egger's regression intercept (Egger et al., 1997), and Duval and Tweedie's trim and fill (Duval & Tweedie, 2000). Additionally, we used the classical fail-safe N (Orwin, 1983) to examine the robustness of our findings.

Univariate meta-regressions, method of moments, were carried for examination of the effects of moderating factors on the effect-size estimates as appropriate.

A kappa coefficient for the inter-rater reliability of study coding was calculated using the standard

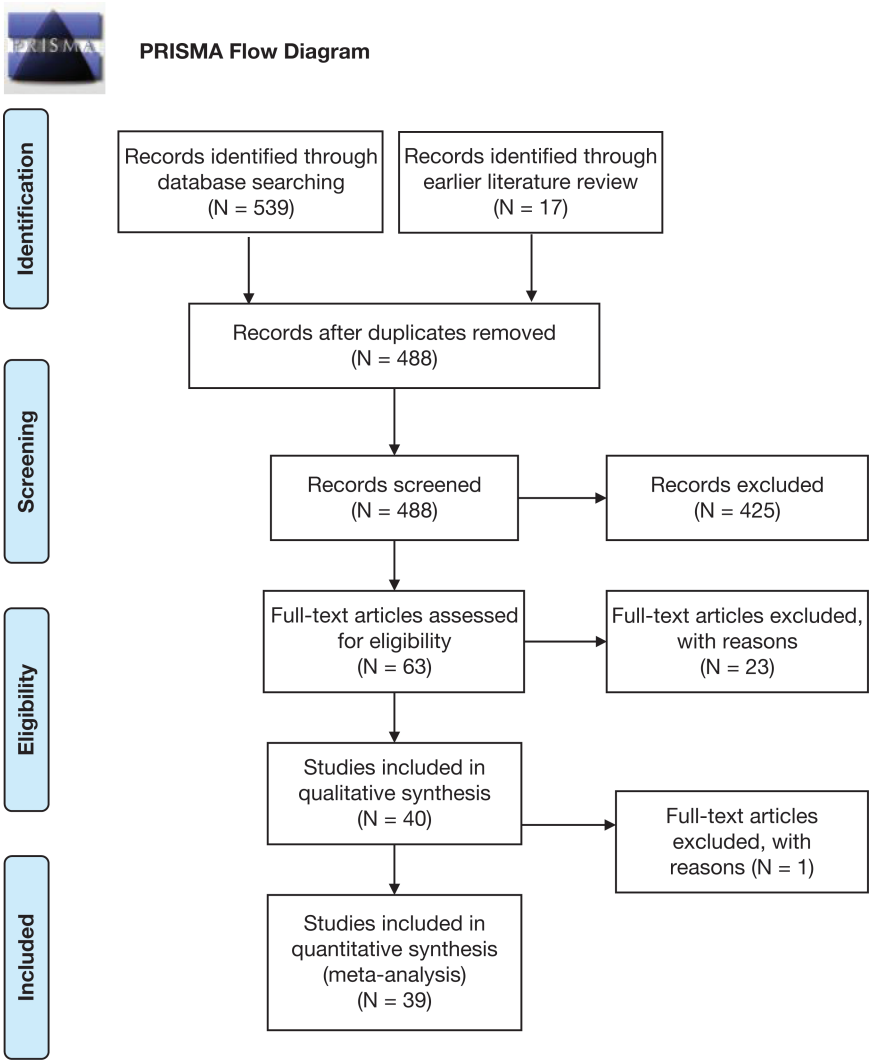

Figure 1. PRISMA-style flow diagram showing study selection for meta-analysis on EMDR for depression literature.

approach via a Microsoft Excel sheet. For all data analysis, we set the alpha level to .05 and used the Comprehensive Meta-Analysis software (Ver. 2.0) (Borenstein et al., 2005).

Results

Study Selection/Demographics

A total of 539 abstracts were retrieved, with an added 17 studies that we had collected during a feasibility assessment for meta-analysis. After duplicates were removed, we screened 488 abstracts and excluded 425 based on *a priori* set selection criteria. Sixty-three remained to be examined at the article level and, after review, 23 did not meet selection criteria, resulting in 40 studies. After further examination with the librarian of the authenticity of published manuscripts, and contact with a journal, we had to eliminate another study, leaving 39 studies for meta-analysis with total N of 1,738 (899 control and 839 EMDR). See Figure 1 for PRISMA flow diagram.

The kappa rate of agreement between study coders (AAS and KL) was 88%, and in the event of a discrepancy, the conflict was resolved by discussion between the coders.

Studies Included

A total of 39 studies provided cross-sectional data [RCTs ($K = 30$), quasi-experimental/observational studies ($K = 9$)] met selection criteria that were published between 1994 and 2019. The included studies had single to multiple comparison arms (e.g., treatment as usual, wait-list, various psychotherapies) with various follow-up durations. Average age distribution of the patients in the EMDR arm ranged between 27.6 and 63, and the sex average distribution was

ranging between 0% and 100% [mean of 60 % (SD = 35)] female. These studies, emerging from the Americas, Asia, Australia, and Europe, included patients currently treated with and without psychotropic medications, with some studies not specifying. The EMDR treatment duration of trials ranged between <1 and 24 weeks. In these studies, depression was either primary ($K = 6$) or secondary ($K = 33$) to a medical or neuropsychiatric condition. Depression status was measured either via full scales (Beck Depression Inventory I or II, Center for Epidemiologic Studies Depression Scale, Hamilton Rating Scale for Depression, Montgomery–Åsberg Depression Rating Scale, and Patient Health Questionnaire-9) or subscales (Hospital Anxiety and Depression Scale-depression, Hopkins Symptom Checklist-depression, Depression Anxiety Stress Scale-21-depression, Problem Report Form-depression, and Symptom Checklist-90R-depression). Three of the 39 studies did not provide baseline data. See e-supplement 6 for description of included studies.

Results of Data Analysis

Depression. At baseline, using the random effect model on all studies (including both primary and secondary depression), either no significant or very small differences emerged between the EMDR arm and the control arms, without significant heterogeneity [Hedges' g (g) = −0.02, 95% CI = −0.16–0.12, p-value = 0.80, I^2 = 43%, K = 36], suggesting that the groups were balanced at onset regarding depression symptoms severity.

At the end of trials, a significant and large, yet heterogeneous, effect-size estimate emerged between treatment and control arms [Hedges' g = 0.89, 95% CI = 0.62–1.17, p-value < .01, I^2 = 84%, K = 39].

Subanalysis for studies examining depression as a primary outcome showed a large, significant, and heterogeneous effect-size estimate [Hedges' g = 1.36, 95% CI = 0.27–2.45, p-value = .01, I^2 = 92%, K = 6], and for depression as a secondary condition/comorbidity, the effect-size estimate was also large, significant, yet heterogeneous [Hedges' g = 0.78, 95% CI = 0.52–1.04, p-value < .01, I^2 = 81%, K = 33]. Examining for the effect of assessment scales (full scale vs. subscale) on EMDR to all control comparisons, the effect-sizes for studies using full scales was large and heterogeneous [Hedges' g = 0.81, 95% CI = 0.57–1.04, p-value < .01, I^2 = 84%, K = 48), as well as those using subscales [Hedges' g = 0.73, 95% CI = 0.31–1.15, p-value < .01, I^2 = 81%, K = 12]. See Figure 2.

EMDR. EMDR significantly improved symptoms of depression in contrast to all control types. All effect-size estimates ranged between medium to large size, and were heterogeneous. See Table 1 for analysis results.

Dose-Response. The effect-size estimates for studies reporting exact and approximate number of EMDR sessions were large and significant, yet heterogeneous (approximate: Hedges' g = 1.099, 95% CI = 0.52–1.68, p-value < .01, I^2 = 83%, K = 7; exact: Hedges' g = 0.82, 95% CI = 0.51–1.13, p-value < .01, I^2 = 85%, K = 32). The univariate meta-regression analysis examining the effect of number of sessions, where the exact average value was reported by the studies (K = 32), the EMDR treatment response for depression was nonsignificant (slope = −0.0293, SE = 0.0297, p-value = .3244).

The effect-size estimates for studies reporting exact and approximate duration of EMDR trials (in weeks) were large in magnitude and significant, yet heterogeneous [approximate: Hedges' g = 1.30, 95% CI = 0.53–2.07, p-value < .01, I^2 = 92%, K = 10; exact: Hedges' g = 0.70, 95% CI = 0.46–0.93, p-value < .01, I^2 = 71%, K = 29]. The univariate meta-regression analysis, examining for the effect of duration of trials where the exact value was reported by the studies (K = 29) on the EMDR treatment response for depression, yielded a nonsignificant effect (slope = −0.0123, SE = 0.0189, p-value = .5155).

The effect-size estimates for studies reporting EMDR session times were significant in favor of EMDR treatment, and medium to large in magnitude, yet heterogeneous (approximate: Hedges' g = 1.05, 95% CI = 0.55–1.54, p-value < .01, I^2 = 91%, K = 18; exact: Hedges' g = 0.67, 95% CI = 0.44–0.90, p-value < .01, I^2 = 56%, K = 21). The univariate meta-regression analysis, examining for the effect of sessions time where the exact value was reported by the studies (K = 21) on the EMDR treatment response for depression, yielded a nonsignificant effect (slope = −0.0004, SE = 0.0073, p-value = .9577]. See Table 1.

Univariate meta-regressions of EMDR average age and percent female showed nonsignificant effect of these moderating factors on the effect-size estimate (age: K = 27, slope = −0.0003, SE = 0.0214, p-value = .9886; percentage of female participants: K = 31, slope = 0.003, SE = 0.0047, p-value = .5312). Similarly, the effect of publication year and quality of studies by STROBE were nonsignificant (publication year: K = 60, slope = 0.0040, SE = 0.0125, p-value = 0.7495; quality: K = 60, Slope = 0.0059;

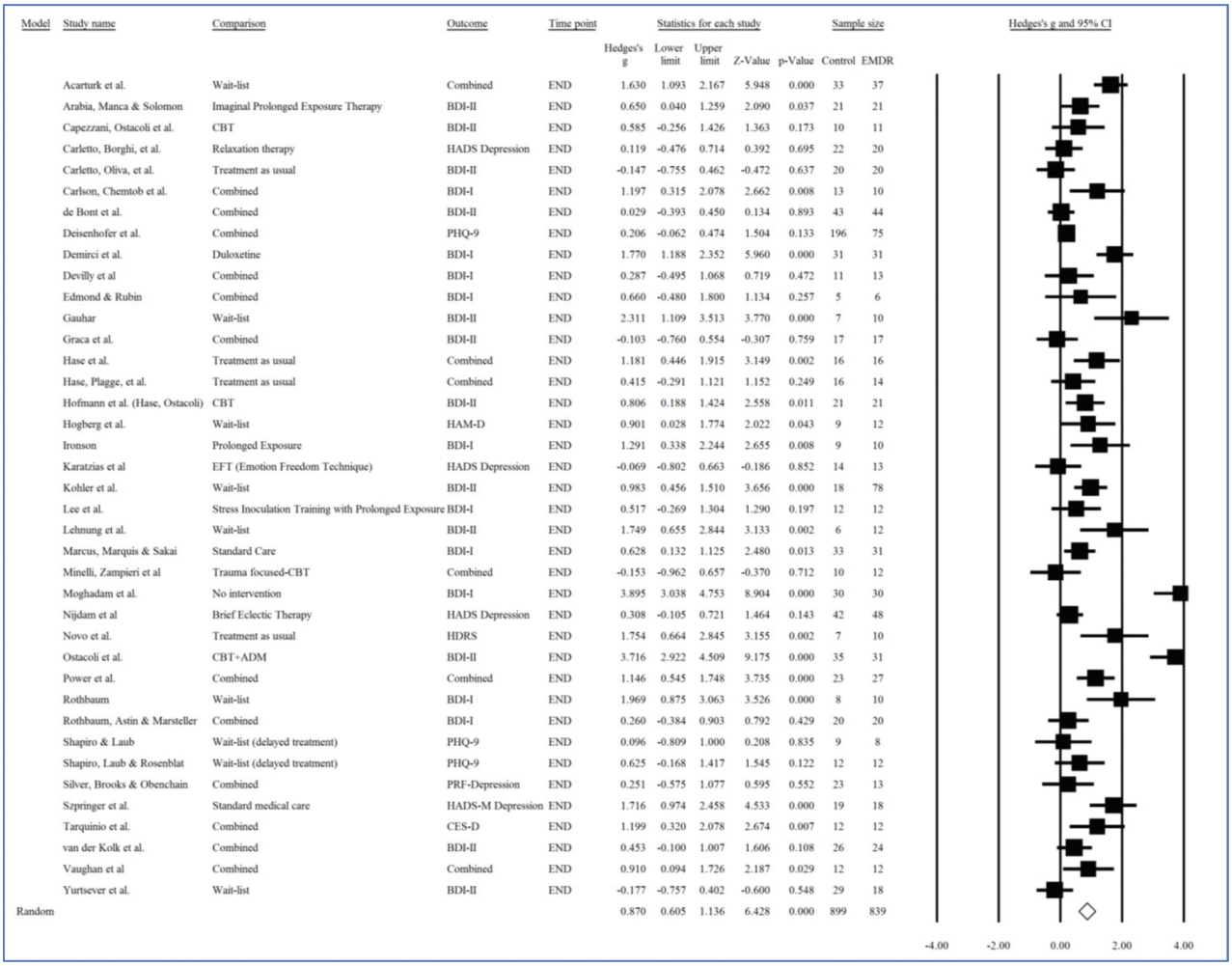

Figure 2. Forest plot showing studies (K = 39) with omnibus effect-size estimate at the endpoint (follow-up not included).

TABLE 1. Effect-Sizes Estimates (Random Effect Model)

		Effect Size and 95% Confidence Interval			Test of Null (Two-Tail)		Heterogeneity			
Groups	*K*	***Effect-size (Hedges' g)***	*Lower limit*	Upper limit	*z*-value	***p*-value**	***Q*-value**	*df (Q)*	*p*-value	I^2 **(%)**
Baseline	36	−0.0172	−0.2461	0.8056	−0.2461	.8056	61.6380	35	.0036	43
END	39	0.8702	0.6049	1.1356	6.4276	.0000	236.7802	38	0	84
Control-Arm Type										
Pharmacotherapy	3	0.8878	0.0421	1.7334	2.0576	.0396	13.5508	2	.0011	85
Therapy	29	0.4444	0.1966	0.6922	3.5155	.0004	131.1848	28	.0000	79
Treatment as usual	10	1.1157	0.4593	1.7721	3.3314	.0009	72.1051	9	.0000	88
Wait-list	18	1.1546	0.8319	1.4773	7.0135	.0000	62.0990	17	.0000	73
Depression type										
Primary	6	1.3571	0.2682	2.4460	2.4427	.0146	58.9102	5	.0000	92
Secondary	33	0.7819	0.5239	1.0399	5.9396	.0000	165.4040	32	.0000	81
Scale type										
Full	48	0.8066	0.5734	1.0398	6.7786	.0000	289.1989	47	.0000	84
Sub	12	0.7306	0.3130	1.1482	3.4292	.0006	55.2758	11	.0000	80

(*continued*)

TABLE 1. Effect-Sizes Estimates (Random Effect Model) (*Continued*)

		Effect Size and 95% Confidence Interval			Test of Null (Two-Tail)		Heterogeneity			
Groups	*K*	***Effect-size (Hedges' g)***	*Lower limit*	Upper limit	*z*-value	***p*-value**	***Q*-value**	*df (Q)*	*p*-value	I^2 **(%)**
Scales										
BDI	34	0.8339	0.5169	1.1509	5.1557	.0000	240.4193	33	.0000	86
CES-D	2	1.1741	−0.5262	2.8744	1.3534	.1759	7.4942	1	.0062	87
HADS Depression	6	0.7454	0.1757	1.3150	2.5646	.0103	27.2534	5	.0001	82
HAM-D	1	0.9008	0.0275	1.7741	2.0217	.0432	0.0000	0	1.0000	0
HDRS	3	1.0731	0.5646	1.5815	4.1366	.0000	1.9859	2	.3705	0
HSCL-Depression	1	1.7059	1.1626	2.2493	6.1535	.0000	0.0000	0	1.0000	0
MADRS	3	0.7219	−0.1383	1.5820	1.6449	.1000	10.2153	2	.0061	80
PHQ-9	4	0.2301	0.0498	0.4105	2.5007	.0124	2.7492	3	.4319	0
PRF-Depression	3	0.2503	−0.7647	1.2653	0.4833	.6289	9.5884	2	.0083	79
SCL-90R depression Subscale	3	0.9284	0.4468	1.4101	3.7779	.0002	2.6455	2	.2664	24
Continents										
Americas	9	0.6316	0.2754	0.9879	3.4750	.0005	16.1609	8	.0401	50
Asia	4	1.7242	−0.0626	3.5110	1.8913	.0586	45.2719	3	.0000	93
Asia-Europe	3	1.0759	−0.1354	2.2873	1.7408	.0817	27.5004	2	.0000	93
Australia	3	0.5620	0.1036	1.0204	2.4029	.0163	1.1893	2	.5518	0
Europe	20	0.8063	0.4621	1.1506	4.5905	.0000	118.8659	19	.0000	84
Medication allowed										
No	10	1.2853	0.5851	1.9855	3.5978	.0003	88.6292	9	.0000	90
NS	13	0.6980	0.3703	1.0257	4.1746	.0000	29.9875	12	.0028	60
Yes	16	0.7300	0.3426	1.1174	3.6929	.0002	96.7023	15	.0000	84
EMDR-trial duration (weeks)										
Approx and NR	10	1.2980	0.5294	2.0666	3.3101	.0009	117.7658	9	.0000	92
Exact	29	0.6990	0.4646	0.9333	5.8467	.0000	97.9879	28	.0000	71
EMDR-session time (min)										
Approx and NR	18	1.0449	0.5498	1.5401	4.1360	.0000	187.0951	17	.0000	91
Exact	21	0.6690	0.4354	0.9027	5.6127	.0000	45.3947	20	.0010	56
EMDR-sessions (#)										
Approx and NR	7	1.0987	0.5205	1.6769	3.7242	.0002	34.8016	6	.0000	83
Exact	32	0.8212	0.5104	1.1320	5.1785	.0000	201.8454	31	.0000	85
Follow-up (Yes/No)										
No	17	0.6979	0.4165	0.9794	4.8608	.0000	60.6172	16	.0000	74
Yes	22	1.0175	0.5626	1.4725	4.3837	.0000	170.8082	21	.0000	88
Randomized/observational										
No	9	0.6438	0.2423	1.0452	3.1431	.0017	32.7092	8	.0001	75
Yes	30	0.9448	0.6099	1.2797	5.5296	.0000	197.0678	29	.0000	85
Number of control arms										
1	27	1.0410	0.6743	1.4077	5.5638	.0000	191.4570	26	.0000	86
2	11	0.4813	0.2097	0.7529	3.4737	.0005	21.3230	10	.0190	53
3	1	0.2507	-0.5752	1.0766	0.5949	.5519	0.0000	0	1.0000	0
EMDR-Sex-reported										
No	8	0.6390	0.2846	0.9934	3.5339	.0004	12.4822	7	.0858	44
Yes	31	0.9224	0.6049	1.2399	5.6935	.0000	223.9426	30	.0000	87

(*continued*)

TABLE 1. Effect-Sizes Estimates (Random Effect Model) (*Continued*)

Groups	*K*	Effect Size and 95% Confidence Interval			Test of Null (Two-Tail)		Heterogeneity			
		Effect-size (Hedges' g)	*Lower limit*	Upper limit	*z*-value	***p*-value**	***Q*-value**	*df (Q)*	*p*-value	I^2 **(%)**
EMDR-Age-reported										
No	11	0.9925	0.4210	1.5640	3.4036	.0007	65.5063	10	.0000	85
Yes	28	0.8243	0.5217	1.1268	5.3401	.0000	167.3947	27	.0000	84
Original condition										
Addiction	1	−0.1466	−0.7550	0.4617	−0.4724	.6366	0.0000	0	1.0000	0
Cancer-PTSD	1	0.5850	−0.2559	1.4259	1.3635	.1727	0.0000	0	1.0000	0
Cardiac -PTSD	1	0.6498	0.0403	1.2593	2.0897	.0366	0.0000	0	1.0000	0
Depression	6	1.3571	0.2682	2.4460	2.4427	.0146	58.9102	5	.0000	92
Glioblastoma	1	1.7162	0.9741	2.4583	4.5325	.0000	0.0000	0	1.0000	0
MI	1	3.8953	3.0378	4.7527	8.9039	.0000	0.0000	0	1.0000	0
MS-PTSD	1	0.1190	−0.4756	0.7137	0.3923	.6948	0.0000	0	1.0000	0
PTS	2	0.3951	−0.2010	0.9911	1.2990	.1940	0.7430	1	.3887	0
PTSD	20	0.5757	0.3344	0.8170	4.6765	.0000	60.7646	19	.0000	69
PTSD-Domestic violence	1	1.1991	0.3203	2.0778	2.6744	.0075	0.0000	0	1.0000	0
PTSD-symptom	1	1.7494	0.6550	2.8437	3.1330	.0017	0.0000	0	1.0000	0
Sexual abuse	1	0.6598	−0.4804	1.8000	1.1341	.2567	0.0000	0	1.0000	0
Somatic symptom disorder	1	1.7698	1.1878	2.3517	5.9603	.0000	0.0000	0	1.0000	0
Subsyndromal Bipolar	1	1.7545	0.6644	2.8446	3.1546	.0016	0.0000	0	1.0000	0
Medical-Psychiatric Comorbidity										
Medical	2	2.7947	0.6594	4.9300	2.5652	.0103	14.1843	1	.0002	93
Mixed	4	0.5686	0.1473	0.9898	2.6456	.0082	4.2213	3	.2385	29
Psychiatric	33	0.7817	0.5188	1.0446	5.8270	.0000	169.0263	32	.0000	81

Note. HDRS = Hamilton Depression Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; PHQ-9 = Patient Health Questionnaire; PTSD = posttraumatic stress disorder; PTS = posttraumatic stress.

SE = 0.0158; P-value = 0.7085). This trend was consistent for the six studies specifically examining primary depression (mean age: slope = −0.0324, SE = 0.0860, *p*-value = .7067; percentage of female participants: Slope = 0.0144, SE = 0.0206, *p*-value = .4853; publication year: slope = −0.0216, SE = 0.3528, *p*-value = .9512; quality: slope = −0.1137, SE = 0.1677, *p*-value = .4978]. Additionally, no significant variation existed on study quality among nonobservational studies ($Z = 0$, $SD = 0$) when the Cochrane ROB 2 tool was implemented, and for observational studies [Slope: 0.0918; SE: 0.1341; *p*-value: .4937] when the NOS was implemented. See e-supplement 7 for graphical representation of meta-regressions.

Heterogeneity/Publication Bias. Publication bias was observed on the funnel plot at the end of trials, but not at the baseline (see Figure 3). Also, evidence of publication bias at the end of studies was observed on statistical analysis (Begg and Mazumdar rank correlation, and Egger's regression intercept). For the Begg and Mazumdar rank correlation, the Kendall's tau with continuity correlation was significant [*p*-value (two-tail) = .004], and for Egger's regression intercept, regression was significant [*p*-value (two-tail) = .006]. This trend was supported by the Duval and Tweedie's trim and fill approach, which asks how the effect-size would shift if the apparent bias were to be removed; we found seven studies to be at the right of the mean within the random effect model, which needed to be adjusted. After the adjustment, the aggregate effect-size estimate increased to 0.93, 95% CI: 0.83–1.02. The aggregate observation from the funnel plot and statistical approaches confirmed the presence of possible publication bias.

Sensitivity Analysis. The classical fail-safe *N* analysis, with alpha .05, at two-tail, with the empirical *z*-value of 1.96 and observed *z*-value of 14.40, and

39 included studies, showed that we would need 2,067 similar studies to raise the *p*-value above the significant alpha level for the obtained effect-size estimate. Thus, it can be concluded that the entire observed effect is not an artifact of bias.

Post Hoc. Examining for the effect of three studies (Kohler et al., 2017; Ostacoli et al., 2018; Silver et al., 1995) that did not provide baseline data, we have obtained a large and significant, yet heterogeneous, effect-size estimate in favor of EMDR [Hedges' g = 0.80, 95% CI = 0.55–1.05, p-value < .01, I^2 = 80%, K = 36].

When reviewing for heterogeneity, we removed the studies by Ostacoli et al. (2018) and Moghadam et al. (2015), given their appearance on the Forest plot, which clearly indicated them as outliers, with the lower end of the confidence interval of both of these studies showing an effect size greater than the best performing of nearly all the other studies. The removal of outliers is a common practice in meta-analysis. After the removal of these outliers, heterogeneity was reexamined and there was a significant and large, yet heterogeneous, effect-size estimate emerged between EMDR and control arm [Hedges' g = 0.70, 95% CI = 0.50–0.89, p-value < .01, I^2 = 70%, K = 37]. However, it is noteworthy to mention that the heterogeneity declined from the original all-inclusive studies of 84%–70%.

Categorical analysis for the effect of follow-up, whether studies included follow-up or not, we found medium to large effect-size estimates, yet heterogeneous, and in favor of EMDR treatment [no follow-up: Hedges' g = 0.70, 95% CI = 0.42–0.97, p-value < .01, I^2= 74%, K = 17; follow-up was present: Hedges' g = 1.02, 95% CI = 0.56–1.47, p-value < .01, I^2 = 88%, K = 22].

Primary conditions (medical vs. psychiatric vs. mixed) did not seem to have an effect on the efficacy of EMDR; however, the magnitude of the effect-size estimates for medical conditions (i.e., myocardial infarction or cancer) appears to be larger in individual studies (see Table 1 for effect sizes), indicating that EMDR has higher efficacy for these patient groups. Noteworthy is the low number of studies for the subgroup analysis in this category, which warrants caution in the interpretation of results. See Table 1 for details.

The possible unique role of the studies' relative (random) weight (<3.0 vs. >3.0), sample size (<50 vs. >50, in the EMDR arm), and variance (>0.3) on heterogeneity did not greatly change the magnitude of heterogeneity (relative weight <3.0: I^2 = 83.41, K = 38; sample size < 50: I^2 = 83.8%, K = 37; variance < 0.3: I^2 = 84.67, K = 35).

Discussion

This is the first meta-analysis (K = 39) specifically examining for the effect of EMDR treatment on depression [primary depressive symptoms (K = 6) or secondary symptoms (K = 33)] when compared to various treatment modalities. We found that the studies were balanced at onset in terms of depression severity, and had a large (Hedges' g: 0.86) and significant (<0.001) effect-size estimate in favor of treatment with EMDR at the end of trials, in contrast to most control modalities [treatment as usual, wait-list, and any therapy (e.g., talk therapy, biofeedback)]. This outcome was irrespective of depression subtype or scale-types (<0.05), or when possible for depression scales (N > 3). The magnitude of the aggregate effect-size estimate was retained when we controlled for various trial methodology, including randomization, number of control arms, trial duration (weeks), and presence of follow-up (N > 3). Additionally, the significance of the aggregate effect-size estimate at the end of trials was not altered by the intake of psychotropic medications, reported demographic variables (age and sex), or EMDR methodology (number and duration of sessions).

Although we have evidence to support the presence of publication bias (see Figure 3) in the studies we have included, elimination or adjustment for the effect of bias shows higher effect-size estimate.

An additional observation was the large magnitude of the effect size estimate for medical-psychiatric primary comorbid conditions when using EMDR. Given the low number of studies in this aggregate analysis, this finding should be interpreted with caution.

Consistent with the evidence emerging from another meta-analysis (Chen et al., 2015), we have also shown that EMDR benefits adult patients with depression more than controls, irrespective of depression or PTSD.

Limitations

Our meta-analysis is not without limitations, and here we present a few. One major limitation of our meta-analysis is that we have had a large and significant heterogeneity that we could not fully explain by methodological variation. One explanation for this is that the heterogeneity may have emerged as a result of the studies' sample distribution, as a few studies did

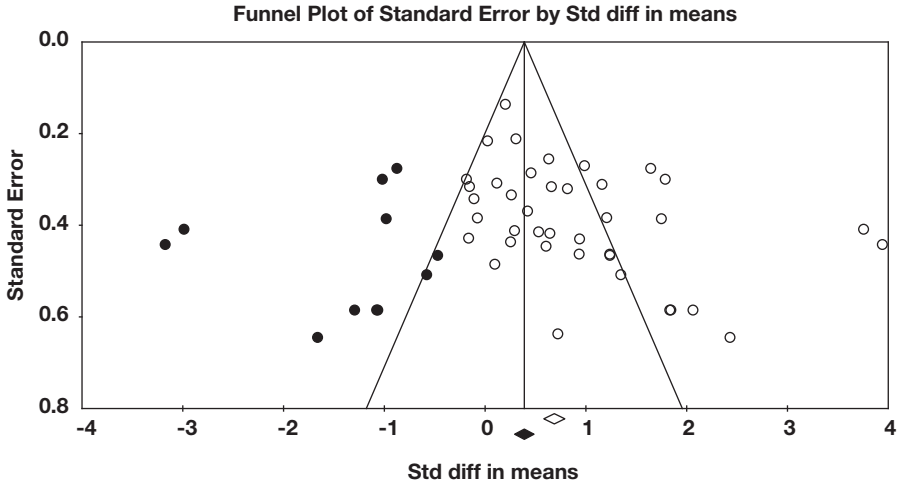

Figure 3. Random effect model funnel plot presenting publication bias at study end.
Note. The open circles represent observed individual studies, and the filled circles represent imputed values for studies. The empty diamond shows the aggregate effect-size, and the filled diamond represent the adjusted aggregate effect-size.

not directly report mean, *SD*, and sample size, therefore, we had to transform the available data presented in these articles (e.g., confidence intervals, standard error, reported effect-size, and *p*-values) for independent group analysis in order to calculate an effect-size estimate. Another is that the studies did not describe depression subtypes. Relationship-based depression (also described as anaclitic, or dependency-based) is different from depression focused on self-definition (also described as introjective, or self-critical) (Blatt, 2015; Lingiardi & McWilliams, 2017). Blatt (2015) describes the former as anaclitic and the latter as introjective, and noted that these psychodynamic subtypes have also been identified by cognitive-behavioral and interpersonal researchers. Relevant to the current study, he noted depression focused on relatedness has been found to be more responsive to the supportive or interpersonal elements of psychotherapy, while depression focused on self-definition has been found to be more responsive to interpretative or explorative aspects of psychotherapy. Thus, another explanation for the posttreatment heterogeneity is that one group responded more favorably to EMDR than the other. An additional explanation can be due to the confidence interval of the studies by Ostacoli et al. (2018) and Moghadam et al. (2015), showing an effect size greater than the best performing of the other studies. This discrepancy accounted for the high heterogeneity of the global analysis, as we have shown at post hoc analysis. Future research should test this hypothesis by separating patients into depression subtype. Finally, we could also speculate that heterogeneity was due to factors such as, by including the lower heterogeneity number of studies included in the analysis was above three, that we could not control for together.

Another shortcoming of our study is that we did not examine for the effect of either duration or outcome of the follow-up phases in the efficacy of EMDR treatment on depression. We did not do this analysis given the yielded aggregate large magnitude effect-size estimate for the end of trials, the robustness of our results based on fail-safe *N*, observation of the similar magnitude of effect across all other analyses, and the unaltered effect due to moderating continuous variables

A further limitation of the current meta-analysis is that only published, peer-reviewed, English-language studies were considered for inclusion. Additionally, file drawer studies, including unpublished dissertations, were also not included. Similarly, another limitation is the use of select databases, including PubMed/Medline and PsycINFO, since we did not have access to other databases, such as Embase or Cochrane, via our institution. However, this should not have affected our results given the high number of studies needed to inverse the significant effect-size estimate we have obtained (see fail safe-N, sensitivity analysis above). Similarly, we did not investigate the effect of clinicians' experience in conducting EMDR or adherence to EMDR, which could have brought methodological heterogeneity given the variation in background of the clinicians. Thus, future studies are needed to examine for this factor in light of the treatment of effect and reason for heterogeneity, and should include a metric of treatment adherence (Purgato, Gastaldon, et al., 2018).

Another possible limitation is that we did not examine, either categorically or otherwise, for the effect of depression severity (e.g., treatment resistant), or personality factors related to depression (e.g., self-critical or socially focused depression). By the same token, we did not examine, per se, for clinical depression, as by scales' cut-off scores, or determine how many individuals out of those treated with EMDR actually improved versus those that did not. Furthermore, future studies are needed to link the EMDR treatment response to neurobiological underpinning.

Conclusions and Future Recommendations

In summary, the current meta-analysis aimed to better understand the effectiveness of EMDR for the treatment of adult depression. Within the sample of studies that were meta-analytically examined, we found that EMDR is an effective treatment for adult depression, irrespective of age or sex. This trend was also irrespective of depression subtype (primary, secondary) or scale-types, or trial methodology, including randomization, number of control arms, trial duration (weeks), and presence of follow-up. Furthermore, the significance of the treatment effect was not altered by the intake of psychotropic medications. To this end, we can make practical recommendations for future studies; it is not clear from the current literature whether EMDR is useful for depression accompanying neurodegenerative conditions such as Alzheimer's disease, which warrants future studies. Additionally, the monitoring of EMDR trials for quality and standardization to keep heterogeneity to a minimum across sites is warranted.

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