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Review article

The potential role of EMDR on trauma in affective disorders: A narrative review

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ABSTRACT

Background: Eye Movement Desensitization and Reprocessing (EMDR) is a psychotherapeutic approach that has originally been developed to treat post-traumatic stress disorder (PTSD). Recently it has been suggested as a complementary therapy in a wide range of clinical conditions. In particular, affective disorders as bipolar disorder (BD) and major depressive disorder (MDD) have a higher lifetime prevalence of traumatic or stressful life events (SLEs) compared to the general population, which makes them good candidates for the application of EMDR.

Methods: A bibliographic search on PUBMED, Scopus, and ScienceDirect of studies applying EMDR to people with a primary diagnosis of bipolar disorder (BD) and major depressive disorder (MDD) (with or without a comorbid PTSD) was conducted.

Results: Literature search retrieved 15 studies, of which 3 were focused on BD and 12 on MDD. Overall, they suggest EMDR as an effective tool in reducing trauma-related but also manic and depressive symptoms, with few effect sides and high adherence rates.

Limitations: Few small studies exist with heterogeneous and not gold-standard methodology, especially for BD.

Conclusions: Overall, retrieved studies can be considered as first attempts at investigating the applicability of EMDR in affective disorders. Although far to be conclusive, preliminary evidence suggests EMDR as a useful adjunctive approach in the treatment of BD and MDD, especially when other treatments have failed. It is now the time to implement such trauma-focused therapy to larger samples of patients using more rigorous methods.

1.Introduction

Eye Movement Desensitization and Reprocessing (EMDR) is a psychotherapeutic approach originally developed by Francine Shapiro (Shapiro, 1989) to treat traumatic memories and the related stress symptoms in people who experienced traumas (Watts et al., 2013; Novo-Navarro et al., 2018; Castelnuovo et al., 2019). Nowadays it is recommended by the National Institute for Care Excellence (NICE; 2005) with a degree of evidence A for the treatment of post-traumatic stress disorder (PTSD) in adults and by World Health Organization (2013) as the first-choice therapy for PTSD in children, adolescents, and adults. Recently, evidence suggests EMDR to be applied to a wide range of clinical situations possibly sharing the presence of childhood trauma (CT) and/or stressful life events (SLEs) as etiopathogenetic factors (John and Gross, 2004). They include anxiety disorders, psychosis, affective disorders, substance use disorders, and chronic back pain (Valiente-Gomez et al., 2017).

The focus of the present narrative review is the application of EMDR to people with affective disorders (bipolar disorder, BD; major depressive disorder, MDD) with or without a comorbid diagnosis of PTSD.

The central aspect of EMDR is the use of bilateral stimulation (nearly always horizontal saccadic eye movements or tapping) which was used to desensitize the distress caused by traumatic memories. Differently from non-traumatic life events, stressful experiences are stored in memory in a disorganized way. Traumatic memories are hence separated from the flow of narration that usually allows people to

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feel part of a history with a past, a present and a future. In these conditions, personal identity and integrity of the self are lost. EMDR procedure focuses on thoughts, emotions, images and bodily sensations composing traumatic memories intending to reprocess and reorganize them as part of the patient personal narrative memory (Fernandez and Giovannozzi, 2012). The classic protocol (Shapiro, 2001) consists of 8 phases: 1) Collection of patient history with a selection of traumatic memories to be worked on; 2) Test of bilateral stimulation); 3) Identification of specific thoughts, emotions and bodily-physical sensations associated with the stressful memory. In this phase, the patient is also asked to identify the most suitable and desirable positive cognition (i.e. 'I am a valid person') to replace the negative one (i.e. 'I am a person without value'). The evaluation of how the patient feels when he/she thinks about the memory is made with the Subjective Units of Distress scale (SUD; Wolpe, 1969) ranging from 0 (minimum) to 10 (maximum level of discomfort) concludes this phase); 4) Desensitization of the memory. In this phase, the patient is asked to bring the traumatic memory to mind together with present emotion and bodily sensations while the therapist starts bilateral stimulation for 30–40 s. The patient is left free to describe thoughts and emotions or new material coming from memory. This phase ends when the traumatic memory no longer causes discomfort in the present moment (SUD score of 0 or 1 at most); (5) Installation of the positive cognition, accompanied by further rounds of bilateral stimulation to link the positive cognition to the original memory; (6) Body scan. The therapist asks the patient to close the eyes and concentrate on bodily sensations while thinking of the memory. Unpleasant or positive sensations are respectively desensitized or reinforced with a 10–12 s round of bilateral stimulation; (7) Debriefing. In this part of the protocol recommendations are given to the patient on how to manage new material like thoughts, insights, memories, and dreams which may follow EMDR sessions; 8) A re-evaluation is made about the effect that patients may experience between sessions and concerning how the traumatic memory has been reprocessed and reorganized (Novo-Navarro et al., 2018).

It is important to specify that the term 'trauma' includes both 'big T traumas' (episodes which are out the common human experience like war, rape, natural disaster, sexual, physical or psychological abuse during childhood) and 'small t traumas' (also called 'stressful life events', SLEs) (referring to positive and negative stressful occurrence like moving house or getting ill, respectively. Such events can be acute or chronic) (Wood et al., 2018). Of note, negative SLE's can generate at least as many PTSD symptoms as traumatic events (Mol et al., 2005).

Many hypotheses have been proposed about how EMDR works (Landing-Romero et al., 2018; Novo-Navarro et al., 2018). Overall, they sustain that symptoms related to traumatic experiences are due to a fault in the processing of stressful memories by different areas of the brain involved in processing emotions, memories, self-perception, attention, REM (rapid eye movement) sleep phase (Rousseau et al., 2019). Bilateral stimulation occurring during EMDR sessions is thought to improve traumatic memories processing by changing functional brain connectivity (Nieuwenhuis et al., 2013), or by favoring physiological changes similar to those observed during the REM (Stickgold et al., 2002) or slow wave sleep (SWS; Pagani et al., 2017) phases; or by reducing the vividness of emotional stimuli by saturating the working memory (Gunter and Bodner, 2008). A recent study by Baek and colleagues in mice suggested that alternating bilateral sensory stimulation (ABS) provides a fear-reducing effect by suppressing the activity of fear-encoding cells and stabilizing inhibitory neurotransmission in a neural circuit including the superior colliculus, the amygdala, and the mediodorsal thalamus with the final effect of attenuating traumatic memories (Baek et al., 2019).

Interestingly, the overall number of adverse experiences (traumas and SLEs) is higher in BD compared to general population (Otto et al., 2004; Dualibe and Osorio, 2017; Lex et al., 2017; Jaworska-Andryszewska et al., 2016; 2019), with the presence of early traumatic experiences representing a poor prognostic factor (Conus et al., 2010; Etain et al., 2017). Furthermore, adversities during childhood seem to interfere with the acquisition of effective abilities to cope with stressors occurring later in life (Aas et al., 2019). Of note, a study by Hernandez et al. (2013) on 3158 bipolar patients showed an overall prevalence rate of 20% for lifetime PTSD in BD (versus 7.8–9.2% lifetime of the general population; Sareen, 2014), being such comorbidity associated with poorer outcome, greater episode severity, more rapid cycling, more depressive and (hypo)manic symptoms, higher relapse rates, more suicide attempts and substance abuse and a lower quality of life, with respect to BD without PTSD (Goodman et al., 2001; Quarantini et al., 2010).

As for MDD, critical events represent risk factors for both the onset and maintaining of depressive symptoms. In particular, a specific psychosocial stressor often precedes primary episodes while later depressive phases may be triggered by smaller or not noticeable events (Post, 1992). Also, SLEs have been identified as the only risk factor to be significantly correlated with the onset of depression (Risch et al., 2009), with risk doubled in case of traumatic events (especially emotional abuse and neglect) lived during childhood. In particular, stressful memories in depressive disorders are often memories of losses, separations, or humiliations (Kendler et al., 2003; Mandelli et al., 2015). Finally, childhood abuse was observed to be associated with the presence of psychotic symptoms (Gaudiano and Zimmerman, 2010).

Given these premises, affective disorders seem to be good candidates for the application of EMDR. Despite that, trauma-focused treatments are hardly offered as part of the clinical management of these patients, also in presence of PTSD comorbidity. This is possibly due to the belief that the treatment of traumatic experiences is harmful and resulting in exacerbation rather than in symptoms improvement. Recent studies in people with severe mental illness (SMI) do not support such view since they showed no negative effects of trauma-focused treatment in patients with SMI in terms of symptom exacerbation, adverse events, and re-victimization (van den Berg et al., 2016; Sin et al., 2017). Moreover, a recent study by de Bont et al. (2019) showed that treating trauma in severe patients would be more economically advantageous than usual care for community treatment services.

2. Methods

In the present narrative review, we focused on EMDR applied to people with BD and MDD. Since the lifetime presence of traumas or SLEs is correlated to worse symptomatology and clinical course, it is extremely relevant to assess the feasibility and effectiveness of EMDR applied to this population. The bibliographic search was performed using PUBMED, Scopus and ScienceDirect databases. The following terms were used for the search: 'EMDR', 'trauma-focused therapy', 'bipolar disorder', 'depression', 'mood disorder'. The inclusion criteria were: (i) papers focused on EMDR therapy in patients with a diagnosis of BD and/or MDD (with the exclusion of post-partum depression); (ii) original publication published in a peer-reviewed journal; (iii) publication date after 2010; (iv) English language; (v) adult population (> 18 years). Animal studies, review papers, qualitative studies, opinion pieces or comments, letters or editorials, study protocols, conference abstracts or posters, published abstracts, and books or book chapters were excluded from the search

The Sackett Scale (Sackett 1989) was used to objectify the quality (i.e., level of evidence) of the selected studies. The scale is characterized by five levels of evidence, ranging from level 1 "large RCTs with clear cut results" to level 5 "case series, studies with no controls".

3. Results

After title and abstract screening, 15 studies were identified and included in the review (Table 1). Of them, 3 were specifically focused on BD (Landin-Romero et al., 2013; Oh and Kim, 2014; Novo-Navarro et al., 2014) and 12 on MDD (Rosas Uribe et al., 2010;

Table 1
Studies on the application of EMDR to people with BD and MDD.

Studies on the application of EMDR to people with BD Reference	Participants	Mean age (s.d); gender (*F* = female, *M* = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
Landin-Romero et al., 2013	1 BD II patient; 30 healthy subjects (only for fMRI)	37; 1F	Case report	HRSD, YMRS, IES, CAPS, FAST, CGI, QoL-PCS; QoL-MCS, cognitive assessment	witnessing a suicide attempt by the sister, conflictive relationship with mother, death of the father, acrimonious divorce	no	14 sessions over 12 weeks (90 min each)	no	Lamotrigine 200 mg/day. Medication as maintained stable during EMDR and until second fMRI scan	1 (100%)	baseline, 12 months	Marked improvement of traumatic symptoms, affective symptoms, functioning, quality of life, verbal and spatial working memory after EMDR. A marked improvement in DMN abnormality was observed as compared to 30 healthy subjects.	5
Oh and Kim, 2014	2 BD patients	32 (ns); 2F	Case report	CAPS	multiple rapes; several traumatic experiences including an accident, sexual assault, and involuntary hospitalization	yes	9–10 sessions	no	mood stabilizer, antipsychotics. Pharmacotherapy dose remained unchanged over the course of EMDR treatment	2 (100%)	baseline, 12 months	Complete resolution of PTSD symptoms at baseline and follow up in both people (final CAPS score = 7 and 18).	5
Novo-Navarro et al., 2014	20 subsyndromal BD patients with a history of traumatic events (10 EMDR group; 10 TAU group)	43.90 (6.87) (EMDR group); 44.80 (6.86) (TAU group); 12F, 8M	Pilot RCT	HRSD, YMRS, CGI-BP, IES-R, CAPS, TAP	At least three documentable (but not specified) traumatic events lifetime, which were still causing clinically relevant distress (at least 5 SUD)	ns	14–18 sessions over 12 weeks (90 min each)	TAU	mood stabilizer, antipsychotics, antidepressants, anxiolytics. During the study a change in the medication was made in 3 participants from each group	10 (100% EMDR group); 7 (70% TAU group)	6 time-points (baseline, 2 weeks, 5 weeks, 8 weeks, 12 weeks, and 24 weeks)	EMDR was superior to TAU in reducing depressive and hypomanic symptoms, symptoms of trauma and trauma impact. The effect was only partly maintained in trauma impact at the 24weeks follow-up visit.	2

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (*F* = female, *M* = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
Rosas Uribe et al., 2010	3 patients with single episode major unipolar depression (2 milds; 1	26 (ns); 2F, 1M	Case report	BDI, The clinical history inventory (Shapiro et al., 2004, 2005)	potential SLEs: divorced parents in childhood, single,	no	11–15 sessions	no	no	3 (100%)	3-time points (baseline, half-way through the treatment,	EMDR had a positive effect both on emotional cognitive processing and on	5

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Table 1 (*continued*)

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (F = female, M = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
	moderate according to BDI)				medium-low socioeconomic status						after the conclusion of the therapy)	long-term memory conceptual organization.	
Hase et al., 2015	32 inpatient with mild-to-moderate depression (16 TAU + EMDR group; 16 TAU group)	46.41 (9.06); 12F, 20M	Matched pairs study	BDI, SCL-90	SLE's below PTSD criterion A threshold	no (SLE's below PTSD criterion A threshold)	4.6 session (mean) (60 min each)	TAU (both group and one-to-one psychodynamic psychotherapy, psychoeducation, physical and relaxation therapies)	19 patients were on medication at the time of admission (7 on SSRI; 6 on NaSSA; 6 other). Five of them were taking more than one drug.	11 (69% EMDR group); 9 (56% TAU group)	12–16 months after the end of treatment	67% of the EMDR group showed full remission at end of treatment (BDI < 12). The EMDR group showed a greater reduction in depressive symptoms as measured by the SCL-90-R depression subscale. At 12–16 months follow up the EMDR group reported fewer problems related to depression and fewer relapses than the control group. No adverse effects were reported during EMDR sessions.	3
Hofmann et al., 2014	51 outpatients with unipolar depression (26 with recurrent episodes) (30 EMDR + CBT; 21 CBT)	40.38 (10.38); 33F, 9M	non-randomized controlled exploratory study	BDI-II	ns	no	a mean of 6.9 sessions (range: 3–16 sessions)	CBT (mean of sessions: 44.5 (EMDR + CBT group); 47.1 (CBT group))	15 patients were on antidepressants at the time of admission (6 SSRI, 1 NaSSA, 8 others).	42 (70% EMDR + CBT group); 21 (100% TAU group)	baseline, end of treatment	86% of the CBT + EMDR group showed full remission at the end of treatment (BDI-II < 12). The CBT + EMDR group showed a greater reduction in depressive symptoms as indexed by the BDI than the CBT group.	3
Gauhar et al., 2016	26 patients with MDD (13 EMDR; 13 waiting list)	29.4 (ns); 10F, 7M	RCT	BDI-II, TSC-40, QLI	potential trauma/SLEs: verbal, physical, sex, child abuse;	no	6–8 weekly sessions (60 min each)	clinical interview regarding presenting complaints	no	10 (77% EMDR); 7 (54% waiting list)	baseline, end of treatment (after 7 weeks) and	After the treatment the EMDR group showed greater improvements in	2

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Table 1 (*continued*)

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (F = female, M = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
					childhood parental neglect; loss of parents; difficult marriage						after 3 months	BDI-II, TSC-40, and QLI scores than the waiting list group and less negative cognitions. After 3 months the EMDR group reported improved sense of well-being and no depressive symptoms occurred.	
Semiz et al., 2016	3 patients with MDD	38 (ns); 3F	case report	BDI, BAI, STAI	potential traumas: workplace accident, violence in childhood, armed attack	no	6–8 sessions	no	all patients were on antidepressants in the last 2–3 months (SNRI, NaSSA or NDRI)	3 (100%)	baseline, end of treatment	EMDR had a positive effects on both depression and anxiety symptoms and negative cognitions.	5
Ostacoli et al., 2018	82 recurrent depression patients (40 ADM + EMDR group; 42 ADM + CBT group)	48.23 (9.66) ADM + EMDR group; 47.54 (12:90) ADM + CBT group	Single-blind, clinical multicentric RCT	BDI-II; MINI-Plus; BAI, IES-R; WHOQOL-Bref; GAF; DES; TAQ	95.5% of reported adverse childhood experiences in the 0–18 years age period	no (as assessed by MINI-Plus)	12–18 sessions	ADM + CBT	stabilized ADMs for at least four weeks	31 (77.5% ADM + EMDR group); 35 (83.3% ADM + CBT group)	6 months	Both groups showed improvement in depressive symptoms in the initial phase of the intervention. In the second phase and at 6-month follow up they had a different trajectory, that is EMDR continued to significantly reduce depression levels until the end of the intervention, while CBT only maintained the gains made in the first phase.	2
Hase et al., 2018	30 inpatients with at least mild depression (16 EMDR + TAU	39.74 (9.52); 3F, 27M	RCT	BDI-II, SCL-90	ns but it is specified that all patients were privately insured	complex PTSD was excluded	4–12 sessions	TAU	current antidepressant treatment was a study inclusion criteria	30 (100%)	baseline, end of treatment	The EMDR + TAU group improved significantly more than the TAU	2

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Table 1 (*continued*)

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (F = female, M = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
	group, 14 TAU group)				through the German Armed Forces							group on the BDI score and the Global Severity Index of the SCL-90. In the EMDR + TAU group, seven out of 14 patients achieved full symptomatic remission, whereas four out of 16 in the TAU group did so.	
Wood et al., 2018	13 patients with recurrent and/or long-term depression (but only 10 entered the treatment)	46 (13.1); 8F, 5M	Single-case with replication study	HRSD, IES-r, PHQ-9, BDI	ns	PTSD was excluded	8–20 sessions (average 17.6)	no	ns but all patients had received at least one antidepressant in the past and must have tried at least one-first-line treatment and not responded	7 (70%)	baseline, end of treatment and after 3 months	All patients except one had clinically significant and statistically reliable improvement on the HRSD score. EMDR was well tolerated by patients.	5
Minelli et al., 2019	26 in-patients with TRD (15 EMDR group; 11 trauma-focused CBT group)	52.3 (10.7) (EMDR group); 53.3 (6.5) (trauma-focused CBT group); 16F, 6M	Pilot RCT	MADRS, BAI, BDI, MINI-ICF-APP, PSQI	a mean of 3.6 childhood adverse events (mother or father hostility/ coldness or neglect; physical abuse, sexual abuse) and a mean of 5 adult SLE's	40% of the sample	24 sessions	trauma-focused CBT	mood stabilizer, antipsychotics, antidepressants, anxiolytics	22 (85%)	4-time points (baseline, 4, 8 and 12 weeks). After 24 weeks, a clinical interview was carried out by phone.	All TRD patients showed a significant improvement in depressive symptomatology; however, post hoc comparisons showed a significant difference between the two treatment groups, with lower depressive symptom scores in the EMDR than in the trauma-focused CBT group at the follow-up (after 12 weeks). This effect was partly	2

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Table 1 (*continued*)

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (F = female, M = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
												maintained at 24 weeks.	
Fereidouni et al., 2019	70 patients with MDD with suicidal thoughts (35 EMDR, 35 TAU)	36.2 (11.68);	RCT	BSSI	60% of traumas related to adulthood (e.g. grief, divorce, physical/ sexual abuse); 25% related to childhood and 15% to both.	ns	9 sessions (45–90 min each) over 3 weeks	ADM	all patients were on antidepressant	70 (100%)	baseline, end of treatment	Both the EMDR and the TAU groups showed reduction of mean BSSI score, but the effect was statistically significant only for the EMDR group.	2
Dominguez et al., 2020	49 out-patients with depressive symptoms (80% with MDD): 16 CBT + EMDR; 16 CBT; 17 CBT + AT)	40 (ns); 29F, 20M	multi-arm parallel RCT	DASS-42	ns	no	3 sessions	CBT (group-based); CBT + AT	44 patients on medication at the time of admission with antidepressants and/or atypical antipsychotic and/or benzodiazepines.	15 (94% CBT + EMDR); 15 (88% CBT + AT); 16 (100% CBT) at the end of treatment.	pre/post intervention and after 6 and 12 weeks.	At the end of training participants treated with CBT + EMDR were less likely to meet criteria for a major depressive episode than those in the other 2 groups. 6-weeks after treatment the CBT-EMDR and the CBT + AT groups were more likely to maintain treatment gains than CBT group. After 12 weeks the CBT + EMDR group showed less depressive symptoms than the CBT + AT group.	2

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Table 1 (*continued*)

Studies on the application of EMDR to people with MDD Reference	Participants	Mean age (s.d); gender (*F* = female, *M* = male)	Study design	Assessment	Trauma or SLE	PTSD	Duration of EMDR	Comparative intervention	Medication	Adherence (number of participants and%)	Follow up	Main results	Level of evidence based on the Sackett scale
Jahanfar et al., 2020	70 patients with MDD (35 ADM + EMDR; 35 ADM)	36.22 (11.70)	RCT	WHOQOL-Bref	ns but it is specified that all patients suffered from psychological trauma	ns	8 sessions of 90 min each over 3 weeks	ADM	all participants were on antidepressants	70 (100%)	pre/post intervention	The ADM + EMDR group showed a greater improvements in all quality of life domains than the ADM group.	2

ADM = antidepressant medication; AT = assertiveness training; BD = bipolar disorder; BAI = Beck Anxiety Inventory (Beck and Steer, 2013); BDI = Beck Depression Inventory (Beck et al., 1996); BSSI = Beck Scale for Suicide Ideation (Beck et al., 1979); CAPS = Clinician-Administered PTSD Scale (Blake et al., 1995); CBT = Cognitive Behavioral Therapy; CGI-BP = Clinical Global Impression-Bipolar Disorder (Spearing et al., 1997); DASS-42 = = Depression, Anxiety and Stress Scale – 42 (Lovibond and Lovibond, 1995); DES = The Dissociative Experiences Scale (DES) (Bernstein and Putnam, 1986); DMN = Default Mode Network; FAST = Functioning Assessment Short Test (Rosa et al., 2007); fMRI = functional Magnetic Resonance Imaging; GAF = Global Assessment of Functioning Scale (American Psychiatric Association, 2000); HRSD = Hamilton Rating Scale for Depression (Hamilton, 1960); IES-*r* = Impact of Event Scale-revised (Weiss and Marmar, 1997); MADRS = Montgomery–Åsberg Depression Rating Scale (Montgomery and Asberg, 1979); MDD = Major depressive disorder; MINI-ICF-APP = MINI-International Classification of Functioning, Disability and Health APP (Balestrieri et al., 2013); MINI-Plus = Mini-International Neuropsychiatric Interview-Plus (Sheehan et al., 1998); NaSSA = Noradrenergic and Specific Serotonin Antidepressants; NDRI = norepinephrine–dopamine reuptake inhibitor; ns = not specified; PHQ-9 = Patient Health Questionnaire – 9 items (Kroenke et al., 2002); PSQI = Pittsburgh Sleep Quality Index (PSQI) (Curcio et al., 2013); PTSD = Post Traumatic Stress Disorder; QLI = Quality of Life Index (Ferrans and Powers, 1985); QoL-PCS/QoL-MCS = Physical/Mental Component of the Quality of Life Scale (Burckhardt and Anderson, 2003); RCT = randomized controlled trial; SCL-90 = Symptom Checklist-90 items (Derogatis, 1994); SLEs = stressful life events; SNRI = Serotonin and norepinephrine reuptake inhibitors; Selective Serotonin Reuptake Inhibitors SSRI = Selective Serotonin Reuptake Inhibitors; STAI = Trait Anxiety Inventory (Spielberger, 1983); SUD = Subjective Units of Disturbance/Distress (Wolpe, 1969); TAQ = The Trauma Antecedent Questionnaire (Luxenberg et al., 2001); TAU = treatment as usual; TAP = Word Accentuation Test [Test de Acentuación de Palabras (Gomar et al., 2011)]; TRD = Treatment-resistant depression; TSC-40 = Trauma Symptoms Checklist-40 (Briere and Runtz, 1989); YMRS = Young mania rating scale (Young et al., 1978); WHOQOL-Bref = World Health Organization-Quality of Life Bref (Skevington et al., 2004).

Hase et al., 2015; Hofmann et al., 2014; Gauhar et al., 2016; Semiz et al., 2016; Hase et al., 2018; Wood et al., 2018; Ostacoli et al., 2018; Fereidouni et al., 2019; Minelli et al., 2019; Dominguez et al., 2020; Jahanfar et al., 2020).

As for the application of EMDR to BD, two out of the three published studies were case reports. For example, Oh and Kim (2014) used EMDR as adjunctive therapy on two women of 25 and 39 years with BD and a comorbid PTSD diagnosis due to repeated traumatic events (accident, sexual assault, involuntary hospitalization). After 9–10 sessions of EMDR, a complete remission of PTSD symptoms were observed in both patients and such therapeutic gain was maintained one year after the end of the treatment. The other case report (Landin-Romero et al., 2013) is the only available study investigating neural changes pre- and post-EMDR in a 37 years old female with a BD-II diagnosis. Of interest, this study focused on the Default Mode Network (DMN) using a functional magnetic resonance imaging (fMRI) working memory task. DMN represents an interconnected series of brain regions (including the medial frontal cortex, MFC, and the posterior cingulate cortex/precuneus) whose dysfunction is currently implicated in major psychiatric disorders like schizophrenia, BD and MDD (Allen et al., 2019). After EMDR, a marked amelioration of clinical measures (trauma-related, hypomanic and depressive symptoms; functioning, quality of life) was observed together with an improvement in DMN abnormality (and especially in the MFC) as compared to 30 healthy subjects. Finally, Novo-Navarro et al. (2014) investigated the effect of EMDR in 20 subsyndromal bipolar patients with a history of traumatic events using a pilot randomized controlled trial (RCT) design. To be included, people should have had at least three documentable (not specified) traumatic events lifetime, which were still causing clinically relevant distress (at least 5 SUD). Ten patients received 14–18 individual sessions of EMDR over a period of 12 weeks, whereas the other 10 patients underwent treatment as usual (TAU). Results showed the superiority of EMDR intervention with respect to TAU in depressive and hypomanic symptoms, symptoms of trauma and trauma impact after the intervention. The effect in trauma impact was only partly maintained at the 24-weeks follow-up visit.

The three studies applying EMDR to BD had a low level of evidence, as two out of three were case reports with no control group (Landin-Romero et al., 2013; Oh and Kim, 2014).

As regards researches on people with MDD, we identified and included 12 studies. They are heterogeneous in terms of study design. In particular, the studies by Rosas-Uribe et al. (2010) and Semiz et al. (2016) are case reports (3 patients each with single episode major unipolar depression), the one by Wood et al. (2018) adopted a single-case with replication design, the study by Hase et al. (2015) is a matched pairs study, the one by Hofmann et al. (2014) is a non-randomized controlled trial and the remaining six researches are RCT (Hase et al., 2018; Ostacoli et al., 2018; Fereidouni et al., 2019; Dominguez et al., 2020; Jahanfar et al., 2020) and pilot RCT (Minelli et al., 2019). The number of included patients was generally small-to-medium, with samples made up of 12–35 people in the experimental groups (without considering the case report studies) Also, nine out of 12 studies used a comparative group (TAU or a waiting-list or another type of CBT or trauma-focused therapy). Regarding the effects of interventions, in 11 out of 12 studies EMDR produced a significant improvement in depressive symptomatology immediately after treatment as measured by the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) or the Beck Depression Inventory (BDI; Beck et al., 1996) or the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979) or the Beck Scale for Suicide Ideation (BSSI; Beck et al., 1979) or the Depression, Anxiety and Stress Scale-42 (DASS-42; Lovibond and Lovibond, 1995). Effects were partly maintained after a 12–24-week follow up (Hase et al., 2015; Gauhar et al., 2016; Ostacoli et al., 2018; Minelli et al., 2019). Overall, therapy was well tolerated by patients with small side effects (i.e. hyper-arousal, intense affect), as showed by a mean adherence to therapy of 87%. Of interest, the study by Hase et al. (2015) explored the patients work status in terms of days of absence from work in the year following EMDR + TAU versus TAU only, showing a distributions of work absences significantly different in favor of the study group, possibly suggesting a positive effect of EMDR on functioning and ability to cope with job demands and stressors.

Overall, the studies that applied EMDR in MDD showed a reasonable level of evidence ranging from 2 to 5 on the Sackett scale. Particularly, only three out of 12 studies did not include control groups i.e., two case reports (Rosas Uribe et al., 2010; Semiz et al., 2016) and one single-case experimental study (Wood et al., 2018) whereas the remaining nine (75% of the total) were small-sample RCTs (Gauhar et al., 2016; Ostacoli et al., 2018; Hase et al., 2018; Minelli et al., 2019; Fereidouni et al., 2019; Dominguez et al., 2020; Jahanfar et al., 2020) or case-control studies (Hase et al., 2015; Hofmann et al., 2014).

4. Discussion and conclusion

Data available on the application of EMDR to people with BD are few and with poor methodology. Despite such important limitations, they overall suggest EMDR as a promising and safe intervention to treat both mood and trauma symptoms in traumatized BD. Further studies with adequate methodology and sample size are now warranted to confirm such preliminary results. A recent protocol has been published aiming at testing the effectiveness of a specific EMDR protocol for patients with BD in reducing affective episodes and symptoms and functional, cognitive and trauma symptoms using a single-blind, randomized, controlled, multicentre trial (Moreno-Alcazar et al., 2017). The authors will apply the original 8-phase protocol (Shapiro, 2001) together with five sub-protocols specifics for BD that target the following areas: 1) mood stabilization; 2) treatment adherence; 3) illness awareness; 4) detection of prodromal symptoms; 5) de-idealization of pleasurable manic symptoms. According to the study inclusion criteria, BD patients should be euthymic that is in clinical remission defined as Bipolar Depression Rating Scale (BDRS; Berk et al., 2007) <8 and Young Mania Rating Scale (YMRS; Young et al., 1978) <6) or at most in a subsyndromal status defined as BDRS ≥ 8 and <14 and/or YMRS ≥ 7 and <12. This advice is also given by Oh and Kim (2014) since the presence of (hypo)manic symptoms possibly make difficult to judge whether the processing of memories in the EMDR procedure is complete or optimistically due to manic ideation. Replication on larger samples is also indispensable to test whether the normalization of the DMN dysfunction may represent a possible neurobiological mechanism of action of EMDR having a mood-stabilizing effect in BD.

As for MDD, 12 studies were retrieved with an overall medium level of evidence. The 67% of them (i.e., 7 studies) did not include patients with comorbid PTSD. Particularly, in Hoffman et al., 2014; Gauhar et al., 2016; Hase et al., 2018; and Wood et al., 2018 the presence of PTSD was an exclusion criterion. This is of interest because, even though the impact of EMDR on PTSD is nowadays established (Wilson et al., 2018), the investigation of how it works in clinical conditions where the PTSD Criterion A threshold is not reached is relatively new. As an example, the study by Gauhar et al. (2016) was the first using an RCT design to examine the impact of EMDR on MDD with a history of SLE's but not PTSD. Conversely, in Minelli et al. (2019) 40% of the sample was made up of patients with a comorbid PTSD diagnosis and in the remaining three studies the presence of co-occurring PTSD was not specified (Semiz et al., 2016; Fereidounin et al., 2019 and Jahanfar et al., 2020). It is worth noticing that the diagnosis of PTSD is often underestimated in primary care setting (Liebschutz et al., 2007) but also in severe mental illnesses (Grubaugh et al., 2011) and depression specifically (Kostaras et al., 2017). As such, more sensitive screening tools are needed to clarify the presence of a MDD-PTSD comorbidity, and further research is warranted to clarify whether EMDR may be an effective adjunctive therapy for both MDD alone and MDD with concomitant PTSD. Overall, the retrieved researches suggest

EMDR as a useful supplementary therapy in the treatment of MDD with and without co-concurrent PTSD, also in the case of recurrent (Hofmann et a., 2014; Ostacoli et al., 2018; Wood et al., 2018), long-term symptomatology (Wood et al., 2018) and TRD (Minelli et al., 2019). Moreover, EMDR can be considered when first-line approaches (i.e. CBT) have been tried and failed. Of interest, a specific protocol for the treatment of depressive disorders has been recently developed (DeprEnd©; Luber, 2018; Ostacoli et al., 2018) aiming at addressing the pathogenic memory networks thought to be involved in the onset and maintenance of depressive symptomatology. The protocol focuses on four main types of memories: classic traumatic memories (Criterion A), often non-Criterion A-based episode triggers, belief systems, and depressive and suicidal states.

To summarize, so far only a few studies have been conducted focusing on the application of EMDR to BD and MDD, with slightly more evidence for MDD than for BD. Although suggesting EMDR as impacting on both mood and traumatic symptoms, they can be considered as first attempts of investigating the applicability and effectiveness of this form of trauma-focused intervention in affective disorders. In particular, small-to-medium sample size and poor study design reduce the generalizability of available results and call for larger and methodologically stronger studies to replicate preliminary evidence. The need for specific protocols adapted to different patients' populations should also be addressed by future studies.

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CRediT authorship contribution statement

Cinzia Perlini: Conceptualization, Writing - original draft, Writing - review & editing, Data curation. **Valeria Donisi:** Writing - review & editing. **Maria Gloria Rossetti:** Writing - review & editing. **Chiara Moltrasio:** Writing - review & editing. **Marcella Bellani:** Writing - review & editing. **Paolo Brambilla:** Conceptualization, Writing - review & editing.

Declaration of competing interest

Authors declare no conflict of interest

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.03.001.

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