

Theoretical Background and Clinical Aspects of the Use of EMDR in Patients With Bipolar Disorder

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Bipolar disorder (BD) is associated with a lifelong episodic course of severe mood and behavioral disturbance. In last decades treatment improved with numerous pharmacological and psychosocial treatments; however, subsequent mood episode rates are still high and possible risk factors for subsequent mood episodes are not sufficiently addressed. Of note, childhood trauma and stressful life events represent significant, under-recognized, and often neglected environmental risk factors in the etiology and course of BD. Here, we summarize the evidence of eye movement desensitization and reprocessing (EMDR) therapy in BD with posttraumatic stress disorder (PTSD) or life traumatic events. So far, one case report study and one pilot randomized controlled trial (RCT) have been published suggesting positive effect of EMDR therapy in BD. Currently, two larger further RCTs are ongoing to increase scientific evidence of the use of EMDR therapy in this indication, especially with a focus on its effect on relapse prevention. In addition, a functional neuroimaging case report of a bipolar subject versus 30 healthy controls showed first evidence that EMDR might modulate the default mode network. These preliminary results suggest that EMDR could be a promising and safe psychotherapeutic approach for the add-on treatment of bipolar subjects, but confirmative large RCT are needed, with two currently being conducted.

Keywords: EMDR; bipolar disorder; psychological trauma; stressful life events; relapse

Bipolar disorder (BD) is a severe chronic psychiatric disorder where patients suffer from serious mood changes in the form of depressive, hypomanic, manic, or mixed episodes. Furthermore, bipolar subjects also experience behavioral alterations, high-risk behavior, frequent cognitive and functional decline, and increased mortality due to cardiovascular incidents and suicide when compared to the general population (Grande, Berk, Birmaher, & Vieta, 2015). The etiology of BD is complex and multifactorial, as it involves both genetic and environmental factors. A recent *Nature Genetics* publication could prove that 30 loci are associated with the etiology of BD (Stahl et al., 2019). Beyond this polygenetic predisposition, childhood adversity has been identified in a recent umbrella meta-analysis as one of the most robust etiological risk factors to develop BD (Bortolato et al., 2017).

Due to the genetic component within BD's etiology, the therapeutic basis of BD consists of a variety of pharmacological drugs, mainly mood stabilizers such as lithium, anticonvulsants, or atypical antipsychotics, and occasionally of antidepressants, in the case of more severe bipolar depressive episodes. Pharmacological treatment is usually recommended for life to avoid or at least reduce numbers of affective relapses across the lifespan. To reach this therapeutic goal, clinicians and researchers became aware in the early 1990s of the necessity of additional psychosocial interventions such as psychoeducation, family-focused intervention, functional remediation, or mindfulness, among others. They have been increasingly studied and added to the individual treatment plan in order to improve the prognosis of this complex and often refractory disorder (Bonnin et al., 2016; Miklowitz & Chung, 2016; Oud et al., 2016; Reinares, Sánchez-Moreno, & Fountoulakis, 2014; Secades-Álvarez & Fernández-Rodríguez, 2017).

Despite these advances, many bipolar-I patients (manic alternating with depressive episodes) and bipolar-II patients (depressive alternating with hypomanic episodes) do not have a complete remission (Paykel, Abbott, Morriss, Hayhurst, & Scott, 2006) and may also suffer from multiple subsequent mood episodes (Radua, Grunze, & Amann, 2017). Radua et al.'s (2017) meta-analysis of observational international long-term studies included 5,837 bipolar-I and -II patients, and reported that 70% of bipolar I and 80% of bipolar-II patients had at least one subsequent mood episode within a 4-year follow-up. They also found that persisting subsyndromal symptoms, which are defined as the presence of minor hypomanic or

depressive symptoms without clinical remission, are a dominant risk factor for rapid subsequent mood episodes. Further risk factors include poor adherence to pharmacological treatment, lack of insight, cognitive deficits, or somatic and psychiatric comorbidities. Among psychiatric comorbid disorders, posttraumatic stress disorder (PTSD) has been identified in 16%–39% of bipolar subjects (Otto et al., 2004). The comorbidity between BD and PTSD has been associated with faster cycles, more suicide attempts, more substance abuse, a lower quality of life, and more (hypo)manic and depressive symptoms than bipolar subjects without PTSD (Goodman et al., 2001; Quarantini et al., 2010). Of importance, life events also increase the risk of suffering from more affective episodes in BD (Simhandl, Radua, König, & Amann, 2015).

Therefore, a further psychosocial/psychotherapeutic intervention focused on psychological trauma is needed within the individual treatment plan of bipolar patients. One candidate hereby is eye movement desensitization and reprocessing (EMDR) (Shapiro, 2001), which is an integrative psychotherapy approach using standardized protocols. It includes elements of cognitive-behavioral therapy, interpersonal and body-centered therapies, as well as dual stimulation in form of mainly horizontal eye movements (Shapiro, 2009; Shapiro, 2001). A recent *Nature* study, using an animal model, revealed its mechanism of action and neuroanatomic pathway (Baek et al., 2019). EMDR therapy has been recommended by the World Health Organization (2013) for the treatment of PTSD in adults and children and adolescents (World Health Organization, 2013), but its use is currently expanding to the treatment of other conditions with comorbid psychological trauma, such as psychosis, BD, unipolar depression, anxiety disorders, and addiction with promising results (Valiente-Gómez et al., 2017). As a matter of fact, there exists no reasonable argument not to treat a comorbid trauma condition in BD, as it is state of art to treat comorbid anxiety disorders, obsessive-compulsive disorders, or substance use disorders in severe mental disorders. Furthermore, so far randomized controlled trials have shown EMDR therapy to be safe in psychosis or BD with comorbid psychological trauma. In this line, a recent article by experts in the field of BD suggested that pragmatic clinical treatment options, including those for comorbid conditions, have to be offered for bipolar subjects, even though scientific clinical evidence might still be preliminary (Post, Yatham, Vieta, & Berk, 2019).

Clinical Aspects of the Current Status of EMDR in BD

It must be stated that the current scientific evidence of the use of EMDR therapy in BD is still limited. So far, one case report study (Oh & Kim, 2014) and one randomized controlled trial (Novo et al., 2014) have been published.

The case report study describes two patients with BD and comorbid PTSD who were treated with 9 and 10 weekly EMDR sessions, respectively (Oh & Kim, 2014). Both were assessed with the Clinician-Administered PTSD Scale (CAPS) before and after EMDR therapy and pharmacotherapy dose was maintained unchanged over EMDR treatment. At the end of the EMDR treatment, both patients achieved full remission of PTSD diagnosis, which was maintained at the 1-year follow-up. EMDR was considered safe in both cases.

In the randomized controlled trial (Novo et al., 2014), 20 bipolar subjects with subsyndromal affective symptoms (see definition above) and a history of traumatic events were enrolled and randomly assigned to EMDR therapy or treatment as usual (TAU). The participants were assessed at baseline, after the treatment, at 12 weeks, and at follow-up visit at 24 weeks. The results of this study showed significant reductions in affective symptom scores, assessed using the Hamilton Depression Rating Scale and the Young Mania Rating Scale, in favor of the EMDR group after treatment. However, changes from baseline to the 24-week follow-up visit did not reach statistical significance. Regarding trauma symptoms, assessed by the CAPS and the Impact Event Scale (IES), results showed a significant improvement in the EMDR group after treatment, in both measures. At the follow-up assessment, only the IES scores remained statistically significant. The EMDR intervention was considered safe, as no adverse events occurred in the EMDR group. The loss of significance in some measures was probably due to the small sample size of this pilot trial. Of note, in this study the Shapiro standard EMDR protocol (2001) was used, with effective results; however, after analyzing in detail the experience of each EMDR therapist, they concluded that a more detailed manual for bipolar subjects would better address the patients' needs due to their often current ongoing stressful events, past complex traumas, traumatic experiences as psychiatric patients, and further comorbidities. Therefore, the same group published a specific EMDR protocol for BD (Amann et al., 2015), which included a summary about the state of art of BD, a detailed inventory to identify traumatic events across clients' lifetime, including also iatrogenic adversities such as

mechanical restraint and involuntary admissions or medication, and first affective episodes with corresponding triggers. In addition to the Shapiro standard protocol (Shapiro, 2001), they included the inverted protocol by Hofmann (Hofmann, 2010), and added new five subprotocols to improve via bilateral stimulation mood stabilization, treatment adherence, insight, a faster treatment of prodromal symptoms, and decreasing idealization symptoms of manic episodes. Currently, this protocol is being tested in a single-blind, randomized controlled, multicenter trial (Moreno-Alcázar et al., 2017), in which 82 patients with BD and a history of traumatic events are randomly allocated to EMDR therapy or supportive therapy (ST). Patients in both groups receive 20 individual EMDR or ST sessions, 60 minutes each during 6 months. The goals of the study are to replicate initial positive preliminary results and to test whether EMDR therapy is effective in the reduction of subsequent mood episodes, affective and trauma-related symptoms, and in the improvement of cognitive performance, social cognition, and functioning after therapy and at 12 and 24 months.

A second randomized controlled trial is currently ongoing in Holland that aims to recruit 36 bipolar subjects with subsyndromal symptoms and a history of traumatic events to test whether or not the EMDR standard protocol (Shapiro, 2001) improves trauma and affective symptoms in this bipolar sample (personal communication Ad de Jongh, 2019).

Can EMDR Modulate Brain Networks?

One female bipolar patient of our randomized controlled trial (Novo et al., 2014), who received 14 EMDR sessions, underwent a functional neuroimaging (fMRI) session before and after the intervention (Landin-Romero et al., 2013). The subject performed a sequential-letter version of the working memory n-back task, which was compared with 30 healthy subjects. The results showed a normalization of the bipolar patient's default mode network (DMN) after the treatment in terms of activation patterns and especially in the failure of deactivation. The DMN is a neural network that consists of a group of several brain regions that show relative hypoactivity during goal-oriented or attention-demanding tasks (Whitfield-Gabrieli & Ford, 2012) and are activated during introspective thinking, remembering personal experiences, making social and emotional judgments, visualizing the future, and performing theoretical tasks

of the mind. In lay words, if subjects have an abnormal DMN functioning, their attention is too much drawn to the past or the future, while their focus on the present is altered. Interestingly, a failure of deactivation is a typical DMN abnormality in major psychiatric disorders, having been documented in schizophrenia, BD, and unipolar depression (Goikolea et al., 2019; Landin-Romero et al., 2015; Rodríguez-Cano et al., 2017).

Our case fits with structural neuroimaging findings, which have found a normalization of important brain regions such as the medial prefrontal cortex, the amygdala, or the hippocampus after cognitive behavioral therapy, prolonged exposure therapy, or EMDR (Boukezzi et al., 2017; Helpman et al., 2016; Levy-Gigi, Szabó, Kelemen, & Kéri, 2013). For further details, we recommend a recent review on the interaction of DMN, psychiatric disorders, and childhood adversities (Allen, Sommer, Jardri, Eysenck, & Hugdahl, 2019).

It is important again to emphasize that evidence of a possible positive modulation of the DMN via EMDR therapy is preliminary with larger studies warranted, but EMDR might have a direct effect on important neurobiological structures and networks implicated in psychiatric disorders and psychological trauma.

Conclusion

In summary, there is preliminary evidence that EMDR therapy may be useful and safe for the treatment of comorbid PTSD symptoms or psychological trauma in subjects with BD. In addition, it appears to improve not only trauma-related symptoms, but also affective subsyndromal symptoms. Whether or not this intervention also prevents subsequent mood episodes has not yet been determined. The idea of a potential mood stabilizing psychotherapy in BD is currently being tested in a large randomized controlled trial with a follow-up of 2 years (Moreno-Alcázar et al., 2017). Further trials of other international groups, such as the Dutch randomized controlled trial, are relevant as well, to replicate first positive results. Considering that one of the most robust risk factors in the onset of BD is having suffered from childhood adversities (Bortolato et al., 2017) and that life events worsen the course of BD (Simhandl et al., 2015), it is a clinical necessity to evaluate and attend to adverse events in this disorders. The principal idea is that EMDR therapy is a further additional psychotherapeutic pragmatic tool for traumatized bipolar subjects, which can be added to other interventions such as psychoeducation or cognitive behavior strategies in this complicated to treat population. The implementation of

EMDR therapy in BD clinic units and mental health services may therefore offer a deeper understanding of the relationship between psychological trauma and mental health.

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