Case Report

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EMDR Therapy Modulates the Default Mode Network in a Subsyndromal, Traumatized Bipolar Patient

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Key Words
Default mode network · EMDR therapy · Bipolar disorder · Subsyndromal symptoms · Functional magnetic resonance imaging · n-back task

Abstract
Background: Some functional imaging abnormalities found in bipolar disorder are state related, whereas others persist into euthymia. It is uncertain to what extent these latter changes may reflect continuing subsyndromal affective fluctuations and whether those can be modulated by therapeutic interventions. ***Method:*** We report functional magnetic resonance imaging (fMRI) findings during performance of the n-back working memory task in a bipolar patient who showed a marked improvement in subsyndromal affective symptoms after receiving eye movement desensitization and reprocessing (EMDR) therapy in the context of a clinical trial. ***Results:*** The patient's clinical improvement was accompanied by marked changes in functional imaging, as compared to 30 healthy subjects. fMRI changes were noted particularly in deactivation, with failure of deactivation in the medial frontal cortex partially normalizing after treatment. ***Conclusions:*** This case supports the potential therapeutic overall benefit of EMDR in traumatized bipolar patients and suggests a possible neurobiological mechanism of action: normalization of default mode network dysfunction.

Introduction

A significant number of patients with bipolar disorder do not show complete remission between episodes, but continue to exhibit subsyndromal mood symptoms [1]. One factor that might contribute to such symptoms is comorbid posttraumatic stress disorder (PTSD), which has been found to be present in 16–39% of patients with bipolar disorder [2] and is associated with affective instability between episodes, especially subthreshold manic symptoms [3].

Whether affective instability between episodes in bipolar patients reflects underlying brain functional changes is unclear. It is known that some brain functional abnormalities associated with bipolar disorder improve or normalize after recovery, whereas others persist into eu-

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Table 1. Clinical and functional assessments at baseline and follow-up visits and differences in pre- and post-EMDR intervention

	Baseline	Visit				Differences pre-/post-EMDR
		2nd week	5th week	8th week	12th week end of trial	
Clinical and functional assessments						
YMRS total	11	8	10	1	1	–10
HDRS-17 total	10	5	6	3	1	–9
CGI total	4	4	4	3	3	–1
FAST total[a]	31	–	–	–	18	–13
CAPS total[b]	55	–	–	–	10	–45
IES1[c]	–2.15	–	–	–	–3.38	–1.23
IES2[c]	–2.81	–	–	–	–3.9	–1.09
IES3[c]	–0.21	–	–	–	–3.33	–3.12
QoL-PCS[d]	42.34	–	–	–	50	+7.66
QoL-MCS[d]	30.68	–	–	–	49.9	+19.32
Cognitive assessments[e]						
Digits span	11	–	–	–	11	0
Letters-numbers sequencing[f]	9	–	–	–	13	+4
Spatial localization-forward[f]	13	–	–	–	16	+3
Spatial localization-backwards	13	–	–	–	13	0
Spatial span-total[f]	13	–	–	–	15	+2

CGI = Clinical Global Impression; FAST = Functioning Assessment Short Test; IES = Impact of Event Scale (events 1–3); QoL-PCS = Physical Component of the Quality of Life Scale; QoL-MCS = Mental Component of the Quality of Life Scale.

[a] Higher scores mean poorer functioning. [b] CAPS >65 is considered as probable diagnosis of PTSD. [c] Higher negative scores are interpreted as presenting with less symptoms of trauma. [d] Higher scores on this scale are interpreted with a better perception of the physical and mental health status and with less difficulties performing everyday tasks. [e] All the cognitive variables are expressed in scaled scores. [f] Main differences are observed in working memory scores pre-/post-EMDR.

thymia [4]. Possibly relevant in this context is default mode network (DMN) dysfunction. First identified in 2001, the DMN is an interconnected series of brain regions, including prominently the medial frontal cortex and also the posterior cingulate cortex/precuneus, which are highly active at rest but deactivate during the performance of attention-demanding tasks [5, 6]. DMN dysfunction is currently implicated in major psychiatric disorders, particularly schizophrenia, but also major depression [7, 8] and bipolar disorder, where it appears to be present in manic [9], depressed [10] and euthymic [11] phases of bipolar disorder. At least 1 study has also found alterations in the DMN in PTSD [12].

We have recently found a positive effect of eye movement desensitization and reprocessing (EMDR) [13], an effective treatment in PTSD [14], in bipolar patients with subsyndromal mood symptoms and a history of traumatic events (unpublished data). Patients were randomly assigned to EMDR therapy or treatment as usual. Subsyndromal mood symptoms were evaluated by a blinded assessor at 5 time points using the Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HDRS). One patient who participated in this study and received active treatment was noted to undergo a marked clinical improvement. Coincidentally, she had also undergone functional imaging before she entered the trial as a part of another project. We therefore rescanned her at the end of the study in order to see whether clinical improvement was associated with changes in brain function. She signed the informed consent and the study was approved by the local ethical committee.

Case Report

The patient was a 37-year-old woman with a 16-year history of illness meeting DSM IV criteria for bipolar II disorder. Over the previous 2 years, despite good compliance with treatment (lamotrigine 200 mg/day) she showed affective instability with approximately 3 subsyndromal hypomanic (YMRS >8 and <14) and 4 subdepressive episodes (HDRS >8 and <14). At baseline, she was suffering from a YMRS score of 11 and an HDRS score of 10, which corresponds to a depressive mixed state with mild symp-

toms of irritability, anxiety, depression, restlessness, reduced need for sleep and negative cognitions. Traumatic events in her history included witnessing a suicide attempt by her sister, a conflictive relationship with her mother, the death of her father and an acrimonious divorce, without fulfilling the diagnosis of PTSD (Clinician-Administered PTSD Scale, CAPS, <65). During the trial the patient received 14 EMDR sessions, 90 min each over 12 weeks, from an EMDR therapist with >10 years' experience. Medication was maintained stable until the end of the active treatment phase and second functional magnetic resonance imaging (fMRI) scanning.

After EMDR treatment, at 12 weeks after baseline, the patient experienced a marked improvement in a set of assessments that included trauma scales (CAPS, Impact of Event Scale (IES), events 1–3), affective scales (YMRS, HDRS, Clinical Global Impression-Bipolar Disorder (CGI-BP)), functioning (Functioning Assessment Short Test, FAST), quality of life (Qol; SF-36 V2), and verbal and spatial working memory (part of a neuropsychological evaluation). Details are shown in table 1.

fMRI scanning during performance of a sequential-letter version of the n-back task was carried out before and after EMDR therapy. Two levels of memory load were used (1-back and 2-back) in a blocked design manner. The patient's scanning data were compared with those of 30 healthy women (mean age = 39.43, SD = 29.29, range = 20 years) during the performance of the same task on the same scanner. Statistical thresholding in the comparison group was performed at the cluster level with z = 2.3 and a corrected p value of 0.05.

Areas of significant activation in the 2-back versus baseline contrast in the controls are shown in figure 1a. Activations were seen in a network of frontal and other regions including the anterior insula bilaterally, basal ganglia, thalamus (extending to the dorsolateral prefrontal cortex), the supplementary motor and the parietal cortex (mean activation value, z = 13.10). The controls also showed areas of task-related deactivations in the medial frontal cortex and the posterior cingulate cortex/precuneus. The anterior cluster extended to include the orbitofrontal cortex and the temporal poles bilaterally (mean deactivation value, z = –14.73).

As can be seen from figure 1b, the patient's mean score was in the high normal range for activations before treatment (z = 25.41) and decreased towards the control group mean following EMDR treatment (z = 13.18). Before treatment she was an outlier for deactivations (z = 11.6), but afterward she had moved close to the mean (z = –7.79).

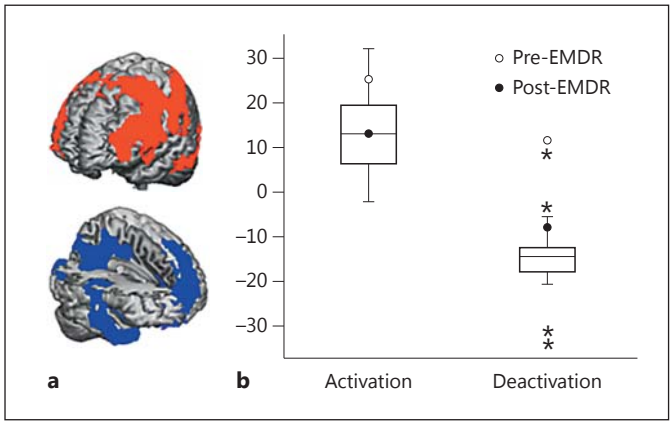

Fig. 1. a Brain images showing the areas of significant activation (above) and deactivation (below) in the control group (n = 30) during the performance of the 2-back task. **b** The box plots are showing the average levels of activation and deactivation in healthy controls across the significant clusters. The white and the black dot represent the patient's pre and post-EMDR mean activation value, respectively, within the significant clusters of the control group.

Discussion

The bipolar patient we report showed marked improvement after receiving EMDR for subsyndromal mood symptoms. The patient also showed changes on fMRI in the direction of normalization. This suggests that some of the persisting neurofunctional changes which have been found to characterize bipolar disorder may not in fact be immutable but can change alongside with changes in clinical status.

Our patient improved hereby particularly in deactivation patterns. Before treatment she was an outlier in comparison to the control group with a positive mean activation value indicative of a failure of deactivation. After treatment her mean deactivation value moved closer to the mean of the control group. Failure of deactivation is a typical DMN abnormality in major psychiatric disorders, having been documented in schizophrenia [6, 15], bipolar disorder [9, 10] and major depression [8]. The DMN is believed to have functions related to introspective or self-directed thought, such as recalling of personal experiences, making social and emotional judgments, envisioning the future and performing theory of mind tasks. Parts of the DMN are also involved in the processing of emotionally salient stimuli, and may play a role in emotional processing related to episodic memory [16].

The mechanism by which EMDR exerts its effect in PTSD is poorly understood. One leading model hypothesizes that eye movements reduce the vividness of emotional stimuli taxing the visuospatial sketchpad of working memory [17, 18]. Interestingly, our patient improved her scores in both the spatial and the verbal components of working memory after therapy, possibly providing support for this hypothesis. But whatever the underlying mechanism is, this case report suggests that EMDR is capable of modulating the function of the DMN.

Limitations of our report include those common of a single case. We suggest that the clinical remission derives

most probably from the EMDR intervention as the patient participated in a positive single-blind, controlled, randomized study (unpublished data); however it cannot be completely excluded that the clinical improvement corresponds to the natural course of the disease.

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Disclosure Statement

Francine Shapiro is the originator of EMDR therapy and shareholder in one of the training organizations. None of the other authors declare any conflicts of interest.

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