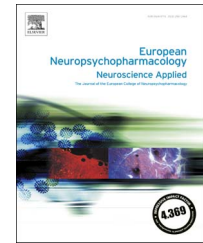




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Do patients with bipolar disorder and subsyndromal symptoms benefit from functional remediation? A 12-month follow-up study

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KEYWORDS

Bipolar disorder;
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Treatment

Abstract

We analyzed the efficacy of functional remediation, in a sample of patients with bipolar disorder who presented with subsyndromal symptoms. From a total sample of 239 patients with bipolar I and II disorder, according to DSM-IV-TR diagnostic criteria, entering a randomized clinical trial, those patients who presented with subsyndromal symptoms were selected based on a method already described by Berk and colleagues was applied. It consists of using the Clinical Global Impression-Bipolar version (CGI-BP) to establish the scores of the Hamilton Depression Rating Scale (HAM-D) and of the Young Mania Rating Scale (YMRS) that correspond with 1 in the CGI-BP. Functional outcome and mood symptoms were assessed at 6 and at 12-month follow-up.

A total of 99 patients were selected for this post-hoc analysis, allocated as follows: functional remediation ($n=33$); psychoeducation ($n=37$) and treatment as usual (TAU, $n=29$). The repeated-measures analyses at 12-month follow-up revealed a significant group \times time interaction in favour of the patients who received functional remediation when compared to psychoeducation and TAU ($F=2.93$; $p=0.02$) at improving psychosocial functioning. Finally, mood symptoms did not significantly change in any of the three groups at any time of follow-up, as shown by the non-significant group \times time interaction effect in HAM-D scores ($F=1.57$; $p=0.18$) and YMRS scores ($F=1.51$; $p=0.20$). Bipolar patients with subsyndromal symptoms improve their functional outcome when exposed to functional remediation regardless of the persistence of mood symptomatology.

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1. Introduction

Subsyndromal symptoms, especially subsyndromal depressive symptoms, have an impact on psychosocial functioning and on neurocognition (Bonnin et al., 2012, 2014; Gitlin et al., 2011; Bourne et al., 2013) in patients with bipolar disorder (BD). How to treat subsyndromal depressive symptoms is an unresolved matter in psychiatry representing a hindrance in the restoration of normal functioning. Hence, in stable patients, it is still unknown whether these types of symptoms are amenable to treatment or maybe they are present in a more severe subsample of bipolar patients. Hence, there is a need to study the efficacy of therapies in patients with subsyndromal symptoms, as well as to design interventions (both pharmacological and psychosocial) to diminish this type of symptomatology (Grande et al., 2016). So far, some studies have proven the reduction of depressive symptoms after an intervention. For instance, Deckersbach and colleagues found a reduction in the Hamilton Depression Scale (HAM-D) in patients with bipolar disorder after receiving cognitive rehabilitation (Deckersbach et al., 2010). Another cognitive-behavioral intervention based on nutrition, exercise and wellness also found a reduction in depressive scores (a four-point change in the MADRS) after treatment (Sylvia et al., 2013). With respect to hypomanic symptoms, Novo et al. (2014) found a statistical significant reduction of subsyndromal hypomanic symptoms after an EMDR intervention in bipolar patients with a history of traumatic events (Novo et al., 2014). However, all these three previous studies included patients mildly symptomatic, and maybe for that reason the reduction in symptomatology were more likely to be found. There exists a subanalysis focused on bipolar II patients reporting an improvement of subsyndromal depressive symptoms in

patients who received functional remediation (FR) (Sole et al., 2015). In that sample patients were required to be stable with strict euthymia criteria (Hamilton Depression Rating Scale = < 8 (HAM-D); Young Mania Rating Scale = < 6 (YMRS)), they improve almost a mean of two points in the HAM-D. In the present subanalysis we focused in euthymic patients with subsyndromal symptoms, that is, those with scores between 3 and 8 in the HAM-D and between 1 and 6 in the Young Mania Rating Scale (YMRS). In contrast to the previous studies (Torrent et al., 2013; Bonnin et al., 2016b) where all the sample was included, in this subanalysis the main objective is to test the efficacy of functional remediation in patients with subsyndromal symptoms both at 6-month and at 12-month follow-up. As a secondary objective, we aimed to explore if the therapy was effective at reducing the HAM-D or YMRS scores and to what extent the improvement in functioning was related to the reduction of HAM-D or YMRS. Finally, changes in neurocognition were also assessed.

We hypothesized that functional remediation will be effective at improving both psychosocial functioning and subsyndromal depressive symptoms at 6-month and at 12-month follow-up. Moreover, the reduction of subsyndromal symptoms will be related to the functional improvement.

2. Experimental procedures**2.1. Participants**

The current study is based on a sample of 99 participants from a larger multicentre study conducted in Spain (Torrent et al., 2013) and was registered with the number NCT 01370668 in www.clinicaltrials.gov. In that original study three groups were compared (functional remediation, psychoeducation and TAU) with the objec

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