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Memory performance predicts recurrence of mania in bipolar disorder following psychotherapy: A preliminary study

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ABSTRACT

Objective: Cognitive complaints are common features of bipolar disorder (BD). Not much is, however, known about the potential moderator effects of these factors on the outcome of talking therapies. The goal of our study was to explore whether learning and memory abilities predict risk of recurrence of mood episodes or interact with a psychological intervention.
Method: We analyzed data collected as part of a clinical trial evaluating relapse rates following Cognitive Behavioral Therapy (CBT) and Supportive Therapy (ST) (Meyer and Hautzinger, 2012). We included cognitive (Auditive Verbal Learning Test, general intelligence - Leistungsprüfsystem) and clinical measures from 76 euthymic patients with BD randomly assigned to either 9 months of CBT or ST and followed up for 2 years.
Results: Survival analyses including treatment condition, AVLT measures, and general intelligence revealed that recurrence of mania was predicted by verbal free recall. The significant interaction between therapy condition and free recall indicated that while in CBT recurrence of mania was unrelated to free recall performance, in ST patients with a better free recall were more likely to remain euthymic, and those with a poorer free recall were less likely to remain mania-free.
Conclusions: These findings constitute first evidence that, when considering treatment outcome in BD, differences in verbal free recall might interact with the kind of psychotherapy provided. More research is needed to determine what other areas of cognitive functioning are related to outcome in psychological interventions.

1. Introduction

The integration of non-pharmacological and pharmacological interventions has been shown to be beneficial and improves the long-term therapeutic outcomes of mood disorder patients (Lobban et al., 2007; Miklowitz et al., 2007; Oestergaard and Møldrup, 2011; Pfennig et al., 2013). The majority of studies in this field had 'prevention of relapse' as the primary outcome measure (Castle et al., 2010; Colom et al., 2003; Oestergaard and Møldrup, 2011), but improvements in medication adherence (Colom and Lam, 2005; Pampallona et al., 2004), mood symptoms (Colom et al., 2009), quality of life, and well-being have also been reported (Zilcha-Mano et al., 2014).

While some studies concluded that interventions such as cognitive behavioral therapy (CBT) are highly effective in bipolar disorder (BD), other trials including heterogeneous populations during both acute and euthymic phases of BD did not show significant changes in mood or relapse (Driessen and Hollon, 2010; Parikh, 2008). However, Colom et al.'s study showed that combining medication and psychosocial intervention in a stabilized population led to a reduced number of relapses and improved medication adherence, as well as improved psychosocial functioning. Notably these effects lasted up to 5 years post-intervention (Colom et al., 2009).

The number of studies investigating the factors predicting the efficacy of psychological treatments is limited and usually focused on predictors such as age of onset or number of prior mood episodes (Lam et al., 2009; Reinares et al., 2014). One potential predictor or moderator of outcome could be cognitive abilities. However, only few studies have investigated this area in psychiatry

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and, to date, no published study has examined cognitive functioning as part of psychological treatments for bipolar disorder (BD). In a study of older adults with anxiety disorders, there was a positive association between general intelligence and improvement in anxiety symptoms in the supportive counseling condition but not CBT (Doubleday et al., 2002). Similar findings by D'Alcante et al. revealed that higher verbal intelligence scores and immediate verbal recall predicted a better treatment response to both CBT and fluoxetine in adults with OCD (D'Alcante et al., 2012). Furthermore, lower intelligence scores appeared to be predictors of poor treatment response in adults with depression (Fournier et al., 2009) and Post-traumatic Stress Disorder (Rizvi et al., 2009). Looking at psychosis, only a very small number of studies have investigated this issue with one study reporting that treatment response to CBT in patients with psychosis was not related to cognitive performance (Granholm et al., 2008).

This kind of research is relevant because memory, executive functions and pre-morbid intelligence are essential for completing daily activities involving goal setting and planning (Lezak, 2004). Thus, it is possible that pre-existing interindividual differences in cognitive abilities affect the extent to which people benefit from different psychological interventions (Doubleday et al., 2002). However, the literature in this field is a) very heterogeneous and b) also still controversial as a number of studies have not found a consistent link between cognitive performance and response to therapy across mood disorders (Knekt et al., 2014; Voderholzer et al., 2013). Thus, further research is needed to test this link.

Results about a potential link between cognitive functioning and outcome of talking therapies are highly relevant to BD as impairment in cognitive functions have been observed across all phases of BD (Bora et al., 2009; Glahn et al., 2007; Quraishi and Frangou, 2002), and cognitive impairment is especially pronounced during the manic and depressive phases of the disorder (Robinson et al., 2006). Additionally, all of the studies we identified and that looked at whether cognitive performance is related to outcome of talking therapies have focused on acute patient populations. However, most studies evaluating psychological interventions for BD, so far, have focused on relapse prevention and recruited patients in remission or immediately after an acute episode. Therefore, it is not known whether neuropsychological functioning in remitted patients will predict or moderate the outcome of talking therapies.

In sum, studies focusing on the impact of neuropsychological performance on treatment response to talking therapies in general and to CBT specifically are lacking. Furthermore, it is unclear whether differences in cognitive performance in patients with BD are prospectively associated with the risk of relapse. The current paper focuses on unpublished neuropsychological data collected as part of a randomized controlled trial (RCT) (Meyer and Hautzinger, 2012) comparing CBT and Supportive Therapy (ST) for remitted patients with BD. In this RCT, CBT and ST were matched with regards to number and duration of sessions, and both conditions included psychoeducation and a mood diary. While CBT additionally included typical cognitive and behavioral strategies and techniques to prevent relapse or how to cope with symptoms (e.g Basco and Rush, 1996). ST had a client-centered focus and was less structured and less directive. While this RCT found no overall difference in relapse rates between CBT and ST over almost 3 years, a higher number of prior mood episodes and a lower number of attended therapy sessions were associated with a shorter time before relapse. These findings suggest that characteristics shared by both treatments may contribute to the outcome. However, this prompted us to explore *post hoc* other potential moderators, and in this case whether indicators of general intelligence, verbal learning and memory predict recurrence of mood episodes during follow-up and whether there is an indication that cognitive performance and treatment interact. Verbal learning and memory were originally chosen because prior research showed that patients with BD demonstrated deficits in this area (Deckersbach et al., 2004; van Gorp et al., 1998).

2. Methods

2.1. Participants

One-hundred-forty adults with BD were either referred by local hospitals, psychiatrists, or self-referred in response to advertisements. Nine of 107 participants who completed the baseline assessment voluntarily withdrew from the study ($n = 9$) and 22 were excluded because they did not have bipolar disorder ($n = 20$) and had current opiate or alcohol dependency ($n = 2$). The analyses for the current paper include the clinical and cognitive data from all 76 participants which were randomized into the RCT (mean age: 44.4 ± 11, 38 women) (Meyer and Hautzinger, 2012). Participants were first invited to a screening session and eligible candidates were asked to provide informed consent. At baseline, participants were administered clinical interviews (e.g. SCID-I and SCID-II) and self-rating questionnaires (e.g. Beck Depression Inventory (BDI), Self-Report Mania Inventory (SRMI)). Participants were included if 1. their primary diagnosis was BD based on the DSM-IV (American Psychiatric Association, 1994), 2. were aged between 18 and 65 years, and 3. were open to continue or start new medication. Exclusion criteria included 1. primary diagnosis was a non-affective disorder including schizo-affective disorder; 2. participants suffered from a major affective episode (depressed, mixed or mania according to SCID-I) or Bech-Rafaelsen Melancholia Scale (Bech and Rafaelsen, 1980); 3. participants suffered from disorders such as substance-induced affective disorder, or affective disorder due to a general medical condition; 4. substance dependency requiring detoxification (abuse would not qualify for exclusion); 5. intellectual disability (IQ < 80); and 6. participants currently undergoing therapy, which means that eligible participants could not take part in additional psychological treatment [for further details see Meyer and Hautzinger, 2012].

2.2. Procedures and measures

At baseline an extensive assessment was undertaken including the SCID-I to assess DSM disorders, as well as neuropsychological tests. A modification of the SCID was used during follow-up to assess recurrence of new mood episodes which only inquired about mood episodes since the last assessment (for further details see Meyer and Hautzinger, 2012). After the initial clinical assessment participants were randomly assigned to the CBT or ST condition including twenty 50–60 min sessions over 9 months. Follow up assessments by raters blind to group allocation occurred at post-treatment, month 3, 6, 9, 12 and 24. In both CBT and ST, therapists provided information on BD and a mood diary was used. While the diary was used only for monitoring mood in ST, in CBT this was strategically used for psychoeducation and jointly elaborating on links between mood changes and other factors (e.g. sleep, work load). ST provided client-centered support for whatever topic the patient brought into the session, while CBT followed a structured manual which is similar to Basco and Rush's (1996) study, including relapse prevention plans, coping strategies, communication and problem solving skills. Therapy sessions were conducted by qualified therapists with at least 1-year postgraduate training in CBT. Prior to the RCT, all therapists attended an additional 2-day workshop focusing on CBT and ST for BD including role play and video training. All therapy sessions were video-taped and weekly