



## Neuropsychological predictors of response to cognitive behavioral therapy for posttraumatic stress disorder in persons with severe mental illness



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### A B S T R A C T

This study examined whether cognitive functioning was related to treatment outcomes in persons with severe mental illness who received a cognitive behavioral therapy (CBT) program for co-occurring posttraumatic stress disorder (PTSD). The study sample was drawn from a larger controlled trial of 108 persons with severe mental illness and PTSD comparing the effects of CBT with treatment as usual on PTSD and related outcomes, with assessments conducted at baseline, post-treatment, and 3- and 6-month follow-ups. Among the 54 persons in CBT, 49 were administered a neuropsychological battery at baseline and 40 were exposed to the CBT program. Statistical analyses of these 40 participants were conducted to evaluate whether cognitive functioning was related to participation in the CBT program, completion of homework assignments, and improvements in PTSD, and other outcomes. Cognitive functioning was not related to participation in CBT or completion of homework. Lower cognitive functioning predicted less learning of information about PTSD at post-treatment and follow-up, but not less clinical benefit from CBT in PTSD diagnosis or symptoms, other symptoms, or health. The results suggest that cognitive impairment does not attenuate response to the CBT for PTSD program in persons with severe mental illness. Clinical Trials.gov Identifier: NCT00053690

### 1. Introduction

Psychologically traumatic events such as physical and sexual abuse/assault, witnessing violence, and the sudden and unexpected death of a loved one are common in persons with psychotic and other severe mental illnesses, both before and following onset of the disorder (Khalifeh et al., 2015; Roy et al., 2014). Trauma exposure in this population is associated with worse psychiatric and other symptoms, higher levels of substance abuse, worse psychosocial functioning, and greater use of acute treatment services (Bebbington et al., 2004; Goodman et al., 2001; Ng et al., 2016). As would be expected from the high rates of trauma in persons with severe mental illness, high rates of posttraumatic stress disorder (PTSD) have also been documented (Grubaugh et al., 2011; Mueser et al., 2004a, 2004b). PTSD has been hypothesized to mediate the association between trauma exposure and worse outcomes in people with severe mental illness (Cusack et al., 2013; Mueser et al., 2002; Subica et al., 2011). To address this problem, recent efforts have focused on developing or adapting treatments for

PTSD designed to accommodate the special challenges of this population, such as lack of social support, psychotic symptoms, cognitive impairment, severe depression, and suicidal ideation (Mueser et al., 2004a, 2004b; Rosenberg et al., 2001).

In the general population, there is strong evidence for the effectiveness of three psychotherapeutic approaches to the treatment of PTSD, including prolonged exposure, cognitive restructuring (also referred to as cognitive processing therapy, cognitive therapy, and cognitive behavioral therapy), and eye movement desensitization and reprocessing (EMDR) therapy (Ehring et al., 2014; Watts et al., 2013). Several randomized controlled trials have established the feasibility and evaluated the effectiveness of adaptations of these interventions for PTSD in persons with severe mental illness. One randomized controlled trial from the Netherlands showed that 8 weekly sessions of prolonged exposure or EMDR were more effective than usual services at reducing PTSD symptoms and diagnoses in 155 persons with a psychotic disorder, with effects maintained at 6 months follow-up (Van den Berg et al., 2015).

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Three randomized controlled trials have evaluated the CBT program for PTSD in persons with severe mental illness, a 12–16 session individual therapy approach that includes psychoeducation about PTSD, breathing retraining, and cognitive restructuring to address trauma-related beliefs (Mueser et al., 2009). The first randomized controlled trial was conducted in a rural area in northeastern U.S. with 108 persons with serious mental illness and severe PTSD, and found that the CBT program more effective than usual services at improving PTSD and depression, with effects maintained three and six months later (Mueser et al., 2008). The second randomized controlled trial was conducted in an urban area in eastern U.S. with 201 persons with serious mental illness and severe PTSD, and compared the CBT program with a brief (three session) program that included just the psychoeducational and breathing retraining components of the full program (Mueser et al., 2015). The CBT program was found to be more effective at improving PTSD outcomes and overall functioning than the brief program, with effects maintained six and 12 months later. A third randomized controlled trial from the United Kingdom comparing the CBT program with usual services in 61 individuals with schizophrenia and PTSD reported significant but comparable reductions in PTSD and other symptoms for both groups at the six month post-treatment assessment and 12-month follow-up (Steel et al., 2017). However, participants in this study had significant less severe PTSD symptoms than those in the two U.S. studies of the CBT program.

The evidence supporting the effectiveness of the CBT program for PTSD in persons with severe mental illness raises the question of whether it is more effective for some clients than others. Cognitive functioning is of particular interest as a potential moderator of treatment effectiveness. Compared to health controls, significantly greater grey matter loss in the anterior insula/dorsal anterior cingulate-based network thought to reflect impaired executive functions has been reported across a diverse range of diagnostic groups (schizophrenia, bipolar disorder, depression, addiction, obsessive-compulsive disorder, and anxiety) and has been hypothesized to reflect a shared neurobiologic substrate to mental illness (Goodkind et al., 2015; McTeague et al., 2017). Cognitive impairment is a common, stable feature of schizophrenia (Harvey, 2013; Heaton et al., 2001) that shows only modest associations with symptoms (Hughes et al., 2003; Dominguez et al., 2009; Rund et al., 2004; Ventura et al., 2010). Two meta-analyses of the research literature on cognitive functioning in schizophrenia conducted 1990–2006 (Dickinson et al., 2007) and 2006–2013 (Schaefer et al., 2013) reported remarkably similar findings, with large mean effect sizes across all cognitive tests of  $g = -0.98$  and  $-1.03$ , respectively, and the worst performance on digit symbol coding,  $g = -1.57$  and  $-1.55$ , respectively. Although severity of cognitive impairment is greater in schizophrenia than bipolar disorder (Bortolato et al., 2015; Depp et al., 2012), reduced cognitive functioning is often present in bipolar disorder (Dickerson et al., 2004), and meta-analyses have found lower cognitive performance in persons with bipolar disorder I compared to healthy controls (Bostock et al., 2017; Torres et al., 2007). Reduced cognitive functioning has also been proposed to reflect a stable marker of major depression (Bortolato et al., 2014; Murrough et al., 2011). A meta-analysis by Ahern and Samkovska (2017) reported that persons with a first episode of major depression demonstrated significant cognitive impairments compared to healthy controls, with remission associated with small improvements in processing speed and shifting but persistent impairment in inhibition and verbal fluency. Meta-analyses of more heterogeneous samples of persons with major depression on the other hand show moderate deficits across the range of cognitive domains (Porter et al., 2015).

Reduced cognitive functioning is also predictive of a greater likelihood of developing PTSD or more severe PTSD symptoms following exposure to a traumatic event (Breslau et al., 2006; McNally and Shin, 1995; Yurgil et al., 2014), and is a common clinical feature associated with the disorder (Golier and Yehuda, 2002; Woon et al., 2010). People with severe mental illness who have lower levels of cognitive

functioning benefit less from psychosocial interventions (Kurtz, 2011) such as social skills training (Kern et al., 1992; Mueser et al., 1991) and supported employment (McGurk et al., 2003). However, research has not examined whether cognitive functioning is predictive of attenuated benefit from cognitive behavioral interventions for PTSD, including the CBT program. The present study addresses this question.

## 2. Methods

This study reports on previously unreported data from a randomized controlled trial of the CBT program (Mueser et al., 2008). While main study results have been reported previously (Mueser et al., 2008), data on cognitive functioning as related to treatment participation and outcomes have not yet been reported. All of the study procedures were approved by the Rutgers and Dartmouth IRBs. The study took place at four publicly funded community mental health centers in the northeastern U.S. (New Hampshire and Vermont) and compared the effectiveness of the CBT program to treatment as usual for improving PTSD and other psychiatric symptoms in 108 persons with serious mental illness, with assessments conducted at post-treatment and 3- and 6-month follow-ups.

Intent-to-treat statistical analyses indicated that participants in the CBT program improved significantly more in PTSD symptoms and diagnosis, knowledge of PTSD, trauma-related cognitions, depression, and anxiety at post-treatment than those in treatment as usual, with treatment gains maintained at the follow-up assessments. Furthermore, reductions in PTSD symptoms in participants who received the CBT program were mediated by decreases in trauma-related cognitions. Finally, participants with higher rates of homework completion improved more in PTSD and other symptoms than those with lower rates of homework completion. The study methods and results have been previously reported (Mueser et al., 2008).

At the baseline assessment participants who were randomized to the CBT program (but not those in treatment as usual) were also administered a neuropsychological battery to assess cognitive functioning. The present report examined the relationship between cognitive functioning at baseline and response to the CBT program at post-treatment and follow-up. These cognitive data have not been previously reported.

### 2.1. Participants

Inclusion criteria for study participants were: 1) minimum 18 years old; 2) meets States of New Hampshire or Vermont definition of severe mental illness as defined by DSM-IV (American Psychiatric Association, 1994) and persistent impairment in work, school, or ability to care for oneself; 3) DSM-IV diagnosis of schizophrenia, schizoaffective disorder, major depression, or bipolar disorder, based on the Structured Clinical Interview for DSM-IV (First et al., 1996); 4) current DSM-IV diagnosis of PTSD, based on the Clinician Administered PTSD Scale (CAPS), schizophrenia version (Blake et al., 1995; Gearon et al., 2004); and 5) interested in receiving treatment for PTSD and legally able to and willing to provide informed consent to participate in the study. Exclusion criteria were: 1) hospitalization or suicide attempt in the past three months, and 2) substance dependence within the past three months. Individuals with a DSM-IV diagnosis of borderline personality disorder, based on the SCID-II (First et al., 1994), were included if they met the other criteria to participate in the study.

A total of 54 participants were randomized to the CBT program, of whom 49 (91%) completed the neurocognitive evaluation. The demographic and clinical characteristics of the participants who received the neurocognitive assessment at baseline are summarized in Table 1. The average age of the participants was in the mid 40 s, with approximately three-quarters being women, 82% had a major mood disorder and 18% had a schizophrenia-spectrum disorder, and 67% had borderline personality disorder.

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