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Predicting trauma-focused treatment outcome in psychosis

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ABSTRACT

Objective: Although TF treatments are effective in patients with psychosis, it is unknown whether specific psychosis-related obstacles limit the effects, and what determines good outcome.
Methods: Baseline posttraumatic stress disorder (PTSD) symptom severity and seven psychosis-specific variables were tested as predictors in patients with a psychotic disorder *and* PTSD ($n = 108$), who received eight sessions of TF treatment (Prolonged Exposure, or Eye Movement Desensitization and Reprocessing therapy) in a single-blind randomized controlled trial. Multiple regression analyses were performed.
Results: Baseline PTSD symptom severity was significantly associated with posttreatment PTSD symptom severity, explaining 11.4% of the variance. Additionally, more severe PTSD at baseline was also significantly associated with greater PTSD symptom improvement during treatment. After correction for baseline PTSD symptom severity, the model with the seven baseline variables did not significantly explain the variance in posttreatment PTSD outcome. Within this non-significant model, the presence of auditory verbal hallucinations contributed uniquely to posttreatment outcome but explained little variance (5.4%). Treatment completers and dropouts showed no significant difference on any of the psychosis-related variables.
Conclusions: Given the low predictive utility of baseline psychosis-related factors, we conclude that there is no evidence-based reason to exclude patients with psychotic disorders from TF treatments. Also, we speculate that patients with psychosis and severe baseline PTSD might derive more benefit if given more than eight sessions.
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1. Introduction

Childhood adversities and comorbid posttraumatic stress disorder (PTSD) are common in psychosis (Achim et al., 2011; de Bont et al., 2015; Matheson et al., 2013), but are often underdiagnosed and undertreated (de Bont et al., 2015; Lommen and Restifo, 2009). A recent randomized controlled trial (RCT) found TF treatments, prolonged exposure (PE) and eye movement desensitization and reprocessing (EMDR) therapy to be effective and safe in patients with long-standing psychotic disorders (van den Berg et al., 2015). Similarly, cognitive restructuring was found to be effective in two controlled trials with

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patients suffering from severe mental illnesses of which a subgroup had a psychotic disorder (Mueser et al., 2015; Mueser et al., 2008). Interestingly, despite the presence of a severe psychiatric disorder, the outcomes and dropout rates in these TF treatment studies were similar to studies with general PTSD samples (Bradley et al., 2005; Hembree et al., 2003).

Based on the above results, it seems that meeting the criteria for a psychotic disorder does not necessarily predict poor TF treatment outcome. However, it remains unclear which factors influence TF treatment outcome in this subgroup of individuals with psychosis and whether specific obstacles need to be taken into account when initiating treatment. It is important to identify these factors in order to disseminate effective TF treatments in psychosis. This information may also elucidate whether it's necessary to adapt TF treatment protocols in this patient group to improve effects and reduce the likelihood of dropout.

Of the many studies examining the potential predictors of TF treatment outcome, most focused on PE, cognitive reprocessing, or other cognitive behavioral therapies. However, the results have not been consistent, e.g. some predictors were found in one study but not others, and vice versa. Consequently, despite the large number of studies on this topic, no robust predictors of TF treatment outcome have been detected, with the exception of baseline severity of PTSD symptoms. Greater baseline PTSD symptom severity has repeatedly predicted greater posttreatment PTSD symptom severity (Blanchard et al., 2003; Hembree et al., 2004; Moser et al., 2010; Popiel and Zawadzki, 2013; Taylor, 2003; van Emmerik et al., 2011; van Minnen et al., 2002). Interestingly, greater baseline PTSD severity was also found to be associated with greater improvements by some (Elliott et al., 2005; Foa et al., 1995; Forbes et al., 2003; Karatzias et al., 2007; Rizvi et al., 2009; Thrasher et al., 2010), although this was not found by others (de Kleine et al., 2014; Speckens et al., 2006). Part of the larger improvements may be explained by regression to the mean. Nevertheless, the broader picture appears to be that patients with high baseline PTSD symptom severity do benefit (perhaps even more than patients with lower scores) from TF treatment with regard to symptom reduction, but their posttreatment end state is still relatively high compared to patients with lower baseline scores.

The present study aimed to determine the predictive value of several baseline factors that characterize patients with a psychotic disorder, that could be expected to influence TF treatment outcome or dropout. Because researchers and clinicians tend to exclude patients with psychotic disorders from effective TF treatments (Becker et al., 2004; Meyer et al., 2014; Ronconi et al., 2014), it is important to test the validity of this assumption. Because the common denominator for excluding patients from treatment is the presence of psychotic symptoms, we included the most important symptom clusters of psychosis, i.e. *paranoia, auditory verbal hallucinations,* and *negative symptoms* as potential predictor variables.

Exclusion of patients with psychotic disorders from TF treatments is likely to be influenced by the fear that these treatments will destabilize patients or exacerbate symptoms and induce suicidal tendencies or other adverse events (Becker et al., 2004; Foa et al., 2013; Gairns et al., 2015). In contrast with these beliefs, in the parent trial of the current study, TF treatment was found to reduce symptom exacerbation and adversities, such as self-harm or psychiatric hospitalization (van den Berg et al., 2016). However, because it remains unclear to what extent the presence of markers of instability at baseline, such as *suicide risk* or *the presence of recent adversities*, affect treatment outcome, we included these potential predictor variables.

Besides symptoms of psychosis and instability factors that are associated with this patient group, we selected two additional factors that are highly prevalent in these patients and are expected to interfere with the ability to benefit from TF treatment, i.e. working memory difficulties, and antipsychotic medication. Working memory problems are common in patients with psychosis (Forbes et al., 2009; Lee and Park, 2005) and the presence of cognitive functioning problems is one of the reasons why clinicians tend to exclude patients from TF treatment (Salyers et al., 2004). We selected this specific cognitive factor, since *working memory capacity* is also associated with TF treatment effects (Gunter and Bodner, 2008; van den Hout et al., 2010; van den Hout et al., 2011). The majority of patients with psychotic disorders use antipsychotic medications, which are associated with many side-effects, e.g. (Young et al., 2015). Moreover, some of these side-effects, e.g. sedation, emotional numbing, and reduced speed of processing (Faber et al., 2012; Moncrieff et al., 2009; Moritz et al., 2013; Saeedi et al., 2006), may undermine the possibility of patients to benefit from TF treatment, e.g. by interfering with the ability to follow treatment procedures, or difficulty to activate the 'fear structure' (Rauch and Foa, 2006). Indeed, the use of psychotropic medication in a sample of veterans was found to be associated with less PTSD symptom reduction during TF treatment (Goodson et al., 2013). Therefore, we included *chlorpromazine hydrochloride dose equivalents* as a potential predictor.

In the present sample of patients, with both psychotic disorder and posttraumatic stress disorder, we first tested the hypothesis that, also in the current sample, baseline posttraumatic stress disorder severity would significantly predict TF treatment outcome. Secondly, we tested the hypothesis that psychosis-specific baseline factors (paranoia, auditory verbal hallucinations, negative symptoms, suicide risk, recent adversities, working memory, and antipsychotic medication) would add unique variance beyond that already explained by baseline posttraumatic stress disorder severity. We also tested the hypothesis that treatment completers and dropouts would differ on these variables at baseline.

2. Experimental materials and methods

2.1. Participants

Participants were 108 patients with a psychotic disorder and PTSD who were allocated to TF treatment (PE or EMDR therapy) in a recently published multicenter single-blind RCT investigating TF treatments in psychosis (van den Berg et al., 2015). The participants were characterized by long-standing psychotic disorders (mean duration = 18.5, SD = 12.5 years). The MINI-International Neuropsychiatric Interview-Plus (Sheehan et al., 1997) DSM-IV-TR diagnoses for the sample were: 60.2% schizophrenia, 29.6% schizoaffective disorder, 3.7% bipolar disorder with psychotic features, 3.7% psychotic disorder not otherwise specified, and 2.8% depression with psychotic features. The mean age of the current sample was 41.5 (10.8) years and 44.4% was male. Most participants had experienced repeated and severe childhood trauma (van den Berg et al., 2015). All participants met the full criteria for chronic PTSD on the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995). Complete details of the study procedure are available elsewhere (de Bont et al., 2013; van den Berg et al., 2015).

2.2. Procedure

Both PTSD symptom severity and the other potential predictor variables were assessed at baseline. PTSD symptom severity was also assessed posttreatment. There were 24 treatment dropouts: 9 never started and 15 dropped-out during treatment (van den Berg et al., 2015). The prediction of posttreatment outcome was performed on the intention-to-treat sample of participants with posttreatment data ($n = 91$). Analyses regarding dropout were performed on the total sample ($n = 108$). The study design was approved by the Medical Ethics Committee of the VU University Medical Center (NL:36,649.029.12).

2.3. Treatment

TF treatment consisted of eight weekly 90-min sessions of either PE or EMDR therapy (Foa et al., 2007; Shapiro, 2001). The first session comprised psycho-education about PTSD and the development of a hierarchy of the most intrusive trauma memories. The active TF treatment

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