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Pharmacotherapy for social anxiety disorder: Interpersonal predictors of outcome and the mediating role of the working alliance

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ABSTRACT

Social anxiety disorder (SAD) is highly prevalent and associated with high levels of impairment and distress. Therapies for SAD leave many patients symptomatic at the end of treatment, and little is known about predictors or mechanisms of treatment outcome. Given the interpersonal dysfunction fundamental to SAD, this study investigated whether prominent interpersonal features of SAD (submissive behavior, childhood maltreatment, suppression of anger, and depression) predicted attrition and response to pharmacotherapy and whether the working alliance mediated these relationships. This is the first study to examine the role of the working alliance in pharmacotherapy for SAD. One hundred thirty-eight treatment-seeking individuals with a primary diagnosis of SAD received 12 weeks of open treatment with paroxetine. Higher levels of depression predicted greater severity of SAD at the end of treatment, and higher levels of submissive behavior and childhood emotional maltreatment predicted a greater probability of attrition from treatment. The psychiatrist-assessed working alliance mediated response to pharmacotherapy for individuals who reported a history of emotional maltreatment. These results identify variables that predict pharmacotherapy outcome and emphasize the importance of the working alliance as a mechanism of treatment response for those with a history of emotional maltreatment. Implications for person-specific treatment selection are discussed.

1. Introduction

Social anxiety disorder (SAD) is highly prevalent, with lifetime rates as high as 12.1% (Kessler et al., 2005), and is associated with significant social, occupational, and educational impairment (Aderka et al., 2012; Kessler, 2003; Schneier et al., 1994). Although several evidence-based treatments exist for SAD (Schneier, Bruce, & Heimberg, 2014), many patients fail to adequately respond. In one study, 42% of patients receiving group cognitive behavioral therapy (CBT) either dropped out of treatment or did not respond (Heimberg et al., 1998), and response rates for selective serotonin reuptake inhibitors (SSRIs) are similar (Liebowitz, Gelenberg, & Munjack, 2005; Van Ameringen et al., 2001). Furthermore, in studies of SSRI pharmacotherapy, only three of four patients complete the trial (Liebowitz et al., 2005; Van Ameringen et al., 2001), indicating that attrition rates, in addition to response rates, are problematic.

The National Institute of Mental Health Strategic Plan (2015) called for the study of personalized mental health care to augment the efficacy of evidence-based treatments. Numerous studies have investigated predictors of outcome of psychological treatments for SAD (e.g., Craske et al., 2014; Mululo et al., 2012). However, only a few studies have identified baseline predictors of pharmacotherapy outcomes. Early childhood onset of SAD, duration of SAD (Van Ameringen, Oakman, Mancini, Pipe, & Chung, 2004), and presence of the minor allele polymorphism of gene RGS2 (Stein et al., 2014) predicted poorer response to treatment with sertraline. In a previous analysis of the dataset which forms the basis of the current paper, a history of emotional maltreatment predicted attrition from paroxetine pharmacotherapy (Bruce, Heimberg, Blanco, Schneier, & Liebowitz, 2012).

Furthermore, researchers have recently explored variables that account for (i.e., mediate) improvements, another line of inquiry pertaining to treatment personalization. Although no study has examined mechanisms of change in pharmacotherapy for SAD, recent studies (e.g., Goldin et al., 2016; Gu, Strauss, Bond & Cavanagh, 2015) have explored mechanisms of change in CBT and acceptance-based interventions. Only one study has jointly considered prediction and

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mediation (Newman & Fisher 2013), although this study focused on GAD rather than SAD.

Research designs that examine baseline predictors and the associated mechanisms through which such variables exert their influence permit the understanding of (a) who is most likely to respond to a given treatment and (b) why individuals with these particular characteristics are more (or less) likely to respond to treatment. Given the centrality of interpersonal concerns to SAD (Heimberg, Brozovich, & Rapee, 2014), the current study focused on interpersonally-focused variables (depression, childhood maltreatment, anger suppression, submissive behavior) that are routinely and robustly associated with SAD and/or with the outcome of pharmacotherapy for SAD and examined whether they exert their influence through the therapeutic relationship.

1.1. The role of the working alliance in social anxiety treatment

The working alliance (WA) is the therapeutic bond and agreement between patient and clinician on tasks and goals (Bordin, 1979). Compared to patients with panic disorder, individuals with SAD have poorer WAs (Haug et al., 2016). The WA predicted end-state social anxiety in an exposure to a feared social situation (Hayes, Hope, VanDyke, & Heimberg, 2007) and in one session of CBT combined with virtual reality therapy (Moldovan & David, 2014). However, these studies did not examine the alliance as a mediator of change.

WA is associated with outcome of pharmacotherapy for adults with major depressive disorder (MDD; Zilcha-Mano, Roose, Barber, & Rutherford, 2015), bipolar disorder (Gaudiano & Miller 2006), substance dependence (Dundon et al., 2008), and psychotic disorders (Wykes, Rose, Williams, & David, 2013). Importantly, no study to date has examined the role of WA in pharmacotherapy for SAD.

1.2. Interpersonal variables associated with SAD

A large number of studies examining predictors of therapeutic outcome in SAD have tended to examine variables only marginally related to core features of the disorder. For example, studies have focused on SAD subtype (e.g., Slaap, van Vilet, Westenberg, & Den Boer, 1996), age of onset (Van Ameringen et al., 2004), and duration of illness (Stein, Stein, Pitts, Kumar, & Hunter, 2002). Still further, although the studies mentioned above indicate predictive utility of the identified variables, other studies contradict their findings (Chen et al., 2007; Slaap et al., 1996), leaving a mixed and mostly inconclusive picture. We believe that when examining variables that may inform treatment selection and treatment process for patients grouped by diagnosis (e.g., SAD), studies should select variables that are central to the diagnostic picture rather than more peripheral. For these reasons we selected interpersonally-oriented variables relevant to SAD as both our predictor variables and our mediating variable (i.e., the therapeutic relationship).

Below, we review the evidence for several interpersonal predictors that have been consistently associated with social anxiety. We briefly discuss 1) the co-occurrence of these predictors and social anxiety, 2) the interpersonal disruption associated with these predictors, and 3) the evidence of their influence on social anxiety treatment outcome. We hypothesize that the interpersonal difficulties associated with these predictors may negatively impact the working alliance and thus pharmacotherapy outcome overall.

1.2.1. Depression

Individuals with SAD have a two-fold increase in risk for developing depression compared to those without SAD (Beesdo et al., 2007), and compared to individuals without a psychiatric disorder, individuals with SAD were 3.5 times more likely to develop a depressive disorder during a period of 34–50 months (Stein et al., 2001). Individuals with depression have poorer quality parental relationships, less optimal peer relationships, and fewer friends (Field, Diego, & Sanders, 2001).

Higher levels of depression are associated with poorer response to CBT for SAD (Chambless, Tran, & Glass, 1997; Collimore & Rector, 2012; Hedman et al., 2012). No research to our knowledge has examined depression as a predictor of the outcome of pharmacotherapy for SAD. The WA mediated the relationship between interpersonal functioning and depressive symptoms in CBT for depression (Howard, Turner, Olkin, & Mohr, 2006). The WA also mediated the association between personality traits and better outcomes for depressed individuals treated with interpersonal therapy, CBT, or antidepressant medication (Kushner, Quilty, Uliaszek, McBride, & Bagby, 2016).

1.2.2. Childhood maltreatment

Simon et al. (2009) found that 70% of a treatment-seeking sample of patients with SAD experienced at least one type of childhood maltreatment. Interpersonally, children with a history of maltreatment display less intimacy, more conflict, and more negative and less positive affect in relationships (Parker & Herrera, 1996). A greater frequency and severity of childhood maltreatment has been associated with a lower quality of the therapeutic alliance in a sample of hospitalized adolescents (Eltz, Shirk, & Sarlin, 1995) and, notably, in a sample of patients with SAD (Alden, Taylor, Laposa, & Mellings, 2006). A history of parental abuse during childhood predicted poorer response to CBT for SAD (Alden et al., 2006), and a history of emotional maltreatment predicted higher rates of attrition from paroxetine pharmacotherapy (Bruce et al., 2012).

1.2.3. Anger suppression

Individuals with SAD report higher levels of anger relative to individuals without SAD (Erwin, Heimberg, Schneier, & Liebowitz, 2003), and they spend more time during the day experiencing anger than non-anxious individuals (Kashdan & Collins, 2010). They also suppress the expression of anger more than their non-anxious counterparts (Erwin et al., 2003; Moscovitch et al., 2008). Among individuals with SAD, those with both high trait anger and the tendency to suppress the expression of anger demonstrated the most distress and impairment (Versella, Piccirillo, Potter, Olino, & Heimberg, 2016). Anger suppression is associated with reduced interest in other people and a decrease in the frequency with which one expresses his or her own feelings, thoughts, and needs (Sperberg & Stabb, 1998). Furthermore, individuals with SAD who suppress their anger have poorer treatment response and higher rates of attrition from CBT (Erwin et al., 2003).

1.2.4. Submissive behavior

According to ethological models, submissive behavior attenuates competition for social status between people (Weeks, Heimberg, & Heuer, 2011). Examples of submissive behaviors include body collapse and vocal pitch peak elevation (Weeks et al., 2011). No research has examined the association of submissive behavior to treatment outcome. Interestingly, animal models have indicated that fluoxetine reduces submissive behavior in rats (Malatynska, Rapp, Harrawood, & Tunnicliff, 2005). Although submissive behavior has a negative impact in the eyes of others (Gilbert, 2014; Weeks et al., 2011), no research to date has examined the influence of submissive behavior on the WA.

1.3. Current study

This study examined various interpersonally-oriented predictors of response to pharmacotherapy and further examined whether these predictors exerted their effect through the WA, a relationship-centric variable, in an open trial of pharmacotherapy for SAD.

We hypothesized that higher levels of childhood maltreatment, depression, anger, and submissive behavior would be related to the following outcomes: smaller reductions in social anxiety, lower probability of achieving responder status, greater attrition, and lower quality of life (QOL). We also hypothesized that the association between the predictors and outcome would be mediated by the WA.[1]