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Clinical presentation and pharmacotherapy response in social anxiety disorder: The effect of etiological beliefs

Jonah N. Cohen [a], Carrie M. Potter [a], Deborah A.G. Drabick [a], Carlos Blanco [b,c], Franklin R. Schneier [b,c], Michael R. Liebowitz [b], Richard G. Heimberg [a,*]

[a] Department of Psychology, Weiss Hall, Temple University, 1701 North 13th Street, Philadelphia, PA 19122, USA
[b] Department of Psychiatry, Columbia University, Harness Pavilion, 180 Ft. Washington Avenue, New York, NY 10032, USA
[c] New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032, USA

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ABSTRACT

Therapies for social anxiety disorder (SAD) leave many patients symptomatic at the end of treatment and little is known about predictors of treatment response. This study investigated the predictive relationship of patients' etiological attributions to initial clinical features and response to pharmacotherapy. One hundred thirty-seven individuals seeking treatment for SAD received 12 weeks of open treatment with paroxetine. Participants completed the Attributions for the Etiology of Social Anxiety Scale at baseline in addition to measures of social anxiety and depression at baseline and over the course of treatment. A latent class analysis suggested four profiles of etiological beliefs about one's SAD that may be characterized as: *Familial Factors*, *Need to be Liked*, *Bad Social Experiences*, and *Diffuse Beliefs*. Patients in the more psychosocially-driven classes, *Need to be Liked* and *Bad Social Experiences*, had the most severe social anxiety and depression at baseline. Patients in the *Familial Factors* class, who attributed their SAD to genetic, biological, and early life experiences, had the most rapid response to paroxetine.# These results highlight the effect of biological and genetically-oriented etiological beliefs on pharmacological intervention, have implications for person-specific treatment selection, and identify potential points of intervention to augment treatment response.

1. Introduction

Social anxiety disorder (SAD) is highly prevalent, with up to 13% of the U.S. population experiencing SAD at some point during their lives (Ruscio et al., 2008). SAD is characterized by a marked and/or persistent fear of one or more social situations and is associated with significant functional impairment (Aderka et al., 2012; American Psychiatric Association, 2013; Schneier et al., 1994). Individuals with SAD have higher rates of alcohol and drug dependence, depression, suicide, and use of medical resources, as well as diminished vocational and educational attainment (Acarturk et al., 2009; Katzelnick et al., 2001; Van Ameringen et al., 2003).

Although there are well-validated treatments for SAD (Heimberg and Magee, 2014; Schneier et al, 2014; Wong et al., 2012), response rates for even the best empirically supported treatments suggest that many treated patients remain symptomatic. For instance, in one study, 35% of patients receiving the monoamine oxidase inhibitor phenelzine and 42% of patients receiving group cognitive behavioral therapy (CBT) were classified as non-responders (Heimberg et al., 1998). Moreover, trials of serotonin-norepinephrine reuptake inhibitors and selective serotonin reuptake inhibitors (SSRIs) suggest similar rates of non-response. For example, non-response rates ranged from 41% with venlafaxine (Liebowitz et al., 2005) to 45% with paroxetine (Stein et al., 1998) to 47% with sertraline (Van Ameringen et al., 2001).

In an effort to augment treatment response for mental disorders, the National Institute of Mental Health (NIMH) called for the study of elements of personalized mental health care in its Strategic Plan (NIMH, 2008). Personalized medicine seeks to identify variables related to both patient and treatment modality that optimize treatment outcomes. The scope of possible avenues of research is wide and include pharmacogenetics, pharmacotherapy dosing schedules, and predictors of treatment outcome that inform patient-treatment matching (Arch and Ayers, 2013).

Only a handful of studies have examined variables that impact treatment outcome in SAD. Having an expectation of benefiting from group CBT predicts enhanced treatment response (Chambless et al., 1997; Safren et al., 1997). Among patients with SAD, certain cognitive characteristics (e.g., cognitive reappraisal self-efficacy, negative cognitive appraisal) may mediate response to CBT (Goldin et al., 2012;

* Correspondence to: Adult Anxiety Clinic of Temple University, Department of Psychology, Weiss Hall, 1701 N. 13th Street, Philadelphia, PA 19122. Tel.: +1 215 204 1575; fax: +1 215 204 5539.
E-mail address: heimberg@temple.edu (R.G. Heimberg).

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Hofmann, 2000). However, only a few published studies have examined predictors of response to pharmacotherapy for SAD (Bruce et al., 2012). To our knowledge, there are no published studies investigating whether and to what extent patients' cognitive characteristics impact response to pharmacotherapy for SAD, information potentially relevant to tailoring to personalizing therapeutic intervention.

1.1. Attributions as a potential predictor of pharmacotherapy response in SAD

Etiological attributions (i.e., causal explanations of the etiology of one's disorder) are one type of cognitive characteristic that may impact treatment response. Causal attributions have been associated with both etiology and maintenance of SAD (Hope et al., 1989). For example, individuals with SAD tend to attribute positive outcomes to external factors and negative outcomes to internal factors. This attributional bias strengthens as social anxiety intensifies (Coles et al., 2001). Though this literature is not specifically focused on attributions about etiology, attributions about causality play an important role in SAD.

In the context of psychopathology more generally, the attributions that individuals make about their disorder may influence the steps they take in the pursuit of treatment (Roth and Eng, 2002). Although there is currently no research that investigates whether etiological beliefs directly influence treatment response, research suggests that etiological beliefs influence *perceived* efficacy of treatment (Furnham, 1995). Thus, matching treatments to patients' etiological beliefs may lead to better treatment response based on expectancy effects, which as noted above, have been associated with response to CBT for SAD (Chambless et al., 1997; Safren et al., 1997). Thus, given the relevance of causal attributions to SAD, investigating the clinical effect of etiological attributions is warranted.

1.2. Present study

Aligned with the NIMH's call for the personalization of mental health care, we sought to identify baseline patient characteristics differentially related to clinical presentation and response to pharmacotherapy, information which may inform ways to augment treatment response. This work has the potential to add to an emerging body of literature on personalization of treatment for SAD (e.g., Craske et al., 2014) and to extend this research by investigating personalization within the context of etiological attributions and pharmacotherapy, two previously unexplored domains.

Thus, we examined whether individuals' attributions about the etiology of their SAD are related to their the initial severity of their symptoms and predictive of their response to pharmacotherapy with paroxetine, an SSRI demonstrated to be efficacious in the treatment of SAD (Allgulander, 1999; Baldwin et al., 1999; Stein et al., 1998). We hypothesized that individuals would differ both in the types of attributions that they endorse (e.g., genetics, family environment, stressful social experiences), as well as frequency of attributions (e.g., moderate vs. high levels of genetic attributions). We used latent class analysis (LCA) to identify distinct profiles of SAD-related etiological attributions. We expected that classes of individuals whose profiles are characterized by genetic/biological attributions would be associated with a more severe clinical presentation at baseline. Additionally, we expected classes of individuals with profiles emphasizing genetic/biological attributions to exhibit better response to paroxetine, as these types of etiological attributions would best match the treatment modality and, in line with previous research (Furnham, 1995), lead to higher expectancy of treatment efficacy.

2. Methods

2.1. Participants

Data for this study were obtained from treatment-seeking outpatients with a principal diagnosis of generalized SAD. Individuals were recruited to participate in an open trial of the treatment of SAD with paroxetine, followed by randomization to augmentation with CBT or continuation of paroxetine. Due to a substantially smaller sample size after randomization, only the open treatment portion of the trial is considered here. Forty-six patients from the Adult Anxiety Clinic of Temple University (AACT) and 92 patients from the Anxiety Disorders Clinic of the New York State Psychiatric Institute (NYSPI) participated. One patient with missing data on the measure of etiological attributions was excluded from analyses; therefore, the analysis sample was 137. Individuals were excluded from this study based on various criteria including current psychotic symptoms, current or past diagnosis of bipolar disorder or major depressive disorder, significant suicidal ideation, past adequate trials of an SSRI or CBT for SAD, unwillingness to discontinue other psychotropic medications, current psychotherapeutic intervention or inability to give consent (Heimberg et al., unpublished results).

2.2. Procedure

Individuals who met inclusion criteria after preliminary screening underwent a structured diagnostic interview. Those patients meeting DSM-IV criteria for generalized SAD and not meeting any exclusionary criteria underwent a comprehensive medical evaluation and then consented to treatment. All procedures were approved by relevant Institutional Review Boards. Patients met with a psychiatrist weekly for the first 6 weeks during titration and then every other week, for a total of nine visits over 12 weeks. Patients started at 10 mg of paroxetine per day and were increased to a therapeutic level on an individual basis (from 20 to 60 mg). The psychiatrist offered general encouragement and support while monitoring clinical progress and medication effects. The psychiatrist instructed patients to expose themselves to feared situations to help overcome avoidance behaviors and explained that the role of paroxetine was to make such exposure easier. However, systematic exposure instructions were not offered. Psychiatrists performed pill counts and asked patients whether they were taking their medication as prescribed. Assessments were conducted at Weeks 0 (baseline), 4, 8, and 12 (end of open treatment).

2.3. Measures

2.3.1. Demographic characteristics

Demographic characteristics, including age, sex, race, ethnicity, employment status, marital status, and religion, were assessed at baseline.

2.3.2. Diagnostics

At the NYSPI, individuals were administered the *Structured Clinical Interview for DSM-IV, Patient Edition with Psychotic Screen* (SCID-I/P; First et al., 2002) at baseline. At the AACT, individuals were administered the *Anxiety Disorders Interview Schedule for the DSM-IV: Lifetime Version* (ADIS-IV-L; Di Nardo et al., 1994). At NYSPI, because the reliability of SAD is lower when based on the SCID-I/P (Zanarini and Franenburg, 2001; Zanarini et al., 2000) than on the ADIS-IV-L, the social phobia module of the ADIS was also administered.

2.3.3. Social anxiety

The Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987) is a 24-item clinician-administered scale that assesses social anxiety and avoidance in performance and social interaction situations. The LSAS has been successfully used in studies that assess change in response to psychotropic medication (Heimberg et al., 1998) and has strong convergent validity (Heimberg et al., 1999). The LSAS was administered to patients at Weeks 0, 4, 8, and 12, and the total score was used to assess social anxiety severity at each time point. Cronbach's α for the LSAS ranged from 0.93 to 0.96 across assessment points in the current study.

2.3.4. Depression

Participants' depressive symptoms were assessed with the Beck Depression Inventory–II (BDI-II; 36), a 21-item self-report measure that assesses symptoms of depression on a scale that ranges from 0 (e.g., "I am not discouraged about my future") to 3 (e.g., "I feel my future is hopeless and will only get worse"). The BDI-II has demonstrated strong test–retest reliability and convergent and divergent validity (Beck et al., 1996). The BDI-II was only administered at Week 0 (α=0.93) and Week 12 (α=0.92).

2.3.5. Etiological attributions of social anxiety

The Attributions for the Etiology of Social Anxiety Scale (AESAS)[1] was created by a panel of experts in SAD for the purposes of this study. Although other

[1] The AESAS is available upon request from the corresponding author.