Characterizing anxiety subtypes and the relationship to behavioral phenotyping in major depression: Results from the EMBARC study


ARTICLE INFO

Keywords:
Anxiety
Depression
Factor analysis
Flanker Task

ABSTRACT

The current study aimed to characterize the multifaceted nature of anxiety in patients with major depression by evaluating distinct anxiety factors. We then related these derived anxiety factors to performance on a Flanker Task of cognitive control, in order to further validate these factors. Data were collected from 195 patients with nonpsychotic chronic or recurrent major depression or dysthymic disorder. At baseline, participants completed self-report measures of anxiety, depression, and other related symptoms (mania, suicidality) and clinicians administered a structured diagnostic interview and the Hamilton Rating Scale for Depression, including anxiety/somatization items. Four discrete factors (State Anxiety, Panic, Neuroticism/Worry, and Restlessness/Agitation) emerged, with high degrees of internal consistency. Discriminant and convergent validity analyses also yielded findings in the expected direction. Furthermore, the neuroticism/worry factor was associated with Flanker Task interference, such that individuals higher on neuroticism/worry responded more incorrectly (yet faster) to incongruent vs. congruent trials whereas individuals higher on the fear/panic factor responded more slowly, with no accuracy effect, to the Flanker Task stimuli. These results parse anxiety into four distinct factors that encompass physiological, psychological, and cognitive components of anxiety. While state anxiety, panic and neuroticism/worry are related to existing measures of anxiety, the Restlessness/Agitation factor appears to be a unique measure of general anxious arousal. Furthermore, two factors were independently validated through the Flanker Task. These results suggest that these anxiety domains have distinct behavioral profiles and could have differential responses to distinct treatments.

1. Introduction

The presence of anxious symptoms in depression significantly reduces the probability of remission when treated with antidepressant medications (Fava et al., 2008). Prior research evaluating anxious symptoms in depression has most often focused on particular aspects of anxiety that align with particular anxiety disorder diagnoses. For example, many questionnaires assess symptoms associated with a specific anxiety disorder, such as Generalized Anxiety (Spitzer et al., 2006), panic disorder (Shear et al., 1997), social anxiety (Iza et al., 2014), and PTSD (Gentes et al., 2014).

While diagnostic-oriented assessment may be helpful in tracking symptoms associated with specific DSM diagnoses and the impact of treatment, there has been a push to evaluate groups of symptoms in an alternative way that will more closely align with the underlying biology and behavior associated with psychopathology. The NIMH Research Domain Criteria (RDoC) initiative (Cuthbert, 2014; Insel et al., 2010) is one approach that suggests novel conceptualizations of

https://doi.org/10.1016/j.jpsychires.2018.04.003

Received 5 October 2017; Received in revised form 29 March 2018; Accepted 5 April 2018

© 2018 Elsevier Ltd. All rights reserved.
psychopathology classification through five organizational domains.

Using diagnostic data, aspects of anxiety have been related to specific underlying biological systems that are distinct from depression (Kocovski et al., 2004). In fact, research has already identified the impact of comorbid anxiety on specific cognitive processes. For example, prior research has demonstrated how anxiety symptoms and disorders are associated with impaired cognition, attention, and behavioral task performance (Eysenck et al., 2007; Farber and Spence, 1956; Robinson et al., 2013). Using functional task-based brain imaging to probe both biological and cognitive abnormalities, Etkin and Schatzberg (2011) observed anxiety disorders to substantially modify emotional conflict regulation in the brain. While these data have elucidated the contribution of anxiety in patients with depression, further characterization of distinct factors within anxiety presentations has been lacking.

The goals of this study are (a) to use a wide selection of anxiety symptoms to determine if distinct anxiety factors can be defined and measured (b) to relate these factors to existing clinical assessments, and most importantly (c) to determine through validation, if they are relevant to performance on a behavioral task, the Flanker Task. To achieve these study aims, we utilized symptoms from six “anxiety” measures evaluating various anxiety facets (i.e., cognitive, physiological, and psychological components; anxiety disorder diagnoses). We used principal component analysis to define factors and report the relationship between these factors and other clinical measures for validation of the derived measures. We further validated these factors by associating them with performance on the Flanker Task, as prior research has revealed anxiety to negatively impact performance on this task (Chen et al., 2016; Huyser et al., 2011).

2. Methods

2.1. Study design and participants

Participants were recruited through advertising, flyers, and physician referrals for the multi-site Establishing Moderators and Biosignatures of Antidepressant Response in Clinical Care (EMBARC) study, a 16-week, placebo-controlled study to determine biological, physiological, cognitive, and genetic biomarkers of response to sertraline and bupropion (Trivedi et al., 2016). The EMBARC study recruited adult participants ages 18–65 from four sites around the United States and required participants to have recurrent or chronic single-episode major depressive disorder (MDD) or dysthymia, with the first onset before age 30. Participants were not included if they failed an antidepressant trial of sufficient dose and duration within the current episode. Key exclusion criteria included a history of inadequate response or poor tolerability to study medications; a history of psychotic or bipolar disorders; or substance dependence (except for nicotine) within the past six months or abuse within the past two months. The 16-week study consisted of two eight-week phases: at study entry, participants were randomized to receive either placebo or sertraline for eight weeks; then, at the 8th week mark, responders stayed on the initial treatment, non-responders to placebo were switched to sertraline, and non-responders to sertraline were switched to bupropion and followed for an additional eight weeks.

The study design was reviewed and approved by each site’s IRB, and, before enrollment, all participants signed written informed consent after the procedures were fully explained. Participants completed a battery of self-report measures at baseline, with behavioral tasks, electroencephalographic (EEG), magnetic resonance imaging (MRI), and other assessments completed within the week prior to randomization. The data presented here include six self-report/clinician forms and behavioral data completed at the initial baseline session and/or at the first EEG session when no participant was currently receiving antidepressant medication. The data presented here encompasses 195 unmedicated participants.

2.2. Measures

Baseline clinician-administered measures included the Structured Clinical Interview for DSM-IV-TR (First et al., 2002) – to determine current or lifetime history of depressive and anxiety diagnoses including Panic Disorder, Social Phobia, Obsessive Compulsive Disorder, Posttraumatic Stress Disorder, Generalized Anxiety Disorder (current only), and Anxiety Disorder Not Otherwise Specified – alongside the anxious distress specifier for a major depressive episode. These items were treated as ordered, using the ratings of 1 (symptoms of the disorder were absent), 2 (subthreshold symptoms present), and 3 (diagnostic threshold met). If there were no current diagnoses present, lifetime diagnoses were used, since, by definition, current disorders were also lifetime disorders. In addition to the six SCID anxiety disorders and the anxious distress specifier for an MDE, six items from the 17-item clinician-rated Hamilton Depression Rating Scale (Hamilton, 1960) related to anxiety (anxiety somatic, anxiety psychic, somatic general, agitation, insight, and hypochondriasis) were also used.

Self-report measures included the neuroticism subscale from the 60-item NEO Five-Factor Inventory – 3 (McCrae and Costa, 2010), as well as the four items that assess for anxiety and the two items that assess for panic from the Concise Associated Symptoms Tracking Scale (Trivedi et al., 2011b). Additional measures included ten items from the Anxious Arousal subscale of a 30-item adaptation of the Mood and Anxiety Symptoms Questionnaire (Wardenaar et al., 2010), one additional item from the General Distress subscale (“I worried about a lot of things”) with face-validity for anxiety, and 20 questions from the state version of the Spielberger State-Trait Anxiety Inventory (Spielberger et al., 1983), all administered before participants began their first EEG session.

Additional measures were selected for follow-up discriminant and convergent validity analyses: Anger Attacks Questionnaire (Fava et al., 1991), Altman Self-Rating Mania Scale (Altman et al., 1997), Concise Health Risk Tracking Scale (Trivedi et al., 2011a), Childhood Trauma Questionnaire (Bernstein et al., 2003), Quick Inventory of Depressive Symptoms (Rush et al., 2003), Social Adjustment Scale (Gameroff et al., 2012), and Snaith-Hamilton Anhedonia Scale (Snaith et al., 1995). All included measures are previously validated measures with strong psychometric data. In order to understand the relationship between identified factors and the clinical measures as they are used, overlapping items were not removed. All measures were scored using standard procedures.

The behavioral Flanker Task required participants to specify (via a button press) whether arrows pointed left or right; these arrows were presented alongside adjacent flankers pointed in the same (congruent) or different (incongruent) direction. Additional details about the Flanker Task’s methodology have been previously described (Webb et al., 2016). Following prior research (Webb et al., 2016), main analytic variables included response time (RT) and accuracy for congruent and incongruent trials considered separately, and the Flanker interference effects, which were assessed by computing a “congruent minus incongruent” score for accuracy and an “incongruent minus congruent” score for RT, such that larger scores on both measures indicate greater interference on incongruent versus congruent trials. These effects control for individual differences in psychomotor processing speed.

2.3. Data analysis

The analyses used data from 200 participants who contributed baseline data to define anxiety/anxious factors based on items that ranged from current mood state (state items from the State Anxiety Inventory) to formal anxiety disorder diagnoses (from the SCID). Of the 200 participants, 195 had complete data on all items; therefore, this subset was included in analyses. Seven participants were missing data on the Flanker Task, leading to N = 188 for these analyses. The analyses were divided into four steps: (1) sample descriptive and demographics; (2) exploratory factor analysis to determine a set of factors
دریافت فوری
متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات