Anxiety and Related Disorders

An Introduction

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Anxiety disorders are characterized by fear and distress in the absence of objective threat and are accompanied by physiological, cognitive, and affective symptoms. Such fear and distress can occur in both anticipatory forms, as generalized anxiety disorder (GAD), and in acute forms, as in panic disorder. With one-year and lifetime prevalence rates of 18.1% and 28.8%, respectively (Kessler, Chiu, Demler, & Walters, 2005a; Kessler et al., 2005b), anxiety disorders are one of the most common psychiatric conditions.

Given the high prevalence of anxiety disorders, it is important to consider their associated disability. Indeed, anxiety disorders are ranked as the sixth leading cause of disability in both high- and low-income countries (Baxter, Vos, Scott, Ferrari, & Whiteford, 2010) and are experienced as equally disabling as many chronic physical conditions (Stein et al., 2005). Such deficits can include problems with social relationships, responsibilities, and self-care among adults (Hendriks et al., 2014) and diminished academic performance in children and adolescents (Nail et al., 2015). Likewise, anxiety disorders are associated with decreased quality of life (Mendlowicz & Stein, 2000). Notably, quality of life is also impaired in subthreshold samples (Mendlowicz & Stein, 2000), suggesting that anxiety-related dysfunction is not limited to those with the most severe disorders. Given such high levels of impairment, it is perhaps unsurprising that anxiety disorders are costly. Anxiety disorders-related disability is associated with an economic burden ranging from $42.3 billion to $46.6 billion annually (Greenberg et al., 1999; Rice & Miller 1998), making anxiety disorders some of the costliest psychiatric conditions (Rice & Miller, 1998).

Despite the high prevalence and associated disability, much remains unknown about the etiology and maintenance of anxiety and related disorders. What is known is that anxiety disorders may be distinguished in part from other forms of psychopathology by the typical age of onset. Indeed, anxiety disorders onset relatively early (median age of onset = 11 years; Kessler et al., 2005b) and are highly prevalent among children (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Although childhood and adolescence appear to represent an important risk window for the development of anxiety symptoms and disorders, researchers continue to struggle to operationalize a comprehensive model that can fully account for this sensitive period.

Research does suggest that treatment for anxiety disorders is often not sought until adulthood (Christiana et al., 2000), indicating several years of untreated symptoms in many individuals with these disorders. This delay between typical age of onset and treatment may contribute to findings that suggest anxiety disorders are generally chronic (Bruce et al., 2005). Prospective research indicates that the majority of anxiety disorders persist over 12 years, with a lower probability of recovery compared to major depressive disorder (Bruce et al., 2005). Recurrence is also highly likely (Scholten et al., 2013), particularly among those with comorbid conditions (Bruce et al., 2005). Further, daily functioning remains diminished in those who remit from an anxiety disorder compared to controls (Iancu et al., 2014). This is notable, given that functional impairment, along with anxiety sensitivity, predicts anxiety disorder recurrence (Scholten et al., 2013).

Anxiety disorders are further complicated by high rates of comorbidity, as approximately 90% of those with an anxiety disorder have a history of additional psychopathology (Kaufman & Charney, 2000. Indeed, half of those with one anxiety disorder meet criteria for another (Kaufman & Charney, 2000). Further, anxiety disorders commonly co-occur with other psychological conditions, including mood disorders, substance use disorders (Kessler et al., 2005a), and eating disorders (Kaye, Bulik, Thornton, Barbarich, & Masters, 2004). Notably, anxiety disorders often precede the development of these disorders (Goodwin & Stein, 2013; Rojo-Moreno et al., 2015; Wittchen, Kessler, Pfister, & Lieb, 2000), suggesting that treating the anxiety disorder may result in improvement in the comorbid condition.

Anxiety disorders also often co-occur with medical conditions. Indeed, anxiety disorders are uniquely associated with medical disorders over and above the effects of mood and substance use disorders (Sareen, Cox, Clara, & Asmundson, 2005a), and this pattern of comorbidity is associated with increased illness severity (Katon, Lin, & Kroenke, 2007). Though anxiety disorders co-occur with a wide range of medical conditions, illnesses characterized by pain are particularly common in those with an anxiety disorder (Harter, Conway, & Merikangas, 2003; Sareen et al., 2005a). Further, reductions in health-related anxiety are associated with improvements in pain conditions (McCracken, Gross, & Eccleston, 2002; Spinhoven, Van der Does, Van Dijk, & Van Rood, 2010), suggesting the utility of targeting anxiety comorbid with medical conditions.

Furthering our understanding of anxiety and related disorders can also save lives, as anxiety disorders are linked to suicidal ideation and attempts, even after adjusting for psychiatric comorbidity, in both cross-sectional (Cougle, Keough, Riccardi, & Sachs-Ericsson, 2008; Nepon, Belik, Bolton, & Sareen, 2010; Sareen et al., 2005b) and longitudinal samples (Sareen et al., 2005b). Further, one study found that among individuals with a history of suicidality, 70% met criteria for an anxiety disorder (Nepon et al., 2010). A similar relationship is also evident among adolescents with anxiety disorders, with increased rates of suicide associated with increased number of anxiety disorders (Boden, Fergusson, & Horwood, 2007). Although the available literature clearly shows that a preexisting anxiety disorder is

an independent risk factor for suicidality and that comorbid anxiety amplifies the risk of suicide attempts among those with mood disorders, the psychobiological processes that may explain this effect remain unclear.

Current understanding of the psychobiological processes associated with anxiety has resulted in significant changes in the diagnostic classification of anxiety disorders in recent years. In the modern classification system, the Diagnostic and Statistical Manual of Mental Disorders (DSM), classes of disorders are clustered around shared phenomenological features, with the defining features of anxiety disorders being symptoms of anxiety and avoidance behavior (APA, 1987). Since the introduction of diagnostic classes in DSM-III (APA, 1980), the anxiety disorders class has consistently included panic disorder with/without agoraphobia, specific phobias, social phobia, GAD, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD). However, DSM-5 has represented a notable departure from this standard, such that OCD and PTSD have been removed from the anxiety disorders and placed within two newly created classes, obsessive-compulsive and related disorders and trauma- and stressor-related disorders, respectively (APA, 2013).

These changes have proved controversial. The obsessive-compulsive and related disorders class was introduced on the assertion that OCD is phenomenologically and biologically distinct from anxiety disorders (Stein et al., 2010). For example, proponents of the obsessive-compulsive and related disorders class suggest that the distinguishing phenomenon of OCD is not anxiety, but repetitive behaviors and emphasize the unique neural profile of hyperactivity in the fronto-striatal loop in OCD (Stein et al., 2010). In contrast, critics of this approach argue that the one of the primary features of OCD is anxiety in response to obsessions and that efforts to adapt classification systems based on findings from neuroimaging research are premature (Abramowitz & Jacoby, 2014). Likewise, while proponents of the changes to PTSD in DSM-5 have praised the addition of symptoms to the diagnostic criteria (Kilpatrick, 2013), others have argued that the new criteria result in excessive heterogeneity (Galatzer-Levy & Bryant, 2013).

Such controversies highlight the limitations inherent to categorical diagnostic approaches. The utility of the diagnostic criteria defined by the DSM is to guide differential diagnosis and selection of treatment and provide a common language for practitioners (APA, 2013). Though the categorical diagnoses contained in the DSM framework arguably imply true distinctions between disorders that represent unique etiologies, DSM-5 notes that such a classification system may not fully account for the various complexities of mental illness (APA, 2013). Indeed, critics of the categorical approach have argued that the excessive rates of comorbidity suggest shared etiology among multiple disorders that the categorical approach would classify as distinct (Widiger & Samuel, 2005). For example, high comorbidity between GAD and depression may reflect shared genetic diatheses and overlap of core phenotypic processes, such as negative affect (Mineka, Watson, & Clark, 1998).

Likewise, the necessity of "black-and-white" boundaries between disorders in a categorical system has contributed to a proliferation of new disorders designed to bridge the gap between extant disorders, a practice that may reflect artificial cutoffs of dimensional domains (Widiger & Samuel, 2005). This practice is seen in the addition of acute stress disorder to DSM-IV to identify pathological stress responses that surpass adjustment disorder but do not meet the minimum duration required for PTSD (Marshall, Spitzer, & Liebowitz, 1999). In contrast, a dimensional framework is arguably a better representation of complex phenotypes that are unlikely to derive from singular etiologies. In addition to addressing the issues of comorbidity and arbitrary distinctions, a dimensional framework also allows for quantitative descriptions of severity and treatment progress and lends itself to empirical elucidation of physiological underpinnings of observable symptoms (Helzer, Kraemer, & Krueger, 2006).

Research has shown that the severity, duration of anxiety, and disability are able to better identify severe chronic course trajectory as compared with DSM-IV categories (Batelaan, Rhebergen, Spinhoven, Van Balkom, & Penninx, 2014). Findings of this sort suggest that a targeted focus on cross-cutting dimensions may explain more variance in anxiety-related processes than diagnostic categories. The purported benefits of such a dimensional approach to psychopathology has led in part to the development of the National Institute of Mental Health (NIH) Research Domain Criteria (RDoC). The RDoC outlines a framework in which five core domains relevant for psychopathology (Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Social Processes, Arousal and Regulatory Systems) can be measured and described at multiple levels ranging from genes to self-report (Insel et al., 2010). RDoC represents a major departure from the categorical diagnoses of the DSM in a push toward defining mental illness by dysfunction along transdiagnostic dimensions. Importantly, in addition to taking a step toward a dimensional diagnostic system, RDoC also asserts that mental illnesses are "brain disorders" that can be understood and measured in terms of dysfunction at genetic and molecular levels (Insel et al., 2010).

The RDoC perspective has been highly debated, particularly among cognitive and behaviorally oriented psychological scientists (Deacon, 2013). The veracity of this perspective remains to be seen, as clinical neuroscience is in its relative infancy. Likewise, the RDoC's impact on the future of anxiety and related disorders research is unclear. Though neurobiology has been critical for delineating certain mechanisms of anxiety-related pathology, such as fear conditioning (Lissek, 2012), there is concern that behavioral or verbal indices are undervalued in a brain disorders framework. Given that an important goal of the RDoC approach is to inform the development of novel, circuit-based interventions and the personalization of treatments available, it will be vital to examine the extent to which this approach complements existing empirically supported models of anxiety and related disorders.

Treatments of anxiety and related disorders have largely centered on two modalities: psychotropic medications and cognitive behavior therapy (CBT). While

a variety of psychotropic medications have been utilized for the treatment of anxiety and related disorders, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the current first-line pharmacological agents due to both efficacy and tolerability (Ravindran & Stein, 2010). CBT for anxiety and related disorders generally includes intervention strategies aimed at reducing maladaptive beliefs (e.g., cognitive restructuring) and behavioral avoidance (e.g., exposure) (Hofmann & Smits, 2008). Considerable research has found CBT to be efficacious for the treatment of anxiety and related disorders (Hofmann & Smits, 2008; Olatunji, Cisler, & Deacon, 2010). Extant research comparing CBT to psychotropic medications indicates comparable efficacy, while evidence for an additive effect of combination treatments (i.e., CBT + medication) is mixed (Bandelow, Seidler-Brandler, Becker, Wedekind, & Ruther, 2007). However, CBT treatment gains are generally sustained over one to two years (Butler, Chapman, Forman, & Beck, 2006), whereas medication effects are generally lost upon discontinuation (see Otto, Smits, & Reese, 2005, for a review). Despite the established efficacy of CBT, a substantial proportion of patients do not respond to CBT or relapse, and a paucity of research examines outcomes beyond two years (Arch & Craske, 2009). These findings highlight major areas for improvement to the current "gold standard" of psychotherapy. Paradigm shifts in research, such as the dimensional approach and emphasis on neurobiology espoused by RDoC, may yield novel treatment targets or personalized medicine insights to increase treatment efficacy and decrease nonresponse and relapse.

Overview of This Book

Much remains unknown about the etiology, maintenance, and treatment of anxiety and related disorders. This volume aims to bridge this gap in knowledge with a focus on the divide between current classification systems and approaches to anxiety and related disorders in a rapidly changing field. This book integrates many levels of information to better explain the basic dimensions of functioning underlying anxiety and related disorders. First, Section 1 outlines basic mechanisms of anxiety. Consistent with a dimensional perspective, Section 1 describes the effects of basic processes of learning, perception, and attention on fear and anxiety. For example, how might learning mechanisms that underlie fear conditioning contribute to clinical fear and anxiety? Can the threat processing that underlies anxiety and its disorders be modeled at the level of sensory perception? Consistent with the RDoC research framework, Section 1 examines basic dimensions of functioning that span the full range of human behavior from normal to abnormal. Section 2 then describes various transdiagnostic processes that may confer risk for the development of anxiety and related disorders. Transdiagnostic processes reflect common psychological *processes* that underlie clinical syndromes. Section 2 highlights that rather than focusing on discrete diagnostic entities, the co-occurrence of many

diagnoses likely reflects different patterns of symptoms that result from shared risk factors and the same underlying processes.

Section 3 of this volume covers assessment, diagnosis, and cultural manifestations of anxiety and related disorders. DSM-5 represents a significant departure in traditional conceptualizations of disorders that fall in the anxiety disorder category. Section 3 highlights these changes as well as their implications for research and practice. Sections 4–6 discuss the etiology and phenomenology of specific anxiety disorders, OCD spectrum disorders, and trauma- and stressor-related disorders. A common theme for Sections 4–6 is a critical analysis of contemporary models of the development of the various disorders that is informed by basic science. Furthermore, this part of the volume examines the potential implications for the RDoC research framework in advancing current knowledge regarding the etiology of anxiety and related disorders. Last, Section 7 examines the treatment and prevention of anxiety and related disorders. This portion of the volume identifies which treatments are most effective for anxiety and related disorders and why. In addition to a survey of existing descriptive and experimental approaches to the study of anxiety and related disorders, an important goal of this book is empirically guided suggestions for the treatment of anxiety and related disorders.

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