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The Nature, Diagnosis, and Treatment of Neuroticism: Back to the Future

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Abstract
We highlight the role of neuroticism in the development and course of emotional disorders and make a case for shifting the focus of intervention to this higher-order dimension of personality. Recent decades have seen great emphasis placed on differentiating disorders into *Diagnostic and Statistical Manual of Mental Disorders* diagnoses; however, evidence has suggested that splitting disorders into such fine categories may be highlighting relatively trivial differences. Emerging research on the latent structure of anxiety and mood disorders has indicated that trait neuroticism, cultivated through genetic, neurobiological, and psychological factors, underscores the development of these disorders. We raise the possibility of a new approach for conceptualizing these disorders—as emotional disorders. From a service-delivery point of view, we explore the possibility that neuroticism may be more malleable than previously thought and may possibly be amenable to direct intervention. The public-health implications of directly treating and even preventing the development of neuroticism would be substantial.

Keywords
anxiety disorders, temperament/personality and psychopathology, comorbidity

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Throughout history, philosophers and researchers have attempted to understand the nature of anxiety and its disorders. As early as 450 BC, the relationship between an individual's discrete emotions in response to stressors and his or her enduring proclivity for such experiences was of interest. For example, the Roman philosopher Cicero proposed a theory of emotion that distinguished between the temporary emotional state of anxiety (*angor*) and the enduring tendency to experience anxiety (*anxietas*; Lewis, 1970). Furthermore, in perhaps one of the best-known historical conceptualizations of anxiety, Freud (1924) distinguished between objective anxiety signaling the presence of an immediate threat (e.g., a loaded gun pressed to the temple) and neurotic anxiety generated when an individual's defense mechanisms are no longer able to successfully repress an early traumatic experience, which results in a persistent state of distress (Reiss, 1997). In this article, we review a variety of research areas with the purpose of shifting focus from the study of discrete anxiety, mood, and related disorders as defined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychiatric Association, APA, 2013) to a broader understanding of emotional or internalizing disorders. In particular, we seek to call attention to higher-order temperamental factors that may be a more appropriate target for assessment and intervention than may symptom-level manifestations of these traits. Although relevant higher-order temperamental dimensions associated with the experience of frequent and intense negative emotions have acquired a number of labels, we focus on the construct of "neuroticism" as the first (Eysenck, 1947) and still most popular (Lahey, 2009) conception of this trait.

Neuroticism is typically defined as the tendency to experience frequent and intense negative emotions in

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response to various sources of stress. These negative emotions are usually broadly construed to include anxiety, fear, irritability, anger, sadness, and so forth, but the greatest focus has been on the experience of anxious or depressive mood. Accompanying this exaggerated negative emotionality is the pervasive perception that the world is a dangerous and threatening place, along with beliefs about one's inability to manage or cope with challenging events. These beliefs often are manifested in terms of heightened focus on criticism, either self-generated or from others, as confirming a general sense of inadequacy and perceptions of lack of control over salient events (Barlow, 2002; L. A. Clark & Watson, 2008; Eysenck, 1947; Goldberg, 1993).

The label *neuroticism* was first used by Eysenck (1947) to describe this statistically derived personality trait; Eysenck coined the term after the commonly used clinical label at that time: *neurosis*—the early *DSM* category comprising people with anxiety, depression, and related disorders. Building on earlier work by Slater (1943), who used the term *neurotic constitution*, Eysenck, no fan of things Freudian even in the 1940s, regretted employing this term and noted that "it would no doubt be preferable in some ways to use a more neutral kind of label" (p. 49). Nevertheless, he made it clear that individuals with the diagnosis of neurosis occupied the pathological extreme of the personality trait of neuroticism. Eysenck also noted, in a prescient bit of writing, that these two constructs could be relatively independent and that "some so called 'neurotic' inmates (of a hospital) show very little evidence of the 'neurotic constitution' and would likely be situated rather towards the normal end of the distribution" (p. 48). He went on to theorize that these individuals would have been subjected to extreme life stress, whereas individuals high on the trait of neuroticism would require relatively little life stress to trigger neurosis, thereby clearly presaging the stress-diathesis model of psychopathology.

Although the study of trait or temperament models of anxiety and related negative emotions has continued for decades, this literature has had decreasing influence on nosological schemes. *DSM-III* (3rd ed.; APA, 1980) represented the advent of an objective, empirically based classification system for mental disorders; patients previously receiving a diagnosis of neurosis were now classified more narrowly into specific anxiety, depressive, and related disorders. These new discrete diagnostic categories indeed had a meaningful impact on the development of pharmacological and individual psychological treatments, particularly for anxiety and mood disorders (e.g., Barlow et al., 1984). This approach allowed for the development of interventions targeting specific forms of psychopathology and the ability to evaluate treatment response on the basis of discrete outcomes. Although this "splitting" approach to nosology ensured high rates of diagnostic reliability, there is evidence that it may have come at the expense of validity; in other words, the current diagnostic system may be overemphasizing categories that are minor variations of a broader underlying syndrome (T. A. Brown & Barlow, 2005, 2009). Neuroticism, combined with other temperamental variables, likely represents this syndrome.

Despite the marked emphasis during the past 30 years on discrete *DSM*-based categories of emotional disorders and their treatment, a few investigators have continued to focus attention on the existence and salience of broader underlying syndromes. For example, Andrews (1990) and Tyrer (1989) each argued for the existence of a "general neurotic syndrome" as a more parsimonious and heuristic account of emotional disorders. In addition, Lahey (2009), summarizing the growing evidence for the public-health significance of neuroticism, documented that neuroticism is strongly associated with and predicts many different mental and physical disorders, as well as treatment seeking for not only mental disorders but also general health services. Indeed, he underscored evidence that neuroticism may act as a salient predictor of the quality and longevity of our lives. Lahey called for a more substantial focus on the nature and origins of neuroticism and the mechanisms through which this trait is linked to both mental and physical disorders. Moreover, Cuijpers et al. (2010) examined the economic cost of the trait of neuroticism and found, in a large representative sample of the Dutch population, that these economic costs were enormous and exceeded costs of common mental disorders. Cuijpers et al. noted that "we should start thinking about interventions that focus not on each of the specific negative outcomes of neuroticism but rather on the starting point itself" (p. 1086).

The current review begins with a section highlighting commonalities among the emotional disorders, including high rates of comorbidity, broad rather than narrow treatment responsiveness among comorbid disorders, and shared neurobiological mechanisms. Next, we present the emerging research on the latent structure of emotional disorders that may underlie these observed commonalities followed by a brief description of theoretical accounts of the origins of neuroticism or trait anxiety. The following section describes common functional relationships in emotional disorders, particularly among emotional expression, negative appraisals under stress, and avoidance, as well as new approaches to conceptualizing these disorders and suggests the possibility of more satisfying dimensional nosological and assessment schemes. Finally, a review of diverse research on the malleability of neuroticism in both normal and pathological expressions sets the stage for a discussion of possible new strategies for treatment and prevention that focus

not on individual negative outcomes of neuroticism in the form of the *DSM*-defined emotional disorders but, rather, on neuroticism itself as well as related temperaments.

Commonalities and Dimensions Among Anxiety and Related Disorders

Empirical conceptions of the anxiety and major emotional disorders are emerging that underscore their commonalities (Barlow, 2002; T. A. Brown, 2007; T. A. Brown & Barlow, 2009). Major developments in at least three areas—high rates of comorbidity, broad treatment response across comorbid disorders, and shared neurobiological mechanisms—support this conception. First, studies of phenomenology and nosology with a particular focus on comorbidity have suggested considerable overlap among disorders. At the diagnostic level, this overlap is most evident in high rates of current and lifetime comorbidity (e.g., Allen et al., 2010; T. A. Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Kessler, Berglund, & Demler, 2003; Kessler et al., 1996; Kessler et al., 1998; Kessler et al., 2008). In a study of 1,127 patients presenting at the Center for Anxiety and Related Disorders (CARD) at Boston University, 55% of patients with a principal anxiety disorder had at least one additional anxiety or depressive disorder at the time of assessment, and this rate increased to 76% when lifetime diagnoses were considered (T. A. Brown et al., 2001). To take one example, of 324 patients diagnosed with *DSM-IV-TR* (4th ed., text rev.; APA, 2000) panic disorder with or without agoraphobia, 60% met criteria for an additional anxiety or mood disorder, breaking down to 47% with an additional anxiety disorder and 33% with an additional mood disorder. When lifetime diagnoses were considered, the percentages rose to 77% of the patients experiencing any comorbid anxiety or mood disorder, breaking down to 56% for an additional anxiety disorder and 60% for a mood disorder. The principal diagnostic categories of posttraumatic stress disorder and generalized anxiety disorder were associated with the highest comorbidity rates. Similarly, Merikangas, Zhang, and Aveneoli (2003) followed approximately 500 individuals for 15 years and found that relatively few people suffered from anxiety or depression alone; when patients did meet criteria for a single disorder at one point in time, an additional anxiety or depressive episode disorder almost certainly emerged at a later time.

These summaries are most likely conservative as a result of artifactual constraints in *DSM-IV-TR* (which were continued in *DSM-5*), such as the nature of inclusion-exclusion criteria used. For instance, when adhering strictly to *DSM-IV-TR* diagnostic rules, the comorbidity between dysthymia and generalized anxiety disorder in the T. A. Brown et al. (2001) study was 5%. However, when the hierarchical rule that generalized anxiety disorder should not be assigned when occurring exclusively during a course of a mood disorder was suspended, the comorbidity estimate increased to 90%. These data also ignore the presence of subthreshold symptoms that did not meet diagnostic thresholds for one disorder or another.

Second, psychological treatments for a given anxiety disorder often produce improvement in additional comorbid anxiety or mood disorders that are not specifically addressed in treatment (Allen et al., 2010; Borkovec, Abel, & Newman, 1995; T. A. Brown, Antony, & Barlow, 1995; Tsao, Lewin, & Craske, 1998; Tsao, Mystkowski, & Zucker, 2002). For example, we examined the course of additional diagnoses in a sample of 126 patients who were being treated at CARD for panic disorder with or without agoraphobia (T. A. Brown et al., 1995). A significant pre- to posttreatment decline in overall comorbidity was noted (40% to 17%, respectively). This effect could represent the generalization of elements of treatment to independent facets of both disorders or the effective targeting of "core" features of emotional disorders. The fact that a wide range of emotional disorders (e.g., major depressive disorder, obsessive-compulsive disorder, panic disorder) respond approximately equivalently to antidepressant medications has also been interpreted by some researchers as indicating shared features among these disorders (e.g., Hudson & Pope, 1990).

There are several possible explanations for high rates of comorbidity and overlapping treatment response that we have reviewed extensively elsewhere (T. A. Brown & Barlow, 2002, 2009), including overlapping definitional criteria, artifactual reasons (e.g., differential base rates of occurrence in our setting), and the possibility that disorders are sequentially related such that the features of one disorder act as risk factors for another disorder. Another more intriguing explanation, noted earlier, is that this pattern of comorbidity argues for the existence of what has been called a general neurotic syndrome (Andrews, 1990, 1996; Tyrer, 1989). Under this conceptualization, heterogeneity in the expression of emotional disorder symptoms (e.g., individual differences in the prominence of social anxiety, panic attacks, anhedonia) is regarded as trivial variation in the manifestation of a broader syndrome. We return to this argument later.

Third, recent research from affective neuroscience has suggested the existence of a biological syndrome that is common across emotional disorders. For example, research among individuals with anxiety and related disorders has suggested that hyperexcitability of limbic structures, along with limited inhibitory control by cortical structures, may be one explanation for the increased negative emotionality among individuals with such

diagnoses (Etkin & Wager, 2007; Mayberg et al., 1999; Porto et al., 2009; Shin & Liberzon, 2010). Specifically, increased "bottom-up" processing through amygdala overactivation, coupled with inefficient or deregulated cortical inhibition of amygdala responses, has been shown in studies of social anxiety disorder (Lorberbaum et al., 2004; Phan, Fitzgerald, Nathan, & Tancer, 2006; Tillfors, Furmark, Marteinsdottir, & Fredrikson, 2002), posttraumatic stress disorder (Shin et al., 2005), generalized anxiety disorder (Etkin, Prater, Hoeft, Menon, & Schatzberg, 2010; Hoehn-Saric, Schlund, & Wong, 2004; Paulesu et al., 2010), specific phobia (Paquette et al., 2003; Straube, Mentzel, & Miltner, 2006), and depression (Holmes et al., 2012). This same amygdala overactivation has also been found in individuals high in the personality dimension of neuroticism (Keightley et al., 2003). Of course, a few unique and idiosyncratic neurobiological factors have also been associated with discrete *DSM-IV-TR* diagnoses (Blair et al., 2008; Chorpita, Albano, & Barlow, 1998), but it seems likely that the broader based genetic and neurobiological commonalities reviewed earlier may better account for the nature of emotional disorders. Although these three commonalities among emotional disorders have garnered attention, a recent focus on the hierarchical structure of emotional disorders may be more heuristic.

Latent Temperamental Structure of Emotional Disorders

Emerging research on the latent dimensional features of emotional disorders has revealed a hierarchical structure that places emphasis on two genetically based core dimensions of temperament: neuroticism and, to a lesser degree, extraversion (Barlow, 2002). Extraversion, commonly associated with social qualities, broadly refers to an energetic approach to the world, including activity and positive emotionality in addition to sociability. Although these traits have received various labels, including *negative affect, behavioral inhibition, trait anxiety*, and *harm avoidance* as alternate terms for neuroticism and *positive affect* or *behavioral activation* as alternate terms for extraversion, substantial existing literature has underscored the roles of these constructs in accounting for the onset, overlap, and maintenance of anxiety, depressive, and related disorders (T. A. Brown, 2007; T. A. Brown & Barlow, 2009; T. A. Brown, Chorpita, & Barlow, 1998; Gershuny & Sher, 1998; Griffith et al., 2010; Kasch, Rottenberg, Arnow, & Gotlib, 2002; Kessler et al., 2011; Krueger, 1999; Watson, Clark, & Carey, 1988).

The study of trait or temperament models of anxiety and related negative emotions has been ongoing for decades in spite of the decreasing influence of this work on nosological schemes. It is interesting that almost every theory of personality structure references neuroticism- and extraversionlike traits, which suggests the fundamental importance of these dimensions for functioning (John & Srivastava, 1999). Current well-accepted personality conceptualizations, such as the Big Three (Eysenck & Eysenck, 1975; Tellegen, 1985; Watson & Clark, 1993) and the Big Five (Digman, 1990; John, 1990; McCrae & Costa, 1987), prominently feature these dimensions of personality despite disagreement on additional traits (e.g., constraint in the Big Three and agreeableness, openness, and conscientiousness in the Big Five) and different methods of formulation.

In addition to understanding the structure of personality, researchers have been interested in the neurobiological basis for such traits. Eysenck's (1961, 1981) influential theory led to the development of the Big Three, and he was the first to implicate neuroticism and extraversion. He based his trait theory on variations in levels of cortical activation and autonomic nervous system reactivity and suggested that extraversion/positive emotion is associated with moderate levels of arousal, whereas neuroticism/negative emotion is associated with under- or overarousal. A number of researchers have examined the relationship of neuroticism (and extraversion) in the development of anxiety and other negative emotions. For example, Gershuny and Sher (1998) found, in a sample composed of 466 young adults, that the combination of high neuroticism and low extraversion at Time 1 seemed to play an important and predisposing role in the emergence of anxiety assessed 4 years later.

Further bolstering the importance of neuroticism and extraversion in the experience of negative emotion, Gray (1982; Gray & McNaughton, 1996) described a similar trait theory and its neurobiological correlates that map onto Eysenck's (1961, 1981) traits, namely, the behavioral inhibition system, behavioral approach system, and fight-flight system. In Gray's theory, the biological basis for anxiety is the behavioral inhibition system's (over)reaction to novel signals or punishment with exaggerated inhibition. High levels on Gray's behavioral inhibition system roughly relate to high levels of neuroticism and low levels of extraversion in Eysenck's model, and the behavioral approach system roughly corresponds to high extraversion and low neuroticism (Barlow, 2002). The fight-flight system involves unconditioned escape behavior (i.e., flight) and defensive aggression (i.e., fight) in response to unconditioned punishment, such as pain, and unconditioned frustrative nonrewards (Gray, 1991; Gray & McNaughton, 1996). As such, the fight-flight system may represent a biological vulnerability specifically to the distinct emotion of fear/panic, as opposed to anxiety more generally.

In another trait theory, Kagan (1989, 1994) examined children's approach-and-withdrawal behavior and created profiles characterizing their levels of behavioral inhibition. Kagan's (1989) definition of *behavioral inhibition* is similar to Gray's (1982) in that it involves a low threshold for limbic arousal and uncertainty regarding unfamiliar events. Kagan considered these stable profiles as representing temperaments; physiological (increased salivary cortisol levels and muscle tension, greater pupil dilation, and elevated urinary catecholamine levels) and external (subsequent development of anxiety disorders) correlates of behavioral inhibition have also been found (Biederman et al., 1993; Hirshfeld-Becker et al., 1992). Robinson, Kagan, Reznick, and Corley (1992) suggested that temperament is clearly heritable; however, only 30% of individuals who clearly met criteria for behavioral inhibition as young children went on to develop anxiety disorders (Biederman, Rosenbaum, Hirshfeld, & Faraone, 1990). Moreover, temperament (as described in Kagan & Snidman, 1991) appears to be somewhat malleable, which suggests that environmental factors are also important determinants in temperament and anxiety vulnerability. These findings support the notion of a "constraining" biological vulnerability (in contrast to a "determining" role of temperament) in the development of anxiety in adolescence and adulthood, a theme to which we return in our later discussion of treatment.

Finally, in one of the best known modern conceptualizations of temperaments related to anxiety and depression, L. A. Clark and Watson (1991) proposed two genetically based core dimensions, neuroticism/negative emotionality and extraversion/positive emotionality, as part of their tripartite theory (L. A. Clark, 2005; L. A. Clark, Watson, & Mineka, 1994; Watson, 2005). These concepts, originally based on Eysenck's (1961, 1981) model, are also closely related to Gray's (1982) constructs of behavioral inhibition and behavioral activation both conceptually and empirically. Although the traits reviewed earlier may turn out to be distinct in some way, current evidence in this area from CARD and elsewhere (L. A. Clark, 2005; Watson, 2005) lump these concepts together in a partially heritable temperament that we have labeled *neuroticism/behavioral inhibition* (or just *neuroticism*[1]) and *behavioral activation/positive affect* (T. A. Brown, 2007; T. A. Brown & Barlow, 2009; T. A. Brown et al., 1998; Campbell-Sills, Liverant, & Brown, 2004).

We have been studying the latent structure of emotional disorders for the past 20 years (e.g., T. A. Brown et al., 1998; Zinbarg & Barlow, 1996) and have confirmed, with some modifications, the tripartite model of emotional disorders first proposed by L. A. Clark and Watson (1991). For example, the findings from T. A. Brown et al. (1998), which used a sample composed of 350 patients with *DSM-IV-TR* anxiety and mood disorders, confirmed a hierarchical structure. In this structure, neuroticism and extraversion emerged as higher-order factors to the *DSM-IV-TR* disorder factors, with significant paths from neuroticism to each of the five *DSM-IV-TR* factors. In accord with a reformulated hierarchical model of anxiety and depression (Mineka, Watson, & Clark, 1998), results showed that extraversion was predictive of unipolar depression and social anxiety disorder only (see also T. A. Brown & McNiff, 2009). In addition, Rosellini, Lawrence, Meyer, and Brown (2010) found recently that agoraphobia (but not panic disorder) was associated with low extraversion, which provided support for the change in *DSM-5* that separates agoraphobia from panic disorder as a distinct, new, diagnosis. In this model, autonomic arousal, which we consider to reflect largely the phenomenon of panic, emerges as a lower-order factor with significant paths from panic disorder and generalized anxiety disorder, which demonstrated a negative relationship with autonomic surges.

These findings on latent structure have recently been extended both by our research team (T. A. Brown, 2007; T. A. Brown & Barlow, 2009) and by other researchers (e.g., Griffith et al., 2010; Kessler et al., 2011). For example, Griffith et al. (2010), studying a large sample of ethnically diverse adolescents and including both self-report and peer-report measures of neuroticism, found that a single internalizing factor was common to lifetime diagnoses of mood and anxiety disorders and that this internalizing factor was all but isomorphic with neuroticism. Noting the replication of earlier findings (e.g., T. A. Brown et al., 1998), Griffith et al. suggested that these results provided further evidence that neuroticism may be the core of "internalizing" disorders. Using factor analysis, Krueger (1999) similarly found that the variance in seven anxiety and mood disorders can be accounted for by the higher-order dimension of internalizing/neuroticism. Although the key features of the *DSM* anxiety and mood disorders (i.e., the specific symptoms used to discriminate between diagnoses) cannot be collapsed indiscriminately into higher-order temperamental dimensions, it seems safe to conclude, on the basis of these studies, that what is common outweighs what is not. Thus, virtually all of the considerable covariance among latent variables corresponding to the *DSM-IV-TR* constructs of depression, social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder was explained by the higher-order dimension of neuroticism (and extraversion); bipolar disorder was not included in these studies.

Our own framework for understanding the origins of neuroticism as well as emotional disorders describes three separate but interacting diatheses or vulnerabilities (i.e., triple vulnerability theory; Barlow, 1988, 2000; Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2013). We

have explicated these vulnerabilities in some detail elsewhere (Barlow et al., 2013) but included a general biological (heritable) vulnerability common across disorders, a general psychological vulnerability consisting of a heightened sense of unpredictability and uncontrollability and associated changes in brain function resulting from adverse early experiences, and a more specific psychological vulnerability, also largely learned, accounting for why one particular emotional disorder may emerge instead of another. It seems increasingly evident that the two generalized vulnerabilities identified in the triple vulnerability theory are implicated in the development and expression of neuroticism itself (T. A. Brown, 2007; T. A. Brown & Barlow, 2009). Indeed, we hypothesize that these two generalized vulnerabilities function as direct risk factors for the development of neuroticism, which in turn mediates risk for the development of anxiety and mood disorders. What is notable for our purposes is that adverse experiences contribute strongly to changes in brain function and that later experiences may alter resulting temperamental expression and associated brain circuits (Kagan & Snidman, 1991; Nemeroff, 2013).

The Nature of Emotional Disorders

Negative reactivity to emotional experience appears fundamentally connected to neuroticism and resulting emotional disorder pathology. *Emotional disorder* is a term that has been used to group anxiety, unipolar mood, and related disorders, such as somatoform and dissociative disorders (Barlow, 1991; Barlow et al., 2011; T. A. Brown & Barlow, 2009). These disorders are characterized by a number of shared emotional disturbances, which appear to be closely linked to neuroticism. As described earlier, individuals with emotional disorders, compared with healthy individuals, have higher levels of negative affect (e.g., T. A. Brown & Barlow, 2009) and report experiencing more frequent and intense negative emotions (Campbell-Sills, Barlow, Brown, & Hofman, 2006; Mennin, Heimberg, Turk, & Fresco, 2005). In addition, individuals with emotional disorders, compared with healthy individuals, report less emotional clarity (Baker, Holloway, Thomas, Thomas, & Owens, 2004; McLaughlin, Mennin, & Farach, 2007; Tull & Roemer, 2007; Weiss et al., 2012) and acceptance of emotional experiences (McLaughlin et al., 2007; Tull & Roemer, 2007; Weiss et al., 2012) and find the experience of negative emotions more unpleasant (Roemer, Salters, Raffa, & Orsillo, 2005).

In view of these reactions to negative emotions, it is not surprising that individuals with emotional disorders also display a range of cognitive and behavioral strategies aimed at reducing encounters with or the impact of negative emotions. Individuals with emotional disorders exhibit early vigilant information-processing biases toward negative information, but then they tend to quickly turn their attention away from such negative information (MacLeod & Mathews, 2012; Mathews & MacLeod, 2005). These individuals also react strongly to negative emotions when they occur with attempts to suppress or avoid the emotional experience (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Baker et al., 2004; Moore, Zoellner, & Mollenholt, 2008; Tull & Roemer, 2007; Turk, Heimberg, Luterek, Mennin, & Fresco, 2005). In addition, individuals with emotional disorders, compared with healthy individuals, display greater intolerance for uncertainty, ambiguity, or situations that are perceived as uncontrollable, which leads to heightened negative affect. For example, intolerance of uncertainty and distress have been demonstrated across a range of disorders, including depression, generalized anxiety disorder, and social anxiety disorder (Boelen, Vrinssen, & van Tulder, 2010; Boswell, Thompson-Hollands, Farchione, & Barlow, 2013; Lee, Orsillo, Roemer, & Allen, 2010; Tolin, Abramowitz, Brigidi, & Foa, 2003). Increased perceptions of emotions as uncontrollable and intolerable as well as increased attempts at emotional control are also evident across disorders. A wide range of research has suggested that these ways of interpreting and responding to negative emotions paradoxically serve to increase and maintain negative emotions and emotional disorder symptomatology. Thus, we consider this pathological reaction to emotional experience as the phenotypic core of emotional disorders. The following section discusses in detail the nature of these response tendencies and their sequelae.

Evidence has suggested that how one interprets or reacts to negative emotions when they occur can affect the intensity and duration of the emotional experience (Sauer & Baer, 2009; Sauer-Zavala et al., 2012). A clear example of how this process unfolds can be seen in early models of panic disorder (Barlow, 1988; D. M. Clark, 1986). In these models, physical symptoms associated with initial panic attacks (e.g., increased heart rate) evoke anxiety about impending consequences (e.g., heart attack), which intensifies anxiety and its related physical symptoms and possibly triggers additional panic attacks. It is important to note that in individuals without panic disorder, occasional panic attacks do not evoke strong emotional reactions (nonclinical panic; Bouton, Mineka, & Barlow, 2001). Thus, the central issue in panic disorder is not the experience of panic attacks but the negative emotional reaction to the intense fear (panic) itself.

Negative reactions or interpretations of emotions that intensify the experience are also prominent in other anxiety and depressive disorders. For example, in research on obsessive-compulsive disorder, Rachman and de Silva (1978) found that the content of ego-dystonic intrusive thoughts under stress are similar in patients diagnosed with obsessive-compulsive disorder and nonclinical

control participants, which supports the notion that the way these thoughts are interpreted and managed has implications for the development of this emotional disorder. In addition, individuals with generalized anxiety disorder may find unexpected, uncontrolled emotional reactions that result from unplanned or mildly threatening situations particularly aversive and may engage in worry or checking behavior to regulate this emotional experience (Newman & Llera, 2011). Once again, the focus of an emotional disorder (panic attacks, intrusive thoughts, and social evaluation) may be determined by early learning experiences; however, the negative emotional reaction itself and one's attempts to cope with or downregulate this emotional reaction are at the core of the disorder.

Several constructs capturing the problematic reactions to emotions that may be implicated in the transdiagnostic development and maintenance of emotional disorders have been identified; specifically, these constructs measure the tendency of individuals to find emotional experiences aversive and, as such, engage in attempts to avoid them. *Anxiety sensitivity*, defined as a propensity for developing beliefs that anxiety-related symptoms will have negative somatic, cognitive, and social consequences (Reiss, 1991), is one such construct. Anxiety sensitivity represents an individual's characteristic way of evaluating and responding to an emotional experience (specifically anxiety) when it occurs, distinct from the frequency or intensity of anxiety itself (Cox, Taylor, & Enns, 1999; Lilienfeld, 1999). Although anxiety sensitivity was originally introduced as a risk factor for panic disorder (Reiss, Peterson, Gursky, & McNally, 1986) and has predominantly been studied in the context of this disorder (e.g., Maller & Reiss, 1992; Plehn & Peterson, 2002; Rassovsky, Kushner, Schwarze, & Wangensteen, 2000), a large literature also has implicated anxiety sensitivity in the development of other anxiety disorders and depression (see Boswell, Farchione, et al., 2013; Naragon-Gainey, 2010; Taylor, 1999).

For example, prospective studies have demonstrated that anxiety sensitivity predicts the onset of anxiety and depressive disorders (Maller & Reiss, 1992; Schmidt, Keough, Timpano, & Richey, 2008) beyond the contributions of the tendency to experience anxiety (see McNally, 1996, for a review) and that reductions in anxiety sensitivity during treatment predict symptom improvement (Gallagher et al., 2013). In addition, anxiety sensitivity has demonstrated incremental validity above trait neuroticism in the prediction of most mood and anxiety disorders (Collimore, McCabe, Carelton, & Asmundson, 2008; Cox, Enns, Walker, Kjernisted, & Pidlubny, 2001; Kotov, Watson, Robles, & Schmidt, 2007; Norton et al., 1997; Reardon & Williams, 2007). These results support the notion that how one relates to negative emotions is just as important in the development of emotional disorders as is the frequency and intensity of emotional experience.

Another transdiagnostic construct that has been implicated in the development and maintenance of emotional disorders is *experiential avoidance*, defined as the unwillingness to remain in contact with uncomfortable internal experience (e.g., thoughts, emotions, sensations, memories, urges) through escape or avoidance (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Self-report studies have demonstrated that individuals with anxiety disorders (Begotka, Woods, & Wetterneck, 2004; Hayes, Luoma, Bond, Masuda, & Lillis, 2006; Kashdan, Breen, Afram, & Terhar, 2010) and depressive disorders (Berking, Neacsiu, Comtois, & Linehan, 2009; Hayes et al., 2006; Shahar & Herr, 2011; Tull, Gratz, Salters, & Roemer, 2004) display high levels of self-reported experiential avoidance. The existing literature also has suggested that experiential avoidance both predicts generalized anxiety disorder symptoms even when the variance associated with frequency of negative affect is parceled out (Lee et al., 2010) and mediates the relationship between neuroticism and posttraumatic stress disorder symptoms (Maack, Tull, & Gratz, 2012; Pickett, Lodis, Parkhill, & Orcutt, 2012). Furthermore, Cheavens and Heiy (2011) recently found that avoidant coping partially mediates the relationship between the experience of negative emotions and major depressive symptoms among individuals high in experiential avoidance. Taken together, these findings suggest that emotional disorder symptoms are not simply a product of high levels of negative affect; instead, the combination of strong negative emotions and how one relates to them when they occur appears to be important for the development of these disorders.

Individuals with emotional disorders also show deficits in mindfulness (Cheavens et al., 2005; Hayes et al., 1996), a related construct that refers to attention and awareness toward the present moment in an accepting manner regardless of how unpleasant the experience (Kabat-Zinn, 1982). Studies have shown that deficits in mindfulness are common across the emotional disorders (Baer, Smith, Hopkins, Kritemeyer, & Toney, 2006; K. Brown & Ryan, 2003; Cash & Whittingham, 2010; Rasmussen & Pidgeon, 2011), which supports the case for similar underlying constructs in these disorders. Results of a recent study on the effects of dispositional mindfulness on response to a laboratory stressor suggested that individuals reporting higher levels of mindfulness display lower levels of self-reported anxiety and an attenuated cortisol response than do individuals endorsing lower levels of this construct (K. Brown, Weinstein, & Creswell, 2011). The impact of mindfulness on stress-related cortisol secretion has been associated with attenuated amygdala activation in response to threat (Creswell,

Way, Eisenberger, & Leiberman, 2007). Consistent with data on experiential avoidance, results from studies have suggested that the degree to which one responds to negative emotions in a mindful manner predicts psychological symptoms over and above the contributions of a traitlike tendency to experience negative emotions (Sauer & Baer, 2009; Segal, Williams, & Teasdale, 2002).

Evidence has suggested that many of the maladaptive behaviors associated with emotional disorders serve a function of facilitating escape or avoidance of intense emotions. Such behaviors include overt situational avoidance as well as more subtle forms of avoidance and safety behaviors. For example, situational avoidance is a hallmark feature of social anxiety disorder, specific phobias, posttraumatic stress disorder, depression, agoraphobia, and panic disorder (APA, 2013). Subtle forms of avoidance are also typical across most emotional disorders. In generalized anxiety disorder and obsessive-compulsive disorder, engaging in worry or compulsions (Newman & Llera, 2011), respectively, are subtle ways of avoiding the distress associated with experiencing anxiety. In social anxiety, subtle avoidance can include behaviors such as decreased eye contact or standing farther away from people during conversations or safety behaviors, such as engaging in social interactions only with a close friend present. In panic disorder, subtle avoidance includes avoiding activities that produce anxietylike sensations, such as exercise or drinking coffee (i.e., interoceptive avoidance). Safety behaviors across disorders include carrying around medications or even empty medication bottles, making sure to always have a cell phone or water on hand, or engaging in certain activities only with a "safe" person.

Addressing such behavioral avoidance is an important element of most cognitive-behavioral treatments for emotional disorders, such as through use of fear and avoidance hierarchies in anxiety disorder protocols or activity scheduling in depression treatments. Some treatment protocols posit behavioral avoidance as comprising the core of the dysfunction, as in the example of behavioral activation, a well-supported treatment for depression, which is based on the notion that depressive symptoms are maintained by chronic avoidance of engagement or activity (Manos, Kanter, & Busch, 2010).

In addition to engaging in problematic avoidant behaviors, individuals with emotional disorders engage in cognitive coping motivated by avoidance. Such processes include emotion suppression and rumination. *Emotion suppression* is a strategy in which individuals deliberately attempt to push unpleasant, emotion-inducing cognitions out of awareness; paradoxically, this strategy has been shown to produce rebound effects in which the suppressed thoughts return with greater frequency and intensity (Rassin, Muris, Schmidt, & Merkelbach, 2000; Wegner, Schneider, Carter, & White, 1987). High levels of emotion suppression have been demonstrated across emotional disorders, including depression, generalized anxiety disorder, obsessive-compulsive disorder, and posttraumatic stress disorder (Purdon, 1999), and have also been shown to exacerbate symptoms (Abramowitz, Tolin, & Street, 2001). In particular, emotional suppression has been associated with increased physiological arousal (Hofmann, Heering, Sawyer, & Asnaani, 2009). It is hypothesized that emotion suppression, like other forms of avoidance, is a negatively reinforced behavior that produces short-term reductions in negative affect, despite then spawning increased negative emotions in the longer term.

Rumination refers to repetitively and passively focusing on negative mood and its possible causes, meanings, and consequences (Nolen-Hoeksema, 1991). Like suppression, rumination can be conceptualized as an avoidant strategy because passive focus on surface matters may serve to protect individuals from more distressing concerns (Lyubomirsky & Nolen-Hoeksema, 1995; Lyubomirsky, Tucker, Caldwell, & Berg, 1999). Rumination has been shown to intensify negative affect (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), which leads to more rumination, in what Selby, Anestis, and Joiner (2008) described as an emotional cascade; this process continues until a maladaptive behavior (reassurance seeking, substance use, binge eating, etc.) interrupts the cycle. Rumination appears to be prominent across emotional disorders (see Aldao et al., 2010) and prospectively predicts increases in anxiety and depressive symptoms (Butler & Nolen-Hoeksema, 1994; Calmes & Roberts, 2007; Hong, 2007; Nolen-Hoeksema, 2000; Nolen-Hoeksema, Larson, & Grayson, 1999; O'Connor, O'Connor, & Marshall, 2007; Sarin, Abela, & Auerbach, 2005; Segerstrom, Tsao, Alden, & Craske, 2000).

It seems clear that negative reactions to strong emotions lead to similar forms of avoidant cognitive coping (e.g., emotion suppression and rumination) common to all emotional disorders. These strategies that intensify already strong negative emotions appear to lead to greater use of disorder-specific behavioral coping. Overall, the literature has suggested that individuals with emotional disorders experience strong negative emotions with frequency and evaluate these experiences as aversive. As a result of these negative reactions to their emotions, such individuals are more likely to engage in avoidant coping strategies to manage emotional experiences, and these strategies, in turn, paradoxically increase the frequency/intensity of negative emotions. Once again, we suggest that this functional relationship, driven by neuroticism, is at the core of disorders of emotion.

Neuroticism/Trait Anxiety, Nosology, and Dimensional Diagnosis of Emotional Disorders

It was long thought that *DSM-IV-TR* represented the zenith of a splitting approach to nosology we described earlier and that began in the 1980s with the publication of *DSM-III*, an approach basically unchanged in *DSM-5*. The advent of an objective empirically based system of classification of mental disorders was an enormous advance over previous systems based on unsupported etiological theories best exemplified by the term *neurosis*. Beginning in the 1980s, with the splitting of neuroses into anxiety, depressive, somatoform, and related disorders, meaningful research on outcomes of pharmacological and individual psychological treatments, particularly cognitive-behavioral therapy, targeting these disorders appeared (e.g., Barlow et al., 1984). It also became clear at that time, on the basis of the pioneering work of Strupp (1973), that clinical trials require the generation of detailed individual therapeutic protocols to specify an independent variable. As a result, these psychotherapeutic treatments were increasingly characterized by well-articulated individual protocols targeted to specific forms of psychopathology as articulated in *DSM-III* and its successors, particularly anxiety and depressive disorders. These treatments were then evaluated empirically and found efficacious in a variety of formats, uses, and settings (Barlow, 1996, 2004, 2008; Barlow, Gorman, Shear, & Woods, 2000; Heimberg, Liebowitz, & Hope, 1998; Nathan & Gorman, 2007).

It is fair to say that these findings have had a substantial impact in that public-health authorities have allocated billions of dollars for training and dissemination of these treatments (McHugh & Barlow, 2010). This approach to nosology also has ensured high rates of diagnostic reliability; however, as mentioned earlier, there was growing suspicion both that advances in classification and treatment development represented by this approach came at the expense of diagnostic validity and that the current system may be overemphasizing categories that are minor variations of broader underlying syndromes. The careful consideration of these broader underlying syndromes as a conceptual approach to nosology would not imply a return to a nonempirical system of classification based on theories of etiology. Rather, this thinking points to a quantitative approach using structural equation modeling to examine the full range of anxiety and mood disorders without the constraints of artificial categories, given their strong relationship and potential overlap. Thus, our evolving view is that *DSM-5* emotional disorder categories do not qualify in any sense as real entities (Kendell, 1975) but do seem to be useful concepts or constructs that emerge as "blips" on a general background of temperament. The conceptualization of emotional disorders in a more dimensional fashion should result in a more satisfactory representation of salient aspects of these disorders that would eliminate vexing issues of comorbidity. But moving from this conceptualization to a dimensional system of diagnostic assessment with implications for treatment has proven an exceedingly difficult task even in areas such as personality disorders in which there is widespread agreement that this would be the preferred approach (Widiger & Crego, 2013). The recent failure to accomplish this goal in *DSM-5* underscores these difficulties.

In a preliminary attempt to conceptualize how this effort might work for emotional disorders, we proposed a dimensional classification scheme to reflect the research described earlier (T. A. Brown & Barlow, 2009). The purpose would be to create a profile that may provide a more complete portrayal of a patient's clinical presentation than would a more categorical approach that often consists of several individual comorbid diagnoses. The profile would highlight levels of constructs thought to be important in forming a useful case conceptualization, including neuroticism, extraversion (referred to as behavioral activation/positive affectivity in this model), avoidance, mood, and specific foci of anxiety (e.g., panic and other autonomic surges, somatic symptoms, intrusive cognitions, social evaluation, and trauma). Scores on the dimension of trait neuroticism, arguably the most important construct in this model, reflect the frequency, intensity, and distress associated with negative emotions, as well as perceptions of uncontrollability regarding future challenges and low self-efficacy regarding one's ability to cope. The higher-order dimension of extraversion/positive affect is also represented because low levels of this trait are specifically associated with major depressive disorder, social anxiety disorder, and agoraphobia, whereas high levels are associated with euthymic states of bipolar and cyclothymic disorders. As highlighted earlier, individuals with high levels of neuroticism are likely to display avoidance behaviors. In this dimensional system, avoidance is broken into two types: behavioral/interoceptive and cognitive/emotional.

Specific examples of disorder profiles highlight the heuristic clinical value associated with dimensional classification of emotional disorders. For example, individuals with a principal diagnosis of panic disorder would likely display profiles with high levels of neuroticism, avoidance, and preoccupation with panic/autonomic arousal and other somatic symptoms. In contrast, patients presenting with posttraumatic stress disorder might display high neuroticism and preoccupation with panic/autonomic arousal (flashbacks) and past trauma. Although

each diagnostic category is linked to a prototypic dimensional profile, this classification system would allow clinicians to determine the extent to which other key features are present that would potentially affect treatment planning. A new measure, the multidimensional emotional disorder inventory (MEDI), recently was developed to assess these important vulnerabilities and characteristics of emotional disorders with a single assessment tool; the ongoing MEDI validation study has suggested that this measure may be a reliable and valid method for assessing important emotional disorder dimensions (Rosellini, 2013). A representation of what a MEDI profile might look like is shown in Figure 1. These data present clinical estimates of constructs composing the dimensional scheme from a patient seen at CARD with a principal diagnosis of posttraumatic stress disorder (motor vehicle accident) and additional diagnoses of generalized anxiety disorder and subclinical depression. Under the current diagnostic system, unless a patient meets full diagnostic criteria for a comorbid disorder, information on the dimensions not associated with the primary diagnosis are discarded. Given that the rates of comorbidity among emotional disorders are high, with even greater overlap at the subclinical level (T. A. Brown & Barlow 2009), a dimensional classification system would allow for the integration of several important areas of functioning.

Malleability of Neuroticism

The evidence regarding the malleability of personality traits over time or in response to therapeutic intervention is mixed. As noted earlier, Kagan (1989, 1994) described his conceptualization of behavioral inhibition as strongly heritable and stable; however, empirical evidence, including Kagan's own work, has suggested that only 30% of children who clearly met criteria for this trait as young children went on to develop anxiety disorders, although some of the participants may have remained shy. Several additional studies have yielded similar results (e.g., Hayward, Killen, Kraemer, & Taylor, 1998; Hirshfeld-Becker et al., 2007; Schwartz, Snidman, & Kagan, 1999). These results led Kagan to view behavioral inhibition as a constraining factor subject to environmental influences. Such influences may include stress and having parents diagnosed with anxiety disorders; behaviorally inhibited third to sixth graders were more likely to experience increased anxiety if they reported more daily hassles (Brozina & Abela, 2006) and were more likely to be diagnosed with an anxiety disorder if their parents also experienced such disorders (Biederman et al., 2001).

L. A. Clark (2009) has reviewed research examining stability and change in personality disorders in adults. Contrary to the thinking of most personality theorists, as well as a statement in the *DSM-5*, which holds that personality traits are stable, inflexible, and pervasive, is Clark's observation that the collection of traits and behaviors that make up the definition of most personality disorders do change, albeit slowly over time, with the greatest change occurring in the behavioral manifestations of these traits. Furthermore, researchers examining longitudinal changes in negative traits, such as neuroticism, in the normal population have observed gradual

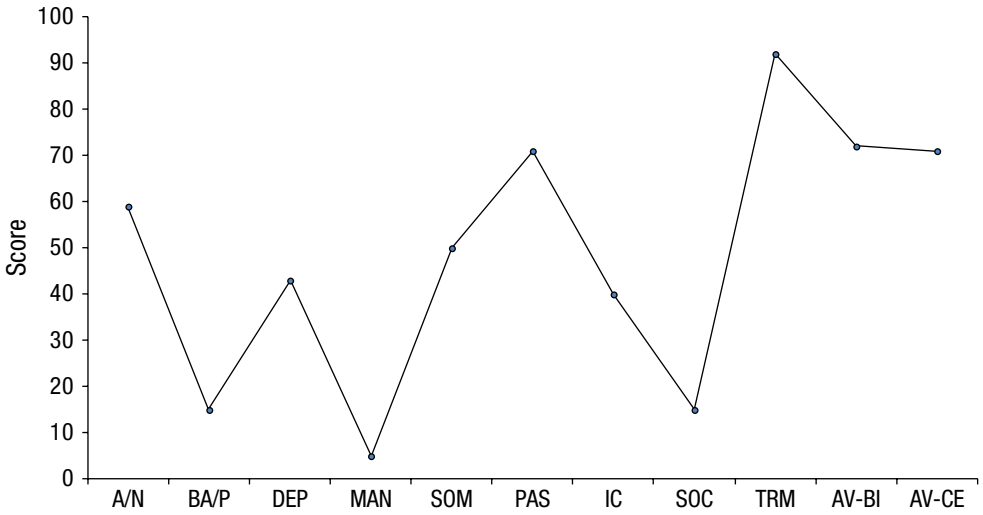

Fig. 1. Example profile of patient evaluated with a dimensional classification system. Higher scores on the *y*-axis indicate higher levels of the *x*-dimension; otherwise, the *y*-axis metric is arbitrary and used for illustrative purposes. A/N = anxiety/neuroticism; BA/P = behavioral activation/positive affect; DEP = unipolar depression; MAN = mania; SOM = somatic anxiety; PAS = panic and related autonomic surges; IC = intrusive cognitions; SOC = social evaluation; TRM = past trauma; AV-BI = behavioral and interoceptive avoidance; AV-CE = cognitive and emotional avoidance.

age-related decreases that continue long into old age (Roberts & Mroczeck, 2008; Roberts, Walton, & Viechtbauer, 2006). Similar age-related decreases in the related higher-order construct of internalizing have also been found; specifically, internalizing means and indicator intercepts were lower for older-aged cohorts (Eaton, Krueger, & Oltmanns, 2011; Oltmanns & Balsis, 2011). This pattern of results is found at the mean level, which suggests that, summed across individuals, neuroticism decreases across time. In addition, change in neuroticism has been examined at the individual level using growth modeling (Mroczek & Spiro, 2003); results suggested that there is great variability in extent of change on temperamental variables, with some people remaining at stable levels and other people changing a great deal (Helson, Jones, & Kwan, 2002; Small, Hertzog, Hultsch, & Dixon, 2003).

At CARD, we have also investigated longitudinal change in neuroticism, with particular focus on responsiveness to psychological intervention, and have encountered mixed findings. For example, in a study on the treatment of panic disorder (T. A. Brown & Barlow, 1995), comorbid anxiety and depressive diagnoses improved immediately after successful treatment even though they were not specifically targeted, which suggests, as described earlier, the existence of an underlying temperamental vulnerability. But at a 2-year follow-up, comorbid diagnoses had returned to a level (30%) that was no longer significantly different from pretreatment. This result occurred despite the fact that, in the aggregate, patients maintained or improved on gains for panic disorder across the follow-up interval, which indicates considerable independence between panic disorder symptoms and related comorbidity. Although speculative, and contrary to the more usual interpretations offered earlier, these findings may suggest that current cognitive-behavioral treatments are generally effective in addressing the specific symptoms and maintaining processes of the targeted disorder (in this case, panic disorder) both immediately and at follow-up but do not result in substantial reductions in general predispositional features (e.g., neuroticism), which leaves patients vulnerable to the emergence or persistence of other disorders. These findings also raise the possibility that current psychological treatments have become overly specialized because they focus on disorder-specific features, such as panic attacks in panic disorder or rituals connected to obsessional thought in obsessive-compulsive disorder, neglecting broader dimensions that might produce more favorable long-term outcomes across all disorders.

In a more direct evaluation of this issue, the temporal stability (8 months) and predictive utility of self-reported levels of neuroticism and extraversion in 41 individuals diagnosed with major depressive disorder (most of whom received some kind of treatment during this time) has also been examined (Eaton et al., 2011; Oltmanns & Balsis, 2011). Low levels of extraversion at Time 1 predicted poorer clinical outcome of major depressive disorder at the 8-month reassessment. Moreover, neuroticism and extraversion were remarkably stable over time, despite changes in clinical state. In fact, although more than one third of depressed participants were classified as no longer depressed at the 8-month follow-up, neuroticism and extraversion displayed the same high level of temporal stability in this group as in a subgroup of participants who were depressed at both assessment points. Despite these overall findings, because there was no information available regarding what types of treatment patients received during this study, it is difficult to determine how specific treatments may have affected the temperamental constructs.

In contrast, other researchers have indeed found changes in neuroticism as a function of time and treatment. For example, we examined the temporal course and temporal structural relationships of dimensions of temperament (neuroticism, extraversion) within *DSM-IV-TR* disorder constructs of depression, social anxiety disorder, and generalized anxiety disorder (T. A. Brown, 2007; T. A. Brown & Barlow, 2009). Outpatients with these disorders (N = 606) were first examined at intake and then reassessed at 1- and 2-year follow-ups. The majority (76%) of patients received some kind of treatment after intake, although not all at CARD, of varying duration and quality. The overall rate of diagnosed anxiety and mood disorders declined significantly during follow-up from 100% at intake to 58% at the 2-year follow-up. Despite the marked decline in *DSM-IV-TR* diagnoses by the 2-year follow-up, test-retest correlations of the factors and unconditional latent growth models indicated that extraversion evidenced a very high degree of temporal stability, consistent with its conceptualization as a trait vulnerability construct that is relatively unaffected by treatment. However, of the five constructs examined, neuroticism evidenced the greatest amount of temporal change and was the dimension associated with the largest treatment effect. In addition to its inconsistency with some prior research, such as that reviewed earlier (e.g., Kasch et al., 2002), this finding is clearly at odds with conceptual assumptions that core dimensions of temperament are stable, inflexible, and more resistant to psychological treatment.

Levels of neuroticism and extraversion have also been explored in a more specified context across a large randomized controlled trial of cognitive therapy compared with placebo for adults with major depressive disorder (Tang et al., 2009). Results indicated that cognitive therapy produced greater changes in both neuroticism and extraversion than did placebo, but contrary to T. A. Brown's (2007) results, cognitive therapy maintained a

significant effect only for extraversion after controlling for changes in depression symptoms during treatment. Nevertheless, the Tang et al. (2009) study differs from Brown's study in the clinical features of the sample (pure major depressive disorder vs. heterogeneous anxiety and unipolar depressive disorders) and the degree of control provided regarding the treatment condition (placebo controlled and with stringent adherence/fidelity procedures vs. naturalistic, heterogeneous treatment).

There is also evidence that neuroticism may operate differently than the *DSM-IV-TR* disorder constructs in several ways (T. A. Brown, 2007). For instance, unconditional latent growth models of each *DSM-IV-TR* disorder construct revealed inverse relations between the intercept and the slope; that is, higher initial disorder severity was associated with greater change over time. However, the intercept and the slope of neuroticism were positively correlated (r = .47), which indicated that patients with higher initial levels of neuroticism tended to show less change in this dimension over time, and, conversely, patients with lower initial levels of neuroticism tended to evidence greater change. Thus, unlike the *DSM-IV-TR* disorders, the stability of neuroticism increased as a function of initial severity. In addition, parallel-process latent growth models indicated that higher initial levels of neuroticism were associated with less change in the *DSM-IV-TR* constructs of generalized anxiety disorder and social anxiety disorder. Although neuroticism alone demonstrated no temporal relation with depression, the presence of chronic stress moderated the relationship such that high neuroticism resulted in less improvement in depression as the level of chronic stress increased (T. A. Brown & Rosellini, 2011). These results are consistent with results from earlier work, as well as theory, that showed that neuroticism has directional temporal effects on Axis I psychopathology (cf. Gershuny & Sher, 1998; Kasch et al., 2002; Meyer, Johnson, & Winters, 2001) but that the converse does not seem to occur; that is, initial levels of the *DSM-IV-TR* disorders did not predict increases in temperament over time.

Finally, evidence has suggested that change in *DSM* disorder constructs (e.g., depression, social anxiety disorder, and generalized anxiety disorder) is significantly related to change in neuroticism (T. A. Brown, 2007). Of particular interest is the finding that all the temporal covariance of the *DSM-IV-TR* disorder constructs was accounted for by change in neuroticism; that is, when neuroticism was specified as a predictor, there was no temporal overlap among disorder constructs. The correlational nature of these findings precludes firm conclusions about the direction of these effects. Nevertheless, and counter to some earlier evidence and conceptualizations (T. A. Brown et al., 1995; Kasch et al., 2002), all of these findings suggest that neuroticism may be therapeutically malleable, and it is this malleability that mediates the extent of change in the emotional disorders.

Some authors have suggested that decreases in neuroticism over time may partly reflect the fact that measures of temperament overlap to some degree with symptomatic measures of anxiety and depression, which results in distortions on estimates of temperament (mood-state distortion; cf. L. A. Clark, Vittengl, Kraft, & Jarrett, 2003; Jylhä & Isometsä, 2006; Widiger, Verheul, & van den Brink, 1999). That is, the measurement of neuroticism consists of some combination of stable temperamental variance (i.e., vulnerability) and variability attributable to generalized distress that would be subject to greater temporal fluctuation and would imply that neuroticism is apt to covary with temporal fluctuations in the severity of disorders. However, results from a recent study have suggested that measures of neuroticism (and extraversion) primarily capture true temperamental variance even in individuals with emotional disorders (Naragon-Gainey, Gallagher, & Brown, 2013). In addition, a number of longitudinal studies have controlled for the periodic occurrence of anxious or depressive symptoms and still found that neuroticism acted independently in predicting anxiety and mood (Lahey, 2009; Spijker, de Graf, Oldehinkel, Nolen, & Ormel, 2007).

In sum, the malleability of neuroticism and other temperamental variables, particularly in response to treatment, remains an unsettled question. The studies described earlier, in which researchers have examined changes in temperamental variables in the context of naturalistic treatments or treatments targeting disorder-specific symptoms, have yielded mixed findings. In some studies, temperament dimensions appeared to change during the course of treatment in the expected directions (e.g., T. A. Brown, 2007; Kennedy, Rapee, & Edwards, 2009), whereas in other studies, no changes in temperament occurred (e.g., Kasch et al., 2002). Inconsistencies also exist in the degree to which the different dimensions of temperament respond to treatment across studies. Indeed, the research reviewed raises questions about the nature and mechanisms of change of temperament during treatment of emotional disorders, how best to measure temperament, and whether directly targeting temperament therapeutically would lead to more definitive results.

Prevention and Treatment of Neuroticism

In most of the studies in which researchers have examined changes in temperament in response to psychological interventions, including the studies described in the

previous section, researchers have not provided a priori hypotheses regarding how and why the study treatment might affect temperament other than as a by-product of symptom reduction. The interventions used were not designed to target features of temperament but, rather, to address symptoms. Within such studies, it is difficult to interpret changes in temperament. One explanation for the mixed findings across studies is that there may be specific interactions between the intervention and the dimensions of temperament that influence which temperament variables respond and to what extent. Such interactions have been largely unexplored in studies of psychological-treatment outcomes. However, recent research from pharmacological-treatment studies has supported this treatment-temperament interaction hypothesis, and emerging research from our own laboratory has suggested that dimensions of temperament can be more directly targeted through specialized treatments. In this section, we review recent evidence for treatments specifically designed to affect temperament and discuss briefly our own efforts to develop a psychological treatment focused on directly addressing neurotic temperament.

Most of the studies in which researchers examine interventions specifically designed to target temperament have come from the literature on psychopharmacology (for a review, see Soskin, Carl, Alpert, & Fava, 2012). Results from these studies have provided some evidence for specific interactions between treatment agents and temperament variables. To summarize, this research has indicated that serotonergic drug agents (i.e., selective serotonin reuptake inhibitors) produce dampening effects on neuroticism (Fu et al., 2004; Harmer et al., 2009; Harmer, Mackay, Reid, Cowen, & Goodwin, 2006; Murphy, Yiend, Lester, Cowen, & Harmer, 2009; Quilty, Meusel, & Bagby, 2008) and possibly to a lesser extent on extraversion (McCabe, Mishor, Cowen, & Harmer, 2010), whereas catecholaminergic (i.e., noradrenergic/dopaminergic) agents produce specific enhancement of extraversion (McCabe et al., 2010; Tomarken, Dichter, Freid, Addington, & Shelton, 2004). The specific neurobiological properties of these agents have been hypothesized to mediate such observed effects on temperament variables. For example, serotonergic agents have been shown to decrease hyperreactivity of the amygdala in response to fear-inducing stimuli and to inhibit dopaminergic neurotransmission in areas of the prefrontal cortex. In contrast, catecholaminergic agents upregulate noradrenergic and dopaminergic neurotransmission, particularly within the mesolimbic reward circuitry (Soskin et al., 2012). Despite the obvious differences between pharmacological and psychological treatments, the studies on preferential effects of pharmacological agents on dimensions of temperament have provided some support for the notion that treatments can be designed to selectively target temperamental variables. As a corollary, the pharmacologic results also suggested that treatments, whether pharmacological or psychological, should not be expected to produce equivalent changes in temperament. Some treatments may produce no effects on temperament, whereas other treatments may produce generalized or specific effects on dimensions of temperament.

Behavioral interventions designed to specifically address temperamental vulnerabilities are limited in number. Rapee, Kennedy, Ingram, Edwards, and Sweeney's (2005) intervention for children identified as behaviorally inhibited was designed with the purpose of preventing the later onset of anxiety and related disorders and serves as one example. The program consists of a parent-focused intervention that includes psychoeducation about the nature of anxiety, traditional cognitive-behavioral strategies (i.e., exposure and cognitive restructuring) directed toward personal concerns, and training in behavior management techniques that prevent an overprotective parenting style. Results from randomized controlled trials (Rapee et al., 2005; Rapee, Kennedy, Ingram, Edwards & Sweeney, 2010) have indicated that this program is clearly successful at preventing anxiety disorders, but for our purposes, the most interesting findings are those on the effects of the program on temperament.

Specifically, using a brief version of this program, Rapee et al. (2010) found that levels of behavioral inhibition did not differ significantly on the basis of either parent report or laboratory observation, despite the success in preventing the later onset of anxiety disorders. However, when the program was administered in a more intensive format with higher risk children, compared with a group that did not receive the treatment, reductions in measures of temperament did occur (Kennedy et al., 2009). Rapee et al. also noted that differences among groups seemed to increase with time, which suggested to them that interventions directed at temperament (and related risk factors) might produce an increasing trajectory of change in temperament over the years, at least in children.

In addition, some work has been conducted in an effort to identify intervention strategies specifically for targeting positive affect (extraversion). For example, in an experience-sampling study, Mata et al. (2012) found that both participants diagnosed with major depressive disorder and control participants reported increases in positive affect directly following physical activity and that depressed participants in particular demonstrated a dose-response effect such that longer and more intense instances of physical activity led to greater increases in positive affect. Speisman, Kumar, Rani, Foster, and Ormerod (2012) recently demonstrated in

animal laboratories that exercise increases neurogenesis, which could possibly be one mechanism of action in successful psychological treatments using exercise. Despite strong preliminary evidence, this theory must now undergo the slow process of scientific confirmation.

Given the clinical promise of therapeutically addressing temperamental vulnerabilities, we have devoted more than a decade to developing a psychological treatment that targets the putative, fundamental, underlying processes of anxiety and mood disorders that may be more closely related to temperament. This treatment, the unified protocol for transdiagnostic treatment of emotional disorders (UP), which has been described in detail elsewhere (Barlow et al., 2011), is a cognitive-behavioral intervention designed to address core temperamental processes in emotional disorders. The UP targets identification and modification of the strong negative reactions to emotions that lead to problematic, avoidant coping across emotional disorders (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010). Amelioration of negative reactions to emotions in turn changes the frequency and intensity of future emotional experiences and thereby affects temperamental constructs.

The UP has now been evaluated for its efficacy in treating anxiety disorders in a series of preliminary trials culminating with a small randomized controlled trial (N = 37) comparing a treatment group with a wait list control group (Ellard et al., 2010; Farchione et al., 2012). Results from these studies have indicated that the UP is an efficacious treatment for a range of anxiety disorders with stable improvements out to an 18-month follow-up (Bullis, Fortune, Farchione, & Barlow, 2013). We have also recently begun a large randomized controlled equivalence trial (N = 250) comparing the UP with four well-established single anxiety disorder treatment protocols on the basis of patients' principal diagnoses (generalized anxiety disorder, obsessive-compulsive disorder, social anxiety disorder, or panic disorder with or without agoraphobia).

In following with the goal of assessing the extent to which the UP addresses temperamental vulnerabilities in addition to current symptoms, we have also conducted an investigation of the effects of the UP on dimensions of temperament (see Carl, Gallagher, Sauer-Zavala, Bentley, & Barlow, 2013) in the context of the randomized controlled trial mentioned in the previous paragraph (i.e., Farchione et al., 2012). In brief, our results indicated that in the treatment group, compared with the wait list group, the UP produced small to moderate effects on both neuroticism and extraversion from pre- to posttreatment, and these changes in temperament are associated with improvements in core symptomatology, functional impairment, and quality of life (Carl et al., 2013). The results of this investigation suggest the importance of changes in temperament as they affect treatment outcomes. Neuroticism and extraversion contributed to both shared and distinct treatment outcomes. Decreased neuroticism at posttreatment and at 6-month follow-up predicted decreased anxiety and depressive symptoms. Increased extraversion was associated with decreased depressive symptoms at posttreatment and decreased anxiety symptoms at 6-month follow-up, and changes in both temperament variables predicted reductions in functional impairment at 6-month follow-up. Finally, extraversion alone was associated with higher quality of life at posttreatment and at 6-month follow-up. Although preliminary, these results suggest that there are both common and differentiated outcomes associated with changes in specific dimensions of temperament. Although both neuroticism and extraversion can affect depression and anxiety symptoms and functional impairment, only extraversion appears to directly influence quality of life. In future research, it will be important to investigate and gain a better understanding of what accounts for the variability in the effects of these temperamental predictors on treatment outcomes.

In summary, contrary to traditional conceptions, a variety of research has suggested that dimensions of temperament may be malleable over time or in response to treatment, but such findings have been mixed, which indicates that more research is required to identify specific conditions that affect temperament. Specifically, recently developed interventions that target dimensions of temperament more directly have provided preliminary support for the notion that psychological interventions can address temperamental vulnerabilities and that such improvements are associated with a range of beneficial treatment outcomes (Carl et al., 2013; Farchione et al., 2012; Kennedy et al., 2009). If confirmed, these findings may shift the focus of investigation into the nature, diagnosis, and treatment of emotional disorders.

Future Research Directions

The construct of neuroticism is almost as old as the study of psychopathology itself, but recent developments described herein suggest fresh, new directions for research. Considered broadly, can we develop targeted psychological interventions for neuroticism? If so, will these interventions provide a more efficient and effective way to affect the broad sweep of phenomena across the spectrum of emotional disorders, including common patterns of comorbidity and subthreshold symptomatic presentations? Will these conceptions move us further along toward the goal of a more satisfactory dimensional system for classifying the emotional disorders and facilitate the development of diagnostic instruments that will greatly simplify the process of assessment? And can we

usefully extend these research objectives to other relevant temperaments, such as positive affect and perhaps constraint? The accumulation of important basic research covered briefly in this review suggests that it may now be possible to translate these concepts into a fundamentally new approach to the diagnosis, assessment, and treatment of emotional disorders.

Author Contributions

D. H. Barlow developed the main thesis of the manuscript. D. H. Barlow, S. Sauer-Zavala, J. R. Carl, J. R. Bullis, and K. K. Ellard all contributed substantially to the literature review and subsequent drafting of the manuscript in support of this thesis.

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The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Note

1. We henceforth refer to this construct as *neuroticism*; however, it should be noted that the individual studies described may have used alternate terms.

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