3

Integrating Temperament into the Study of Emotional Disorders

During the last two decades of the twentieth century, the study of temperament and personality proceeded largely independently from research on anxiety, depressive, and related disorders. Now that we have explicated our theory of the origins of neuroticism, the temperamental tendency to experience negative emotions, it is necessary to take a step back to outline the developments in clinical science that resulted in a new and more empirical focus on incorporating temperamental constructs into any consideration of the nature, classification, and treatment of emotional disorders (see Bullis, Boettcher, Sauer-Zavala, Franchione, & Barlow, 2019).

EVIDENCE-BASED TREATMENTS AND THE DSM

Prior to 1980, the emergence of anxiety and depressive disorders, along with other related conditions, was generally accounted for by widely accepted but empirically unsubstantiated theories of personality development, and these conditions were classified very broadly under the umbrella term *neurosis*. Then two advances in clinical science profoundly changed the landscape of how the development and treatment of these emotional disorders were viewed. First, methods of scientific verification were enhanced during the 1970s and 1980s, resulting in an ability to determine, in an objective fashion, the efficacy of psychological and pharmacological interventions for these conditions. This was accomplished primarily by the refinement and increasing sophistication of clinical trial methodology, including the introduction of rigorous, cost-effective single-case experimental designs capable of establishing the efficacy of interventions for individual patients, that could then

be replicated in additional cases (Barlow, Nock, & Hersen, 2009; Barlow & Hersen, 1984). Also, clinical scientists began to realize, based partly on the pioneering work of Hans Strupp (1973), that successfully evaluating interventions required defining their therapeutic procedures sufficiently such that other clinicians could deliver these treatments in the manner in which they were intended, albeit with flexible adaptations for particular patients or other local circumstances. Thus detailed individual therapeutic protocols began to appear, each targeting specific forms of psychopathology, particularly anxiety and depressive disorders.

Indeed, results from the clinical trials during that era began to show efficacy of both psychological and pharmacological treatments tailored to various specific disorders (e.g., phobic disorders, depression; cf. Barlow & Hersen, 1984). These positive outcomes in treating discrete disorders with manualized protocols, accompanied by a growing mandate for evidence-based practice by heath care policymakers and third-party payers (Baker, 2001; Barlow, 1996, 2004; Sackett, Strauss, Richardson, Rosenberg, & Haynes, 2000), began to undermine the credibility of the more traditional broad-based, but nonspecific, treatment approaches focused on problems with personality development more generally.

A second influence, perhaps having an even greater impact on the shift away from personality-based conceptions of psychopathology and treatment, was the appearance of the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; American Psychiatric Association, 1980) in 1980. In this revolutionary approach to diagnosis, global conceptions of psychopathology based on unsubstantiated theories (i.e., neuroses) were eschewed in favor of an atheoretical, empirically derived taxonomy focused on observable presenting problems. Thus individuals who had received a diagnosis of neurosis during the preceding years of the 20th century were now classified more narrowly into specific anxiety, depressive, dissociative, and related disorder categories. See Chapter 5 in this volume for detailed treatment of the evolution of the DSM system.

The impact of this development is hard to imagine 40 years later, but suffice it to say that the "death of neurosis" (Barlow, 1982) was extremely contentious, provoking outrage in some circles; indeed, this controversy played out not only in scholarly outlets such as journals and professional meetings, but also in the popular press. Nevertheless, the result was a completely transformed nosological system consisting of narrowly construed and thinly sliced definitional criteria for psychopathology that, for the first time, made possible operational definitions of behavioral disorders. Thus clinical investigators were better able to identify dependent variables in clinical trials (the disorders) in a reliable fashion. This development complemented the increasing specificity of independent variables in clinical trials research, the psychological interventions that had also been operationalized into fairly

detailed guidelines or manuals, as noted above (e.g., Barlow, 1985, 2004). These advances in clinical science led to an explosion of efficacy trials testing discrete interventions for each DSM-III disorder during the 1990s, with strong support from funding agencies around the world. As a result, a new gold standard for psychological care, evidence-based interventions for narrowly defined conditions, emerged that, in turn, had broad impact on mental health policy, service delivery, and funding (Barlow, 2004; Barlow, Bullis, Comer, & Ametaj, 2013; McHugh & Barlow, 2010).

However, even during that era, with its focus on discrete disorders, clinicians and investigators recognized phenomena that were common across large classes of mental illness and began focusing once again, but with more experimental rigor, on features characterizing psychopathology more generally (Barlow, 1988). An age-old tension exists in the science of classification of mental disorders between researchers who came to be called "splitters," advocating the advantages of narrowly defined slices of psychopathology, and those called "lumpers," who found more value in drilling down to common underlying factors among disorders (Brown & Barlow, 2005, 2009). The rationale among "lumpers" was that ensuring adequate reliability of diagnostic categories might have been achieved at the expense of validity, in that DSM-III and its successive iterations were overemphasizing categories that are minor variations of a broader underlying syndrome. (See Chapter 5, this volume, for a description of prominent proposals for the classification of mental disorders that highlight shared features across disorders rather than emphasizing differences.)

COMMONALITIES ACROSS DIAGNOSES: ANXIETY AND FEAR/PANIC

With the development and embrace of DSM-III, it was no longer acceptable to use *neurosis* as an umbrella term for similar conditions (Barlow, 1982). And yet the apparent shared features of these conditions prompted a closer examination of commonalities across disorders along the traditional neurotic spectrum. One parallel across the anxiety disorders was the presence of similar affective states, including anxiety, fear, and the newly introduced (in 1980) phenomenon of panic, which were explored with more objective, experimental rigor.

Fear/Panic

In the mid- to late 1980s, it became clear that the constructs of anxiety and fear, terms that had previously been used interchangeably, actually refer to different emotional states. Both of these states occur across all emotional

disorders, and each plays a unique role in the origins and presentations of them (Barlow, 1988). By the 1990s, it had also become widely accepted that the newly recognized phenomenon of panic attacks encompassed the well-known fight-or-flight component of fear, albeit occurring at inappropriate times (i.e., when there was nothing to be afraid of; Barlow, 1988; Barlow et al., 1985; Cannon, 1929). Two primary types of evidence supported this distinction between anxiety and fear/panic, which was to become increasingly important in the conceptions of psychopathology that would ultimately inform nosology and etiology of emotional disorders (Bouton, 2005; Bouton, Mineka, & Barlow, 2001).

First, outpatient reports of anxiety and mood symptoms subjected to quantitative analyses seemed to clearly differentiate a state of fear or panic, characterized by high autonomic arousal, from a more general state of apprehension, tension, and worry, which seemed to fit better with conceptions of anxiety (Brown, Chorpita, & Barlow, 1998). Anxiety in this context was best described as trait anxiety (Barlow, 1988; Cattell, 1962), although the important distinction between trait and state anxiety was not always made clear at that time. Second, findings from behavioral neuroscience research, mostly from the animal laboratories, distinguished anxiety and fear at neural and behavioral levels. For example, a number of investigators demonstrated that lesions of the amygdala eliminate fear conditioning in rats but do not eliminate behavioral manifestations of anxiety in these animals (Fanselow, 1994; LeDoux, 1996). On the other hand, different investigators (e.g., Davis, Walker, & Lee, 1997) suggested that lesions in the bed nucleus of the stria terminalis (BNST), with downstream effects on the CRF system, eliminate anxious responding in the form of well-established behavioral measures of anxiety without affecting fear conditioning.

Thus evidence from both outpatient clinical samples and basic neuroscience (see Barlow, 2002; Suárez et al., 2009) converge to underscore the distinction between fear and anxiety. In short, fear arises when danger is perceived as actual and present; anxiety represents a focus on the possibility of future threat accompanied by a sense of one's inability to predict, control, or obtain desired outcomes if these negative events unfolded. If one were to put anxiety into words, one might say, "That terrible event could happen again, and I might not be able to deal with it, but I've got to be ready to try." The behavior driven by these emotions also differs. Fear activates immediate escape behaviors or (if escape is impossible) attack directed at the source of threat—better known as the fight–flight response. LeDoux (1996) even established one fear circuit that directly bypasses the cortex (the high road) for a direct connection from the retina to the emotional brain (the low road), which makes possible the activation of the fight–flight response before the organism is even aware of the nature of the danger—a useful evolutionary adaptation. Anxiety, on the other hand, is more associated with

the behavioral action tendency that Jeffrey Gray had called "stop, look, and listen" (sometimes called *freezing*), reflecting a state of heightened vigilance and apprehension as the organism prepares to cope with future threat (Gray, 1982; Gray & McNaughton, 1995).

Despite narrow conceptions of panic attacks as restricted to panic disorder, panic proved to be ubiquitous across anxiety disorders (Barlow & Craske, 1988; Barlow, 2002) and came to play an important role in new conceptions of the etiology of emotional disorders and the relation of emotional disorders to temperament. But we also recognized that an even more common thread running through anxiety and related disorders is, of course, the emotion of anxiety itself, although not the vaguely conceptualized construct from prior decades.

Chronic (Trait) Anxiety

During the 1980s and 1990s, conceptions of anxiety, now research-based, broadened and deepened to describe a unique but coherent cognitive-affective structure within a defensive motivational system (Barlow, 2000, 2002; Lang, 1979, 1985). As noted previously, anxiety was clearly distinguished from the emotion of fear, reflecting a sense of uncontrollability focused on the possibility of future threat, danger, or other potentially negative events. This perception of uncontrollability could also be described as a state of helplessness in which the organism struggles to plan effectively for dealing with what seems like overwhelming stress with little confidence in a successful outcome (i.e., limited self-efficacy). Associated with this negative affective state is a distinct physiological component that seems best described as a substrate of readiness to prepare the organism to counteract future challenges. Research at that time linked the somatic aspect of anxiety to activation of distinct brain circuits, including the CRF system and, more importantly, Gray's BIS (Chorpita & Barlow, 1998; Gray & McNaughton, 1995). Once again, the characteristic behavioral profile associated with this state is best described as reflecting vigilance or an expectation of danger in the surrounding environment, along with an ongoing effort to prepare for additional threats. Thus trait anxiety came to be typified by persistent central nervous system tension and arousal, as well as autonomic inflexibility (Thayer, Friedman, & Borkovec, 1996), which seemed to reflect the consequences of a state of perpetual readiness to confront threat or danger, real or imagined. A description of trait anxiety as then conceptualized is presented in Figure 3.1. This is an illustration of the process of chronic trait anxiety, and not a description of the etiology of anxiety or emotional disorders.

It also became clear that conscious evaluation was not necessary for this process to occur. That is, the triggers could be "implicit" in that individuals often experience anxiety with little awareness of cues that may prompt

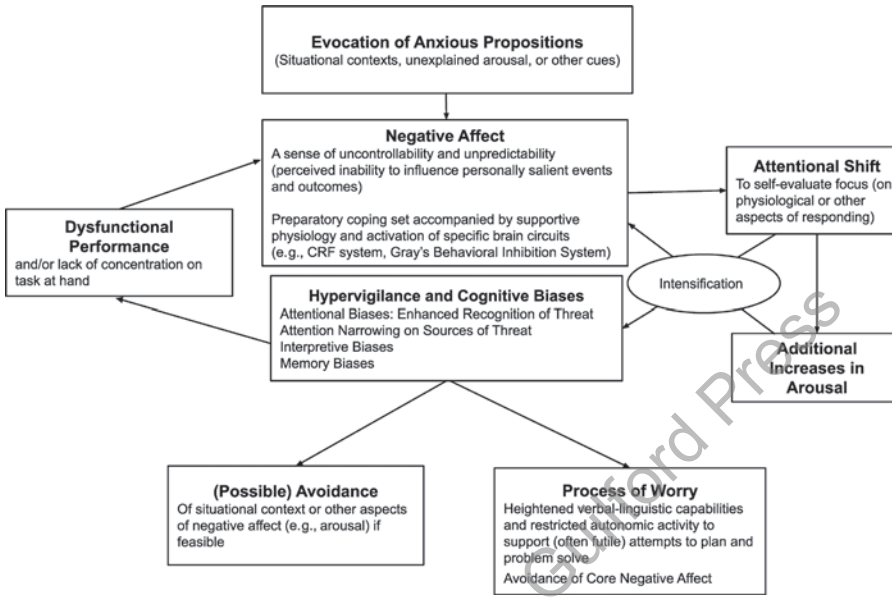

FIGURE 3.1. The nature of anxious apprehension. From Barlow (2002). Copyright © 2002 The Guilford Press. Reprinted with permission.

this emotional state. Indeed, implicit cues in emotional reactivity have come to be foundational in studies of emotion and psychopathology (LeDoux, 1996; Öhman, Flykt, & Lundqvist, 2000). This is, perhaps, most evident in the addictions (Wiers & Stacy, 2013) and posttraumatic stress disorder (PTSD; Lindgren, Kaysen, Werntz, Gasser, & Teachman, 2013), but it also is observed across the emotional disorders.

Another important area of study in that era focused on attentional shifts during the experience of anxiety. Although it had been well known that attentional focus on potentially threatening cues increases during anxiety (and fear), it also became clear that attention can shift to a hyperfocus inward, resulting in a characteristically critical, irrational, and inaccurate evaluation of the self. Indeed, studies of patients indicated that attention often rapidly shifts in its focus from the potentially threatening stimulus to the inadequate capacity of the individual to deal with the threat. Increasing self-focused attention was further found to increase arousal and negative affect in a feedback loop leading to increased intensity of the emotion (Barlow et al., 1995; Barlow, 1988, 2002).

Narrowing of attention, along with the activation of interpretive biases or *schemas* related to a sense of uncontrollability, leads to distorted

information processing of internal and external cues. This narrow and intense focus on threatening cues and self-evaluation disrupts concentration and performance in the moment, potentially fulfilling an expectation of inadequate functioning, as best demonstrated in the case of sexual dysfunction (Barlow, 1986). Briefly, research during the 1980s demonstrated that, contrary to the theories of Masters and Johnson (1966), it was not anxious arousal that interfered with sexual response (erectile adequacy in males, lubrication in females) but rather a distracting internal focus on possible inadequate responding and its consequences. Thus the individual is literally "distracted" from processing sexual cues that would ordinarily result in adequate sexual arousal (Barlow, 1986, 2002; Cranston-Cuebas & Barlow, 1990; Wiegel, Scepkowski, & Barlow, 2007). What also became clear during that period is that, although anxiety is normal and can be adaptive even at intense levels when it occurs periodically in response to real challenges or threats, what most defines pathological trait anxiety is intensity, chronicity, and a consistent interference with performance, engagement, and adaptive functioning. Affect intensity was found to significantly predict the perceived intensity of panic-relevant physical (e.g., breathlessness, smothering sensations) and cognitive (e.g., fear of going crazy) symptoms, but not objective physiological arousal (e.g., heart rate), following a hyperventilation physiological challenge test (Vujanovic et al., 2006). Most likely this finding reflects the attention narrowing onto somatic cues mentioned earlier.

Anxiety-Driven Emotion-Regulation Strategies

As a negative affect state, intense anxiety feels uncomfortable and, for some, intolerable. As this research unfolded, it seemed that there were at least two primary consequences of the process of chronic or trait anxiety that develop as one attempts to cope with anxiety and its triggers, as depicted in Figure 3.1. First, a propensity to avoid entering a state of anxiety is constantly present. This tendency becomes more prominent, noticeable, and interfering as the intensity of the anxiety increases and the cues or context that evoke the anxiety are more relevant and specific. Of course, as anxiety becomes more severe and generalizes to many different cues or contexts, overt behavioral avoidance (e.g., completely avoiding crowded places) may not be an available coping strategy, leading to the development of equally maladaptive, yet more subtle, cognitive or behavioral avoidance (e.g., engagement in rituals or superstitious behaviors, attachment to objects or persons who offer an illusory sense of safety).

The second consequence of trait anxiety noted at that time was the development of chronic worry that can be difficult to control at more severe levels (Borkovec, 1994; Borkovec, Alcaine, & Behar, 2004; Borkovec & Inz, 1990; Brown, Dowdall, Côté, & Barlow, 1994c). Borkovec and colleagues

pointed out that this worry process could be best understood as another unsuccessful attempt to cope with (regulate) the unpleasant affective and physical experience of anxiety by activating brain functions that tend to suppress pure (negative) affective experience. As with anxiety itself, the process of worry is not always maladaptive and interfering; in some cases, it is warranted and even adaptive until it becomes frequent, intense, unproductive (in that one does not achieve a rational plan or solution to the challenge or threat), and uncontrollable. Indeed, the "uncontrollability" of worry became the defining diagnostic criteria for GAD in DSM-IV (American Psychiatric Association, 1994).

Of course, the fact that the constructs of anxiety (and fear/panic) were common across anxiety and related disorders was not thought to be particularly significant in terms of predictive validity among nosologists constructing various iterations of the DSM. Rather, specific symptomatic presentations—such as perceptual derealization, phobic avoidance of blood, sensitivity to social evaluation, intrusive thoughts, flashbacks of traumatic experiences, cognitive rituals, and psychomotor retardation, among other symptoms—continued to be the basis for categorical classification through DSM-IV (and DSM-5). And yet all of these diverse phenomena are included under the more encompassing general classification of anxiety or mood disorders.

COMORBIDITY

Earlier we reviewed the ubiquity of the constructs of anxiety and fear (panic) across the emotional disorders. Other approaches to phenomenology and nosology have supported additional phenotypic similarities across the anxiety and depressive disorders, including studies describing high rates of comorbidity among common conditions.

Brown, Barlow, and Liebowitz (1994b), upon reflecting on one particular condition, GAD, noted, during the creation of DSM-IV, the extremely high rates of comorbidity of additional anxiety and mood disorders accompanying GAD and suggested that this disorder may be better conceptualized as a vulnerability to developing more diagnoses. Other evidence supported this suggestion, including the earlier age of onset for this condition than for other anxiety and mood disorders, with other comorbid presentations developing later. Thus Brown and colleagues (1994b) went on to say that contemporary classification systems may be "erroneously distinguishing phenomena on the basis of differing manifestations of a common pathophysiology" (p. 1278). They cited a study largely overlooked at the time in the context of psychopathology and classification, reporting that anxiety and mood disorders seemed to respond in a very similar fashion to antidepressant medication (Hudson &

Pope, 1990), a distinct departure from the orthodoxy of the day that different DSM disorders had not only different phenotypes but also different pathophysiology and would require unique pharmacological treatments.

Moving beyond the diagnosis of GAD, it became increasingly clear that the constructs of anxiety and depression, in general, were more closely related than previously thought. Data from a number of studies conducted during that period supported this contention. For example, one of our early large-scale diagnostic reliability studies of anxiety and depressive disorder criteria in DSM-IV included a sample of 1,127 patients presenting at the Center for Anxiety and Related Disorders at Boston University (CARD) and looked at the presence of disorders over a lifetime. We found that major depression was by far the most common additional diagnosis in patients with a principal anxiety disorder of any type (Brown, Campbell, Lehman, Grisham, & Mancill, 2001a; Brown, Di Nardo, Lehman, & Campbell, 2001b). Another interesting finding was the relative infrequency of cases presenting with a mood disorder without current or past anxiety disorders (cf. Mineka, Watson, & Clark, 1998). Specifically, in our study mentioned above, of the 670 patients who had a lifetime diagnosis of major depression or dysthymia, only 5% ($n = 33$) did not have a current or past anxiety disorder. Also, in a large majority of cases, anxiety disorders were most likely to precede rather than follow the onset of mood disorders, particularly in cases of major depressive disorder. These findings were consistent with psychometric studies of anxiety and depression that reported very high correlations among prominent self-report measures or clinical rating scales of the two constructs (Zinbarg & Barlow, 1996).

It was also notable that, when groups of patients with anxiety disorders could be differentiated from those with depressive disorders, it was depressive signs and symptoms and not anxious signs and symptoms that best discriminated these groups. That is, almost all patients with depression are anxious, but not all patients with anxiety are depressed. Specific symptoms that do seem to discriminate individuals with depression from those with anxiety could be characterized under the heading of low positive affect, or anhedonia, as reflected in loss of pleasurable engagement. Along with cognitive and motor slowing, these symptoms are often referred to as the classic "melancholic" cluster (Rush & Weissenburger, 1994).

When lifetime rates of comorbidity are considered across the full range of anxiety and depressive disorders, co-occurrence of these common mental disorders is even more striking (e.g., Allen et al., 2010; Brown et al., 2001a; Kessler et al., 1996, 1998, 2003, 2008). In the study of 1,127 patients mentioned previously, 55% of patients with a principal anxiety disorder had at least one additional anxiety or depressive disorder at the time of assessment. This rate increased to 76% when lifetime diagnoses were examined (Brown et al., 2001a). Although the principal diagnostic categories of PTSD and

GAD were associated with the highest comorbidity rates, substantial comorbidity was associated with all disorders. To take one example, of 324 patients diagnosed with DSM-IV panic disorder, 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 are considered, the percentages rise to 77% experiencing any comorbid anxiety or mood disorder, breaking down to 56% for an additional anxiety disorder and 60% for a mood disorder. Relatedly, Merikangas and colleagues (2003) followed almost 500 individuals for 15 years and found that relatively few people suffer from a specific anxiety or depressive disorder alone; when patients did meet criteria for a single disorder at one point in time, an additional anxiety or depressive episode disorder almost always emerged at a later time.

These summaries are most likely conservative due to artifactual constraints that were present in DSM-IV, constraints that continue in DSM-5, such as the nature of inclusion–exclusion criteria used. For instance, when adhering strictly to DSM-IV diagnostic rules, the comorbidity between dysthymia and GAD was 5%. However, when we suspend the hierarchical rule that GAD should not be assigned when occurring exclusively during a course of a mood disorder, the comorbidity estimate increases to 90%. These data also ignore the presence of subthreshold symptoms that did not meet diagnostic thresholds for one disorder or another.

Thus it began to be clear that anxiety and depressive disorders might be variable manifestations of a more fundamental common diathesis (Barlow, 1991; Gray & MacNaughton, 1995). Indeed, there was emerging evidence to suggest that the origins of sadness and depressive disorders may also be similar to the origins of anxiety and anxiety disorders in that both states may arise out of a common set of vulnerabilities: a shared generalized psychological vulnerability emerging from early experiences and instilling a sense of uncontrollability (accompanied by a heritable disposition to experience negative affect, as reviewed in Chapter 2). Supporting this view, Alloy, Kelly, Mineka, and Clements (1990) referred to depression emerging out of a state of anxiety as "hopelessness depression." In this conception, depression would reflect an extreme vulnerability to experiences of unpredictability and uncontrollability and would be dependent on the extent of one's psychological vulnerability, the severity of the current stressor, and the coping mechanisms at one's disposal. In more recent research, temperamental variables (neuroticism and extraversion), as well as trait anxiety, remained stable over time, and depression emerged episodically out of these traits (Prenoveau et al., 2011).

Depressive disorders and anxiety disorders may both arise out of early experiences instilling a sense of uncontrollability.

BROAD IMPACT OF PSYCHOLOGICAL TREATMENTS

In addition to common phenotypic presentations (i.e., the occurrence of anxiety, panic, and sadness across conditions) and high rates of comorbidity among anxiety and depressive disorders, broad response to specific treatment also points to important similarities in these conditions. Specifically, psychological treatments for a given anxiety disorder often produce improvement in additional comorbid anxiety or depressive disorders that are not explicitly addressed by the intervention (Allen et al., 2010; Borkovec, Abel, & Newman, 1995; Brown, Antony, & Barlow, 1995; Tsao, Lewin, & Craske, 1998; Tsao, Mystkowski, Zucker, & Craske, 2002). Early on, we examined the course of additional diagnoses in a sample of 126 patients who were being treated for panic disorder at our Center (Brown et al., 1995). A significant pre- to posttreatment decline in overall comorbidity was noted (40% to 17%, respectively). More recently, we examined effects on comorbidity across 179 adults seeking outpatient treatment at our Center. Patients were randomized to receive either a transdiagnostic cognitive-behavioral protocol that addresses emotional disorders generally (Barlow et al., 2017a, 2017b) or established single-disorder protocols that target specific diagnoses, such as panic disorder (Steele et al., 2018). The principal (most severe) diagnoses in this study were panic disorder, social anxiety disorder, OCD, and GAD. In both treatment conditions, participants' mean number of comorbid diagnoses dropped significantly from baseline to posttreatment and from baseline to the 12-month follow-up assessment. Interestingly, changes were particularly robust in terms of comorbid GAD, social anxiety disorder, and depression, in addition to any changes in the principal (most severe) diagnosis.

A COMMON NEUROBIOLOGICAL SYNDROME

There are a number of possible explanations for high rates of comorbidity and overlapping treatment response. We have reviewed these explanations extensively elsewhere (Brown & Barlow, 2002, 2009). One possibility is overlapping definitional criteria; that is, the criteria sets defining one disorder often are similar to criteria sets defining other disorders, even if they are considered distinct disorders. Another possibility is that disorders are sequentially related, such that the features of one disorder (e.g., social anxiety disorder) act as risk factors for another disorder (e.g., depression). However, a more intriguing explanation, noted above, is that these patterns of comorbidity reflect the existence of a higher order factor, such as trait anxiety or neuroticism, with implications for both classification and treatment of common mental health conditions. If this is true (and the thesis of this book supposes it is), then the mix of symptoms that define emotional disorders

(e.g., panic attacks, anhedonia, dissociative symptoms) can be understood as variations in the manifestation of a broader syndrome. These findings could suggest (but do not prove) that treatments, when successful, are targeting "core" features of emotional disorders. Also, the fact that a wide range of emotional disorders (e.g., major depressive disorder, OCD, panic disorder) respond approximately equivalently to antidepressant medications, including selective serotonin reuptake inhibitors (SSRIs), has also been interpreted by some as indicating that these medications may be targeting shared features of these disorders (e.g., Gorman, 2007; Hudson & Pope, 1990).

Indeed, recent research from affective neuroscience suggests the existence of common neurobiological patterns across emotional disorders. Specifically, research among individuals with anxiety and related disorders suggests 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). Thus increased "bottom up" processing through amygdala overactivation, coupled with inefficient or deregulated cortical inhibition of amygdala responses, is found across a number of emotional disorders, including social anxiety disorder (Lorberbaum et al., 2004; Phan, Fitzgerald, Nathan, & Tancer, 2006; Tillfors, Furmark, Marteinsdottir, & Fredrikson, 2002), PTSD (Shin et al., 2005), GAD (Ellard, 2013; 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. Indeed, a recent meta-analysis of 367 functional imaging studies across 4,500 patients with various mood, anxiety, and trauma-based disorders strongly supported transdiagnostic deficits in cortical inhibitory control (Janiri et al., 2020). This same neurobiological pattern of amygdala overactivation has also been found in individuals high in the personality dimension of neuroticism itself (Keightley et al., 2003). Of course, discrete DSM diagnoses have also been associated with several unique and idiosyncratic neurobiological factors (Blair et al., 2008; Chorpita, Albano, & Barlow, 1998a), but it seems likely that the increasingly robust neurobiological syndrome reviewed above may be a more fundamental characteristic of emotional disorders.

THE LATENT STRUCTURE OF EMOTIONAL DISORDERS

In addition to these three phenotypic commonalities among emotional disorders (anxiety, panic, and sadness), sophisticated quantitative studies have shed some light on the structure and nature of these disorders. At the heart of this line of inquiry is a focus on traits or temperaments.

Traits and Temperament: A Brief Review

The study of traits, personality, and temperament has been ongoing for decades, as outlined in Chapter 1, despite a relative lack of influence on nosological schemes for anxiety and related emotional disorders. This may be because the focus of personality research mostly fell within normal samples rather than psychopathological samples that included individuals with emotional disorders. To review briefly, major personality conceptualizations such as the Big Three (Eysenck & Eysenck, 1975; Tellegen, 1985; Watson & Clark, 1993) and Big Five (Digman, 1990; John, 1990; McCrae & Costa, 1987) prominently feature neuroticism and extraversion, 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.

Many of these investigators have also been interested in the neurobiological basis for such traits as one approach to better understanding the structure of personality. Hans Eysenck, whose influential theory (1961, 1981) led to the development of the Big Three, was first to explicate the traits of neuroticism and extraversion and their characteristics and relationships. He based his theory on variations in levels of cortical activation and autonomic nervous system reactivity, suggesting that extraversion/positive emotion is associated with moderate levels of arousal, whereas neuroticism/negative emotion is associated with under- or overarousal. Decades later, following up on this influential theoretical position, investigators began to examine the relationship of traits such as neuroticism (and extraversion) to the development and course of psychopathology, such as anxiety and related negative emotions (Clark & Watson, 2008). For example, Gershuny and Sher (1998) found, in a sample 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 clinical levels of anxiety assessed 4 years later.

Further bolstering the importance of neuroticism and extraversion in the experience of clinical levels of negative emotions, albeit utilizing data largely from animal labs, Jeffrey Gray (1982; Gray & McNaughton, 1995) described a similar trait theory and its neurobiological correlates that map onto Eysenck's traits: the BIS, the behavioral activation system (BAS), and the fight–flight system (FFS). In Gray's theory, the biological basis for anxiety is the BIS's (over)reaction to either novel signals or punishment with exaggerated inhibition. High levels on Gray's BIS roughly relate to elevated levels of neuroticism and low levels of extraversion in Eysenck's model, and elevations in the BAS roughly correspond to high extraversion and low neuroticism (Barlow, 2002). The FFS involves unconditioned escape behavior (i.e., flight) and/or defensive aggression (i.e., fight) in response to unconditioned

punishment, such as pain, and unconditioned frustrative nonrewards (Gray, 1991; Gray & McNaughton, 1995). As such, the FFS would seem to represent a biological vulnerability to the distinct emotion of fear/panic specifically, as opposed to anxiety more generally.

In another trait theory, Kagan (1989, 1994) examined children's approach and withdrawal behavior and characterized a profile he also termed *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, and he considered this stable profile to be a temperament, which he suggested is clearly heritable (Robinson, Kagan, Reznick, & Corley, 1992). This temperament showed marked physiological characteristics, including increased salivary cortisol levels and muscle tension, greater pupil dilation, and elevated urinary catecholamine levels, and children with this profile were at risk for the subsequent development of anxiety disorders (Biederman et al., 1993; Hirshfeld et al., 1992). However, only 30% of individuals who clearly met criteria for behavioral inhibition as young children went on to develop anxiety disorders (Biederman et al., 1990), and this temperament appeared to be somewhat malleable, which suggests that environmental factors are also important determinants in the expression of this temperament and possibly subsequent anxiety (Kagan & Snidman, 1991). 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 when we discuss treatment in subsequent chapters.

The Relationship between Temperament and Emotional Disorders

In the 1990s, we began to explore further the discrepant views of emotional disorders from the perspectives of "splitters" versus "lumpers," mentioned earlier. To accomplish this, we investigated the latent structure of anxiety and mood disorders (Brown et al., 1998; Zinbarg & Barlow, 1996), following in the footsteps of other investigators who were working along similar lines at the time (e.g., Clark & Watson, 1991; Clark, 2005; Tellegen, 1985; Watson, 2005). The basic finding, from a sample of 350 patients with DSM-IV anxiety and mood disorders, was that the data confirmed a hierarchical model of anxiety and mood disorders, with negative affectivity or behavioral inhibition (terms we used at the time) representing a higher order factor common to anxiety and depressive disorders and lower order factors contributing to the unique DSM definitions of specific disorders (Brown et al., 1998). This model, presented in Figure 3.2, illustrated that anxiety and mood disorders are closely related, with a substantial contribution from the higher order factor of negative affectivity.

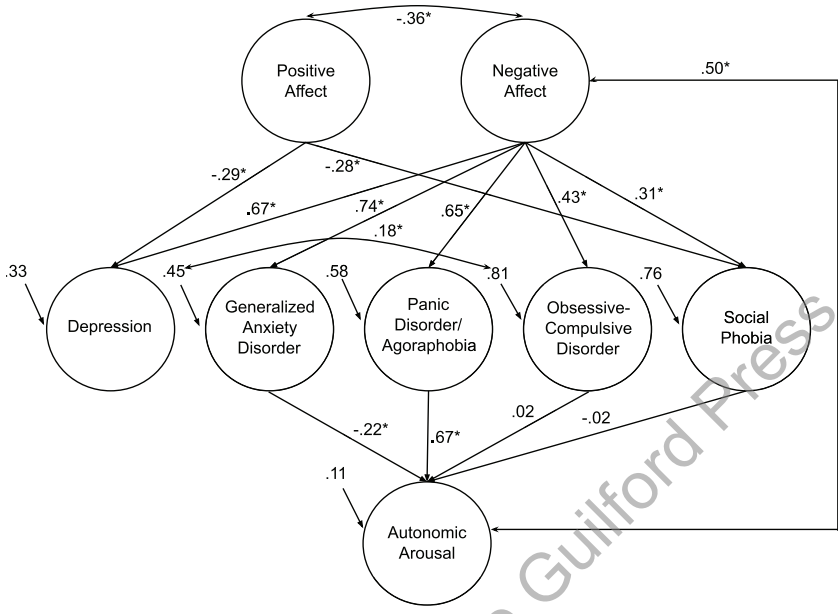

FIGURE 3.2. Structural model of the interrelationships of DSM-IV disorder constructs and negative affect, positive affect, and autonomic arousal. Completely standardized estimates are shown (path coefficients with asterisks are statistically significant, $p > .01$). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. From Brown, Chorpita, and Barlow (1998). Copyright © 1998 American Psychological Association. Reprinted with permission.

Positive affectivity (extraversion) also contributed to this model. Specifically, low positive affect constituted an important facet of depression and social anxiety disorder (Brown & McNiff, 2009). This finding was mostly consistent with a reformulation of Clark and Watson's hierarchical model (Mineka et al., 1998). Later investigations also discovered that low positive affect was a characteristic of agoraphobia (in addition to depression and social anxiety disorder) when this phenotypic presentation was split from panic disorder in DSM-5 (Rosellini, Lawrence, Meyer, & Brown, 2010). Anxious arousal, which formed the third part of the tripartite model in Clark and Watson's conceptions (1991), was now identified as a separate lower order factor closely associated with panic attacks that contributed to the disorders in an expected fashion, with particularly high loadings on, for example, panic disorder. GAD and depression, consistent with research reported earlier, were very closely related, with high contributions from negative affectivity as reflected in the

highest zero-order correlations found in the model: 0.67 between negative affect and depression and 0.74 between negative affect and GAD. This high correlation with GAD further supported notions of GAD as a "basic" disorder, or even perhaps a vulnerability (Barlow, Brown, & Craske, 1994).

These initial findings on latent structure were extended by our research team (Brown, 2007; Brown & Barlow, 2009) and others (e.g., Griffith et al., 2010; Kessler et al., 2011; Kotov 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 measures of neuroticism. Noting the marked similarity to earlier findings utilizing somewhat different terminology, such as negative affect or behavioral inhibition (e.g., Brown et al., 1998), Griffith and colleagues (2010) suggested that these results provide further evidence that neuroticism itself may be at the core of "internalizing" disorders. Hong, Lee, Tsai, and Tan (2017) picked up a very similar internalizing factor "pervaded with a sense of uncontrollability and vulnerability" (p. 299) as early as age 7 that remained stable through childhood and predicted internalizing symptoms. Krueger (1999) also found that the variance in seven anxiety and mood disorders could be accounted for by the higher order dimension of "internalizing"/neuroticism.

Recent Updates

In recent years, research on a hierarchical structure of emotional disorders has broadened and deepened. To take just a few examples, Zinbarg et al. (2016), in an important prospective study, reported that neuroticism predicted initial onsets of anxiety and unipolar mood disorders and, to a somewhat lesser extent, substance use disorders in a sample of high school students over a period of 3 years. Conway, Craske, Zinbarg, and Mineka (2016), in a similar fashion, found that negative temperament was a robust predictor of both new onsets and recurrences of internalizing disorders. Naragon-Gainey, Gallagher, and Brown (2013) ruled out the potentially confounding effect of mood-state distortion in accounting for these findings, strongly suggesting that the contribution of temperament in the prediction of anxiety and related disorders could not be accounted for by variability in mood during periodic assessments. Brown and Rosellini (2011) also examined the contribution of chronic stress to the influence of temperament on the course of emotional disorders and found that chronic stress moderated this relationship, adding another important element to conceptions of emotional disorders.

Finally, several groups of investigators have used sophisticated analytical procedures and broadened the scope to include hierarchical structural analysis of almost all behavioral disorders. Prominent among these are

Lahey, Krueger, Rathouz, Waldman, and Zald (2017), who found evidence for a general factor of psychopathology, referred to as the *p* factor, that is largely contributory to the full range of psychopathology. They also demonstrate that this factor is closely related to neuroticism, suggesting that this trait makes some contribution to all psychopathology, not just the emotional disorders. The strong overlap of the *p* factor with neuroticism has now been replicated in children (Brandes, Herzhoff, Smack, & Tackett, 2019). Other investigators (Oltmanns, Smith, Oltmanns, & Widiger, 2018) suggest that this general *p* factor may simply be tapping into level of impairment rather than representing a different higher order construct that is broader than neuroticism. These efforts will undoubtedly increase our understanding of psychopathology and have substantial implications for assessment and treatment in the years to come.

Perhaps the most significant advance in this area has been the development of the HiTOP, an empirical quantitative approach to the classification of psychopathology (Kotov et al., 2017). This approach ignores artificial categorical boundaries and began by assembling a comprehensive list of symptoms from all emotional disorders to quantitatively determine the most homogeneous components or sets of symptoms. These components are then sorted into empirically derived syndromes, which are, in turn, grouped under higher order factors. Consistent with research summarized above, all emotional disorders fall under a superordinate factor termed *Internalizing.* Also, three subfactors emerged, replicating previous research, that have been termed *Distress, Fear,* and, somewhat counterintuitively, *OCD/Mania* (Waszczuk, Kotov, Ruggero, Gamez, & Watson, 2017). As noted previously in this chapter, fear and distress seem to correspond to fear/panic and anxiety in our original conceptions.

In any case, although the "key features" of the DSM anxiety and depressive disorders (i.e., the specific symptoms used to discriminate among diagnoses) cannot be collapsed indiscriminately into higher order temperamental dimensions, it seemed safe to conclude, based on studies previously reviewed in this chapter, that what is common outweighs what is not and that these disorders need to be conceptualized in a hierarchical fashion. Summarizing these studies, virtually all the considerable covariance among latent variables corresponding to the DSM constructs of emotional disorders can be accounted for by higher order dimensions.

What is common outweighs what is not.

A NEW FOCUS ON NEUROTICISM

Of course, even when it was less in vogue, some investigators had remained more interested in the possibility of broader underlying syndromes for the

variety of specific emotional disorders. For example, Andrews (1990, 1996) and Tyrer (1989) each considered the evidence for the existence of a "general neurotic syndrome" to be stronger and more parsimonious in classifying emotional disorders than individual narrow categories defined by specific symptom presentations. Even earlier, Achenbach, working mostly with children, had identified broad, higher order dimensions of psychopathology that he termed *internalizing* and *externalizing* factors, with the internalizing factor notably encompassing anxiety and depressive symptoms (Achenbach, 1966; Achenbach & Edelbrock, 1978). Now, a substantial literature has accumulated underscoring the roles of these constructs in accounting for the onset, overlap, and maintenance of anxiety, depressive, and related disorders, much as predicted by Tyrer, Andrews, and Achenbach (Brown et al., 1998; Brown, 2007; Brown & Barlow, 2002, 2009; Chorpita et al., 1998a; Gershuny & Sher, 1998; Griffith et al., 2010; Kasch, Rottenberg, Arnow, & Gotlib, 2002; Kessler et al., 2011; Krueger, 1999; Watson, Clark, & Carey, 1988; Watson et al., 1995).

Thus it was becoming clearer during the late 1990s, spilling over into the 21st century, that drilling down into the nature of the coherent cognitive-affective structure of trait anxiety revealed the trait or temperamental nature of this construct. Indeed, various research groups studying the latent structure of anxiety and depressive disorders in both adult and child clinical samples uncovered higher order dimensions that appeared to reflect the temperamental tendency to experience negative emotions. These dimensions carried various labels, including *negative affect*, *behavioral inhibition*, *trait anxiety, internalizing*, *harm avoidance*, and, more recently, *dispositional negativity* (Shackman et al., 2016), all of which are closely related to if not synonymous with *neuroticism*. Also, *positive affect*, *behavioral activation*, or *externalizing* appeared as alternate terms for *extraversion*. We have chosen to call the first dimension *neuroticism*, the oldest term for this trait (Eysenck, 1947) and the most widely used (e.g., Cuijpers et al., 2010; Lahey, 2009). This new focus on neuroticism, we believe, is likely to lead to a more rich and fruitful perspective on the origins, nature, and treatment of emotional disorders (Barlow et al., 2014b; Brown & Barlow, 2009; Campbell-Sills, Liverant, & Brown, 2004).

AVERSIVE REACTIVITY TO EMOTIONS: A BRIDGE FROM TEMPERAMENT TO DISORDER

Early in this chapter, we discussed the growing concern during the 1990s with splitting diagnostic definitions of emotional disorders into ever narrower slices of psychopathology. We then reviewed the beginnings of

research and conceptualizations focused on phenomena that were common across emotional disorders and the emerging consensus that the DSM taxonomy may well be overemphasizing categories that are minor variations of a broader underlying syndrome. Referring back to Figure 3.1, we now believe that the process originally conceptualized as trait anxiety can be broadened to represent neuroticism itself. To briefly review, at the core of neuroticism is the experience of intense and frequent negative emotionality, accompanied by a sense of uncontrollability and unpredictability over stressful or challenging events. This sense of limited control could be described as a perceived inability to influence personally salient events and outcomes, along with a preparatory coping set accompanied by supportive physiology. The sense of uncontrollability, of course, drives an aversion or negative reaction to the experience of an event, including the emotional experience itself (Izard, 1971; Tomkins, 1962). These perceptions are an integral component of the neurotic temperament and, as noted earlier and elaborated on later (see Chapter 4), it is negative reactivity to emotions, rather than the discrete emotional experience itself, that contributes to the development and maintenance of pathology (Barlow, 1988, 1991; Bullis et al., 2019).

As part of that process, we also described two "consequences," represented in Figure 3.1, that develop as one attempts to cope with anxiety (neuroticism) and its triggers. The first is a tendency to down-regulate negative affect and its associated sense of uncontrollability through avoidant behavior that becomes more prominent as the affect increases in intensity; the second is the development of chronic "worry" or repetitive but unproductive negative cognitive activity. Recently, repetitive negative thinking has been shown once again to be transdiagnostically central to anxiety and mood disorders in a sophisticated network analysis (Everaert & Joormann, 2019). The function of this verbal-linguistic activity has also been traditionally described as avoidance or down-regulation of the experience of intense negative affect (Barlow, 2002; Borkovec, 1994).

For the past 20 years, research on constructs found transdiagnostically across the emotional disorders, such as avoidance and worry, that function to regulate emotion has greatly expanded, necessitating further additions and refinements to Figure 3.1. Most of these constructs were originally considered and continue to be conceived as only narrowly associated with one DSM disorder or another; others could be considered more sophisticated elaborations of broad concepts outlined in Figure 3.1. These constructs include those that reflect aversive reactivity to emotional experiences (i.e., anxiety sensitivity, experiential avoidance, intolerance of uncertainty, distress intolerance) and related avoidant coping (e.g., overt situational avoidance, subtle forms of avoidance and safety behaviors, deficits in emotional clarity, emotion/thought suppression, perfectionism, and repetitive negative

cognitive activity, which includes both worry and rumination). These constructs, and their functional relationship to both the maintenance of neuroticism and the development of emotional disorders, are reviewed in Chapter 4.

In considering these phenomena more recently, questions began to arise concerning their relationship to well-established temperaments, particularly neuroticism on the one hand and emotional disorders on the other. For example, Paulus, Talkovsky, Heggeness, and Norton (2015) evaluated the relationship of negative affectivity to what they called *transdiagnostic risk factors*, specifically anxiety sensitivity and intolerance of uncertainty, in a proposed hierarchical model using structural equation modeling. They found that these constructs added some information, particularly in the relationship between negative affect and panic disorder for anxiety sensitivity and negative affect and intolerance of uncertainty for several disorders, compared with models without these transdiagnostic risk factors. In each example, though, negative affect alone accounted for most of the variance.

In another example, Naragon-Gainey and Watson (2018), highly respected theorists in the area of temperament, affect, and emotional disorders, chose to describe a subset of the phenomenon mentioned above—specifically, anxiety sensitivity, intolerance of uncertainty, perfectionism, and experiential avoidance—as "social-cognitive vulnerabilities." They noted that these vulnerabilities describe "individual differences in thoughts, emotional experiences, and behaviors that are hypothesized to be related to the onset and/or maintenance of internalizing symptoms, such as anxiety and depression" (p. 143). They also note, as we did earlier, that several of these vulnerabilities arose in the context of theorizing and some experimental work looking at predisposing diatheses for single DSM disorders. For example, anxiety sensitivity is still thought to be primarily a risk factor for panic disorder (e.g., Reiss & McNally, 1985; Reiss, Peterson, Gursky, & McNally, 1986), and both worry and intolerance of uncertainty are thought to be closely related to the onset of GAD (Barlow, Blanchard, Vermilyea, Vermilyea, & DiNardo, 1986; Dugas, Gagnon, Ladouceur, & Freeston, 1998). Naragon-Gainey and Watson (2018) then go on to review a substantial body of literature demonstrating that the four vulnerabilities they focused on were all primarily associated with neuroticism more generally, a finding also reported by Hong and Cheung (2015), but that at least some of the vulnerabilities accounted for a small amount of additional variance beyond the temperament of neuroticism when describing at least some emotional disorders, although not all.

Interestingly, in a paper published a few months later, Naragon-Gainey, McMahon, and Park (2018) changed the label of these same vulnerabilities to "affect-laden clinical traits" and then described these constructs as more "proximal individual differences that can better describe who is likely to

develop which specific symptoms beyond the broad risk conferred by affective traits" (p. 1177). While admitting that these traits were largely indistinguishable from neuroticism in their previous study, they point out that there is still some evidence for incremental validity in predicting specific disorders and that these traits comprise more proximal and convenient targets for treatment. This distinction mirrors to some extent the "splitting versus lumping" controversy that has so permeated classification of mental disorders; that is, the initial tendency is to associate one construct or "clinical trait" with one disorder, whereas further analysis reveals not only more general transdiagnostic characteristics but also that these traits are, for the most part, an integral part of neuroticism itself. Of course, as suggested by Naragon-Gainey et al. (2018), this does not mitigate their utility. Indeed, a number of these "clinical traits" have already been targeted in a transdiagnostic treatment for emotional disorders (Barlow et al., 2011, 2017a).

Indeed, in a conceptual paper offering a uniform definition of emotional disorders with accompanying criteria reflecting this definition, we suggest that each of these constructs represents negative reactivity to intense emotional experience, which is then accompanied by a range of cognitive and behavioral strategies to down-regulate negative affect (Barlow et al., 2014b; Bullis et al., 2019). These clinical traits, presented in Figure 3.3 and reviewed in Chapter 4, fall under the broad heading of negative reactivity to emotional experience, often leading to related cognitive and behavioral strategies to down-regulate negative affect, which we refer to as *avoidant emotional behaviors*. This functional relationship, negative avoidant reactivity and resulting temporary down-regulation of negative affect, forms the important bridge between neuroticism and the common core of emotional disorders.

CONCLUSIONS

Overall, the findings reviewed in this chapter suggest that individuals with emotional disorders experience strong negative emotions with frequency and evaluate these experiences as aversive. Because of these negative reactions to their emotions, they are more likely to engage in strategies to down-regulate their emotional experiences, and these strategies, in turn, paradoxically increase the frequency and intensity of negative emotions through a negative reinforcement mechanism. We suggest that this functional relationship, driven by neuroticism, is at the core of disorders of emotion. This relationship, and the evidence supporting it, are reviewed in considerably more detail in Chapter 4.

Thus the study of temperament and personality on the one hand and the psychopathology of emotional disorders on the other, which were largely

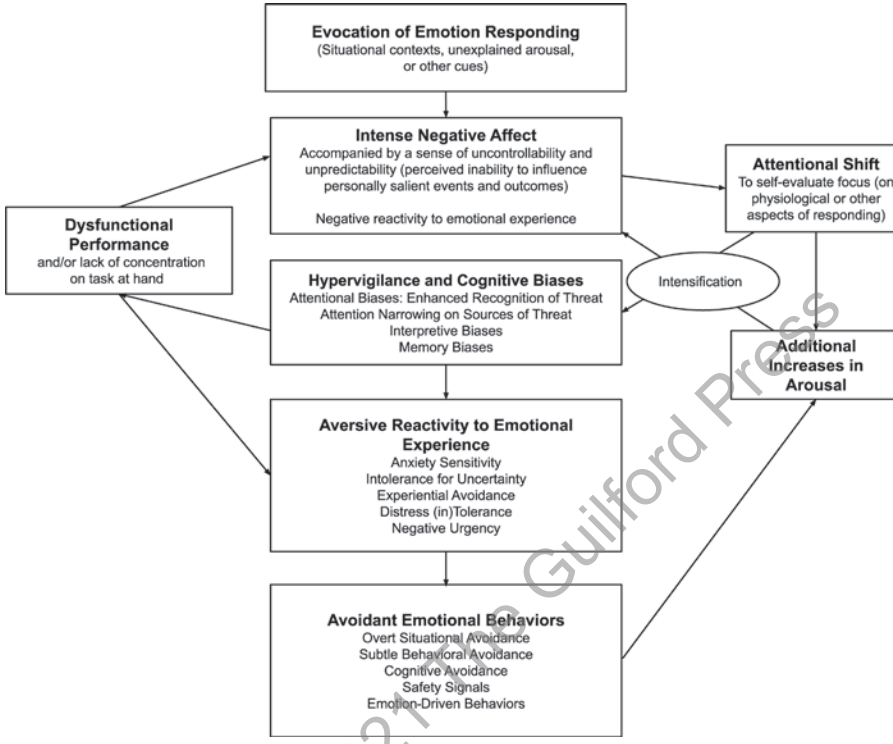

FIGURE 3.3. The process of neuroticism.

unrelated to each other during the last decades of the 20th century, would now seem to be inextricably interrelated. Indeed, at the core of disorders of emotion are relatively stable patterns of temperament, particularly but not limited to neuroticism and extraversion, and advances in our understanding of emotional disorders cannot proceed without a deeper focus on temperamental contributions.