

Chapter 1

Anxiety

A Common but Multifaceted Condition

Love looks forward, hate looks back, anxiety has eyes
all over its head.

—MIGNON MCLAUGHLIN (American journalist, 1915–)

Anxiety is ubiquitous to the human condition. From the beginning of recorded history, philosophers, religious leaders, scholars, and more recently physicians as well as social and medical scientists have attempted to unravel the mysteries of anxiety and to develop interventions that would effectively deal with this pervasive and troubling condition of humanity. Today, as never before, calamitous events brought about by natural disasters or callous acts of crime, violence, or terrorism have created a social climate of fear and anxiety in many countries around the world. Natural disasters like earthquakes, hurricanes, tsunamis, and the like have a significant negative impact on the mental health of affected populations in both developing and developed countries with symptoms of anxiety and posttraumatic stress showing substantial increases in the weeks immediately following the disaster (Norris, 2005).

Elevated levels of anxiety and other posttraumatic symptoms spike in the first few weeks after acts of terrorism, war, or other large-scale acts of community violence. In 5–8 weeks after the September 11, 2001, terrorist attacks on the World Trade Center towers in New York City, symptoms of posttraumatic stress disorder (PTSD) doubled (Galea et al., 2002). An Internet-based survey ($N = 2,729$) found that 17% of individuals outside New York City reported PTSD symptoms 2 months after 9/11 (Silver, Holman, McIntosh, Poulin, & Gil-Rivas, 2002). The National Tragedy Study, a telephone survey of 2,126 Americans, found that 5 months after the 9/11 terrorist attacks month, 30% of Americans reported difficulty sleeping, 27% felt nervous or tense, and 17% indicated they worried a great deal about future terrorist attacks (Rasinski, Berkold, Smith, & Albertson, 2002). The Gallup Youth Survey of American teenagers conducted 2½ years after 9/11 found that 39% of teens were either “very” or “somewhat” worried that they or someone in their families will become a victim of terrorism (Lyons, 2004).

Although large-scale threats have their greatest impact on the psychological morbidity of individuals directly affected by the disaster in the weeks immediately following the traumatic event, their wider effects are evident months and years later in the heightened concerns and worries of a significant proportion of the general population.

Fear, anxiety, and worry, however, are not the exclusive domain of disaster and other life-threatening experiences. In the majority of cases anxiety develops within the context of the fluctuating pressures, demands, and stresses of daily living. In fact anxiety disorders represent the single largest mental health problem in the United States (Barlow, 2002), with more than 19 million American adults having an anxiety disorder in any given year (National Institute of Mental Health, 2001). Approximately 12–19% of primary care patients meet diagnostic criteria for an anxiety disorder (Anseau et al., 2004; Olfson et al., 1997). Moreover, antidepressants and mood stabilizers are the third most prescribed pharmacotherapy class, having 2003 global sales of \$19.5 billion (IMS, 2004). Thus millions of people worldwide mount a daily struggle against clinical anxiety and its symptoms. These disorders cause a significant economic, social and health care burden for all countries, especially in developing countries that face frequent social and political upheavals and high rates of natural disaster.

This chapter provides an overview of the diagnosis, clinical features, and theoretical perspectives on the anxiety disorders. We begin by examining definitional issues and the distinction between fear and anxiety. The diagnosis of anxiety disorders is then considered with particular attention to the problem of comorbidity, especially with depression and substance abuse disorders. A brief review of the epidemiology, course, and consequence of anxiety is presented, and contemporary biological and behavioral explanations for anxiety are considered. The chapter concludes with arguments for the validity of a cognitive perspective for understanding the anxiety disorders and their treatment.

ANXIETY AND FEAR

The psychology of emotion is rich with diverse and opposing views on the nature and function of human emotions. All emotion theorists who accept the existence of basic emotions, however, count fear as one of them (Öhman & Wiens, 2004). As part of our emotional nature, fear occurs as a healthy adaptive response to a perceived threat or danger to one's physical safety and security. It warns individuals of an imminent threat and the need for defensive action (Beck & Greenberg, 1988; Craske, 2003). Yet fear can be maladaptive when it occurs in a nonthreatening or neutral situation that is misinterpreted as representing a potential danger or threat. Thus two issues are fundamental to any theory of anxiety: how to distinguish fear and anxiety, and how to determine what is a normal versus an abnormal reaction.

Defining Fear and Anxiety

Many different words in the English language relate to the subjective experience of anxiety such as “dread,” “fright,” “panic,” “apprehension,” “nervous,” “worry,” “fear,” “horror,” and “terror” (Barlow, 2002). This has led to considerable confusion and inaccuracy in the common use of the term “anxious.” However, “fear” and “anxiety”

must be clearly distinguished in any theory of anxiety that hopes to offer guidance for research and treatment of anxiety.

In his influential volume on the anxiety disorders, Barlow (2002) stated that “fear is a primitive alarm in response to present danger, characterized by strong arousal and action tendencies” (p. 104). Anxiety, on the other hand, was defined as “a future-oriented emotion, characterized by perceptions of uncontrollability and unpredictability over potentially aversive events and a rapid shift in attention to the focus of potentially dangerous events or one’s own affective response to these events” (p. 104).

Beck, Emery, and Greenberg (1985) offered a somewhat different perspective on the differentiation of fear and anxiety. They defined fear as a cognitive process involving “the *appraisal* that there is actual or potential danger in a given situation” (1985, p. 8, emphasis in original). Anxiety is an emotional response triggered by fear. Thus fear “is the appraisal of danger; anxiety is the unpleasant feeling state evoked when fear is stimulated” (Beck et al., 1985, p. 9). Barlow and Beck both consider fear a discrete, fundamental construct whereas anxiety is a more general subjective response. Beck et al. (1985) emphasize the cognitive nature of fear and Barlow (2002) focuses on the more automatic neurobiological and behavioral features of the construct. On the basis of these considerations, we offer the following definitions of fear and anxiety as a guide for cognitive therapy.

Clinician Guideline 1.1

Fear is a primitive automatic neurophysiological state of alarm involving the **cognitive appraisal** of imminent threat or danger to the safety and security of an individual.

Clinician Guideline 1.2

Anxiety is a complex cognitive, affective, physiological and behavioral response system (i.e., **threat mode**) that is activated when anticipated events or circumstances are deemed to be highly aversive because they are perceived to be unpredictable, uncontrollable events that could potentially threaten the vital interests of an individual.

A couple of observations can be derived from these definitions. Fear as the basic automatic appraisal of danger is the core process in all the anxiety disorders. It is evident in the panic attacks and acute spikes of anxiousness that people report in specific situations. Anxiety, on the other hand, describes a more enduring state of threat or “anxious apprehension” that includes other cognitive factors in addition to fear such as perceived aversiveness, uncontrollability, uncertainty, vulnerability (helplessness), and inability to obtain desired outcomes (see Barlow, 2002). Both fear and anxiety involve a future orientation so that “what if?” questions predominate (e.g., “What if I ‘bomb’ this job interview?”, “What if my mind goes blank during the speech?”, “What if my heart palpitations trigger a heart attack?”).

The distinction between fear and anxiety can be illustrated by Bill, who suffers from obsessive–compulsive disorder (OCD) due to a fear of contamination and so engages in compulsive washing. Bill is hypervigilant about the possibility of encountering “dan-

gerous” contaminants, and so he avoids many things that he perceives as possible contamination. He is in a continual state of high arousal and subjectively feels nervous and apprehensive due to repetitive doubts of contamination (e.g., “What if I become contaminated?”). This cognitive–behavioral–physiological state, then, describes anxiety. If Bill touches a dirty object (e.g., the doorknob in a public building) he quickly experiences fear, which is the perception of imminent danger (e.g., “I’ve touched this dirty doorknob. A cancer patient may have recently touched it. I could contract cancer and die.”). Thus we describe Bill’s immediate response to the doorknob as “fear,” but his almost continuous negative affective state as “anxiety.” Anxiety, then, is of greater concern for those individuals who seek treatment for a heightened state of “nervousness” or agitation that causes considerable distress and interference in daily living. Consequently it is anxiety and its treatment that is the focus of the present volume.

Normal versus Abnormal

It would be difficult to find someone who hasn’t experienced fear or felt anxious about an impending event. Fear has an adaptive function that is critical to the survival of the human species by warning and preparing the organism for response against life-threatening dangers and emergencies (Barlow, 2002; Beck et al., 1985). Moreover, fears are very common in childhood, and mild symptoms of anxiety (e.g., occasional panic attacks, worry, social anxiety) are frequently reported in adult populations (see Craske, 2003, for review). So, how are we to distinguish abnormal from normal fear? At what point does anxiety become excessive, so maladaptive that clinical intervention is warranted?

We suggest five criteria that can be used to distinguish abnormal states of fear and anxiety. It is not necessary that all these criteria be present in a particular case, but one would expect many of these characteristics to be present in clinical anxiety states.

1. *Dysfunctional cognition.* A central tenet of the cognitive theory of anxiety is that abnormal fear and anxiety derive from a false assumption involving an erroneous danger appraisal of a situation that is not confirmed by direct observation (Beck et al., 1985). The activation of dysfunctional beliefs (schemas) about threat and associated cognitive-processing errors leads to marked and excessive fear that is inconsistent with the objective reality of the situation.

For example, the sight of a loose Rotweiler charging toward you with teeth bared and raised fur on a lonely country road would likely elicit the thought “I am in grave danger of being attacked; I better get out of here fast.” The fear experienced in this situation is perfectly normal, because it involves a reasonable deduction based on an accurate observation of the situation. On the other hand, anxiety elicited by the sight of a toy poodle dog held on a leash by its owner is abnormal: the threat mode is activated (e.g., “I’m in danger”) even though direct observation indicates this is a “nonthreatening” situation. In this latter case we would suspect that the person has a specific animal phobia.

2. *Impaired functioning.* Clinical anxiety will directly interfere with effective and adaptive coping in the face of a perceived threat, and more generally in the person’s daily social or occupational functioning. There are instances in which the activation of fear results in a person freezing, feeling paralyzed in the face of danger (Beck et al., 1985). Barlow (2002) notes that rape survivors often report physical paralysis at some point

during the attack. In other cases the fear and anxiety may lead to a counterproductive response that actually increases risk of harm or danger. For example, a woman anxious about driving after being involved in a rear-end collision would constantly check her rear-view mirror and so pay less attention to the traffic in front of her, increasing the chance that she would cause the very accident she feared.

It is also recognized that clinical fear and anxiety usually interfere in a person's ability to lead a productive and fulfilling life. Consequently, in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR; American Psychiatric Association [APA], 2000), marked distress or "significant interference with the person's normal routine, occupational (or academic) functioning, or social activities or relationships" (p. 449) is one of the core diagnostic criteria for most of the anxiety disorders.

3. *Persistence*. In clinical states anxiety persists much longer than would be expected under normal conditions. Recall that anxiety prompts a future-oriented perspective that involves the anticipation of threat or danger (Barlow, 2002). As a result, the person with clinical anxiety can feel a heightened sense of subjective apprehension by just thinking about an impending potential threat, regardless of whether it eventually materializes. Thus it is not uncommon for anxiety-prone individuals to experience elevated anxiety on a daily basis over many years.

4. *False alarms*. In anxiety disorders one often finds the occurrence of false alarms, which Barlow (2002) defines as "marked fear or panic [that] occurs in the absence of any life-threatening stimulus, learned or unlearned" (p. 220). A spontaneous or uncued panic attack is one of the best examples of a "false alarm." The presence of panic attacks or intense fear in the absence of threat cues or very minimal threat provocation would suggest a clinical state.

5. *Stimulus hypersensitivity*. Fear is a "stimulus-driven aversive response" (Öhman & Wiens, 2004, p. 72) to an external or internal cue that is perceived as a potential threat. However, in clinical states fear is elicited by a wider range of stimuli or situations of relatively mild threat intensity that would be perceived as innocuous to the nonfearful individual (Beck & Greenberg, 1988). For example, most people would be quite fearful about approaching a Sydney funnelweb spider, which has the most lethal spider venom in the world for humans. On the other hand, a spider phobic patient was referred to our clinical practice who exhibited intense anxiety, even panic attacks, at the sight of a spider web produced by the smallest, most harmless Canadian household spider. Clearly the number of spider-related stimuli that elicits a fear response in the phobic individual is far greater than the spider-related stimuli that would elicit fear in the nonphobic individual. In the same way individuals with an anxiety disorder would interpret a broader range of situations as threatening compared to individuals without an anxiety disorder. Clinician Guideline 1.3 presents five questions to determine if a person's experience of fear or anxiety is sufficiently exaggerated and pervasive to warrant further assessment, diagnosis, and possible treatment.

Clinician Guideline 1.3

1. Is fear or anxiety based on a false assumption or faulty reasoning about the potential for threat or danger in relevant situations?
2. Does the fear or anxiety actually interfere in the person's ability to cope with aversive or difficult circumstances?

3. Is the anxiety present over an extended period of time?
4. Does the individual experience false alarms or panic attacks?
5. Is fear or anxiety activated by a fairly wide range of situations involving relatively mild threat potential?

ANXIETY AND THE PROBLEM OF COMORBIDITY

Over the last several decades clinical research on anxiety has recognized that the older term “anxiety neurosis” had limited heuristic value. Most theories and research on anxiety now recognize that there are a number of specific subtypes of anxiety that cluster under the rubric “anxiety disorders.” Even though these more specific anxiety disorders share some common features such as the activation of fear in order to detect and avoid threat (Craske, 2003), there are important differences with implications for treatment. Thus the present volume, like most contemporary perspectives, will focus on specific anxiety disorders rather than treat clinical anxiety as a single homogenous entity. Table 1.1 lists the core threat and cognitive appraisal associated with the five DSM-IV-TR anxiety disorders discussed in this book (for similar summary, see Dozois & Westra, 2004).

Psychiatric classification systems like DSM-IV assume that mental disorders like anxiety consists of more specific disorder subtypes with diagnostic boundaries that sharply demarcate one type of disorder from another. However, a large body of epidemiological, diagnostic, and symptom-based research has challenged this categorical approach to psychiatric nosology, offering much stronger evidence for the dimensional nature of psychiatric disorders like anxiety and depression (e.g., Melzer, Tom, Brugha, Fryers, & Meltzer, 2002; Ruscio, Borkovec, & Ruscio, 2001; Ruscio, Ruscio, & Keane, 2002).

One of the strongest challenges to the categorical perspective is the evidence of extensive symptom and disorder comorbidity in both anxiety and depression—that is, the cross-sectional co-occurrence of one or more disorders in the same individual (Clark, Beck, & Alford, 1999). Only 21% of respondents with a lifetime history of disorder had only one disorder in the National Comorbidity Survey (NCS; Kessler et al., 1994), a National Institute of Mental Health (NIMH) epidemiological study of mental disorders involving a randomized nationally representative sample of 8,098 Americans who were administered the Structured Clinical Interview for DSM-III-R. Based on a sample of 1,694 outpatients from the Philadelphia Center for Cognitive Therapy evaluated between January, 1986, and October, 1992, only 10.5% of those with a primary mood disorder and 17.8% with panic disorder (with or without agoraphobia avoidance) had a “pure diagnosis” without Axis I or II comorbidity (Somoza, Steer, Beck, & Clark, 1994). Clearly then, diagnostic comorbidity is the norm rather than the exception, with *prognostic comorbidity*, in which one disorder predisposes an individual to the development of other disorders (Maser & Cloninger, 1990) also important to consider in the pathogenesis of psychiatric conditions.

Numerous clinical states have reported a high rate of diagnostic comorbidity within the anxiety disorders. For example, a large outpatient study ($N = 1,127$) found that

TABLE 1.1. Core Features of Five DSM-IV-TR Anxiety Disorders

Anxiety disorder	Threatening stimulus	Core appraisal
Panic disorder (with or without agoraphobia)	Physical, bodily sensations	Fear of dying (“heart attack”), losing control (“going crazy”) or consciousness (fainting), having further panic attacks
Generalized anxiety disorder (GAD)	Stressful life events or other personal concerns	Fear of possible future adverse or threatening life outcomes
Social phobia	Social, public situations	Fear of negative evaluation from others (e.g., embarrassment, humiliation)
Obsessive–compulsive disorder (OCD)	Unacceptable intrusive thoughts, images, or impulses	Fear of losing mental or behavioral control or otherwise being responsible for a negative outcome to self or others
Posttraumatic stress disorder (PTSD)	Memories, sensations, external stimuli associated with past traumatic experiences	Fear of thoughts, memories, symptoms, or stimuli associated with the traumatic event

two-thirds of anxiety disorder patients had another current Axis I disorder, and over three-fourths had a lifetime comorbid diagnosis (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). Individuals with an anxiety disorder, then, are much more likely to have at least one or more additional disorders than would be expected by chance (Brown et al., 2001).

Comorbid Depression

Anxiety disorders are more likely to co-occur with some disorders than with others. Much of the research on comorbidity has focused on the relationship between anxiety and depression. Approximately 55% of patients with an anxiety or depressive disorder will have at least one additional anxiety or depressive disorder, and this rate jumps to 76% when considering lifetime diagnoses (Brown & Barlow, 2002). In the Epidemiologic Catchment Area (ECA) study individuals with a major depression were 9 to 19 times more likely to have a coexisting anxiety disorder than individuals without major depression (Regier, Burke, & Burke, 1990). Fifty-one percent of anxiety disorder cases in NCS had major depressive disorder, and this increased to 58% for lifetime diagnoses (Kessler et al., 1996). Moreover, anxiety disorders are more likely to precede depressive disorders than the reverse, although the strength of this sequential association does vary across specific anxiety disorders (Alloy, Kelly, Mineka, & Clements, 1990; Mineka, Watson, & Clark, 1998; Schatzberg, Samson, Rothschild, Bond, & Regier, 1998). Results from the ECA survey waves indicated that simple phobia, obsessive–compulsive disorder (OCD), agoraphobia, and panic attacks were associated with increased risk for major depression 12 months later (Goodwin, 2002).

Research into comorbidity has important clinical implications for the treatment of all psychological disorders. Clinical depression comorbid with an anxiety disorder is associated with a more persistent course of disturbance, greater symptom severity, and greater functional impairment or disability (Hunt, Slade, & Andrews, 2004; Kessler & Frank, 1997; Kessler et al., 1996; Olfson et al., 1997; Roy-Byrne et al., 2000). In addi-

tion, anxiety disorders with a comorbid depression show a poorer treatment response, higher relapse and recurrence rates, and greater service utilization than cases of pure anxiety (Mineka et al., 1998; Roy-Byrne et al., 2000; Tylee, 2000).

Comorbid Substance Use

Substance use disorders, especially use of alcohol, are another category of conditions that are often seen in the anxiety disorders. In their review Kushner, Abrams, and Borchardt (2000) concluded that presence of an anxiety disorder (except simple phobia) doubles to quadruples the risk of alcohol or drug dependence, with anxiety frequently preceding the alcohol use disorder and contributing to its persistence, although alcohol misuse can also lead to anxiety. Even at subthreshold diagnostic levels, individuals with an anxiety condition are significantly more likely to use drugs and alcohol than non-clinical controls (Sbrana et al., 2005).

It is evident that a special relationship exists between alcohol use disorders and anxiety. Compared with mood disorders, anxiety disorders more often precede substance use disorders (Merikangas et al., 1998), leading to the assumption that anxious individuals must be “self-medicating” with alcohol. However, this “self-medicating” assumption was not supported in a 7-year prospective study in which alcohol dependence was as likely to increase risk of developing a subsequent anxiety disorder as was the reverse temporal relationship (Kushner, Sher, & Erickson, 1999). Kushner and colleagues concluded that anxiety and alcohol problems likely have reciprocal and interacting influences that will lead to an escalation of both anxiety and problem drinking (Kushner, Sher, & Beitman, 1990; Kushner et al., 2000). The end result can be a “downward self-destructive spiral” leading to helplessness, depression, and increased risk for suicide (Barlow, 2002).

Comorbidity within Anxiety Disorders

The presence of one anxiety disorder significantly increases the probability of having one or more additional anxiety disorders. In fact, pure anxiety disorders are less frequent than comorbid anxiety. In their large clinical study, Brown, DiNardo, Lehmann, and Campbell (2001) found that comorbidity for another anxiety disorder ranged from 27% for specific phobia to 62% for posttraumatic stress disorder (PTSD). Generalized anxiety disorder (GAD) was the most common secondary anxiety disorder, followed by social phobia. For PTSD, which had the highest comorbid rate for another anxiety disorder, panic disorder and GAD were the most common secondary anxiety conditions. Social phobia and GAD tended to precede many of the other anxiety disorders. Analysis of lifetime diagnoses revealed even higher rates for occurrence of a secondary anxiety disorder.

Clinician Guideline 1.4

A case conceptualization of anxiety should include a broad diagnostic assessment that covers investigation of comorbid conditions, especially major depression, alcohol abuse, and other anxiety disorders.

PREVALENCE, COURSE, AND OUTCOME OF ANXIETY

Prevalence

The anxiety disorders are the most prevalent form of psychological disturbance (Kessler, Chiu, Demler, & Walters, 2005). Epidemiological studies of adult community samples have been remarkably consistent in documenting a 25–30% lifetime prevalence rate for at least one anxiety disorder. For example the 1-year prevalence for any anxiety disorder in the NCS was 17.2%, compared with 11.3% for any substance abuse/dependence and 11.3% for any mood disorder (Kessler et al., 1994). The NCS lifetime prevalence, which includes all individuals who ever experienced an anxiety disorder, was 24.9%, but this may be an underestimate because OCD was not assessed. In a recent replication of the NCS (NCS-R), involving a nationally representative sample of respondents ($N = 9,282$) interviewed between 2001 and 2003, 12-month prevalence for any anxiety disorder was 18.1% and estimated lifetime prevalence was 28.8%, findings that are remarkably similar to the first NCS (Kessler et al., 2005; Kessler, Berglund, Demler, Robertson, & Walters, 2005).

National surveys conducted in other Western countries like Australia, Great Britain, and Canada have also reported high rates of anxiety disorders in the general population, although the actual prevalence rates vary slightly across studies because of different interview methodologies, diagnostic decision rules, and other design factors (Andrews, Henderson, & Hall, 2001; Jenkins et al., 1997; Canadian Community Health Survey, 2003). The World Health Organization (WHO) World Mental Health Survey Initiative found that anxiety was the most common disorder in every country except the Ukraine (7.1%), with 1-year prevalence ranging from 2.4% in Shanghai, China, to 18.2% in the United States (WHO World Mental Health Survey Consortium, 2004).

Anxiety disorders are also common in childhood and adolescence, with 6-month prevalence rates ranging from 6% to 17% (Breton et al., 1999; Romano, Tremblay, Vitaro, Zoccolillo, & Pagani, 2001). The most frequent disorders are specific phobia, GAD, and separation anxiety (Breton et al., 1999; Whitaker et al., 1990). Some disorders like social phobia, panic, and generalized anxiety significantly increase during adolescence, whereas others like separation anxiety show a decrease (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Kashani & Orvaschel, 1990). Girls suffer higher rates of anxiety disorders than boys (Breton et al., 1999; Costello et al., 2003; Romano et al., 2001), comorbidity between anxiety and depression is high (Costello et al., 2003), and anxiety disorders that arise during childhood and adolescence often persist into early adulthood (Newman et al., 1996).

Individuals suffering from anxiety disorders often first come to the attention of family physicians in primary care settings because of unexplained physical symptoms like noncardiac chest pain, palpitations, faintness, irritable bowel syndrome, vertigo, and dizziness. These complaints may reflect an anxiety condition such as panic disorder (see discussion by Barlow, 2002). Moreover, patients with anxiety disorders seek out medical advice in disproportionate numbers. Studies of primary care patients find that 10–20% have a diagnosable anxiety disorder (Ansseau et al., 2004; Olfson et al., 1997, 2000; Sartorius, Ustun, Lecrubier, & Wittchen, 1996; Vazquez-Barquero et al., 1997). Sleath and Rubin (2002) found that anxiety was mentioned in 30% of visits to a university medical clinic family practice. Anxiety disorders, then, place a considerable burden on health service resources.

A large percentage of the general adult population experiences occasional or mild symptoms of anxiety. There is some evidence that individuals are at increased risk for developing a full-blown anxiety disorder if they experience panic attacks, sleep disturbance, or have obsessional concerns that are not sufficiently frequent or intense to meet diagnostic criteria (i.e., subclinical forms), or have high anxiety sensitivity (see Craske, 2003). Worry, the cardinal feature of GAD, is reported by a majority of nonclinical individuals who express concerns with work (or school), finances, family, and the like (e.g., Borkovec, Shadick, & Hopkins, 1991; Dupuy, Beaudoin, Rhéaume, Ladouceur, & Dugas, 2001; Tallis, Eysenck, & Mathews, 1992; Wells & Morrison, 1994). Problems with sleep are reported by 27% of British women and 20% of British men (Jenkins et al., 1997). In the U.S. 1991 National Sleep Foundation Survey, 36% of participants had occasional or chronic insomnia (Ancoli-Israel & Roth, 1999). Other studies indicate that 11–33% of nonclinical students and community adults have experienced at least one panic attack in the last year (Malan, Norton, & Cox, 1990; Salge, J. G. Beck, & Logan, 1988; Wilson et al., 1992). Thus symptoms of anxiety and its disorders are prevalent problems that threaten the physical and emotional well-being of a significant number of people in the general population.

Clinician Guideline 1.5

Given the high rate of anxiety disorders and symptoms in the general population, clinical assessment should include specification of symptom frequency and intensity as well as measures that enable differential diagnosis between disorders.

Gender Differences

Women have a significantly higher incidence of most anxiety disorders than men (Craske, 2003), with the possible exception of OCD, where the rates are approximately equal (see Clark, 2004). In the NCS women had a lifetime prevalence of 30.5% for any anxiety disorder, compared with 19.5% for men (Kessler et al., 1994). Other community-based and epidemiological studies generally have confirmed a 2:1 ratio of women to men in prevalence of anxiety disorders (e.g., Andrews et al., 2001; Jenkins et al., 1997; Olfson et al., 2000; Vazquez-Barquero et al., 1997). Since these gender differences were found in community-based surveys, the preponderance of anxiety disorders in women cannot be attributed to greater service utilization. In a critical review of research on gender differences in the anxiety disorders, Craske (2003) concluded that women may have higher rates of anxiety disorders because of an increased vulnerability such as (1) higher negative affectivity; (2) differential socialization patterns in which girls are encouraged to be more dependent, prosocial, empathic but less assertive and controlling of everyday challenges; (3) more pervasive anxiousness as evidenced by less discriminating and more overgeneralized anxious responding; (4) heightened sensitivity to reminders of threat and contextual threat cues; and/or (5) tendency to engage in more avoidance, worry, and rumination about potential threats.

Cultural Differences

Fear and anxiety exist in all cultures but their subjective experience is shaped by culture-specific factors (Barlow, 2002). Comparing the prevalence of anxiety across different cul-

tures is complicated by the fact that our standard diagnostic classification system, DSM-IV-TR (APA, 2000), is based on American conceptualizations and experiences of anxiety that may not have high diagnostic validity in other cultures (van Ommeren, 2002). Cross-cultural generalizability is not necessarily improved by using the WHO's classification of anxiety disorders, the International Classification of Diseases—Tenth Revision (ICD-10), because of the dominance of the European-influenced Western experience (World Health Organization, 1992). Thus our standard diagnostic and assessment approaches to anxiety may overemphasize aspects of anxiety that are prominent in the European Western experience and omit significant expressions of anxiety that are more culture-specific.

Barlow (2002) concluded in his review that apprehension, worry, fear, and somatic arousal are common in all cultures. For example, a large community survey of 35,014 adult Iranians found that 20.8% had anxiety symptoms (Noorbala, Bagheri-Yazdi, Yasamy, & Mohammad, 2004). Even in remote rural or mountainous regions of developing countries where modern industrial amenities and pressures are minimal, the occurrence of anxiety and panic disorders is similar to rates reported in Western community surveys (Mumford, Nazir, Jilani, & Yar Baig, 1996). Nevertheless, countries do appear to have different population rates of the anxiety disorders. The WHO World Mental Health Surveys found that 1-year prevalence of DSM-IV anxiety disorders ranged from a low of 2.4%, 3.2%, and 3.3% in Shanghai, Beijing, and Nigeria, respectively, to 11.2%, 12%, and 18.2% in Lebanon, France, and the United States, respectively (WHO World Mental Health Survey Consortium, 2004). This broad variability in prevalence rates raises the possibility that culture may influence the actual rate of anxiety disorders across countries, although methodological differences across sites cannot be ruled out as an alternative explanation for the differences.

There is substantial evidence that culture does play a significant role in the expression of anxious symptoms. Barlow (2002) noted that somatic symptoms appear more prominent in emotional disorders in most countries other than those of the European-influenced West. Table 1.2 presents a select number of culture-bound syndromes with a significant anxiety component.

Clinician Guideline 1.6

Assessment for anxiety should include a consideration of the individual's culture and social/familial environment and their influence on the development and subjective experience of anxiety.

Persistence and Course

In contrast to major depression, anxiety disorders are often chronic over many years with relatively low remission but more variable rates of relapse after complete recovery (Barlow, 2002). The Harvard–Brown Anxiety Disorder Research Program (HARP), an 8-year prospective study, found that only one-third to one-half of patients with social phobia, GAD, or panic disorder achieved full remission (Yonkers, Bruce, Dyck, & Keller, 2003).¹ The Zurich Cohort Study found that nearly 50% of individuals with an initial

¹Although these remission rates are very low, especially for social phobia and panic disorder, they probably overestimate the true remission rates for the anxiety disorders since 80% of the subjects had some form of pharmacological treatment over the 8-year follow-up.

TABLE 1.2. Select Culture-Bound Syndromes in Which Anxious Symptoms Play a Prominent Role

Syndrome name	Description	Country
<i>dhat</i>	Severe anxiety about the loss of semen through nocturnal emissions, urination, or masturbation. (Sumathipala, Siribaddana, & Bhugra, 2004)	Males in India, Sri Lanka, China
<i>koro</i>	Sudden and intense fear that one's sexual organs will retract into the abdomen eventually causing death. (APA, 2000)	Mainly occurs in males in south and east Asia
<i>pa-leng</i>	Morbid fear of the cold and wind in which the individual worries about further loss of body heat that could eventually lead to death. The person wears several layers of clothes even on warm days to keep out wind and cold. (Barlow, 2002)	Chinese cultures
<i>taijin kyofusho</i>	An intense fear that one's body parts or functions are displeasing, offensive, or embarrassing to other people by their appearance, odor, facial expressions, or movements. (APA, 2000).	Japan

anxiety disorder later developed depression alone or depression comorbid with anxiety at a 15-year follow-up (Merikangas et al., 2003). A Dutch longitudinal study of 3,107 older individuals found that 23% of subjects with an initial DSM-III anxiety disorder continued to meet criteria 6 years later, whereas another 47% suffered from subclinical anxiety (Schuermans et al., 2005). It is evident the anxiety disorders persist for many years when not treated (Craske, 2003). Given that the majority of these disorders have their onset in childhood and adolescence (Newman et al., 1996), the chronic nature of anxiety is a significant component of its overall disease burden.

Clinician Guideline 1.7

Consider the chronicity of anxiety and its influence on the development of other conditions when conducting a cognitive assessment. We can expect that early onset and a more persistent course would be more challenging for treatment.

Consequences and Outcome

The presence of an anxiety disorder, or even just anxious symptoms, is associated with a significant reduction in quality of life as well as in social and occupational functioning (Mendlowicz & Stein, 2000). In a meta-analytic review of 23 studies, Olatunji, Cisler, and Tolin (2007) found that all individuals with anxiety disorders experienced significantly poorer quality of life outcomes compared with control samples, and overall quality of life impairment was equivalent across the anxiety disorders. Individuals with an anxiety disorder have an increase in number of work loss days (Kessler & Frank, 1997; Olfson et al., 2000), more disability days (Andrews et al., 2001; Marcus, Olfson, Pincus, Shear, & Zarin, 1997; Weiller, Bisslerbe, Maier, & LeCrubier, 1998), and elevated rates of financial dependence in the form of disability payments, chronic unemployment, or welfare payments (Leon, Portera, & Weissman, 1995). Anxiety also tends

to reduce the quality of life and social functioning in patients with a comorbid chronic medical illness (Sherbourne, Wells, Meredith, Jackson, & Camp, 1996). Olfson et al. (1996) even found that primary care patients who did not meet diagnostic criteria for GAD, panic, or OCD but had symptoms of these disorders reported significantly more days of lost work, marital distress, and visits to a mental health professional. The negative impact of anxiety disorders in terms of distress, disability, and utilization of services can be even greater than for individuals whose main problem is a personality disorder or substance abuse (Andrews, Slade, & Issakidis, 2002). In fact, individuals with panic disorder evidence significantly lower social and role functioning in daily activities than patients with a chronic medical illness like hypertension (Sherbourne, Wells, & Judd, 1996).

Individuals with a diagnosable anxiety disorder make more visits to mental health professionals and are more likely to consult with their general practitioners for psychological problems compared with nonclinical controls (Marciniak, Lage, Landbloom, Dunayevich, & Bowman, 2004; Weiller et al., 1998). A large-scale study of employed Americans found that individuals with anxiety disorders were significantly more likely than the nonclinical control group to visit medical specialists, more likely to use inpatient services, and more likely to visit emergency rooms (Marciniak et al., 2004; see also Leon et al., 1995, for similar results). However, the majority of individuals with an anxiety disorder never receive professional treatment, and even fewer come to the attention of mental health practitioners (Coleman, Brod, Potter, Buesching, & Rowland, 2004; Kessler et al., 1994; Olfson et al., 2000). Family physicians, for example, are particularly poor at recognizing anxiety, with at least 50% of anxiety disorders missed in primary care patients (Wittchen & Boyer, 1998).

Given the adverse personal and social effects of anxiety disorders, the economic costs of anxiety are substantial in both the direct costs of services and the indirect costs of lost productivity. Self-reported anxiety in one American study accounted for an estimated 60.4 million days per year in lost productivity, which is equivalent to the level of lost productivity associated with the common cold or pneumonia (Marcus et al., 1997). Greenberg et al. (1999) estimated the annual cost of anxiety disorders at \$42.3 billion in 1990 U.S. dollars, whereas Rice and Miller (1998) found that the economic costs of anxiety were greater than for schizophrenia or the affective disorders.²

Clinician Guideline 1.8

Given the significant morbidity associated with anxiety, the negative impact of the disorder on work/school productivity, social relations, personal finances, and daily functioning must be included in the clinical assessment.

²There is evidence that a significant offset of the costs of anxiety can be achieved by early detection and treatment (Salvador-Carulla, Segui, Fernández-Cano, & Canet, 1995). Health economic studies have consistently shown that cognitive-behavioral therapy (CBT) for anxiety disorders is cheaper than medication and produces significant reduction in health care costs (Myhr & Payne, 2006). As the most common of the mental disorders, anxiety inflicts a significant human and social cost on our society, but increased provision of cognitive and cognitive-behavioral treatment could reduce the personal and economic costs of these disorders.

BIOLOGICAL ASPECTS OF ANXIETY

Anxiety is multifaceted, involving diverse elements of the physiological, cognitive, behavioral, and affective domains of human function. Table 1.3 lists the symptoms of anxiety divided into the four functional systems involved in an adaptive response to threat and danger (Beck et al., 1985, 2005).

The automatic physiological responses that typically occur in the presence of threat or danger are considered *defensive responses*. These responses, seen in the fear-eliciting contexts of both animals and humans, involve autonomic arousal that prepares the organism to deal with danger by fleeing (i.e., flight) or by directly confronting the danger (i.e., fight), a process known as the “fight-or-flight” response (Canon, 1927). The behavioral features primarily involve escape or avoidance as well as safety-seeking responses. The cognitive variables provide the meaningful interpretation of our internal state as that of anxiety. Finally the affective domain is derived from cognitive and physiological activation, and constitutes the subjective experience of feeling anxious. In the following sections, we briefly discuss the physiological, behavioral, and emotional aspects of anxiety. The cognitive features of anxiety are the focus of subsequent chapters.

Psychophysiology

As evident from Table 1.3, many of the symptoms of anxiety are physiological in nature, reflecting activation of the sympathetic (SNS) and parasympathetic (PNS) nervous systems. Activation of the SNS is the most prominent physiological response in anxiety, and it leads to hyperarousal symptoms such as constriction of the peripheral blood vessels, increased strength of the skeletal muscles, increased heart rate and force of contraction, dilation of the lungs to increase oxygen supply, dilation of the pupils for possible improved vision, cessation of digestive activity, increase in basal metabolism, and increased secretion of epinephrine and norepinephrine from the adrenal medulla (Brad-

TABLE 1.3. Common Features of Anxiety

Physiological symptoms

(1) Increase heart rate, palpitations; (2) shortness of breath, rapid breathing; (3) chest pain or pressure; (4) choking sensation; (5) dizzy, lightheaded; (6) sweaty, hot flashes, chills; (7) nausea, upset stomach, diarrhea; (8) trembling, shaking; (9) tingling or numbness in arms, legs; (10) weakness, unsteady, faintness; (11) tense muscles, rigidity; (12) dry mouth

Cognitive symptoms

(1) fear of losing control, being unable to cope; (2) fear of physical injury or death; (3) fear of “going crazy”; (4) fear of negative evaluation by others; (5) frightening thoughts, images, or memories; (6) perceptions of unreality or detachment; (7) poor concentration, confusion, distractible; (8) narrowing of attention, hypervigilance for threat; (9) poor memory; (10) difficulty in reasoning, loss of objectivity

Behavioral symptoms

(1) avoidance of threat cues or situations; (2) escape, flight; (3) pursuit of safety, reassurance; (4) restlessness, agitation, pacing; (5) hyperventilation; (6) freezing, motionless; (7) difficult speaking

Affective symptoms

(1) nervous, tense, wound-up; (2) frightened, fearful, terrified; (3) edgy, jumpy, jittery; (4) impatient, frustrated

ley, 2000). All of these peripheral physiological responses are associated with arousal but cause various perceptible symptoms such as trembling, shaking, hot and cold spells, heart palpitations, dry mouth, sweating, shortness of breath, chest pain or pressure, and muscle tension (see Barlow, 2002).

The role of PNS excitation, which causes a conservation of certain physiological responses, has not been as well researched in anxiety. The PNS is involved in symptoms like tonic immobility, drop in blood pressure, and fainting, which are a type of “conservation-withdrawal” response strategy (Friedman & Thayer, 1998). The effects of PNS stimulation include decreased heart rate and force of contraction, constricted pupils, relaxed abdominal muscles, and constriction of the lungs (Bradley, 2000). Moreover, research on heart rate variability in panic attacks indicates that the cardiovascular activity associated with anxiety should not be seen simply in terms of excessive SNS activation but also reduced compensatory PNS excitation. Thus the PNS probably plays a greater role in anxiety than previously considered.

Barlow (2002) concluded that one of the most robust and enduring findings in the past 50 years of psychophysiological research is that chronically anxious individuals exhibit a persistently elevated autonomic arousal level often in the absence of an anxiety-producing situation. For example, Cuthbert et al. (2003) reported significantly elevated heart rate base levels for panic and specific phobias but not social phobia or posttraumatic stress disorder (PTSD) groups. Other researchers, however, have linked anxiety (or neuroticism) to excess autonomic lability and reactivity rather than to enduring tonic levels of activation (Costello, 1971; Eysenck, 1979). Craske (2003) proposed that heightened cardiovascular reactivity might be a predisposing factor for panic disorder such that a tendency to experience intense and acute autonomic activation could increase the salience and therefore threat attributed to bodily sensations.

Empirical support for autonomic differences between anxious and nonanxious controls in response to stressful or threatening stimuli has not been consistently obtained across studies (Barlow, 2002). Friedman and Thayer (1998) also noted that psychophysiological findings of *reduced* heart rate and electrodermal variability challenge the view that anxiety is characterized by excessive autonomic lability and reactivity. Nevertheless, anxious individuals do show a slower decline in their physiological response to stressors (i.e., slow habituation), but this is probably due to their higher initial baseline arousal level (Barlow, 2002). In addition Lang and colleagues found greater physiological arousal to fear-relevant imagery in snake phobic individuals, but reactivity was less evident in those with panic (Cuthbert et al., 2003; Lang, 1979; Lang, Levin, Miller, & Kozak, 1983). Together these results suggest that heightened physiological reactivity to fear stimuli may be greatest in specific phobic conditions but less evident in other anxiety states like panic disorder or PTSD. However, a heightened basal arousal level and slower habituation rate might be seen more consistently across various anxiety disorders, thereby providing the physiological basis for chronically anxious individuals to misinterpret their persistent state of hyperarousal as evidence of an anticipated threat or danger.

Recent psychophysiological research suggests that individuals with chronic anxiety exhibit *diminished autonomic flexibility* in response to stressors (Noyes & Hoehn-Saric, 1998). This is characterized by a weak but sustained response to stressors, indicating a poor habituation trajectory. In a study of heart rate reactivity under baseline, relaxation, and worry conditions, Thayer, Friedman, and Borkovec (1996) found that

individuals with GAD or those actively engaged in worry had lower cardiac vagal control, which supports the view that GAD is characterized by autonomic inflexibility.

In sum it would appear that important psychophysiological features of anxiety such as elevated basal arousal level, slower habituation, and diminished autonomic flexibility might contribute to the misinterpretation of threat that is the core cognitive feature of anxiety. However, a different physiological response pattern may distinguish phobia, panic disorder, and GAD, which prevents generalizing research findings across the anxiety disorders. Furthermore, it is unclear whether the anxiety state is primarily an excess of SNS activation and a withdrawal of vagal activity, or if SNS activity is depressed and PNS activity remains normal under the conditions of daily living (see Mussgay & Rüdell, 2004, for discussion).

Clinician Guideline 1.9

Assessment of anxiety disorders must include a thorough evaluation of the type, frequency, and severity of physiological symptoms experienced during acute anxiety episodes, as well as the patient's interpretation of these symptoms. Baseline as well as patterns of physiological reactivity should be assessed using diaries and daily rating scales.

Genetic Factors

There is considerable empirical evidence that anxiety runs in families (see Barlow, 2002, for review). In a meta-analysis of family and twin studies for panic disorder, GAD, phobias, and OCD, Hettema, Neale, and Kendler (2001) concluded there is significant familial aggregation for all four disorders, with the strongest evidence for panic disorder. Across all disorders, estimates of heritability ranged from 30 to 40%, leaving the largest proportion of the variance due to individual environmental factors. Even at the symptomatic level, heritability accounts for only 27% of the variability by predisposing individuals to general distress, with environmental factors determining the development of specific anxiety or depressive symptoms (Kendler, Heath, Martin, & Eaves, 1987).

Barlow (2002) raised the possibility that a separate genetic transmission might be evident for anxiety and panic. In a structural equation modeling of diagnostic data collected on a large female twin sample, Kendler et al. (1995) found separate genetic risk factors for major depression and GAD (i.e., anxiety), on the one hand, and for acute, short-lived anxiety like phobias and panic, on the other. An earlier study also found a common genetic diathesis for major depression and GAD with disorder-specificity determined by exposure to different life events (Kendler, Neale, Kessler, Heath, & Eaves, 1992a).

There is less evidence that individuals inherit specific anxiety disorders and stronger empirical support for inheritance of a general vulnerability to develop an anxiety disorder (Barlow, 2002). This nonspecific vulnerability for anxiety could be neuroticism, high trait anxiety, negative affectivity, or what Barlow, Allen, and Choate (2004) called a "negative affect syndrome." Vulnerable individuals might show a stronger (or at least more sustained) emotional response to aversive or stressful situations. However, environmental and cognitive factors would interact with this genetic predisposition to determine which of the specific anxiety disorders is experienced by a particular individual.

Clinician Guideline 1.10

A diagnostic interview should include questions about the prevalence of anxiety disorders in first-degree relatives.

Neurophysiology

In the last decade rapid advances have been made in our understanding of the neurobiological basis of fear and anxiety. One important finding that has emerged is the central role of the amygdala in emotional processing and memory (see discussion by Canli et al., 2001). Human and nonhuman research indicates that the amygdala is involved in the emotional modulation of memory, the evaluation of stimuli with affective significance, and the appraisal of social signals related to danger (see Anderson & Phelps, 2000). Research on auditory fear conditioning by LeDoux (1989, 1996, 2000) has contributed most to implicating the amygdala as the neural substrate for the acquisition of conditioned fear responses. LeDoux (1996) concluded that the amygdala is the “hub in the wheel of fear” (p. 170), that it is “in essence, involved in the appraisal of emotional meaning” (p. 169).

LeDoux (1989) contends that one of the most important tasks of the emotional brain is to evaluate the affective significance (e.g., threat vs. nonthreat) of mental (thoughts, memories), physical, or external stimuli. He proposed two parallel neural pathways in the amygdala’s processing of fear stimuli. The first pathway involves direct transmission of a conditioned fear stimulus through the sensory thalamus to the lateral nucleus of the amygdala, bypassing the cortex. The second pathway involves transmission of fear stimulus information from the sensory thalamus through the sensory cortex and on to the lateral nucleus. Within the amygdala region the lateral nucleus, which receives inputs in fear conditioning, innervates the central nucleus that is responsible for the expression of the conditioned fear response (see also Davis, 1998). Figure 1.1 illustrates the two parallel pathways of LeDoux’s conditioned fear reaction system.

LeDoux (1996) draws a number of implications from his dual pathway of fear. The more direct thalamo–amygdala path (called “the low road”) is quicker, more rudimentary, and occurs without thinking, reasoning, and consciousness. The thalamo–cortical–amygdala path (labeled “the high road”) is slower but involves more elaborative processing of the fear stimulus because of extensive involvement of higher cortical regions of the brain. Although LeDoux (1996) discusses the obvious evolutionary advantage of an automatic, preconscious neural basis to information processing of fear stimuli, his research demonstrated that the cortical pathway is necessary for fear conditioning to more complex stimuli (i.e., when the animal must discriminate between two similar tones in which only one is paired with the unconditioned stimulus [UCS]).

The central role of the amygdala in fear is entirely consistent with its neuroanatomical connections. It has multiple output projections via the central nucleus to the hypothalamus, hippocampus, and upward to various regions of the cortex, as well as downward to various brainstem structures involved in autonomic arousal and neuroendocrine responses associated with stress and anxiety like the periaqueductal gray region (PAG), the ventral tegmental area, the locus ceruleus, and the raphe nuclei (Barlow, 2002). All of these neural structures have been implicated in the experience of anxiety, including the bed nucleus of the stria terminalis (BNST; Davis, 1998), which may be the most important neural substrate of anxiety (Grillon, 2002).

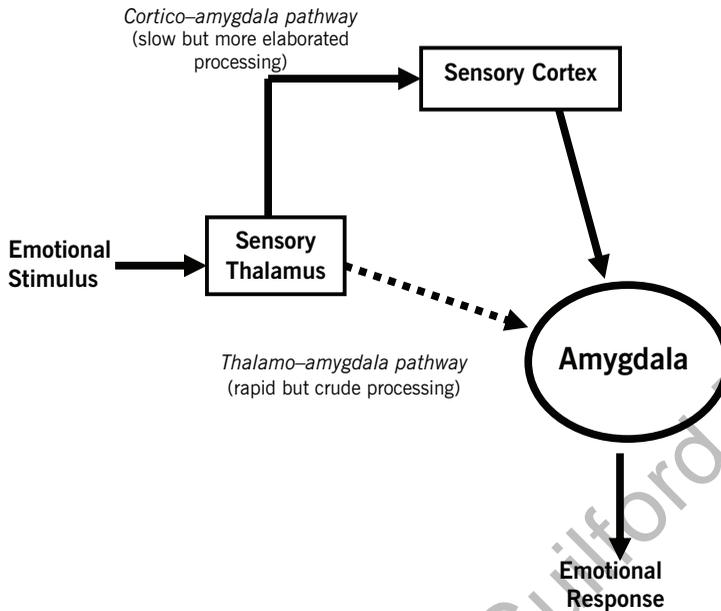


FIGURE 1.1. LeDoux's parallel neural pathways in auditory fear conditioning.

The role of conscious cognitive processing in fear is a much debated issue in light of LeDoux's research suggesting a rapid and rudimentary noncortical thalamo-amygdala pathway in the processing of conditioned fear. In fact LeDoux (1996) found that fear-relevant stimuli can be implicitly processed by the amygdala through the subcortical thalamo-amygdala pathway without conscious representation. Neuroimaging studies have found that fearful or negatively valenced stimuli are associated with relative increases in regional cerebral blood flow (rCBF) in the secondary or associative visual cortex and relative reductions in rCBF in the hippocampus, prefrontal, orbitofrontal, temporopolar, and posterior cingulate cortex (e.g., see Coplan & Lydiard, 1998; Rauch, Savage, Alpert, Fishman, & Jenike, 1997; Simpson et al., 2000). These findings have been interpreted as evidence that fear can be preconscious without the occurrence of higher cognitive processing.

Evidence for a subcortical, lower order pathway to immediate conditioned fear processing should not divert attention away from the critical role that attention, reasoning, memory, and subjective appraisal or judgments play in human fear and anxiety. LeDoux (1996) found that the thalamo-cortico-amygdala pathway was activated in more complex fear conditioning. Moreover, the amygdala has extensive connections with the hippocampus and cortical regions, where it receives inputs from cortical sensory processing areas, the transitional cortical area, and the medial prefrontal cortex (LeDoux, 1996, 2000). LeDoux emphasizes that the hippocampal system involving explicit memory and the amygdala system involving emotional memory will be activated simultaneously by the same stimuli and will function at the same time. Thus cortical brain structures involved in *working memory*, such as the prefrontal cortex and the anterior cingulate and orbital cortical regions, and structures involved in long-term *declarative memory*,

like the hippocampus and temporal lobe, are implicated with amygdala-dependent emotional arousal to provide the neural basis to the subjective (conscious) experience of fear (LeDoux, 2000). The neural substrates of cognition, then, can be expected to play a critical role in the type of fear acquisition and persistence that characterizes complex human fears and anxiety disorders. This is supported by various neuroimaging studies that found differential activation of various medial prefrontal and frontotempororbital regions of the cortex (e.g., Connor & Davidson, 1998; Coplan & Lyiard, 1998; Lang, Bradley, & Cuthbert; 1998; McNally, 2007; van den Heuvel et al., 2004; Whiteside, Port, & Abramowitz, 2004).

In their review Luu, Tucker, and Derryberry (1998) argued that fear-relevant mental representations of the cortex influence emotional functioning not only at the later stage of fear expression and responsivity, but cortical influence can also serve an anticipatory function even before sensory information is physically available. The authors conclude that “with our highly evolved frontal networks, we humans are capable of cognitively mediating our actions, and of inhibiting the more reflexive responses triggered by limbic and subcortical circuits” (Luu et al., 1998, p. 588). This sentiment was recently echoed in a review paper by McNally (2007a) in which he concludes that activation in the medial prefrontal cortex can suppress conditioned fear acquisition that is mediated by the amygdala. Thus prefrontal executive functions (i.e., conscious cognitive processes) can have fear-inhibiting effects that involve learning new inhibitory associations or “safety signals” that suppress fear expression (McNally, 2007a). Frewen, Dozois, and Lanius (2008) concluded in their review of 11 neuroimaging studies of psychological interventions for anxiety and depression that CBT alters functioning in brain regions such as the dorsolateral, ventrolateral, and medial prefrontal cortices; anterior cingulate; posterior cingulate/precuneus; and the insular cortices that are associated with problem solving, self-referential and relational processing, and regulation of negative affect. Clearly, then, the extensive involvement of higher order cortical regions of the brain in emotional experiences is consistent with our contention that cognition plays an important role in the production of anxiety and that interventions like cognitive therapy can effectively inhibit anxiety by engaging cortical regions responsible for higher order reasoning and executive function.

Neurotransmitter Systems

Neurotransmitter systems such as the benzodiazepine–gamma-aminobutyric acid (GABA), noradrenergic, and serotonergic, as well as the corticotropin-releasing hormonal pathway, are important to the biology of anxiety (Noyes & Hoehn-Saric, 1998). The serotonergic neurotransmitter system has become of increasing interest in research on anxiety and panic. Serotonin acts as a neurochemical break on behavior, with blockade of serotonin receptors in humans associated with anxiety (Noyes & Hoehn-Saric, 1998). Although low levels of serotonin have been implicated as a key contributor to anxiety, direct neurophysiological evidence is mixed on whether abnormalities in serotonin can be found in anxiety disorders like GAD compared to controls (Sinha, Mohlman, & Gorman, 2004). The serotonergic system projects to diverse areas of the brain that regulate anxiety like the amygdala, septo-hippocampal, and prefrontal cortical regions and so may have a direct influence on anxiety or an indirect influence by alter-

ing the function of other neurotransmitters (Noyes & Hoehn-Saric, 1998; Sinha et al., 2004).

A subgroup of the inhibitory transmitter GABA contains benzodiazepine receptors that enhance the inhibitory effects of GABA when benzodiazepine molecules bind to these receptor sites (Gardner, Tully, & Hedgecock, 1993). Evidence that generalized anxiety may be due to a suppressed benzodiazepine-GABA system comes from the anxiolytic effects of benzodiazepine drugs (e.g., lorazepam [Ativan], alprazolam [Xanax]), which appear to have their clinical effectiveness by enhancing benzodiazepine-GABA inhibition (Barlow, 2002).

Corticotropin-releasing hormone (CRH) is a neurotransmitter that is primarily stored in the hypothalamic paraventricular nuclei (PVN). Stressful or threatening stimuli can activate certain brain regions like the locus ceruleus, amygdala, hippocampus, and prefrontal cortex, which then releases CRH. CRH then stimulates secretion of adrenocorticotrophic hormone (ACTH) from the anterior pituitary gland and other pituitary–adrenal activity that results in increased production and release of cortisol (Barlow, 2002; Noyes & Hoehn-Saric, 1998). The CRH, then, not only mediates endocrine responses to stress but also other broad brain and behavioral responses that play a role in the expression of stress, anxiety, and depression (Barlow, 2002). Overall, then, abnormalities at the neurotransmitter level appear to have anxiogenic or anxiolytic effects that play an important contributory role in heightened physiological states that characterize fear and anxiety. However, the exact nature of these abnormalities is still unknown. Table 1.4 provides a summary of the biological aspects of anxiety that might underlie the cognitive features of these disorders discussed later in this volume.

Clinician Guideline 1.11

Discuss the neural basis of anxiety when educating the client about the cognitive model of anxiety. The rationale for cognitive therapy should include a discussion of how the higher order cortical centers of the brain involved in memory, reasoning, and judgment can “override” or inhibit subcortical emotional brain structures, thereby reducing the subjective experience of anxiety.

TABLE 1.4. Biological Concomitants of Cognition in Anxiety

Biological factors	Cognitive sequelae
<ul style="list-style-type: none"> • Elevated tonic autonomic activation • Slower habituation rate • Diminished autonomic flexibility • Genetic predisposition for negative emotionality • Subcortical fear potentiation 	<ul style="list-style-type: none"> • Increased salience of threat-related stimuli • Sustained attention to threat • Reduced ability to shift attention • Hypervalent schemas of threat and danger • Preconscious fear stimulus identification and immediate physiological arousal
<ul style="list-style-type: none"> • Extensive cortical afferent and efferent pathways to subcortical emotion-relevant circuitry 	<ul style="list-style-type: none"> • Cognitive appraisal and memory influence fear perception and modulates fear expression and action

BEHAVIORAL THEORIES

Over several decades experimental psychologists grounded in learning theory have demonstrated that fear responses can be acquired through an associative learning process. Theoretical and experimental work from this perspective has focused on the physiological and behavioral responses that characterize an anxious or fearful state. Early learning theory focused on the acquisition of fears or phobic reactions through classical conditioning.

Conditioning Theories

According to classical conditioning, a neutral stimulus, when repeatedly associated with an aversive experience (unconditioned stimulus [UCS] that leads to the experience of anxiety (unconditioned response [UCR]), becomes associated with the aversive experience, it acquires the capability to elicit a similar anxiety response (conditioned response [CR]) (Edelmann, 1992). The emphasis in classical conditioning is that human fears are acquired as a result of some neutral stimulus (e.g., visit to a dentist's office) coming into association with some previous anxiety-provoking experience (e.g., a highly painful and terrifying experience at the dentist office when a child). Although numerous experimental studies over the past 80 years have demonstrated that fears can be acquired in the laboratory by repeatedly pairing a neutral stimulus (e.g., tone) with an unconditioned stimulus (e.g., mildly aversive electric shock), the model could not provide a credible explanation for the remarkable persistence of human fears in the absence of repeated UCS–CS pairings (Barlow, 2002).

Mowrer (1939, 1953, 1960) introduced a major revision to the conditioning theory in order to better account for avoidance behavior and the persistence of human fears. Referred to as “two-factor theory,” it became a widely accepted behavioral account of the etiology and persistence of clinical fears and anxiety states throughout the 1960s and early 1970s (e.g., Eysenck & Rachman, 1965). Although no longer considered a tenable theory of anxiety, the two-factor theory is important for two reasons. First, many of the behavioral interventions that have proven so effective in the treatment of anxiety disorders had their origins in the two-factor model. And second, our current cognitive models of anxiety were in large part born out of the criticisms and inadequacies of the two-factor theory.

Figure 1.2 provides an illustration of how the two-factor theory might be used to explain Freud's case study of Little Hans (Freud, 1909/1955). Little Hans was a 5-year-old Austrian boy who developed a fear that a horse would bite him, and so experienced considerable anxiety whenever he ventured outside for fear of seeing a horse. The onset of the “horse phobia” occurred after he witnessed a large “bus-horse” fall down and violently kick its feet in an effort to get up. Little Hans then became frightened that horses, particularly those pulling carts, would fall down and bite him. (Of course Freud interpreted the real source of Little Hans's phobia as his repressed sexual affection for his mother and hostility toward his father that became transposed [displaced] onto horses.)

In the two-factor model, the first stage of fear acquisition is based on classical conditioning. Little Hans experiences a traumatic event: seeing a large horse fall to the street and thrash about violently (UCS). This elicits a strong fear response (UCR), so that the sight of horses (CS) through association with the UCS is now capable of elic-

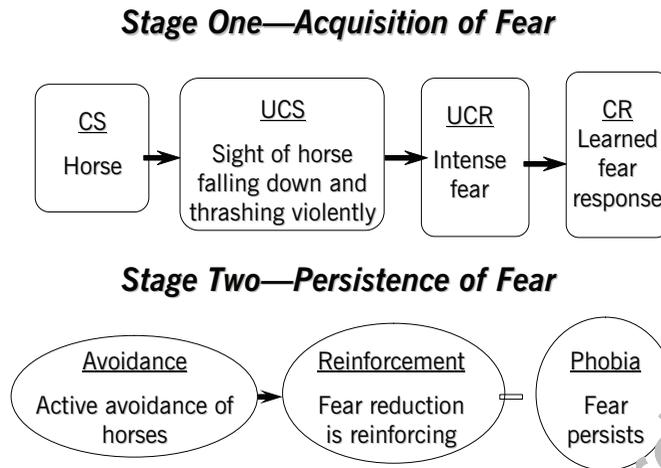


FIGURE 1.2. A two-factor theory of fear acquisition explanation of Freud's case study of Little Hans.

iting a CR (fear response). However, fear persistence is explained at the second stage because of extensive avoidance of the CS. In other words, Little Hans stays indoors and so avoids the sight of horses (the CS). Because avoidance of horses ensures that Little Hans will not experience fear or anxiety, the avoidance behavior is negatively reinforced. Avoidance is maintained because fear reduction is a powerful secondary reinforcer (Edelmann, 1992). Furthermore, because he stays indoors, Little Hans fails to learn that horses do not regularly fall down (i.e., he does not experience repeated CS-only presentations that would lead to extinction).

By the late 1970s serious problems were raised with the two-factor model explanation for human phobias (Rachman, 1976, 1977; see also Davey, 1997; Eysenck, 1979). First, classical conditioning assumes that any neutral stimulus can acquire fear-eliciting properties if associated with a UCS. However, this assumption was not supported in aversive conditioning experiments in which some stimuli (e.g., pictures of spiders and snakes) produced a conditioned fear response much more easily than other stimuli (e.g., pictures of flowers or mushrooms; for review, see Öhman & Mineka, 2001). Second, many individuals who develop clinical phobias can not recall a traumatic conditioning event. Third, there is considerable experimental and clinical evidence of nonassociative learning of fears through vicarious observation (i.e., witnessing someone else's trauma) or informational transmission (i.e., when threatening information about specific objects or situations is conveyed to the individual). Fourth, people often experience traumatic events without developing a conditioned fear response (Rachman, 1977). Again the two-factor model requires considerable refinement to explain why only a minority of individuals develop phobias in response to a traumatic experience (e.g., painful dental work). And finally, the two-factor theory has difficulty explaining the epidemiology of phobias (Rachman, 1977). For example, fear of snakes is much more common than dental phobia, and yet many more people experience the pain of dental work than are bitten by snakes.

Although various refinements were proposed, it became clear that the two-factor theory of conditioning was unable to explain the development and persistence of human fears and anxiety disorders. Many behavioral psychologists concluded that cognitive constructs were needed to provide an adequate account of the development and maintenance of anxiety, even phobic states (e.g., Brewin, 1988; Davey, 1997). A variety of cognitive concepts were proposed (e.g., expectancies, self-efficacy, attentional bias, or threat-related schemas) as mediators between the occurrence of a fear-eliciting stimulus and the anxious response (see Edelman, 1992). Not all behavioral psychologists, though, embraced cognitive mediation as a causal mechanism in the development of anxiety. An example of a more “noncognitive” perspective is the fear module proposed by Öhman and Mineka (2001).

The Fear Module

Öhman and Mineka (2001) state that because fear evolved as a defense against predators and other threats to survival, it involves a *fear module* composed of behavioral, psychophysiological, and verbal-cognitive components. A fear module is defined as “a relatively independent behavioral, mental, and neural system that is specifically tailored to help solve adaptive problems encountered by potentially life-threatening situations in the ecology of our distant forefathers” (Öhman & Mineka, 2001, p. 484).

They discuss four characteristics of the fear module. First, it is *selectively sensitized* to respond to stimuli that are evolutionarily prepotent because they posed particular threats to the survival of our ancestors. They reviewed a large experimental literature that demonstrated selective association in human aversive conditioning in which individuals evidence better conditioning and greater resistance to extinction for phylogenetic stimuli (e.g., slides of snakes or spiders) than for ontogenetic materials (e.g., slides of houses, flowers, or mushrooms). Öhman and Mineka (2001) concluded that (1) evolutionarily prepared fear-relevant stimuli have preferential access to the human fear module and (2) selective association of these prepared stimuli is largely independent of conscious cognition.

A second characteristic of the fear module is its *automaticity*. Öhman and Mineka (2001) state that because the fear module evolved to deal with phylogenetic threats to survival, it can be automatically activated without conscious awareness of the triggering stimulus. Evidence for automatic preconscious activation of fear includes physiological fear response (e.g., SCR) to fear stimuli that are not consciously recognized, continued conditioned fear response to nonreportable stimuli, and the acquisition of a conditioned fear response to fear-relevant stimuli that were not amenable to conscious awareness.

A third feature is *encapsulation*. The fear module is assumed to be “relatively impenetrable to other modules with which it lacks direct connections” (Öhman & Mineka, 2001, p. 485) and so will tend to run its course once activated with few possibilities that other processes can stop it (Öhman & Wiens, 2004). Even though the fear module is relatively impenetrable to conscious influences, Öhman and Mineka argue that the fear module itself can have a profound influence by biasing and distorting conscious cognition of the threat stimulus. In support of their contention of the independence of the fear module from the influence of conscious cognition, Öhman and Weins (2004) cite evidence that (1) masking of stimuli affects conscious appraisals but not condi-

tioned responses (SCRs), (2) instructions that alter explicit UCS–CS expectancies do not affect conditioned response to biological fear-relevant stimuli, (3) individuals can acquire conditioned fear responses to masked stimuli outside conscious awareness, and (4) conditioned fear responses to masked stimuli can affect conscious cognition in the form of expectancy judgments.

A final characteristic is its *specific neural circuitry*. Öhman and Mineka (2001) consider the amygdala the central neural structure involved in the control of fear and fear learning and contend that fear activation (i.e., emotional learning) occurs via LeDoux's (1996) subcortical, noncognitive thalamo–amygdala pathway, whereas cognitive learning occurs via the hippocampus and higher cortical regions. The authors contend that the amygdala has more afferent than efferent connections to the cortex and so has more influence on the cortex than the reverse. Based on this view of the neural structure of the fear module, they conclude that (1) nonconscious activation of the amygdala occurs via a neural route that does not involve the cortex, (2) this neural circuitry is specific to fear, and (3) any conscious cognitive processes associated with fear are a consequence of the activated fear module (i.e., amygdala) and thus play no causal role in fear activation. Thus biased appraisals and beliefs are a product of automatic fear activation and the production of psychophysiological and reflexive defensive responses (Öhman & Weins, 2004). Exaggerated beliefs in danger may play a role in maintaining anxiety over time but they are the consequence rather than the cause of fear.

Clinician Guideline 1.12

Given the substantial evidence concerning the importance of learning in the development of anxiety, the clinician should explore with patients past anxiety-related learning experiences (e.g., trauma, life events, exposure to threat-related information).

THE CASE FOR COGNITION

Öhman and Mineka's (2001) perspective on fear and anxiety is at variance with the cognitive perspective advocated by Beck and colleagues (Beck et al., 1985, 2005; Beck & Clark, 1997; D. M. Clark, 1999). Although they acknowledge that cognitive phenomena should be targeted in treatment because they play a key role in the longer term maintenance of anxiety, they still consider anxious thinking, beliefs, and processing biases a consequence of fear activation. Öhman and Mineka (2001) do not consider conscious cognition critical in the pathogenesis of fear itself, which is contrary to the conceptualization of fear that we offered earlier in this chapter. This noncognitive view of fear is evident in other learning theorists like Bouton, Mineka, and Barlow (2001), who argue that interoceptive conditioning in panic disorder occurs without conscious awareness and is quite independent of declarative knowledge systems. Nevertheless, we consider cognitive appraisal a core element of fear and critical to understanding the etiology, persistence, and treatment of anxiety disorders. This view is based on several arguments.

Existence of Preconscious Cognition

Critics of cognitive models tend to overemphasize conscious awareness when discussing cognition, arguing that the substantial experimental evidence of conditioned fear responses without conscious awareness fails to support basic tenets of the cognitive perspective (e.g., Öhman & Mineka, 2001). However, there is equally robust experimental research demonstrating preconscious, automatic cognitive and attentional processing of fear stimuli (see MacLeod, 1999; Wells & Matthews, 1994; Williams, Watts, MacLeod, & Matthews, 1997). Thus the cognitive perspective on anxiety is misrepresented when cognition is characterized only in terms of conscious appraisal.

Cognitive Processes in Fear Acquisition (i.e., Conditioning)

Öhman and Mineka (2001) argue that cognitive processes are a consequence of fear activation and so play little role in their acquisition. However, over the last three decades many learning theorists have argued that cognitive concepts must be incorporated into conditioning models to explain the persistence of fear responses. Davey (1997), for example, reviews evidence that outcome expectancies as well as one's cognitive representation of the UCS will influence the strength of the fear CR in response to a CS. In other words, CRs increase or decrease in strength depending on how the person evaluates the meaning of the UCS or trauma (see also van den Hout & Merckelbach, 1991). According to Davey (1997), then, cognitive appraisal is a key element in Pavlovian fear conditioning.

It has long been recognized that outcome expectancies (i.e., expectations that in a particular situation a certain response will lead to a given outcome) play a critical role in aversive conditioning (e.g., Seligman & Johnston, 1973; de Jong & Merckelbach, 2000; see also experiments on covariation bias by de Jong, Merckelbach, & Arntz, 1995; McNally & Heatherton, 1993). In his influential review paper Rescorla (1988) argued that modern learning theory views Pavlovian conditioning in terms of learning the relations among events (i.e., associations) that must be perceived and that are complexly represented (i.e., memory) by the organism. For most behaviorally oriented clinical researchers, then, the acquisition and elicitation of fear and anxiety states will involve learning contingencies that recognize the influence and importance of various cognitive mediators (for further discussion, see van den Hout & Merckelbach, 1991).

Conscious Cognitive Processes Can Alter Fear Responses

Öhman and Mineka (2001) contend that the fear module is impenetrable to conscious cognitive control. However, this view is difficult to reconcile with empirical evidence that cognitive or informational factors can lead to a reduction in fear (see discussion by Brewin, 1988). Even with exposure-based interventions, which are directly derived from conditioning theory, there is evidence that long-term habituation of fear responses requires conscious directed attention and processing of the fear-relevant information (Foa & Kozak, 1986). Brewin (1988) succinctly makes a case for the influence of cognition on fear responses, stating that "a theory that assigns a role to conscious thought processes is necessary to explain how people can alternately frighten and reassure them-

selves by thinking different thoughts, test out a variety of different coping responses, set goals and reward or punish themselves depending on the outcome, etc.” (p. 46).

The Amygdala Is Not Specific to Fear

A central argument of Öhman and Mineka (2001) is that a direct thalamus–amygdala link in fear activation and emotional learning accounts for the automaticity of the fear module and so is dissociable from declarative acquisition of information via the hippocampus. Thus activation of the amygdala begins a fear response which then leads to more complex cognition and memory processes via projections to the hippocampus and higher cortical brain regions (see also Morris, Öhman, & Dolan, 1998).

Although experimental research has been quite consistent in showing amygdaloid activation in the processing of fearful stimuli, there is evidence that the amygdala may also be involved in other emotional functions such as the appraisal of the social and emotional significance of facial emotions (Adolphs, Tranel, & Damasio, 1998; Anderson & Phelps, 2000). Neuroimaging studies suggest greater activation occurs in the prefrontal cortex, amygdala, other midbrain structures, and the brainstem when processing any generally negative, arousing emotional stimuli, which suggests that the amygdala and other structures involved in emotional processing may not be specific to fear but rather to the valence of emotional stimuli (e.g., Hare, Tottenham, Davidson, Glover, & Casey, 2005; Simpson et al., 2000; see also amygdala activation when processing sad film excerpts, Lévesque et al., 2003). In addition the amygdala is responsive to positively valenced stimuli, although this response seems to be more variable and elaborative in nature than the fixed, automatic response seen to fear expressions (Somerville, Kim, Johnstone, Alexander, & Whalen, 2004; see also Canli et al., 2002). Thus there is experimental evidence that the amygdala may not be the seat of anxiety specifically but an important neural structure of emotion processing more generally (see also Gray & McNaughton, 1996).

Other neuroimaging research suggests that the amygdala can be influenced by cognitive processes mediated by higher cortical regions of the brain. McNally (2007a) reviewed evidence that the medial prefrontal cortex can suppress conditioned fear acquired via activation of the amygdala. For example, in one study perceptual processing of threatening pictorial scenes was associated with a strong bilateral amygdala response that was attenuated by cognitive evaluation of the fear stimuli (Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003). Together these findings suggest that conscious cognitive processes mediated by other cortical and subcortical regions of the brain have an important influence on the amygdala and together provide an integrated neural account of the experience of fear.

Role of Higher Order Cortical Regions in Fear

The critical issue for a cognitive perspective on anxiety is whether conscious cognitive processes play a sufficiently important role in the propagation and amelioration of anxiety to warrant an emphasis at the cognitive level. As discussed previously, there is considerable neurophysiological evidence that higher cortical regions of the brain are involved in the type of human fear and anxiety responses that are the target of clinical

interventions. LeDoux (1996) has shown that the hippocampus and related areas of the cortex involved in the formation and retrieval of memories are implicated in more complex contextual fear conditioning. It is this type of conditioning that is particularly relevant to the formation and persistence of anxiety disorders. Moreover, LeDoux (1996, 2000) notes that the subjective feeling associated with fear will involve connections between the amygdala and the prefrontal cortex, anterior cingulate, and orbital cortical regions, as well as the hippocampus. From a clinical perspective, it is the subjective experience of anxiety that brings individuals to the attention of clinicians, and it is the elimination of this aversive subjective state that is the main criteria for judging treatment success. In sum, it is apparent that the neural circuitry of fear is consistent with a prominent role for cognition in the pathogenesis of anxiety.

SUMMARY AND CONCLUSION

In many respects anxiety is a defining feature of contemporary society and the tenacity of its clinical manifestations represents one of the greatest challenges facing mental health research and treatment. The pervasiveness, persistence, and deleterious impact of anxiety disorders have been well documented in numerous epidemiological studies. In this chapter, a number of issues in the psychology of anxiety disorders were identified. One of the most basic confusions arises from the definition of anxiety and its relation to fear. Taking a cognitive perspective, we defined fear as the automatic appraisal of imminent threat or danger, whereas anxiety is the more enduring subjective response to fear activation. The latter is a more complex cognitive, affective, physiological, and behavioral response pattern that occurs when events or circumstances are interpreted as representing highly aversive, uncertain, and uncontrollable threats to our vital interests. Fear, then, is the basic cognitive process underlying all the anxiety disorders. However, anxiety is the more enduring state associated with threat appraisals, and so the treatment of anxiety has become a major focus in mental health.

Another fundamental issue associated with anxiety is the differentiation between normal and abnormal states. Although fear is necessary for survival because it is essential for preparing the organism for response to life-threatening dangers, fear is clearly maladaptive when present in the anxiety disorders. Once again a cognitive perspective can be helpful in identifying the boundaries between normal anxiety or fear, and their clinical manifestations. Fear is maladaptive and more likely associated with an anxiety disorder when it involves an erroneous or exaggerated appraisal of danger, causes impaired functioning, shows remarkable persistence, involves a false alarm, and/or creates hypersensitivity to a wide range of threat-related stimuli. The challenge for practitioners is to offer interventions that “dampen down” or normalize clinical anxiety so it becomes less distressing and interfering in daily living. The elimination of all anxiety is neither desirable nor possible, but its reduction to within the normal range of human experience is the common goal of treatment regimens for anxiety disorders.

Anxiety states are multifaceted, involving all levels of human function. There is a significant biological aspect to anxiety, with particular cortical and subcortical neural structures playing a critical role in emotional experience. This strong neurophysiological element gives anxiety states a sense of urgency and potency that makes modification

difficult. At the same time anxiety is often acquired through the organism's interaction with the environment even though this learning process may occur outside awareness and beyond rational consideration. And yet cognitive mediation such as expectancies, interpretations, beliefs, and memories play a critical role in the development and persistence of anxiety. As a subjective experience, anxiety may feel like a storm that surges and recedes throughout the day. Relief from this state of personal turmoil can be a potent motivator even when it elicits response patterns, such as escape and avoidance, that are ultimately counterproductive to the vital interests of the individual.

Despite its complexity, we have argued in this chapter that cognition plays a key role in understanding both normal and abnormal states of anxiety. The essence of maladaptive anxiety is a faulty or exaggerated interpretation of threat to an anticipated situation or circumstance that is perceived to have significance for the person's vital resources. In the last two decades substantial progress has been made in elucidating the cognitive structures and processes of anxiety. Based on the cognitive model of anxiety first proposed by Beck et al. (1985), this book presents a more refined, elaborated, and extended cognitive formulation that incorporates major advances made within cognitive-clinical research of anxiety. A systematic evaluation of the empirical status of this reformulation is presented along with theory-driven strategies for cognitive assessment and treatment. In subsequent chapters disorder-specific cognitive theories, research, and treatment are presented for the major forms of anxiety disorders: panic disorder, social phobia, GAD, OCD, and PTSD. It is our contention that the cognitive perspective continues to hold much promise for the advancement of our understanding of anxiety and the provision of innovative treatment approaches.