Diagnostic Criteria for Panic Disorder

A. Both 1 and 2:
   1. Recurrent unexpected panic attacks.
   2. At least one of the attacks has been followed by one month (or more) of one (or more) of the following:
      a. a persistent concern about having additional attacks;
      b. worrying about the implications of the attack or its consequences (e.g., losing control, having a heart attack, going crazy insane);
      c. a significant change in behavior related to the attacks.

B. The panic attacks are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

C. The panic attacks are not better accounted for by another mental disorder, such as social phobia (e.g., occurring on exposure to feared social situations), specific phobia (e.g., on exposure to a specific phobic situation), obsessive-compulsive disorder (OCD) (e.g., on exposure to dirt in someone with an obsession about contamination), posttraumatic stress disorder (PTSD) (e.g., in response to stimuli associated with a severe stressor), or separation anxiety disorder (e.g., in response to being away from home or close relatives).

Panic Disorder (PD) is divided into categories of with or without agoraphobia.
**Diagnostic Criteria for Agoraphobia**

A. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed panic attack or panic-like symptoms. Agoraphobic fears typically involve characteristic clusters of situations that include being outside the home alone; being in a crowd or standing in a line; being on a bridge; and traveling in a bus, train, or automobile.

B. The situations are avoided (e.g., travel is restricted), or else are endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion.

C. The anxiety or phobic avoidance is not better accounted for by another mental disorder, such as social phobia (e.g., avoidance limited to social situations because of fear of embarrassment), specific phobia (e.g., avoidance limited to a single situation like elevators), OCD (e.g., avoidance of dirt in someone with an obsession about contamination), PTSD (e.g., avoidance of stimuli associated with a severe stressor), or separation anxiety disorder (e.g., avoidance of leaving home or relatives).

**Diagnostic Criteria for a Panic Attack**

The diagnostic criteria for a panic attack include a discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes:

1. heart palpitations, pounding heart, or accelerated heart rate;
2. sweating;
3. trembling or shaking;
4. sensations of shortness of breath or smothering;
5. feeling of choking;
6. chest pain or discomfort;

Like OCD and PTSD, SAD?
7. nausea or abdominal distress;
8. feeling dizzy, unsteady, lightheaded, or faint;
9. derealization (feelings of unreality) or depersonalization (being detached from oneself);
10. fear of losing control or going insane;
11. fear of dying;
12. paresthesias (numbness or tingling sensations);
13. chills or hot flushes.

**Features of Panic Disorder and Agoraphobia**

*Panic Disorder* is characterized by *recurrent panic attacks* (or, sudden rushes of intense fear or discomfort). A panic attack is defined by a cluster of physical and cognitive symptoms, including heart palpitations, shortness of breath, derealization, paresthesia, trembling, and fears of dying, going insane, or losing control. Panic attacks are common to all anxiety disorders. PD is distinguished by *unexpected attacks*, that is, attacks that occur without an obvious trigger; and at least one month of persistent apprehension about the recurrence of panic or its consequences; or a significant behavioral change.

*Agoraphobia* refers to avoidance or endurance with dread of situations from which escape might be difficult or help unavailable in the event of a panic attack, or panic-like symptoms, such as loss of bowel control. Typical agoraphobia situations include shopping malls, waiting in lines, being at movie theaters, traveling by car or bus, being in crowded restaurants and stores, and being alone.

The National Comorbidity Survey-Replication (NCS-R) provides prevalence estimates of 12-month and lifetime PD as 2.7% and 4.7%, respectively (Kessler, Chiu, Demler, Merikangas, & Walters, 2005; Kessler, Berglund, Demler, Jin, Merikangas, & Walters, 2005). Conservative estimates suggest that an additional 3.3–4.6% experience *nonclinical panic* (or, occasional panic attacks). The level of anxiety about the re-
currence of panic and catastrophic cognitions during panic seem to differentiate nonclinical panic from PD.

Epidemiological studies report relatively high rates for agoraphobia without a history of PD: 2.8% in the last 12 months and 4.7% in a lifetime (Kessler et al., 2005). In contrast, individuals with agoraphobia who seek treatment almost always report a history of panic which preceded development of their avoidance (Wittchen, Reed, & Kessler, 1998). There are at least two explanations for the contrast between population-based and clinic-based data. First, epidemiological data may vastly overestimate the prevalence of agoraphobia due to misdiagnosis of specific phobias, generalized anxiety, or “normal” cautiousness about certain situations (e.g., walking in unsafe urban districts) as agoraphobia. Second, individuals who panic are more likely to seek help.

Rarely does the diagnosis of PD, with or without agoraphobia, occur in isolation. Commonly co-occurring Axis I conditions include specific phobias, social phobia, dysthymia, generalized anxiety disorder, major depressive disorder, and substance abuse. From 25–60% of persons with PD also meet criteria for a personality disorder, mostly avoidant and dependent personality disorders (see Roy-Byrne, Craske, & Stein, 2006).

The modal age of onset is late teenage years and early adulthood (Kessler et al., 2005), although treatment is usually sought at a much later age, around 34 years. A large percent (approximately 70%) report the presence of identifiable stressors around the time of the first panic attack. Finally, PD and agoraphobia tend to be chronic conditions with severe financial and interpersonal costs. That is, only a minority of patients remit without subsequent relapse within a few years (30%), although a similar number experience notable improvement, albeit with a waxing and waning course (35%) (Roy-Byrne & Cowley, 1995). Fortunately, PD responds well to specifically targeted treatments, described in our workbook.

Psychobiological Conceptualization

For a full presentation and original citations for psychobiological conceptualization, see Barlow (2000) and Craske (2003).
Biological Factors

From a genetic perspective, it is believed that PD, like other psychiatric disorders, is a complex disorder with multiple genes conferring vulnerability through as-yet-undetermined pathways. Either there is substantial genetic heterogeneity with multiple etiologically distinct forms of the disorder, or the superficially similar phenotype actually reflects a more unified, broad genetic vulnerability to panic and anxiety. Studies involving multivariate genetic analyses of large samples of subjects tend to support the latter model, to suggest the existence of relatively broad or nonspecific genetic factors that influence the vulnerability to panic and anxiety. Thus, the workbook educates the reader to think of certain biological factors that may be inherited or passed on through genes and thus may lead some people to be more likely to panic. Many believe that what is inherited is overly sensitive parts of the nervous system which increase the likelihood of all negative emotions, including anger, sadness, guilt, and shame, as well as anxiety and panic. However, inheriting vulnerabilities to experience negative emotions does not guarantee panic attacks or PD. In other words, panic is not inherited in the same way that eye color is inherited.

Biological factors (whatever they might be) probably help explain why panic disorder tends to run in families. In other words, if one family member has PD, then another person in the same family is more likely to have PD than are others in the general population. That is, whereas 5–8% of the American population has PD and/or agoraphobia, 15–20% of first-degree relatives (parents, siblings, children) of someone with panic disorder themselves develop PD.

Psychological Factors

The psychological conceptualization of panic disorder emphasizes fear of bodily sensations, characterized by tendencies to misappraise these sensations in a catastrophic manner or to misappraise them as being much more dangerous than they really are. Usually, the misappraisals are of impending physical or mental danger, such as believing that a feeling of breathlessness as evidence of impending breathing cessation and death,
viewing palpitations of the heart as evidence of an impending heart attack, thinking that lightheadedness is evidence of an impending loss of consciousness, or viewing shakiness as evidence of impending loss of control and insanity.

The trait of anxiety sensitivity, a set of beliefs that anxiety is harmful along social, physical and mental domains, is believed to predispose toward the fear of bodily sensations. In support, several longitudinal studies find that high scores on a measure of anxiety sensitivity are predictive of the development of panic attacks in nonclinical groups and of the maintenance of panic disorder in untreated PD groups.

We believe that anxiety sensitivity is acquired insidiously from a lifetime of direct aversive experiences (such as a personal history of significant illness or injury), vicarious observations (such as exposure to significant illnesses or death among family members or to family members who display a fear of body sensations through hypochondriasis), and/or informational transmissions (such as parental warnings or overprotectiveness regarding physical well-being).

Also associated with anxiety sensitivity is an enhanced attentional selectivity toward, or interoception for, physical cues. Individuals with panic disorder have heightened awareness of, or ability to detect, bodily sensations of arousal, although discrepant findings exist as to whether they are more accurate in their detection. Ability to perceive one's heartbeat, in particular, appears to be a relatively stable individual difference variable. Thus, along with anxiety sensitivity, the ability to detect interoceptive cues may predispose an individual toward PD.

Many (48%) panic clients report similar but less intense or less frightening panic-like sensations prior to their first panic attack. Also, previous experiences of cardiac symptoms and shortness of breath predict later development of panic attacks and PD. Perhaps such prior experiences reflect a state of autonomic vulnerability which only develops into full-blown panic when instances of autonomic arousal occur in threatening contexts or under stressful conditions (i.e., when the sensations are more likely to be perceived as harmful).

Earlier theorists emphasized separation anxiety as a specific precursor for agoraphobia and panic. Bowlby (1973) suggested that abnormal parent-
child bonding induces a specific form of anxious attachment in children, resulting in enduring separation anxiety, which in turn leads to agoraphobia when the individual is confronted with personally threatening situations as an adult. Some retrospective findings support the link between separation anxiety and agoraphobia. However, there is also reason to believe that separation anxiety is a vulnerability for all anxiety disorders, as well as for depression. Thus, separation anxiety may be best viewed as a component of a broader vulnerability.

Initial Panic Attacks

The large majority of initial panic attacks occur outside of the home, while driving, walking, or simply being at work or at school, in public in general, and on a bus, plane, subway, or in social evaluative situations. Furthermore, settings for initial panic attacks often are rated retrospectively as somewhat difficult to escape. Situations that block escape behavior, the natural action tendency associated with panic, intensify the urgency to escape, as well as the associated fear and panic. Furthermore, initial panic attacks may be most likely to occur in situations in which feared physical sensations are perceived as particularly threatening due to possible impairment (e.g., driving), entrapment (e.g., air travel, elevators), negative social evaluation (e.g., job, formal social events), or distance from safety (e.g., unfamiliar locales).

In addition to a vulnerability to instances of elevated autonomic arousal, an array of factors may explain surges of physiological sensations on the occasion of an initial panic attack. These include benign physiological events (ranging from normal variations in bodily state to illnesses), distal and proximal stress (e.g., impending divorce, rushing to an appointment, meeting a deadline), stimulants (e.g., caffeine, hallucinogenic drugs, prescription medications), environmental conditions (e.g., heat and humidity), and anticipatory anxiety about the immediate situation or an upcoming event (e.g., receiving a work evaluation).

A stress-diathesis interaction seems to account for initial panic attacks. In other words, the initial panic attack is viewed as a false alarm that is prone to activation under stressful conditions. Just as some people experience irritable bowel syndrome, others experience panic attacks in re-
sponse to stressful events. Certainly, the majority of individuals associate their initial panic attacks with stressful events. Typical stressful life events include the unexpected loss of a significant other, illness, or aversive drug experiences.

**Maintenance Factors**

Acute “fear of fear” (really, anxiety about fear or panic) that develops after initial panic attacks refers to fear of specific bodily sensations associated with panic attacks (e.g., racing heart, dizziness, paresthesia). This anxiety is attributed to two factors. The first is interoceptive conditioning (i.e., learned anxiety focused on internal states via aversive associations—such as learning to be anxious about elevated heart rate because of a previous association between elevated heart rate and a panic attack). The second factor is the misappraisal of bodily sensations (i.e., misinterpretation of sensations as signs of imminent death, loss of control, and so forth). “Fear of fear” can be construed as the sensitization of the predisposing trait of anxiety sensitivity due to the experience of panic attacks.

In support of the notion of “fear of fear,” clients with panic disorder have strong beliefs and fears of physical or mental harm arising from bodily sensations that are associated with panic attacks, and these clients are more likely to interpret bodily sensations in a catastrophic fashion. Also, persons with PD are more likely to focus anxiety on procedures that elicit bodily sensations similar to the ones experienced during panic attacks, including benign cardiovascular, respiratory, and audiovestibular exercises, as well as more invasive procedures, such as carbon dioxide inhalations. Furthermore, these individuals become anxious about signals that ostensibly reflect heightened arousal, even in the absence of actual heightened arousal, as shown through false physiological feedback paradigms. Not only is misappraisal associated with anxiety, but reappraisal lessens anxiety. For example, persons with PD and nonclinical panickers report significantly less anxiety and panic during laboratory-based panic provocation procedures, such as hyperventilation and carbon dioxide inhalation, when they perceive that the procedure is safe or controllable, when accompanied by a safe person, or after successful cognitive-behavioral treatment.
The pattern of learned anxiety to certain somatic sensations typically results in an acute sensitivity to otherwise normal bodily sensations. Hence, different daily activities that elicit sensations similar to the sensations experienced during panic may trigger panic attacks. Examples include a racing heart from exercise; sweating from hot weather conditions; excitement from suspenseful movies, arguments, or sexual arousal; trembling from ingestion of caffeine; and feelings of floating or heaviness from deep relaxation. Note, however, that anxiety focused on sensations is moderated by occasion setters, which vary greatly across individuals. For example, elevated heart rate may be anxiety provoking while sitting but not while running, depending on the individual. Furthermore, if the bodily sensation occurs in association with an established safety signal or a safe context, anxiety will be diminished. For example, a racing heart may be anxiety provoking when an individual is alone but not anxiety provoking when that person is in close proximity to others and, especially, to medical help.

Several features distinguish anxiety focused on bodily sensations from anxiety triggered by external stimuli. First, autonomic arousal generated by anxiety from sensations in turn intensifies the sensations, thus creating a reciprocating cycle of anxiety and sensations. The cycle is sustained until physiological arousal is exhausted or perceptions of safety are achieved. In contrast, anxiety triggered by external stimuli does not intensify the object of fear. Second, cues that trigger panic attacks (i.e., bodily sensations) are not always immediately obvious, thus generating the perception of unexpected or “out of the blue” panic attacks. Furthermore, even when interoceptive cues are identifiable, they tend to be less predictable than external stimuli. Third, bodily sensations are more difficult to escape, on average, than external objects; that is, sensations are relatively uncontrollable. Unpredictability and uncontrollability elevate anxiety about upcoming aversive events, in general, and panic attacks, in particular. Consequently, the unpredictable and uncontrollable nature of panic attacks is hypothesized to contribute to high levels of chronic anxious apprehension and to maintaining anticipatory anxiety about the recurrence of panic. In turn, anxious apprehension increases the likelihood of panic by directly increasing the availability of sensations that have become conditioned cues for panic or by increasing attentional vigilance for these bodily cues. Thus, a maintaining cycle of panic and anxious apprehension develops.
Also, anxiety develops over specific contexts in which the occurrence of panic would be particularly troubling (i.e., situations involving impairment, entrapment, negative social evaluation, or distance from safety). These anxieties contribute to agoraphobia. Note, however, that agoraphobia is predicted by other variables as well, as described in the next section.

Finally, subtle avoidance behaviors are believed to maintain negative beliefs about feared bodily sensations. Examples include holding on to objects or persons for fears of fainting, sitting and remaining still for fears of heart attack, and moving slowly or searching for an escape for fears of acting foolish.

**Development of Agoraphobia**

Not all persons who panic develop agoraphobia, and the extent of agoraphobia that emerges is highly variable. Agoraphobia tends to increase as an individual’s history of panic lengthens; however, a significant proportion of persons panic for many years without developing agoraphobic limitations. Nor is agoraphobia avoidance related to age of onset or frequency of panic. Some researchers report more intense symptomatology during panic attacks in individuals who are more agoraphobic. Others fail to find such differences. Agoraphobic individuals may be more concerned with social consequences of panicking, and the anticipation of panic in specific agoraphobia situations predicts agoraphobia avoidance. Whether the latter two variables are precursors or are secondary to agoraphobia remains to be determined.

Occupational status predicts agoraphobia avoidance, accounting for 18% of the variance: “the more one is forced to leave the house by means of employment, the less one is likely to suffer from agoraphobia.” Perhaps the strongest predictor of agoraphobia, however, is gender. Females increasingly predominate the sample as agoraphobia worsens. Sex-role expectations and behaviors may contribute to these effects.
Nocturnal Panic

The psychobiological model described above applies equally to nocturnal panic, that is, waking from sleep in a state of panic (a recent review is provided by Craske & Tsao, 2005). Nocturnal panic does not refer to waking from sleep and panicking after a lapse of waking time, nighttime arousals induced by nightmares or environmental intrusions, night terrors, sleep paralysis, sleep seizures, or flashbacks to traumatic events. Nocturnal panics occur without apparent reason and are similar symptomatically to daytime panic attacks. They tend to occur in non-REM sleep and, particularly, during the transition between late Stage 2 and early Stage 3 sleep. While epidemiological studies have not been conducted, surveys of select clinical and nonclinical groups suggest that nocturnal panic is a relatively common phenomenon. From 44–71% of PD clients report having experienced nocturnal panic at least once, and from 18–45% have regular and frequent occurrences.

We believe that fears of bodily sensations contribute directly to nocturnal panic. In support of this claim, we find that individuals who are re-
assured that episodes of physiological arousal during sleep are safe and expected are less fearful of signals of such arousal than individuals who are not reassured and who do not expect episodes of arousal to occur. In other words, we found that the latter group awoke with more self-reported distress, panic, and symptoms in response to these signals of arousal.

We propose that, like daytime panic attacks, nocturnal panics are triggered by changes in an individual’s physiological state during sleep through a process of interoceptive conditioning, whereby low-level somatic sensations of arousal or anxiety become conditional stimuli, so that early somatic components of the anxiety response come to elicit anxiety or panic. In addition, interoceptive conditional responses are not dependent on conscious awareness of triggering cues such that, once acquired, these responses can be elicited under anesthesia, even in humans. Consequently, changes in relevant bodily functions which are not consciously recognized due to sleep or sleep-like states may elicit conditional fear due to previous pairings with panic. The role of precipitating physiological events has received some support from reports of short muscle twitches, increased EEG frequency, body movements, breathing irregularities, and increases in heart rate and skin conductance in the minutes and seconds preceding panicky awakenings. It may be necessary for these physiological events to co-occur with Stage 2 or Stage 3 sleep, as one shifts from semivigilance to nonvigilance; a shift that may be particularly anxiety provoking for individuals who have frequent nocturnal panic attacks.

Fortunately, as mentioned earlier, panic control treatment modified slightly for sleep is effective for nocturnal panic attacks (Craske, Lang, Aikins, & Mystkowksi, 2005).