

## CHAPTER 1

# Panic Disorder and Agoraphobia

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The treatment protocol described in this chapter represents one of the success stories in the development of evidence-based psychological treatments. Results from numerous studies indicate that this approach provides substantial advantages over placebo medication or alternative psychosocial approaches containing “common” factors, such as positive expectancies and helpful therapeutic alliances. In addition, this treatment forms an important part of every clinical practice guideline in either public health or other sources from countries around the world, describing effective treatments for panic disorder and agoraphobia. Results from numerous studies evaluating this treatment protocol, both individually and in combination with leading pharmacological approaches, suggest that this approach is equally effective as the best pharmacological approaches in the short term and more durable over the long term. But this treatment protocol has not stood still. For example, we have learned a great deal in recent years about neurobiological mechanisms of action in fear reduction, and the best psychological methods for effecting these changes and newly developed acceptance-based procedures have proven efficacious. In this chapter we present the latest version of this protocol, incorporating these changes and additions in the context of changes to diagnostic criteria in DSM-5, all as illustrated in a comprehensive account of the treatment of “Julie.”—D. H. B.

Advances continue in the development of biopsychosocial models and cognitive-behavioral treatments for panic disorder and agoraphobia. The conceptualization of panic disorder as an acquired fear of certain bodily sensations, and agoraphobia as a behavioral response to the anticipation of related bodily sensations or their crescendo into a full-blown panic attack, continues to be supported by experimental, clinical, and longitudinal research. Furthermore, the efficacy of cognitive-behavioral treatments that target fear of bodily sensations and associated agoraphobic situations is well established. In addition to presenting an up-to-date

review of treatment outcome data, this chapter covers recent theoretical and empirical developments in reference to etiological factors, the role of comorbid diagnoses in treatment, ways of optimizing learning during exposure therapy, and the effect of medication on cognitive-behavioral treatments. The chapter concludes with a detailed, session-by-session outline of cognitive-behavioral treatment for panic disorder and agoraphobia. This protocol has been developed in our clinics; the full protocol is detailed in available treatment manuals (Barlow & Craske, 2006; Craske & Barlow, 2006).

## NATURE OF PANIC AND AGORAPHOBIA

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### *Panic Attacks*

“Panic attacks” are discrete episodes of intense fear or discomfort, accompanied by physical and cognitive symptoms, as listed in the DSM-5 panic attack checklist (American Psychiatric Association, 2013). Panic attacks are discrete by virtue of their sudden or abrupt onset and brief duration, as opposed to gradually building anxious arousal. Panic attacks in panic disorder often have an unexpected quality, meaning that from the patient’s perspective, they appear to happen without an obvious trigger or at unexpected times. Indeed, the diagnosis of panic disorder is defined by recurrent “unexpected” panic attacks, followed by at least 1 month of persistent concern about their recurrence and their consequences, or by a significant change in behavior consequent to the attacks (American Psychiatric Association, 2013).

As with all basic emotions (Izard, 1992), panic attacks are associated with strong action tendencies: Most often, these are urges to escape, and less often, urges to fight. These fight and flight tendencies usually involve elevated autonomic nervous system arousal needed to support such fight–flight reactivity. Furthermore, perceptions of imminent threat or danger, such as death, loss of control, or social ridicule, often accompany such fight–flight reactivity. However, the features of urgency to escape, autonomic arousal, and perception of threat are not present in every self-reported occurrence of panic. For example, despite evidence for elevated heart rate or other indices of sympathetic nervous system activation during panic attacks on average (e.g., Wilkinson et al., 1998), Margraf, Taylor, Ehlers, Roth, and Agras (1987) found that 40% of self-reported panic attacks were not associated with accelerated heart rate. Moreover, in general, patients with panic disorder are more likely than nonanxious controls to report arrhythmic heart rate in the absence of actual arrhythmias (Barsky, Cleary, Sarnie, & Ruskin, 1994). Heightened anxiety about signs of autonomic arousal may lead patients to perceive cardiac events when none exist (Barlow, Brown, & Craske, 1994; Craske & Tsao, 1999). We believe that self-reported panic in the absence of heart rate acceleration or other indices of autonomic activation reflects anticipatory anxiety rather than true panic (Barlow et al., 1994), especially because more severe panic attacks are more consistently associated with accelerated heart rate (Margraf et al., 1987). Sometimes

individuals report intense abrupt fear in the absence of perceptions of threat or danger. This has been termed “nonscognitive” panic (Rachman, Lopatka, & Levitt, 1988; see Kircanski, Craske, Epstein, & Wittchen, 2009). Finally, the urgency to escape is sometimes weakened by situational demands for continued approach and endurance, such as performance expectations or job demands, thus creating discordance between behavioral responses on the one hand, and verbal or physiological fear responses on the other.

A subset of individuals with panic disorder experience nocturnal panic attacks. “Nocturnal panic” refers to waking from sleep in a state of panic with symptoms that are very similar to panic attacks during wakeful states (Craske & Barlow, 1989; Uhde, 1994). Nocturnal panic does *not* refer to waking from sleep and panicking after a lapse of waking time, or nighttime arousals induced by nightmares or environmental stimuli (e.g., unexpected noises). Instead, nocturnal panic is an abrupt waking from sleep in a state of panic, without an obvious trigger. Nocturnal panic attacks reportedly most often occur between 1 and 3 hours after sleep onset, and only occasionally more than once per night (Craske & Barlow, 1989). Surveys of select clinical groups suggest that nocturnal panic is relatively common among individuals with panic disorder: 44–71% report having experienced nocturnal panic at least once, and 30–45% report repeated nocturnal panics (Craske & Barlow, 1989; Krystal, Woods, Hill, & Charney, 1991; Mellman & Uhde, 1989; Roy-Byrne, Mellman, & Uhde, 1988; Uhde, 1994). Individuals who suffer frequent nocturnal panic often become fearful of sleep and attempt to delay sleep onset. Avoidance of sleep may result in chronic sleep deprivation, which in turn precipitates more nocturnal panics (Uhde, 1994).

“Nonclinical” panic attacks occur occasionally in approximately 3–5% of people in the general population who do not otherwise meet criteria for panic disorder (Norton, Cox, & Malan, 1992). Also, panic attacks occur across a variety of anxiety and mood disorders (Barlow et al., 1985), as well as substance use, personality disorders and psychoses (Craske et al., 2010) and are not limited to panic disorder. Indeed, the ubiquity of panic attacks has been emphasized in DSM-5 (American Psychiatric Association, 2013) where panic attacks are designated as a potential specifier for any DSM disorder. As stated earlier, the defining feature of panic disorder is not the presence of panic attacks *per se*, but involves additional anxiety about the recurrence of panic or its consequences, or a significant behavioral

change because of the panic attacks. It is the additional anxiety about panic combined with catastrophic cognitions in the face of panic that differentiate between the person with panic disorder and the occasional nonclinical panicker (e.g., Telch, Lucas, & Nelson, 1989) or the person with other anxiety disorders who also happens to panic. The following scenario exemplifies the latter point.

PATIENT: Sometimes I lay awake at night thinking about a million different things. I think about what is going to happen to my daughter if I get sick. Who will look after her, or what would happen if my husband died and we didn't have enough money to give my daughter a good education? Then I think about where we would live and how we would cope. Sometimes I can work myself up so much that my heart starts to race, my hands get sweaty, and I feel dizzy and scared. So I have to stop myself from thinking about all those things. I usually get out of bed and turn on the TV—anything to get my mind off the worries.

THERAPIST: Do you worry about the feelings of a racing heart, sweating, and dizziness happening again?

PATIENT: No. They're unpleasant, but they are the least of my concerns. I am more worried about my daughter and our future.

This scenario illustrates the experience of panic that is *not* the central focus of the person's anxiety. More likely, this woman has generalized anxiety disorder, and her uncontrollable worry leads her to panic on occasion. The next example is someone with social anxiety disorder, who becomes very concerned about panicking in social situations, because the possibility of a panic attack increases her concerns about being judged negatively by others.

PATIENT: I am terrified of having a panic attack in meetings at work. I dread the thought of others noticing how anxious I am. They must be able to see my hands shaking, the sweat on my forehead, and worst of all, my face turning red.

THERAPIST: What worries you most about others noticing your physical symptoms?

PATIENT: That they will think that I am weird or strange.

THERAPIST: Would you be anxious in the meetings if the panic attacks were gone?

PATIENT: I would still be worried about doing or saying the wrong thing. It is not just the panic attacks that worry me.

THERAPIST: Are you worried about panic attacks in any other situations?

PATIENT: Formal social events and sometimes when I meet someone for the first time.

In this case, even though the patient experiences panic attacks, the real concern is about being judged negatively by others consequent to panic attacks, and the panic attacks do not occur in situations other than social ones. Hence, this presentation is most aptly described as social anxiety.

### ***Agoraphobia***

“Agoraphobia” refers to avoidance or endurance with dread of situations from which escape might be difficult or help is unavailable in the event of a panic-like symptoms (including but not limited to panic attacks) or other incapacitating symptoms, such as loss of bowel control or vomiting, disorientation (especially in children), or sense of falling (especially in older adults) (American Psychiatric Association, 2013). Typical agoraphobic situations include shopping malls, waiting in line, movie theaters, traveling by car or bus, crowded restaurants, and being alone. “Mild” agoraphobia is exemplified by the person who hesitates about driving long distances alone but manages to drive to and from work, prefers to sit on the aisle at movie theaters but still goes to movies, and avoids crowded places. “Moderate” agoraphobia is exemplified by the person whose driving is limited to a 10-mile radius from home and only if accompanied, who shops at off-peak times and avoids large supermarkets, and who avoids flying or traveling by train. “Severe” agoraphobia refers to very limited mobility, sometimes even to the point of becoming housebound.

### ***Relationship between Panic and Agoraphobia***

The relationship between panic and agoraphobia is complex. On the one hand, not all persons who panic develop agoraphobia, and the extent of agoraphobia that emerges is highly variable (Craske & Barlow, 1988). Various factors have been investigated as potential predictors of agoraphobia. Although agoraphobia tends to increase as history of panic lengthens, a significant

proportion of individuals panic for many years without developing agoraphobic limitations. Nor is agoraphobia related to age of onset or frequency of panic (Cox, Endler, & Swinson, 1995; Craske & Barlow, 1988; Kikuchi et al., 2005; Rapee & Murrell, 1988). Some studies report more intense physical symptoms during panic attacks when there is more agoraphobia (e.g., de Jong & Bouman, 1995; Goisman et al., 1994; Noyes, Clancy, Garvey, & Anderson, 1987; Telch, Brouillard, Telch, Agras, & Taylor, 1989). Others fail to find such differences (e.g., Cox et al., 1995; Craske, Miller, Rotunda, & Barlow, 1990). On the one hand, fears of dying, going crazy, or losing control do not relate to level of agoraphobia (Cox et al., 1995; Craske, Rapee, & Barlow, 1988). On the other hand, concerns about social consequences of panicking may be stronger when there is more agoraphobia (Amering et al., 1997; de Jong & Bouman, 1995; Rapee & Murrell, 1988; Telch, Brouillard, et al., 1989). In addition, Kikuchi and colleagues (2005) found that individuals who develop agoraphobia within 6 months of the onset of panic disorder have a higher prevalence of generalized anxiety disorder but not major depression. However, whether social evaluation concerns or comorbidity are precursors or are secondary to agoraphobia remains to be determined. Occupational status also predicts agoraphobia, accounting for 18% of the variance in one study (de Jong & Bouman, 1995). Perhaps the strongest predictor of agoraphobia is sex; the ratio of males to females shifts dramatically in the direction of female predominance as level of agoraphobia worsens (e.g., Thyer, Himle, Curtis, Cameron, & Nesse, 1985).

On the other hand, not everyone with agoraphobia has a history of panic attacks or even panic-like symptoms, although a history of panic is much more common in treatment-seeking samples of individuals with agoraphobia than in epidemiological samples (Wittchen, Gloster, Beesdo-Baum, Fava, & Craske, 2010). Nonetheless, the prevalence of agoraphobia without a history of panic disorder, panic attacks, or panic-like symptoms was reported to be at least as high as the combined rates of panic disorder with and without agoraphobia across all epidemiological studies (Wittchen et al., 2010). Approximately 50% of individuals from community samples who endorse agoraphobia do not endorse panic attacks. Furthermore, agoraphobia without panic-like features appears to be as impairing as panic disorder without agoraphobia, although the combination is usually associated with even more impairment. In addition, some differences exist between

them in terms of incidence, comorbidity, and response to treatment (Wittchen et al., 2010). For these reasons, panic disorder and agoraphobia are now recognized as two distinct, albeit highly comorbid, disorders in DSM-5 (American Psychiatric Association, 2013).

## PRESENTING FEATURES

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From the latest epidemiological study, the National Comorbidity Survey Replication (NCS-R; Kessler, Berglund, Demler, Jin, & Walters, 2005; Kessler, Chiu, Demler, & Walters, 2005) 12-month prevalence estimates for panic disorder are approximately 2% in adults and adolescents. Lower estimates have been reported for some Asian, African and Latin American countries, ranging from 0.1 to 0.8% (Lewis-Fernandez et al., 2010). The 12-month rates for agoraphobia are approximately 1.7%, and the lifetime morbid risk is 3.7% (Kessler et al., 2012).

The modal age of onset for panic disorder is late teenage years and early adulthood (Kessler, Berglund, et al., 2005). In fact, although panic disorder is rare below the age of 14, a substantial proportion of adolescents report panic attacks (e.g., Hayward et al., 1992), and panic disorder in children and adolescents tends to be chronic and comorbid with other anxiety, mood, and disruptive disorders (Biederman, Faraone, Marris, & Moore, 1997). Treatment is usually sought much later, around age 34 (e.g., Noyes et al., 1986). Similarly, agoraphobia may occur in childhood but the incidence peaks in late adolescence and early adulthood (Beesdo, Knappe, & Pine, 2007; Bittner et al., 2007); the mean age of onset is 17 years (Kessler et al., 2012), and older in the absence of history of panic disorder or panic attacks. Rates of panic disorder decline in older adults, possibly diminishing to subclinical levels (Wolitzky-Taylor, Castriotti, Lenze, Stanley, & Craske, 2010). Similarly, 12-month prevalence rates for agoraphobia reduce to 0.4% in individuals over the age of 65 years (Kessler et al., 2006). The overall ratio of females to males is approximately 2:1 (Kessler et al., 2006) and, as mentioned already, the ratio shifts dramatically in the direction of female predominance as level of agoraphobia worsens (e.g., Thyer et al., 1985).

Rarely do the diagnoses of panic disorder or 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 (e.g., Brown,

Campbell, Lehman, Grishman, & Mancill, 2001; Golsman, Goldenberg, Vasile, & Keller, 1995; Kessler, Chiu, et al., 2005). Also, 25–60% of persons with panic disorder also meet criteria for a personality disorder, mostly avoidant and dependent personality disorders (e.g., Chambless & Renneberg, 1988). However, the nature of the relationship with personality disorders remains unclear. For example, comorbidity rates are highly dependent on the method used to establish Axis II diagnosis, as well as the co-occurrence of depressed mood (Alneas & Torgersen, 1990; Chambless & Renneberg, 1988). Moreover, the fact that abnormal personality traits improve and some “personality disorders” even remit after successful treatment of panic disorder (Black, Monahan, Wesner, Gabel, & Bowers, 1996; Mavissakalian & Hamman, 1987; Noyes, Reich, Suelzer, & Christiansen, 1991) raises questions about the validity of Axis II diagnoses. The issue of comorbidity with personality disorders and its effect on treatment for panic disorder and agoraphobia is described in more detail in a later section.

Finally, panic disorder and agoraphobia tend to be chronic conditions, with severe financial and interpersonal costs (Wittchen et al., 2010). Only a minority of untreated individuals remit without subsequent relapse within a few years if not treated (Emmelkamp & Wittchen, 2009; Katschnig & Amering, 1998; Roy-Byrne & Cowley, 1995). Also, individuals with panic disorder overutilize medical resources compared to the general public and individuals with other “psychiatric” disorders (e.g., Katon et al., 1990; Roy-Byrne et al., 1999).

### **HISTORY OF PSYCHOLOGICAL TREATMENT FOR PANIC DISORDER AND AGORAPHOBIA**

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It was not until the publication of DSM-III (American Psychiatric Association, 1980) that panic disorder with or without agoraphobia was recognized as a distinct anxiety problem. Until that time, panic attacks were viewed primarily as a form of free-floating anxiety. Consequently, psychological treatment approaches were relatively nonspecific. They included relaxation and cognitive restructuring for stressful life events in general (e.g., Barlow, O’Brien, & Last, 1984). Many presumed that pharmacotherapy was necessary for the control of panic. In contrast, the treatment of agoraphobia was quite specific from the 1970s onward, with primarily exposure-based approaches to target fear and

avoidance of specific situations. However, relatively little consideration was given to panic attacks in either the conceptualization or treatment of agoraphobia. The development of specific panic control treatments in the middle to late 1980s shifted interest away from agoraphobia. Interest in agoraphobia was subsequently renewed, specifically in terms of whether panic control treatments are sufficient for the management of agoraphobia, and whether their combination with treatments that directly target agoraphobia is superior overall. We address these questions in more detail after describing the conceptualization that underlies cognitive-behavioral approaches to the treatment of panic and agoraphobia.

### **CONCEPTUALIZATION OF ETIOLOGICAL AND MAINTAINING FACTORS FOR PANIC DISORDER AND AGORAPHOBIA**

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Several independent lines of research (Barlow, 1988; Clark, 1986; Ehlers & Margraf, 1989) converged in the 1980s on the same basic conceptualization of panic disorder as an acquired fear of bodily sensations, particularly sensations associated with autonomic arousal. Psychological and biological predispositions are believed to enhance the vulnerability to acquire such fear. These interacting vulnerabilities have been organized into an etiological conception of anxiety disorders in general, referred to as “triple vulnerability theory” (Barlow, 1988, 2002; Suárez, Bennett, Goldstein, & Barlow, 2008). First, genetic contributions to the development of anxiety and negative affect constitute a generalized (heritable) biological vulnerability. Second, evidence supports a generalized psychological vulnerability to experience anxiety and related negative affective states, characterized by a diminished sense of control arising from early developmental experiences. Although the unfortunate co-occurrence of generalized biological and psychological vulnerabilities may be sufficient to produce anxiety and related states, particularly generalized anxiety disorder and depression, a third vulnerability seems necessary to account for the development of at least some specific anxiety disorders, including panic disorder; that is, early learning experiences in some instances seem to focus anxiety on particular areas of concern. In panic disorder, the experience of certain somatic sensations becomes associated with a heightened sense of threat and danger. This specific psychological vulnerability, when coordi-



nated with the generalized biological and psychological vulnerabilities mentioned earlier, seems to contribute to the development of panic disorder. Fear conditioning, avoidant responding, and information-processing biases are believed to perpetuate such fear. It is the perpetuating factors that are targeted in the cognitive-behavioral treatment approach. What follows is a very brief review of some contributory factors with practical relevance for panic disorder.

## ***Vulnerability Factors***

### *Genetics and Temperament*

The temperament most associated with anxiety disorders, including panic disorder, is neuroticism (Eysenck, 1967; Gray, 1982), or proneness to experience negative emotions in response to stressors. A closely linked construct, “negative affectivity,” is the tendency to experience a variety of negative emotions across a variety of situations, even in the absence of objective stressors (Watson & Clark, 1984). Structural analyses confirm that negative affect is a higher-order factor that distinguishes individuals with each anxiety disorder (and depression) from controls with no mental disorder: Lower-order factors discriminate among anxiety disorders, with “fear of fear” being the factor that discriminates panic disorder from other anxiety disorders (Brown, Chorpita, & Barlow, 1998; Prenoveau et al., 2010; Zinbarg & Barlow, 1996). The anxiety disorders load differentially on negative affectivity, with more pervasive anxiety disorders, such as generalized anxiety disorder, loading more heavily, panic disorder loading at an intermediate level, and social anxiety disorder loading the least (Brown et al., 1998).<sup>1</sup> However, these findings derive from cross-sectional datasets.

Longitudinal prospective evidence for the role of neuroticism in predicting the onset of panic disorder is relatively limited. Specifically, neuroticism predicted the onset of panic attacks in adolescents (Hayward, Killen, Kraemer, & Taylor, 2000; Schmidt, Lerew, & Jackson, 1997, 1999), and “emotional reactivity” at age 3 was a significant variable in the classification of panic disorder in 18- to 21-year-old males (Craske, Poulton, Tsao, & Plotkin, 2001). Ongoing studies, such as the Northwestern/UCLA Youth Emotion Project, are comprehensively evaluating the role of neuroticism in the prediction of subsequent panic disorder.

Numerous multivariate genetic analyses of human twin samples consistently attribute approximately 30–50% of variance in neuroticism to additive genetic fac-

tors (Eley, 2001; Lake, Eaves, Maes, Heath, & Martin, 2000). In addition, anxiety and depression appear to be variable expressions of the heritable tendency toward neuroticism (Kendler, Heath, Martin, & Eaves, 1987). Symptoms of panic (i.e., breathlessness, heart pounding) may be additionally explained by a unique source of genetic variance that is differentiated from symptoms of depression and anxiety (Kendler et al., 1987) and neuroticism (Martin, Jardine, Andrews, & Heath, 1988).

Analyses of specific genetic markers remain preliminary and inconsistent. For example, panic disorder has been linked to a locus on chromosome 13 (Hamilton et al., 2003; Schumacher et al., 2005) and chromosome 9 (Thorgeirsson et al., 2003), but the exact genes remain unknown. Findings regarding markers for the cholecystokinin-B receptor gene have been inconsistent (cf. Hamilton et al., 2001; van Megen, Westenberg, Den Boer, & Kahn, 1996). Also, association and linkage studies implicate the adenosine receptor gene in panic disorder (Deckert et al., 1998; Hamilton et al., 2004). An allele of the neuropeptide S receptor gene on chromosome 7 was linked in a male-specific manner to panic disorder and not to schizophrenia or attention deficit disorder (Okamura et al., 2011), whereas the same gene was linked in a female-specific manner to panic disorder compared to healthy controls (Domschke et al., 2011). Thus, at this stage, the results are rather piecemeal and sometimes inconsistent, and there is no evidence at this point for a specific link between genetic markers and temperament, on the one hand, and panic disorder on the other. Rather, neurobiological factors seem to comprise a nonspecific biological vulnerability.

### *Anxiety Sensitivity*

As described earlier, neuroticism is viewed as a higher-order factor characteristic of all anxiety disorders, with “fear of fear” being more unique to panic disorder. The construct “fear of fear” overlaps with the construct “anxiety sensitivity,” or the belief that anxiety and its associated symptoms may cause deleterious physical, social, and psychological consequences that extend beyond any immediate physical discomfort during an episode of anxiety or panic (Reiss, 1980). Anxiety sensitivity is elevated across most anxiety disorders, but it is particularly elevated in panic disorder (e.g., Taylor, Koch, & McNally, 1992; Zinbarg & Barlow, 1996), especially the Physical Concerns subscale of the Anxiety Sensitivity Index (Zinbarg & Barlow, 1996; Zinbarg,

Barlow, & Brown, 1997). Therefore, beliefs that physical symptoms of anxiety are harmful seem to be particularly relevant to panic disorder and may comprise a specific psychological vulnerability.

Anxiety sensitivity is presumed to confer a risk factor for panic disorder because it primes fear reactivity to bodily sensations. In support, anxiety sensitivity predicts subjective distress and reported symptomatology in response to procedures that induce strong physical sensations, such as CO<sub>2</sub> inhalation (Forsyth, Palav, & Duff, 1999), balloon inflation (Messenger & Shean, 1998), and hyperventilation (Sturges, Goetsch, Ridley, & Whittal, 1998) in nonclinical samples, even after researchers control for the effects of trait anxiety (Rapee & Medoro, 1994). In addition, several longitudinal studies indicate that high scores on the Anxiety Sensitivity Index predict the onset of panic attacks over 1- to 4-year intervals in adolescents (Hayward et al., 2000), college students (Maller & Reiss, 1992), and community samples with specific phobias or no anxiety disorders (Ehlers, 1995). The predictive relationship remains after researchers control for prior depression (Hayward et al., 2000). In addition, Anxiety Sensitivity Index scores predicted spontaneous panic attacks and worry about panic (and anxiety more generally), during an acute military stressor (i.e., 5 weeks of basic training), even after researchers control for history of panic attacks and trait anxiety (Schmidt et al., 1997, 1999). Finally, panic attacks themselves elevate anxiety sensitivity over a 5-week period in adults (Schmidt et al., 1999), and over a 1-year period in adolescents, albeit to a lesser extent (Weems, Hayward, Killen, & Taylor, 2002).

However, Bouton, Mineka, and Barlow (2001) have noted that the relationship between anxiety sensitivity and panic attacks in these studies is relatively small, not exclusive to panic, and weaker than the relationship between panic and neuroticism. Furthermore, these studies have evaluated panic attacks and worry about panic but not the prediction of diagnosed panic disorder. Thus, the causal significance of anxiety sensitivity for panic disorder remains to be fully understood.

### *History of Medical Illness and Abuse*

Other studies highlight the role of medical illnesses as contributing to a specific psychological vulnerability for panic disorder. For example, using the Dunedin Multidisciplinary Study database, we found that experience with personal respiratory disturbance (and parental poor health) as a youth predicted panic disorder

at age 18 or 21 (Craske et al., 2001). This finding is consistent with reports of more respiratory disturbance in the history of patients with panic disorder compared to other patients with anxiety disorders (Verburg, Griez, Meijer, & Pols, 1995). Furthermore, first-degree relatives of patients with panic disorder had a significantly higher prevalence of chronic obstructive respiratory disease, and asthma in particular, than first-degree relatives of patients with other anxiety disorders (van Beek, Schruers, & Friez, 2005).

Childhood experiences of sexual and physical abuse may also prime panic disorder. Retrospective reports of such childhood abuse were associated with panic disorder onset at ages 16–21 years in a longitudinal analysis of New Zealanders from birth to age 21 (Goodwin, Fergusson, & Horwood, 2005). This finding is consistent with multiple cross-sectional studies in both clinical and community samples (e.g., Bandelow et al., 2002; Kendler et al., 2000; Kessler, Davis, & Kendler, 1997; Moisan & Engels, 1995; Stein et al., 1996). The association with childhood abuse is stronger for panic disorder than for other anxiety disorders, such as social phobia (Safren, Gershuny, Marzol, Otto, & Pollack, 2002; Stein et al., 1996) and obsessive-compulsive disorder (Stein et al., 1996). In addition, some studies report an association between panic disorder and exposure to violence between other family members, generally interparental violence (e.g., Bandelow et al., 2002; Moisan & Engels, 1995), whereas another study did not (Goodwin et al., 2005). Retrospective reporting of childhood abuse and familial violence in all of these studies, however, limits the findings.

### *Interoceptive Awareness*

Patients with panic disorder, as well as nonclinical panickers, appear to have heightened awareness of, or ability to detect, bodily sensations of arousal (e.g., Ehlers & Breuer, 1992, 1996; Ehlers, Breuer, Dohn, & Feigenbaum, 1995; Zoellner & Craske, 1999). Discrepant findings (e.g., Antony et al., 1995; Rapee, 1994) exist but have been attributed to methodological artifact (Ehlers & Breuer, 1996). Ability to perceive heartbeat, in particular, appears to be a relatively stable individual-difference variable given that it does not differ between untreated and treated patients with panic disorder (Ehlers & Breuer, 1992), or from before to after successful treatment (Antony, Meadows, Brown, & Barlow, 1994; Ehlers et al., 1995). Thus, interoceptive accuracy may be a predisposing trait for panic disorder that increases the probability of perceiving sensa-

tions that in turn may trigger a panic attack. Whether interoceptive awareness is learned, and represents another specific psychological vulnerability, or is more dispositional remains to be determined.

Separate from interoception is the issue of propensity for intense autonomic activation. As noted earlier, some evidence points to a unique genetic influence on the reported experience of breathlessness, heart pounding, and a sense of terror (Kendler et al., 1987). Conceivably, cardiovascular reactivity presents a unique physiological predisposition for panic disorder. In support of this, cardiac symptoms and shortness of breath predict later development of panic attacks and panic disorder (Keyl & Eaton, 1990). Unfortunately, these data derive from *report* of symptoms, which is not a good index of actual autonomic state (Pennebaker & Roberts, 1992) and may instead reflect interoception.

### **Initial Panic Attacks**

From an evolutionary standpoint, fear is a natural and adaptive response to threatening stimuli. However, the fear experienced during the first unexpected panic attack is often unjustified due to the lack of an identifiable trigger or antecedent; hence, it represents a “false alarm” (Barlow, 1988, 2002). The large majority of initial panic attacks are recalled as occurring outside of the home, while driving, walking, at work, or at school (Craske et al., 1990), generally in public (Lelliott, Marks, McNamee, & Tobena, 1989), and on a bus, plane, subway, or in social-evaluative situations (Shulman, Cox, Swinson, Kuch, & Reichman, 1994). Barlow (1988) and Craske and Rowe (1997b) believe situations that set the scene for initial panic attacks are ones in which bodily sensations are perceived as posing the most threat because of impairment of functioning (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). Entrapment concerns may be particularly salient for the subsequent development of agoraphobia (Faravelli, Palianti, Biondi, Paterniti, & Scarpato, 1992).

### **Maintenance Factors**

Acute “fear of fear” (or, more accurately, anxiety focused on somatic sensations) that develops after initial panic attacks in *vulnerable individuals* refers to anxiety about certain bodily sensations associated with panic attacks (e.g., racing heart, dizziness, paresthe-

sias) (Barlow, 1988; Goldstein & Chambless, 1978), and is attributed to two factors. The first is interoceptive conditioning, or conditional fear of internal cues, such as elevated heart rate, because of their association with intense fear, pain, or distress (Razran, 1961). Specifically, interoceptive conditioning refers to low-level somatic sensations of arousal or anxiety becoming conditional stimuli, so that early somatic components of the anxiety response come to elicit significant bursts of anxiety or panic (Bouton et al., 2001). An extensive body of experimental literature attests to the robustness of interoceptive conditioning (e.g., Dworkin & Dworkin, 1999), particularly with regard to early interoceptive drug-onset cues becoming conditional stimuli for larger drug effects (e.g., Sokolowska, Siegel, & Kim, 2002). In addition, interoceptive conditional responses are not dependent on conscious awareness of triggering cues (Razran, 1961); thus, they have been observed in patients under anesthesia (e.g., Block, Ghoneim, Fowles, Kumar, & Pathak, 1987). Within this model, then, slight changes in relevant bodily functions that are not consciously recognized may elicit conditional anxiety or fear and panic due to previous pairings with panic (Barlow, 1988; Bouton et al., 2001); the result would be an unexpected panic attack. Further support for a conditioning model comes from evidence that individuals with panic disorder, as well as other anxiety disorders, show elevated fear conditioning and weakened fear extinction in laboratory paradigms (Lissek et al., 2005), suggesting that they are more prone to developing fear through negative associations, and once acquired, their fear is less likely to diminish with time. This pattern seems to be compounded for individuals with panic disorder who additionally show impaired safety learning (Lissek et al., 2009) and greater fear generalization (Lissek et al., 2010) in laboratory paradigms. In other words, once fear of specific bodily sensations is acquired, individuals with panic disorder may have difficulty perceiving other sensations as being harmless and may be more likely to generalize their fear to various bodily states.

The second factor, offered by Clark (1986) to explain acute fear of panic-related body sensations, is catastrophic misappraisals of bodily sensations (misinterpretation of sensations as signs of imminent death, loss of control, etc.). We have taken issue with the purely cognitive model of panic disorder by stating that it cannot account for panic attacks devoid of conscious cognitive appraisal without turning to constructs such as “automatic appraisals,” which prove to be untestable



(Bouton et al., 2001). Catastrophic misappraisals may accompany panic attacks because they are a natural part of the constellation of responses that go with panic, or because they have been encouraged and reinforced much like sick role behaviors during childhood. In addition, such thoughts may become conditioned stimuli that trigger anxiety and panic, as demonstrated via panic induction through presentation of pairs of words involving sensations and catastrophic outcomes (Clark et al., 1988). In this case, catastrophic cognitions may well be sufficient to elicit conditioned panic attacks, but not necessary.

Whether cognitively or noncognitively based, excessive anxiety over panic-related bodily sensations in panic disorder is well supported. Persons with panic disorder endorse strong beliefs that bodily sensations associated with panic attacks cause physical or mental harm (e.g., Chambless, Caputo, Bright, & Gallagher, 1984; McNally & Lorenz, 1987). They are more likely to interpret bodily sensations in a catastrophic fashion (Clark et al., 1988) and to allocate more attentional resources to words that represent physical threat, such as “disease” and “fatality” (e.g., Ehlers, Margraf, Davies, & Roth, 1988; Hope, Rapee, Heimberg, & Dombek, 1990); catastrophe words, such as “death” and “insane” (e.g., Maidenberg, Chen, Craske, Bohn, & Bystritsky, 1996; McNally, Riemann, Louro, Lukach, & Kim, 1992); and heartbeat stimuli (Kroeze & van den Hout, 2000; however, attentional bias is not always found; e.g., DeCort, Hermans, Spruyt, Griez, & Schruers, 2008). Also, individuals with panic disorder show enhanced brain potentials in response to panic-related words (Pauli, Amrhein, Muhlberger, Dengler, & Wiedemann, 2005). In addition, they are more likely to become anxious in procedures that elicit bodily sensations similar to the ones experienced during panic attacks, including benign cardiovascular, respiratory, and audiovestibular exercises (Antony, Ledley, Liss, & Swinson, 2006; Jacob, Furman, Clark, & Durrant, 1992), as well as more invasive procedures, such as CO<sub>2</sub> inhalations, compared to patients with other anxiety disorders (e.g., Perna, Bertani, Arancio, Ronchi, & Bellodi, 1995; Rapee, 1986; Rapee, Brown, Antony, & Barlow, 1992) or healthy controls (e.g., Gorman et al., 1994). The findings are not fully consistent, however, because patients with panic disorder did not differ from patients with social phobia in response to an epinephrine challenge (Veltman, van Zijderveld, Tilders, & van Dyck, 1996). Nonetheless, individuals with panic disorder also fear signals that ostensibly reflect height-

ened arousal and false physiological feedback (Craske & Freed, 1995; Craske, Lang, et al., 2002; Ehlers, Margraf, Roth, Taylor, & Birnbaumer, 1988).

Distress over bodily sensations is likely to generate ongoing distress for a number of reasons. First, in the immediate sense, autonomic arousal generated by fear in turn intensifies the feared sensations, thus creating a reciprocating cycle of fear and sensations that is sustained until autonomic arousal abates or the individual perceives safety. Second, because bodily sensations that trigger panic attacks are not always immediately obvious, they may generate the perception of unexpected or “out of the blue” panic attacks (Barlow, 1988) that causes even further distress (Craske, Glover, & DeCola, 1995). Third, the perceived uncontrollability, or inability to escape or terminate bodily sensations, again, is likely to generate heightened anxiety (e.g., Maier, Laudenslager, & Ryan, 1985; Mineka, Cook, & Miller, 1984). Unpredictability and uncontrollability, then, are seen as enhancing general levels of anxiety about “When is it going to happen again?” and “What do I do when it happens?”, thereby contributing to high levels of chronic anxious apprehension (Barlow, 1988, 2002). In turn, anxious apprehension increases the likelihood of panic by directly increasing the availability of sensations that have become conditioned cues for panic and/or attentional vigilance for these bodily cues. Thus, a maintaining cycle of panic and anxious apprehension develops. Also, subtle avoidance behaviors are believed to maintain negative beliefs about feared bodily sensations (Clark & Ehlers, 1993). Examples include holding onto objects or persons for fear of fainting, sitting and remaining still for fear of a heart attack, and moving slowly or searching for an escape route because one fears acting foolish (Salkovskis, Clark, & Gelder, 1996). Such avoidance includes “experiential avoidance,” or being unwilling to remain in contact with particular private experiences, in this case bodily sensations and catastrophic cognitions. Experiential avoidance is believed to contribute to overall distress and dysfunction in general (Hayes et al., 1996), and appears to correlate with panic-related worries and disability in individuals with panic disorder (Kampfe et al., 2012). Further support for the role of experiential avoidance comes from evidence for instructions to accept symptoms of panic to result in less fear and avoidance in patients with panic disorder (Campbell-Sills, Barlow, Brown, & Hofmann, 2006; Eifert & Heffner, 2003), including CO<sub>2</sub> inhalation challenges (Levitt, Brown, Orsillo, & Barlow, 2004). Finally, anxiety may develop

over specific contexts in which the occurrence of panic would be particularly troubling (i.e., situations associated with impairment, entrapment, negative social evaluation, and distance from safety). These anxieties may contribute to agoraphobia, which in turn maintains distress by preventing disconfirmation of catastrophic misappraisals and extinction of conditioned responding. Clearly, this model targets panic disorder and agoraphobia, and is not as relevant to agoraphobia in the absence of panic attacks or panic-like symptoms.

## TREATMENT VARIABLES

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### Setting

There are several different settings for conducting cognitive-behavioral therapy for panic disorder and agoraphobia. The first, the outpatient clinic-office setting, is suited to psychoeducation, cognitive restructuring, assignment, and feedback regarding homework assignments and role-play rehearsals. In addition, certain exposures can be conducted in the office setting, such as interoceptive exposure to feared bodily sensations we describe later. Outpatient settings have extended from mental health settings to primary care suites (e.g., Craske, Roy-Byrne, et al., 2002; Craske et al., 2011; Roy-Byrne, Craske, et al., 2005; Roy-Byrne et al., 2010; Sharp, Power, Simpson, Swanson, & Anstee, 1997). This extension is particularly important because of the higher prevalence of panic disorder in primary care settings (e.g., Shear & Schulberg, 1995; Tiemens, Ormel, & Simon, 1996). However, whether a mental health or a primary care office is being used, the built-in safety signals of such an office may limit the generalizability of learning that takes place in that setting. For example, learning to be less afraid in the presence of the therapist, or in an office located near a medical center, may not necessarily generalize to conditions in which the therapist is not present, or when the perceived safety of a medical center is not close by. For this reason, homework assignments to practice cognitive-behavioral skills in a variety of different settings are particularly important.

In the second setting, the natural environment, cognitive restructuring and other anxiety management skills are put into practice as the patient faces feared situations. The latter is called *in vivo* exposure and can be conducted with the aid of the therapist or alone. Therapist-directed exposure is particularly use-

ful for patients who lack a social network to support *in vivo* exposure assignments, and more valuable than self-directed exposure for patients with more severe agoraphobia (Holden, O'Brien, Barlow, Stetson, & Infantino, 1983). Therapist-directed exposure is essential to "guided mastery exposure," in which the therapist gives corrective feedback about the way the patient faces feared situations to minimize unnecessary defensive behaviors. For example, patients are taught to drive in a relaxed position and to walk across a bridge without holding the rail. On the one hand, guided mastery exposure has been shown to be more effective than "stimulus exposure" when patients attempt simply to endure the situation alone until fear subsides, without the benefit of ongoing therapist feedback (Williams & Zane, 1989). On the other hand, self-directed exposure is very valuable also, especially to the degree that it encourages independence and generalization of the skills learned in treatment to conditions in which the therapist is not present. Thus, the most beneficial approach in the natural environment is to proceed from therapist-directed to self-directed exposure.

In telephone-guided treatment, an interesting variation that combines the office and the natural environment, therapists direct patients with agoraphobia by phone to conduct *in vivo* exposure to feared situations (NcNamee, O'Sullivan, Lelliot, & Marks, 1989; Swinson, Fergus, Cox, & Wickwire, 1995) or provide instruction in panic control skills (Cote, Gauthier, Lamberge, Cormier, & Plamondon, 1994). In addition, one small study showed that cognitive-behavioral therapy was as effective when delivered by videoconference as in person (Bouchard et al., 2004).

Self-directed treatments, with minimal direct therapist contact, take place in the natural environment and are beneficial for highly motivated and educated patients (e.g., Ghosh & Marks, 1987; Gould & Clum, 1995; Gould, Clum, & Shapiro, 1993; Lidren et al., 1994; Schneider, Mataix-Cols, Marks, & Bachofen, 2005). On the other hand, self-directed treatments are less effective for more severely affected patients (Holden, O'Brien, Barlow, Stetson, & Infantino, 1983); for those with more comorbidity (Hecker, Losee, Roberson-Nay, & Maki, 2004), less motivation, and less education; or for patients who are referred as opposed to recruited through advertisement (Hecker, Losee, Fritzler, & Fink, 1996). Self-directed treatments have expanded beyond workbooks and manuals to computerized and Internet versions (e.g., Carlbring, Ekselius, & Andersson, 2003; Richards, Klein, & Aus-

tin, 2006; Richards, Klein, & Carlbring, 2003). In general, these treatments yield very positive results with strong effect sizes (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010), and at least two studies indicate that they are as effective as therapist-led cognitive-behavioral therapy for panic disorder (Carlbring et al., 2005; Kiropoulos et al., 2008). However, attrition rates may be higher with self-directed computer/Internet programs in the absence of any therapist contact (e.g., Carlbring et al., 2003).

The third setting, the inpatient facility, is most appropriate when conducting very intensive cognitive-behavioral therapy (e.g., daily therapist contact) or treating severely disabled persons who can no longer function at home. In addition, certain medical or drug complications may warrant inpatient treatment. The greatest drawback to the inpatient setting is poor generalization to the home environment. Transition sessions and follow-up booster sessions in an outpatient clinic-office or in the patient's own home facilitate generalization.

### Format

Cognitive-behavioral therapy for panic disorder and agoraphobia may be conducted in individual or group formats. Several clinical outcome studies have used group treatments (e.g., Bohni, Spindler, Arendt, Houggaard, & Rosenberg, 2009; Craske, DeCola, Sachs, & Pontillo, 2003; Craske et al., 2007; Evans, Holt, & Oei, 1991; Feigenbaum, 1988; Hoffart, 1995; Telch et al., 1993). The fact that their outcomes are generally consistent with the summary statistics obtained from individually formatted treatment suggests that group treatment is as effective as individual therapy. In direct comparisons, albeit few in number, a slight advantage is shown for individual formats. Specifically, Neron, Lacroix, and Chaput (1995) compared 12–14 weekly sessions of individual or group cognitive-behavioral therapy ( $N = 20$ ), although the group condition received two additional 1-hour individual sessions. The two conditions were equally effective for measures of panic and agoraphobia at posttreatment and 6-month follow-up. However, the individual format was more successful in terms of generalized anxiety and depressive symptoms by the follow-up point. In addition, individual treatments resulted in more clinically significant outcomes than group formats in primary care (Sharp, Power, & Swanson, 2004). Furthermore, 95% of individuals assigned to the waiting-list condition in the latter study

stated a clear preference for individual treatment when given the choice at the end of the waiting list.

Most studies of cognitive-behavioral therapy for panic and agoraphobia involve 10–20 weekly treatment sessions. Several studies show that briefer treatments may be effective as well. Evans and colleagues (1991) compared a 2-day group cognitive-behavioral treatment to a waiting-list condition, although without random assignment. The 2-day program comprised lectures (3 hours); teaching skills, such as breathing, relaxation, and cognitive challenge (3 hours); *in vivo* exposure (9 hours); and group discussion plus a 2-hour support group for significant others. Eighty-five percent of treated patients were reported to be either symptom-free or symptomatically improved, and these results were maintained 1 year later. In contrast, the waiting-list group did not demonstrate significant changes. A pilot study similarly indicated effectiveness with intensive cognitive-behavioral therapy over 2 days (Deacon & Abramowitz, 2006). Other studies have evaluated the effectiveness of cognitive-behavioral therapy when delivered over fewer sessions. In a randomized study, patients with panic disorder with agoraphobia who awaited pharmacotherapy treatment were assigned to four weekly sessions of either cognitive-behavioral therapy or supportive nondirective therapy (Craske, Maidenberg, & Bystritsky, 1995). Cognitive-behavioral therapy was more effective than supportive therapy, particularly with less severely affected patients, although the results were not as positive as those typically seen with more sessions. Also, we found that up to six sessions (average of three sessions) of cognitive-behavioral therapy combined with medication recommendations yielded significantly greater improvements on an array of measures, including quality of life, compared to treatment as usual for individuals with panic disorder in primary care settings (Roy-Byrne, Craske, et al., 2005). Notably, however, the treatment effects substantially increased as the number of cognitive-behavioral therapy sessions (up to six) and follow-up booster phone call sessions (up to six) increased (Craske et al., 2006). In our subsequent primary care study, an average of seven sessions of cognitive-behavioral therapy and/or medication recommendations was superior to usual care, and in this case, usual care often involved several active treatment elements (Craske et al., 2011). Finally, in a direct comparison, results were equally effective whether cognitive-behavioral therapy was delivered across the standard 12 sessions or across approximately six sessions (Clark et al., 1999).

### ***Interpersonal Context***

Interpersonal context variables have been researched in terms of the development, maintenance, and treatment of agoraphobia. The reason for this research interest is apparent from the following vignettes:

“My husband really doesn’t understand. He thinks it’s all in my head. He gets angry at me for not being able to cope. He says I’m weak and irresponsible. He resents having to drive me around, and doing things for the kids that I used to do. We argue a lot because he comes home tired and frustrated from work only to be frustrated more by the problems I’m having. But I can’t do anything without him. I’m so afraid that I’ll collapse into a helpless wreck without him, or that I’ll be alone for the rest of my life. As cruel as he can be, I feel safe around him because he always has everything under control. He always knows what to do.”

This vignette illustrates dependency on the significant other for a sense of safety despite a nonsympathetic response that may only serve to increase background stress for the patient. The second vignette illustrates inadvertent reinforcement of fear and avoidance through attention from the significant other:

“My boyfriend really tries hard to help me. He’s always cautious of my feelings and doesn’t push me to do things that I can’t do. He phones me from work to check on me. He stays with me and holds my hand when I feel really scared. He never hesitates to leave work to help me if I’m having a bad time. Only last week we visited some of his friends, and we had to leave. I feel guilty because we don’t do the things we used to enjoy doing together. We don’t go to the movies anymore. We used to love going to ball games, but now it’s too much for me. I am so thankful for him. I don’t know what I would do without him.”

Perhaps some forms of agoraphobia represent a conflict between desire for autonomy and dependency in interpersonal relationships (Fry, 1962; Goldstein & Chambless, 1978). In other words, the “preagoraphobic” is trapped in a domineering relationship without the skills needed to activate change. However, the concept of a distinct marital system that predisposes toward agoraphobia lacks empirical evidence. That is not to say that marital or interpersonal systems are un-

important to agoraphobia. For example, interpersonal discord/dissatisfaction may represent one of several possible stressors that precipitate panic attacks. Also, interpersonal relations may be negatively impacted by the development of agoraphobia (Buglass, Clarke, Henderson, & Presley, 1977) and in turn contribute to its maintenance. Not unlike one of the earlier vignettes, consider the woman who has developed agoraphobia and now relies on her husband to do the shopping and other errands. These new demands upon the husband lead to resentment and marital discord. The marital distress adds to background stress, making progress and recovery even more difficult for the patient.

Aside from whether interpersonal dysregulation contributes to the onset or maintenance of panic disorder or agoraphobia, some studies suggest that poor marital relations adversely impact exposure-based treatments (Bland & Hallam, 1981; Dewey & Hunsley, 1989; Milton & Hafner, 1979). However, other studies show no relationship between marital distress and outcome from cognitive-behavioral therapy (Arrindell & Emmelkamp, 1987; Emmelkamp, 1980; Himadi, Cerny, Barlow, Cohen, & O’Brien, 1986). Another line of research suggests that involving significant others in every aspect of treatment may override potential negative impacts of poor marital relations on phobic improvement (Barlow et al., 1984; Cerny, Barlow, Craske, & Himadi, 1987). Furthermore, involvement of significant others resulted in better long-term outcomes from cognitive-behavioral therapy for agoraphobia (Cerny et al., 1987). Similarly, communications training with significant others, compared to relaxation training, after 4 weeks of *in vivo* exposure therapy, resulted in significantly greater reductions on measures of agoraphobia by posttreatment (Arnou, Taylor, Agras, & Telch, 1985), an effect that was maintained over an 8-month follow-up. Together, these studies suggest the value of including significant others in the treatment for agoraphobia. On the other hand, treatment focused specifically on interpersonal relationships, via interpersonal therapy, was not as effective as cognitive-behavioral therapy for panic disorder and agoraphobia (Vos, Huibers, Diels, & Arntz, 2012).

Yet another question is the degree to which treatment for panic disorder and agoraphobia influences marital/interpersonal relations. Some have noted that successful treatment can have deleterious effects (Hafner, 1984; Hand & Lamontagne, 1976). Others note that it has no effect or a positive effect on marital functioning (Barlow, O’Brien, & Last, 1984; Himadi et al., 1986)



and interpersonal functioning in general (Hoffart, 1997). We (Barlow et al., 1983) suggested that when negative effects do occur, it may be because exposure therapy is conducted intensively, without the significant other's involvement, which causes major role changes that the significant other perceives as being beyond his or her control. This again speaks to the value of involving significant others in the treatment process.

### **Therapist Variables**

Only a few studies have evaluated therapist variables in relation to cognitive-behavioral treatments for anxiety disorders, let alone panic disorder or agoraphobia. Williams and Chambless (1990) found that patients with agoraphobia who rated their therapists as caring/involved, and as modeling self-confidence, achieved better outcomes on behavioral approach tests. However, an important confound in this study was that patient ratings of therapist qualities may have depended on patient responses to treatment. Keijsers, Schaap, Hoogduin, and Lammers (1995) reviewed findings on therapist relationship factors and behavioral outcome. They concluded that empathy, warmth, positive regard, and genuineness assessed early in treatment predict positive outcome; patients who view their therapists as understanding and respectful improve the most; and patient perceptions of therapist expertness, self-confidence, and directiveness relate positively to outcome, although not consistently. In their own study of junior therapists who provided cognitive-behavioral treatment for panic disorder with or without agoraphobia, Keijsers and colleagues found that more empathic statements and questioning occurred in Session 1 than in later sessions. In Session 3, therapists became more active and offered more instructions and explanations. In Session 10, therapists employed more interpretations and confrontations than previously. Most importantly, directive statements and explanations in Session 1 predicted poorer outcome. Empathic listening in Session 1 related to better behavioral outcome, whereas empathic listening in Session 3 related to poorer behavioral outcome. Thus, they demonstrated the advantages of different interactional styles at different points in therapy.

Most clinicians assume that therapist training and experience improve the chances of successful outcome. Some believe this to be the case particularly with respect to the cognitive aspects of cognitive-behavioral therapy (e.g., Michelson et al., 1990), and some indirect evidence for this supposition exists. Specifically,

cognitive-behavioral therapy conducted by "novice" therapists in a medical setting (Welkowitz et al., 1991) was somewhat less effective in comparison to the same therapy conducted by inexperienced but highly trained therapists in a psychological setting (Barlow, Craske, Czerny, & Klosko, 1989), or by experienced and highly trained therapists in a community mental health setting (Wade, Treat, & Stuart, 1998). Huppert and colleagues (2001), who directly evaluated the role of therapist experience, found that, in general, therapist experience positively related to outcome, seemingly because these therapists were more flexible in administering the treatment and better able to adapt it to the individual being treated. Obviously, there is a need for more evaluation of the role of therapist experience and training in cognitive-behavioral therapy.

In our primary care work, we developed a computer guide to assist novice clinicians in implementing a cognitive-behavioral program for panic disorder (plus other anxiety disorders and depression) (Craske et al., 2009), called *Calm Tools for Living*. The clinician and patient sit side by side as both view the program on-screen. Throughout, the program prompts clinicians to engage in specific tasks, such as helping patients to establish a fear hierarchy, demonstrating breathing skills, practicing cognitive skills, conducting interoceptive exposure, or designing *in vivo* exposure assignments. The program also provides learning tools for patients, such as didactic information, interactive exercises, video vignettes, and quizzes. The goal of the computerized program is to enhance the integrity of cognitive-behavioral therapy in the hands of novice and relatively untrained clinicians.

### **Patient Variables**

There has been interest in the effect of comorbidity upon the outcomes of cognitive-behavioral therapy for panic disorder and agoraphobia. Brown, Antony, and Barlow (1995) found that comorbidity with other anxiety disorders did not predict response to cognitive-behavioral therapy overall, although social phobia was unexpectedly associated with superior outcome for panic disorder and agoraphobia. In contrast, Tsao, Lewin, and Craske (1998) found a trend for comorbidity that comprised mostly other anxiety disorders to be associated with slightly lower rates of overall success. In a subsequent study, however, we replicated the finding by Brown and colleagues of no relationship between baseline comorbidity comprising mostly other anxiety

disorders, and either immediate or 6-month outcome for panic disorder and agoraphobia (Tsao, Mystkowski, Zucker, & Craske, 2002).

Research on how comorbid depression affects the course and outcome of panic disorder treatment has yielded mixed results. Studies focused on cognitive-behavioral therapy for all anxiety disorders and treatment participation have found that comorbidity with depression is associated with increased rates of refusal to enter treatment (Issakidis & Andrews, 2004); however, once patients have entered treatment, the comorbidity has no effect on rates of attrition (Allen et al., 2010; Brown et al., 1995). Preliminary research investigating the effects of comorbidity on engagement with treatment has revealed that comorbid depression has no effect on compliance with cognitive-behavioral therapy homework (McLean, Woody, Taylor, & Koch, 1998) or compliance with cognitive-behavioral treatment as a whole (Murphy, Michelson, Marchione, Marchione, & Testa, 1998), though it does increase levels of distress associated with treatment (Murphy et al., 1998). Interestingly, comorbid depression has no effect on the response to cognitive-behavioral therapy for panic disorder at posttreatment or follow-up and in both referred and primary care settings (Allen et al., 2010; McLean et al., 1998; Roy-Byrne, Craske, et al., 2005). It seems contradictory that comorbid depression would have significant impact on the severity and persistence of panic disorder (Baldwin, 1998) but would not affect the outcomes of panic disorder treatment. This may be a product of limitations to the current treatment literature. For example, studies have recruited patients for the treatment of panic disorder and have often excluded patients who are very extremely depressed or suicidal. Thus, the majority of patients are mildly to moderately depressed. Many of these studies also exclude patients with bipolar disorder, and therefore exclude an entire group of individuals who experience major depressive episodes. However, it may also be that the effects of cognitive-behavioral therapy for panic disorder are sufficiently potent to impact depressive symptoms either directly or indirectly.

A relatively high co-occurrence exists between panic disorder and agoraphobia, and avoidant, dependent, and histrionic personality disorders (e.g., Reich et al., 1994). Questions of diagnostic reliability and validity aside, comorbid personality disorders are sometimes associated with poorer response than usual to cognitive-behavioral therapy for panic disorder or agoraphobia (e.g., Hoffart & Hedley, 1997; Marchand, Goyer, Dupuis, & Main-

guy, 1998). However, closer examination reveals that although individuals with comorbid personality disorders have greater severity of panic or agoraphobia pre- and post-cognitive-behavioral therapy, the rate of decrease in panic or agoraphobia symptoms usually is not affected by the comorbid personality disorder. Thus, Dreessen, Arntz, Lutjels, and Sallaerts (1994) and van den Hout, Brouwers, and Oomen (2006) found that comorbid personality disorders did not affect response to cognitive-behavioral therapy for panic or agoraphobia. Moreover, Hofmann and colleagues (1988) found that scores on questionnaire subscales reflecting Axis II personality disorders did not predict panic disorder treatment response to either cognitive-behavioral therapy or to medication. In fact, some personality traits may associate positively with outcome, as was reported by Rathus, Sanderson, Miller, and Wetzler (1995) with respect to compulsive personality features.

Substance-related disorders also commonly co-occur with panic disorder and agoraphobia, but very few treatment studies have addressed this important comorbidity. In a series of single cases ( $N = 3$ ), Lehman, Brown, and Barlow (1998) demonstrated successful control of panic attacks in individuals who were abusing alcohol. Also, the addition of anxiety treatment to a relapse prevention program for abstinent individuals with a primary diagnosis of alcohol dependence and a comorbid diagnosis of panic disorder or social phobia decreased anxiety symptoms relative to a relapse prevention program alone (Schade et al., 2005). However, adding the anxiety treatment did not affect rates of alcohol relapse in that study.

Another source of comorbidity is medical conditions, such as cardiac arrhythmias or asthma, that may slow improvement rates given the additional complications involved in discriminating between anxiety and disease symptomatology, increases in actual medical risk, and the stress of physical diseases. We found that medically ill patients with panic disorder, although more severely affected than their nonmedically ill counterparts at baseline, responded just as favorably to cognitive-behavioral therapy with psychotropic medication recommendations (Roy-Byrne, Stein, et al., 2005). Also, cognitive-behavioral therapy for panic disorder has been shown to alleviate self-reported physical health symptoms (Schmidt et al., 2003). Similarly, we found that cognitive-behavioral therapy and/or psychotropic medication recommendations for anxiety disorders (including panic disorder) significantly improve physical health functioning (Niles et al., 2013).

Other patient variables include socioeconomic status and general living conditions. We evaluated perceived barriers to receiving mental health treatment in our primary care study of panic disorder (Craske, Golinelli, et al., 2005). Commonly reported barriers included inability to find out where to go for help (43%), worry about cost (40%), lack of coverage by one's health plan (35%), and inability to get an appointment soon enough (35%). Also, in our multicenter trial, attrition from cognitive-behavioral and/or medication treatment for panic disorder with minimal agoraphobia was predicted by lower education, which in turn was dependent on lower income (Grilo et al., 1998). Similarly, levels of education and motivation were associated with drop-out rates in another sample, although the effects were small (Keijsers, Kampman, & Hoogduin, 2001). Low education-income may reflect less discretionary time to engage in activities such as weekly treatment. Consider a woman who is the mother of two, a full-time clerk, whose husband is on disability due to a back injury, or the full-time student who works an extra 25 hours a week to pay his way through school. Under these conditions, treatment assignments of daily *in vivo* exposure exercises are much less likely to be completed. Frustration with lack of treatment progress is likely to result. Therapeutic success requires either a change in lifestyle that allows the cognitive-behavioral treatment to become a priority or termination of therapy until a later time, when life circumstances are less demanding. In fact, these kinds of life circumstance issues may explain the trend for African Americans to show less treatment benefit, in terms of mobility, anxiety, and panic attacks, than European Americans (Friedman & Paradis, 1991; Williams & Chambless, 1994). Although, in contrast to these two studies, Friedman, Paradis, and Hatch (1994) found equivalent outcomes across the two racial groups, and the results from another study yielded outcomes from a female African American sample that were judged to be comparable to those of European Americans (Carter, Sbrocco, Gore, Marin, & Lewis, 2003). The influence of ethnic and cultural differences on treatment outcome and delivery clearly needs more evaluation.

Finally, patients' understanding of the nature of their problem may be important to the success of cognitive-behavioral treatments. Given the somatic nature of panic disorder, many patients seek medical help first. Beyond that, however, differences in the way the problem is conceptualized could lead to the perception that pharmacological or analytical treatment approaches

are more credible than cognitive-behavioral treatment approaches. For example, individuals who strongly believe their condition is due to "a neurochemical imbalance" may be more likely to seek medication and to refute psychological treatments. Similarly, individuals who attribute their condition to "something about my past—it must be unconscious influences" may resist cognitive-behavioral interpretations. Also, Grilo and colleagues (1998) found that patients with panic disorder or agoraphobia who attributed their disorder to specific stressors in their lives were more likely to drop out of cognitive-behavioral or medication treatment, perhaps because they saw the offered treatment as irrelevant.

### **Concurrent Pharmacological Treatment**

Many more patients receive medications than cognitive-behavioral therapy for panic disorder and agoraphobia, partly because primary care physicians are usually the first line of treatment. Thus, one-half or more of patients with panic disorder who attend psychology research clinics already are taking anxiolytic medications. The obvious questions, therefore, are the extent to which cognitive-behavioral therapy and medications have a synergistic effect, and how medications impact cognitive-behavioral therapy.

Results from large clinical trials, including our own multisite trial (Barlow, Gorman, Shear, & Woods, 2000), suggest no advantage during or immediately after treatment of combining cognitive-behavioral and pharmacological approaches. Specifically, both individual cognitive-behavioral and drug treatment, and a combination treatment were immediately effective following treatment. Furthermore, following medication discontinuation, the combination of medication and cognitive-behavioral therapy fared worse than cognitive-behavioral therapy alone, suggesting the possibility that state- (or context-) dependent learning in the presence of medication may have attenuated the new learning that occurs during cognitive-behavioral therapy. In contrast, in the primary care setting, we found that the addition of even just one component of cognitive-behavioral therapy to medications for panic disorder resulted in statistically and clinically significant improvements at posttreatment and 12 months later (Craske, Golinelli, et al., 2005).

More recently, our multisite collaborative team has been investigating long-term strategies in the treatment of panic disorder. We examined sequential combination

strategies to determine whether this approach is more advantageous than simultaneously combining treatments. In the initial phase, 256 patients with panic disorder and all levels of agoraphobia completed 3 months of initial treatment with cognitive-behavioral therapy (Aaronson et al., 2008; White et al., 2010). Patients were then triaged into two clinical trials. Responders were randomized to 9 months of monthly booster sessions ( $N = 79$ ) or no booster sessions ( $N = 78$ ), then followed for an additional 12 months without treatment (White et al., 2013). Booster sessions produced significantly lower relapse rates (5.2%) and reduced work and social impairment compared to the assessment-only condition without booster sessions (18.4%) at 21-month follow-up. Multivariate Cox proportional hazards models showed that residual symptoms of agoraphobia at the end of acute-phase treatment were independently predictive of time to relapse during 21-month follow-up (hazard rate = 1.15,  $p < .01$ ). Thus, booster sessions aimed at reinforcing acute treatment gains to prevent relapse and offset disorder recurrence improved long-term outcome for panic disorder with and without agoraphobia. Fifty-eight of the original patients did not reach an optimal level of functioning (high end-state functioning) and entered a trial in which they received either continued cognitive-behavioral therapy for 3 months or paroxetine for 3 months. Patients doing well with one treatment or the other continued with the respective treatment for an additional 9 months (Payne et al., 2012). Results indicated significantly lower panic disorder symptoms for individuals in the paroxetine condition compared to those in continued cognitive-behavioral therapy at 3 months. However, group differences had disappeared 9 months later. Results were maintained when excluding individuals with comorbid major depression. These data suggest a more rapid treatment response when switching to paroxetine after not responding optimally to cognitive-behavioral therapy; however, both treatments ultimately achieved similar outcomes.

In another study with similar results, patients who did not respond to cognitive-behavioral therapy also benefited more from the addition of a serotonergic drug (paroxetine) to continued cognitive-behavioral therapy than from the addition of a drug placebo, with substantially different effect sizes (Kampman, Keijsers, Hoogduin, & Hendriks, 2002). Conversely, individuals who are resistant to pharmacotherapy may respond positively to cognitive-behavioral therapy, although these findings were part of an open trial without randomization (Heldt et al., 2006).

Findings from the combination of fast-acting anxiolytics, specifically, the high-potency benzodiazepines, and behavioral treatments for agoraphobia are contradictory (e.g., Marks et al., 1993; Wardle et al., 1994). Nevertheless, several studies have reliably demonstrated the detrimental effects of chronic use of high-potency benzodiazepines on short-term and long-term outcome in cognitive-behavioral treatments for panic or agoraphobia (e.g., Otto, Pollack, & Sabatino, 1996; van Balkom, de Beurs, Koele, Lange, & van Dyck, 1996; Wardle et al., 1994). Specifically, there is evidence for more attrition, poorer outcome, and more relapse with chronic use of high-potency benzodiazepines. In addition, use of benzodiazepines as needed was associated with poorer outcome than regular use or no use in one small naturalistic study (Westra, Stewart, & Conrad, 2002).

Finally, the cost-effectiveness of cognitive-behavioral and medication treatments alone rather than in combination requires further evaluation; currently, cognitive-behavioral therapy is considered to be more cost-effective (e.g., disability costs, work days missed, health care use) than pharmacotherapy (Heuzenroeder et al., 2004).

Understanding the ways in which psychotropic medications influence cognitive-behavioral therapy may prove useful for developing methods that optimize the combination of these two approaches to treatment. First, medications, particularly fast-acting, potent medications that cause a *noticeable* shift in state and are used on an as-needed basis (e.g., benzodiazepines, beta-blockers), may contribute to relapse because therapeutic success is attributed to them rather than to cognitive-behavioral therapy. Patients' resultant lack of perceived self-control may increase relapse potential when medication is withdrawn or contribute to maintenance of a medication regimen under the assumption that it is necessary to functioning. In support, attribution of therapeutic gains to alprazolam, and lack of confidence in coping without alprazolam, even when given in conjunction with behavioral therapy, predicted relapse (Basoglu, Marks, Kilic, Brewin, & Swinson, 1994). Second, medications may assume the role of safety signals, or objects to which persons erroneously attribute their safety from painful, aversive outcomes. Safety signals may contribute to maintenance of fear and avoidance in the long term (Hermans, Craske, Mineka, & Lovibond, 2006) and may interfere with corrections of misappraisals of bodily symptoms (see below for further discussion of this issue). Third,



medications may reduce the motivation to engage in practices of cognitive-behavioral skills, yet completion of between-session assignments is a positive predictor of outcome from cognitive-behavioral therapy (e.g., Glenn et al., in press). Finally, learning that takes place under the influence of medications may not necessarily generalize to the time when medications are removed, thus contributing to relapse (Bouton & Swartzentruber, 1991). Some of these points are illustrated in the following vignettes:

"I had been through a program of cognitive-behavioral therapy, but it was really the Paxil that helped. Because I was feeling so much better, I considered tapering off the medication. At first I was very concerned about the idea. I had heard horror stories about what people go through when withdrawing. However, I thought it would be OK as long as I tapered slowly. So, I gradually weaned myself off. It really wasn't that bad. Well, I had been completely off the medication for about a month when the problem started all over again. I remember sitting in a restaurant, feeling really good because I was thinking about how much of a problem restaurants used to be for me before, and how easy it seemed now. Then, whammo. I became very dizzy and I immediately thought, 'Oh no, here it comes.' I had a really bad panic attack. All I could think of was why didn't I stay on the medication?"

"I started to lower my dose of Xanax. I was OK for the first couple of days. . . . I felt really good. Then, when I woke up on Friday morning, I felt strange. My head felt really tight and I worried about having the same old feelings all over again. The last thing I want to do is to go through that again. So I took my usual dose of Xanax and, within a few minutes, I felt pretty good again. I need the medication. I can't manage without it right now."

In what ways might such negative effects of medications be offset? One possibility is that continuation of exposure after medication is withdrawn may offset relapse because it enhances attributions of personal mastery and reduces the safety signal function of medications. In addition, opportunities to practice exposure and cognitive and behavioral strategies without the aid of medication overcome state dependency and enhance generalization of therapeutic gains once treatment is over.

## CASE STUDY

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Julie, a 33-year-old European American mother of two, lives with Larry, her husband of 8 years. For the past 3 years she has been chronically anxious and panic stricken. She describes her panic attacks as unbearable and increasing in frequency. The first time she felt panicky was just over 3 years ago, when she was rushing to be by her grandmother's side in the last moments before she died. Julie was driving alone on the freeway. She remembers feeling as if everything were moving in slow motion, as if the cars were standing still, and things around her seemed unreal. She recalled feeling short of breath and detached. However, it was so important to reach her destination that she did not dwell on how she felt until later. After the day was over, she reflected on how lucky she was not to have had an accident. A few weeks later, she experienced the same feeling again when driving on the freeway. This time it occurred without the pressure of getting to her dying grandmother. It scared Julie because she was unable to explain the feelings. She pulled to the side of the road and called her husband, who came to meet her. She followed him home, feeling anxious the entire way.

Now, Julie has these feelings in many situations. She describes her panic attacks as feelings of unreality, detachment, shortness of breath, a racing heart, and a general fear of the unknown. It is the unreality that scares her the most. Consequently, Julie is sensitive to anything that produces "unreal" types of feelings, such as the semiconsciousness that occurs just before falling asleep, the period when daylight changes to night, bright lights, concentrating on the same thing for long periods of time, alcohol or drugs, and being anxious in general. Even though she has a prescription for Klonopin (a high-potency benzodiazepine), she rarely, if ever, uses it because of her general fear of being under the influence of a drug, or of feeling an altered state of consciousness. She wants to be as alert as possible at all times, but she keeps the Klonopin with her in the event that she has no other way of managing her panic. She does not leave home without the Klonopin. Julie is very sensitive to her body in general; she becomes scared of anything that feels a little different than usual. Even coffee, which she used to enjoy, is distressing to her now because of its agitating and racy effects. She was never a big exerciser, but to think of exerting herself now is also scary. Julie reports that she is constantly waiting for the next panic attack to occur. She avoids freeways, driving on familiar surface

streets only. She limits herself to a 10-mile radius from home. She avoids crowds and large groups as well, partly because of the feeling of too much stimulation and partly because she is afraid to panic in front of others. In general, she prefers to be with her husband or her mother. However, she can do most things as long as she is within her “safety” region.

Julie describes how she differs from the way she used to be: how weak and scared she is now. The only other incident that is similar to her current panic attacks occurred in her early 20s, when she had a negative reaction to smoking marijuana. Julie became very scared of the feeling of losing control and feared that she would never return to reality. She has not taken drugs since then. Otherwise, there is no history of serious medical conditions or any previous psychological treatment. Julie had some separation anxiety and was shy as a young child and throughout her teens. However, her social anxiety improved throughout her 20s to the point that until the onset of her panic attacks, she was mostly very comfortable around people. Since the onset of her panic attacks, Julie has become concerned that others will notice that she appears anxious. However, her social anxiety is limited to panic attacks and does not reflect a broader social phobia.

In general, Julie’s appetite is good, but her sleep is restless. At least once a week she wakes abruptly in the middle of the night, feeling short of breath and scared, and she has great difficulty going to sleep when her husband travels. In addition to worrying about her panic attacks, Julie worries about her husband and her children, although these latter worries are secondary to her worry about panicking and not excessive. She has some difficulty concentrating but is generally able to function at home and at work because of the familiarity of her environment and the safety she feels in the presence of her husband. Julie works part time as the manager of a business that she and her husband own. She sometimes becomes depressed about her panic and the limitations on how far she can travel. Occasionally she feels hopeless about the future, doubting whether she will ever be able to escape the anxiety. Although the feelings of hopelessness and the teariness never last than more than a few days, Julie has generally had a low-grade depressed mood since her life became restricted by the panic attacks.

Julie’s mother and her uncle both had panic attacks when they were younger. Julie is now worried that her oldest child is showing signs of being overly anxious because he is hesitant about trying new things or spending time away from home.

## ASSESSMENT

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A functional behavioral analysis depends on several different modes of assessment, which we describe next.

### *Interviews*

An in-depth interview is the first step in establishing diagnostic features and the profile of symptomatic and behavioral responses. Several semistructured and fully structured interviews exist. The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Di Nardo, Brown, & Barlow, 1994) and for DSM-5 (ADIS-5; Brown & Barlow, in press) primarily assesses anxiety disorders, as well as mood and somatoform disorders. Psychotic and drug conditions are screened by this instrument also. The ADIS facilitates gathering the necessary information to make a differential diagnosis among anxiety disorders and offers a means to distinguish between clinical and subclinical presentations of a disorder. Data on the frequency, intensity, and duration of panic attacks, as well as details on avoidance behavior, are embedded within the ADIS; this information is necessary for tailoring treatment to each individual’s presentation. The value of structured interviews is their contribution to a differential diagnosis and interrater reliability. Interrater agreement ranges from satisfactory to excellent for the various anxiety disorders using the ADIS-IV (Brown, Di Nardo, Lehman, & Campbell, 2001). Similar analysis for the ADIS-5 are under way.

Similarly, the Schizophrenia and Affective Disorders Schedule—Lifetime Version (modified for the study of anxiety) produces reliable diagnoses for most of the anxiety disorders (generalized anxiety disorder and simple phobia are the exceptions) (Manuzza, Fyer, Liebowitz, & Klein, 1990), as does the Structured Clinical Interview for DSM (SCID), which covers all of the mental disorders (First, Spitzer, Gibbon, & Williams, 1994), and will be updated for DSM-5 diagnostic criteria.

Differential diagnosis is sometimes difficult because, as described earlier, panic is a ubiquitous phenomenon (Barlow, 1988) that occurs across a wide variety of emotional disorders. It is not uncommon for persons with specific phobias, social phobia, generalized anxiety disorder, obsessive-compulsive disorder, and posttraumatic stress disorder to report panic attacks. For Julie, there was a differential diagnostic question regarding social anxiety disorder, and panic disorder and agoraphobia. Shown in Figure 1.1 are the ADIS-IV questions that address this differentiation (Julie’s answers are in italics).

**Parts of ADIS-IV Panic Disorder Section**

Do you currently have times when you feel a sudden rush of intense fear or discomfort? *Yes.*

**In what kinds of situations do you have those feelings?** *Driving, especially on freeways . . . alone at home . . . at parties or in crowds of people.*

**Did you ever have those feelings come “from out of the blue,” for no apparent reason, or in situations where you did not expect them to occur?** *Yes.*

**How long does it usually take for the rush of fear/discomfort to reach its peak level?** *It varies, sometimes a couple of seconds and at other times it seems to build more slowly.*

**How long does the fear/discomfort usually last at its peak level?** *Depends on where I am at the time. If it happens when I’m alone, sometimes it is over within a few minutes or even seconds. If I’m in a crowd, then it seems to last until I leave*

**In the last month, how much have you been worried about, or how fearful have you been about having another panic attack?**

0	1	2	3	4	5	6	7	8
No worry no fear	Rarely worried/mild fear		Occasionally worried/moderate fear		Frequently worried/ severe fear		Constantly worried/ extreme fear	

**Parts of ADIS-IV Social Phobia Section**

**In social situations, where you might be observed or evaluated by others, or when meeting new people, do you feel fearful, anxious, or nervous?** *Yes.*

**Are you overly concerned that you might do and/or say something that might embarrass or humiliate yourself in front of others, or that others may think badly of you?** *Yes.*

**What are you concerned will happen in these situations?** *That others will notice that I am anxious. My face turns white and my eyes look strange when I panic. I am worried that I’ll flip out in front of them, and they won’t know what to do.*

**Are you anxious about these situations because you are afraid that you will have an unexpected panic attack?** *Yes (either a panic or that I’ll feel unreal).*

**Other than when you are exposed to these situations, have you experienced an unexpected rush of fear/anxiety?** *Yes.*

FIGURE 1.1. Julie’s responses to ADIS-IV questions.

As demonstrated in Figure 1.1, Julie experiences panic attacks in social situations and is concerned about being negatively evaluated by others if her anxiety becomes visibly apparent. However, despite her history of shyness, Julie’s current social discomfort is based primarily on the possibility of panicking. Because of this, and because she meets the other criteria for panic

disorder (i.e., unexpected /nonsocial panic attacks and pervasive apprehension about future panic attacks), the social distress is best subsumed under the domain of panic disorder and agoraphobia. If Julie reported that she experiences panic attacks in social situations only, or that she worries about panic attacks in social situations only, then a diagnosis of social anxiety disorder

would be more probable. A report of unexpected panic attacks, as well as self-consciousness about things that she might do or say in social situations regardless of the occurrence of panic, would be consistent with a dual diagnosis of panic disorder–agoraphobia and social anxiety disorder. In general, an individual with panic disorder may continue to feel anxious even when playing a passive role in a social setting, whereas a patient with social phobia is more likely to feel relaxed when he or she is not the center of attention and does not anticipate being evaluated or judged (Dattilio & Salas-Auvert, 2000).

The same types of diagnostic questioning are useful for distinguishing between panic disorder–agoraphobia and claustrophobia. Other differential diagnostic issues can arise with respect to somatoform disorders, real medical conditions, and avoidant or dependent personality disorders.

Following completion of a diagnostic assessment, a dimensional assessment specifically designed for panic disorder, such as the Panic Disorder Severity Scale (PDSS; Shear et al., 1997), may be helpful. This clinician-completed scale rates seven areas of responding using a 0- to 4-point severity rating scale: panic attack frequency; distress; anticipatory anxiety; agoraphobic and interoceptive-related fears; avoidant behavior; and work and social impairment. A cutoff score of 8 on the PDSS identifies patients with panic disorder with high sensitivity and acceptable specificity (Shear et al., 2001).

### **Medical Evaluation**

A medical evaluation is generally recommended because several medical conditions should be ruled out before assigning the diagnosis of panic disorder. These include thyroid conditions, caffeine or amphetamine intoxication, drug withdrawal, or pheochromocytoma (a rare adrenal gland tumor). Furthermore, certain medical conditions can exacerbate panic disorder, although panic disorder is likely to continue even when the symptoms are under medical control. Mitral valve prolapse, asthma, allergies, and hypoglycemia fall into this latter category. According to the model described earlier, these medical conditions exacerbate panic disorder to the extent that they elicit the feared physical sensations. For example, mitral valve prolapse sometimes produces the sensation of a heart flutter, asthma produces shortness of breath, and hypoglycemia produces dizziness and weakness, all of which overlap

with symptoms of panic and may therefore become conditional cues for panic.

### **Self-Monitoring**

Self-monitoring is a very important part of assessment and treatment for panic disorder and agoraphobia. Retrospective recall of past episodes of panic and anxiety, especially when made under anxious conditions, may inflate estimates of panic frequency and intensity (Margraf et al., 1987; Rapee, Craske, & Barlow, 1990). Moreover, such inflation may contribute to apprehension about future panic. In contrast, ongoing self-monitoring generally yields more accurate, less inflated estimates (for a comprehensive review of self-monitoring for panic and anxiety, see Craske & Tsao, 1999). Also, ongoing self-monitoring is believed to contribute to an objective self-awareness. Objective self-monitoring replaces negative, affect-laden self-statements such as “I feel horrible. This is the worst it has ever been—my whole body is out of control” with “My anxiety level is 6. My symptoms include tremulousness, dizziness, unreal feelings, and shortness of breath—and this episode lasted 10 minutes.” Objective self-awareness usually reduces negative affect. Finally, self-monitoring provides feedback for judging progress and useful material for in-session discussions.

Panic attacks are recorded in the Panic Attack Record, a version of which is shown in Figure 1.2. This record, which is to be completed as soon as possible after a panic attack occurs, is therefore carried on-person (wallet size). Daily levels of anxiety, depression, and worry about panic are monitored with the Daily Mood Record shown in Figure 1.3. This record is completed at the end of each day. Finally, activities may be recorded by logging daily excursions in a diary, or by checking off activities completed from an agoraphobia checklist.

A common problem with self-monitoring is non-compliance. Sometimes noncompliance is due to misunderstanding or lack of perceived credibility in self-monitoring. Most often, however, noncompliance is due to anticipation of more anxiety as a result of monitoring. This is particularly true for individuals whose preferred style of coping is to distract themselves as much as possible because thoughts of panic might otherwise become overwhelming: “Why should I make myself worse by asking myself how bad I feel?” In Julie’s case, the self-monitoring task was particularly difficult because explicit reminders of her anxiety elicited strong



Date 2/16/06 Time began 5:20 PM.  
 Triggers Home alone and shortness of breath  
 Expected x Unexpected \_\_\_\_\_

Maximum Fear 0—1—2—3—4—5—6—7—8—9—10  
 None Mild Moderate Strong Extreme

Check all symptoms present to at least a mild degree:

Chest pain or discomfort	_____	Sweating	<u>x</u> _____
Heart racing/palpitations/pounding	<u>x</u> _____	Nausea/upset stomach	_____
Short of breath	<u>x</u> _____	Dizzy/unsteady/lightheaded/faint	_____
Shaking/trembling	<u>x</u> _____	Chills/hot flushes	_____
Numbness/tingling	_____	Feelings of unreality	<u>x</u> _____
Feelings of choking	_____	Fear of dying	_____
Fear of losing control/going crazy	<u>x</u> _____		

Thoughts: *I am going crazy, I will lose control*

Behaviors: *Called my mother*

FIGURE 1.2. Julie's Panic Attack Record.

	0—1—2—3—4—5—6—7—8—9—10			
	None	Mild	Moderate	Strong Extreme
Date	Average anxiety	Average depression	Average worry about panic	
2/16	7	5	7	
2/17	5	4	5	
2/18	4	4	5	
2/19	4	3	4	
2/20	4	4	5	
2/21	2	1	1	
2/22	2	2	2	

FIGURE 1.3. Julie's Daily Mood Record.

concerns about losing touch with reality. Prompting, reassurance that anxiety would subside with perseverance at self-monitoring, and emphasis on objective versus subjective self-monitoring were helpful for Julie. In addition, therapist attention to the self-monitored information and corrective feedback about the method of self-monitoring at the start of each treatment session reinforced Julie's self-monitoring.

### **Standardized Inventories**

Several standardized self-report inventories provide useful information for treatment planning and are sensitive markers of therapeutic change. The Anxiety Sensitivity Index (Reiss, Peterson, Gursky, & McNally, 1986) and the multidimensional Anxiety Sensitivity Index-3 (Taylor et al., 2007) have received wide acceptance as a trait measure of threatening beliefs about bodily sensations. Both display good psychometric properties and tend to discriminate panic disorder and agoraphobia from other anxiety disorders (e.g., Taylor et al., 1992; Telch, Sherman, & Lucas, 1989), especially the Physical Concerns subscale (Zinbarg et al., 1997). More specific information about which particular bodily sensations are feared most and what specific misappraisals occur most often may be obtained from the Body Sensations Questionnaire and the Agoraphobia Cognitions Questionnaire, respectively (Chambless, Caputo, Bright, & Gallagher, 1984). Both scales have strong to excellent psychometric properties and are sensitive to change following treatment (see Keller & Craske, 2008). The Mobility Inventory (Chambless, Caputo, Gracely, Jasin, & Williams, 1985) lists agoraphobic situations, which are rated in terms of degree of avoidance when alone and when accompanied. This instrument is very useful for establishing *in vivo* exposure hierarchies and, again, is well supported psychometrically.

In addition, we have developed two standardized self-report inventories that are useful for panic disorder and agoraphobia. The first, the Albany Panic and Phobia Questionnaire (Rapee, Craske, & Barlow, 1995), assesses fear and avoidance of activities that produce feared bodily sensations (e.g., exercise, caffeine), as well as more typical agoraphobia and social situations. Factor analyses confirmed three distinct factors labeled Agoraphobia, Social Phobia, and Interoceptive Fears. The questionnaire has adequate psychometric properties and is useful in profiling agoraphobic versus interoceptive avoidance. The second, the Anxiety Control

Questionnaire, assesses perceived lack of control over anxiety-related events and occurrences, such as internal emotional reactions or externally threatening cues (Rapee, Craske, Brown, & Barlow, 1996). This scale is designed to assess locus of control, but in a more specific and targeted manner relevant to anxiety and anxiety disorders compared to more general locus-of-control scales. A revised 15-item version yields three factors—Emotion Control, Threat Control, and Stress Control—with a higher-order dimension of perceived control (Brown, White, Forsyth, & Barlow, 2004). Changes in this scale from pre to posttreatment predicted reductions in comorbidity at follow-up in one study (Craske et al., 2007). A more detailed review of each questionnaire listed herein and the complete assessment for panic disorder and agoraphobia is provided by Keller and Craske (2008).

### **Behavioral Tests**

The behavioral test is a useful measure of degree of avoidance of specific interoceptive cues and external situations. Behavioral approach tests can be standardized or individually tailored. The standardized behavioral test for agoraphobic avoidance usually involves walking or driving a particular route, such as a 1-mile loop around the clinic setting. Standardized behavioral tests for anxiety about physical sensations involve exercises that induce panic-like symptoms, such as spinning in a circle, running in place, hyperventilating, and breathing through a straw (Barlow & Craske, 2006). Anxiety levels are rated at regular intervals throughout the behavioral tests, and actual distance or length of time is measured. The disadvantage of standardized behavioral tests is that the specific task may not be relevant to all patients (e.g., a 1-mile walk or running in place may be only mildly anxiety provoking to some but highly distressing to others); hence, the value of individually tailored tasks. In the case of agoraphobia, this usually entails attempts at three to five individualized situations that the patient has identified as ranging from *Somewhat difficult* to *Extremely difficult*, such as driving two exits on freeway, waiting in a bank line, or shopping in a local supermarket for 15 minutes. For anxiety about physical sensations, individually tailored behavioral tests entail exercises designed specifically to induce the sensations feared most by a given patient (e.g., nose plugs to induce sensations of difficulty breathing). As with standardized tests, ongoing levels of anxiety and degree of approach behavior are mea-

sured in relation to individually tailored behavioral tests.

Individually tailored behavioral tests are more informative for clinical practice, although they confound between-subject comparisons for research purposes. Behavioral tests are an important supplement to self-report of agoraphobic avoidance because patients tend to underestimate what they can actually achieve (Craske et al., 1988). In addition, behavioral tests often reveal important information for treatment planning of which the individual is not yet fully aware. For example, the tendency to remain close to supports, such as railings or walls, may not be apparent until one observes the patient walking through a shopping mall. In Julie's case, the importance of change from daylight to night was not apparent until she was asked to drive on a section of road as a behavioral test. Her response was that it was too late in the day to drive because dusk made her feel as if things were unreal. Similarly, it was not until Julie completed a behavioral test that we recognized the importance of air-conditioning when she was driving. Julie believed that the cool air blowing on her face helped her to remain "in touch with reality." Finally, we noticed that her physical posture while driving was a factor that contributed to anxiety: Julie's shoulders were hunched, and she leaned toward the steering wheel and held it very tightly. All of these were targeted in the treatment: Driving at dusk was included in her hierarchy; air-conditioning was regarded as a safety signal from which she should be weaned; and driving in a more relaxed position was part of mastery exposure.

### *Psychophysiology*

Ongoing physiological measures are not very practical tools for clinicians, but they can provide important information. In particular, the discrepancy described earlier between reports of symptoms and actual physiological arousal (i.e., report of heart rate acceleration in absence of actual heart rate acceleration) may serve as a therapeutic demonstration of the role of attention and cognition in symptom production. Similarly, actual recordings provide data to disconfirm misappraisals such as "My heart feels like it's going so fast that it will explode" or "I'm sure my blood pressure is so high that I could have a stroke at any minute." Finally, resting levels of physiological functioning, which are sometimes dysregulated in anxious individuals, may be sensitive measures of treatment outcome (e.g., Craske, Lang, et al., 2005).

### *Functional Analysis*

The various methods of assessment provide the material for a full functional analysis for Julie. Specifically, the topography of her panic attack is as follows: The most common symptoms include a feeling of unreality, shortness of breath, and racing heart; average frequency of panic attacks is three per week; each panic attack on average lasts from a few seconds to 5 minutes, if Julie is not in a crowd, where the panicky feelings last until she exits the crowd; in terms of apprehension, Julie worries about panic 75% of the day; and most of her panic attacks are expected, but she has some unexpected ones as well. Julie has both situational and internal antecedents to her panic attacks. The situational antecedents include driving on freeways; crowds of people; being alone, especially at night; restaurants; dusk; reading and concentrating for long periods of time; and aerobic activity. The internal antecedents include heart rate fluctuations, lightheaded feelings, hunger feelings, weakness due to lack of food, thoughts of the "big one" happening, thoughts of not being able to cope with this for much longer, and anger. Her misappraisals about panic attack symptoms include beliefs that she will never return to normality, that she will go crazy or lose control, and that others will think she is weird. Her behavioral reactions to panic attacks include escape behaviors such as pulling off to the side of the road, leaving restaurants and other crowded places, calling her husband or mother, and checking for her Klonopin. Her behavioral reactions to the anticipation of panic attacks include avoidance of driving long distances alone, driving on unfamiliar roads and freeways or at dusk, crowded areas, exercise, quiet time with nothing to do, and doing one thing for a long period of time. In addition, she tries not to think about anxiety or feelings of unreality. Her safety signals and safety-seeking behaviors include having her Klonopin on hand at all times, always knowing the location of her husband, and having the air-conditioning on. The consequences of her panic disorder with agoraphobia affect her family: Julie's husband is concerned and supportive, but her mother thinks she should pull herself together because "it's all in her head." In addition, Julie works but has cut back the number of hours, and she travels and socializes much less. Her general mood includes some difficulty concentrating and sleeping, restlessness, headaches, and muscular pains and aches. In addition, she is occasionally tearful, sad, and hopeless, and generally feels down.

## COMPONENTS OF COGNITIVE-BEHAVIORAL THERAPY

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The components of the cognitive-behavioral treatment described in this section are integrated into a session-by-session treatment program in the next section.

### **Education**

The treatment begins with education about the nature of panic disorder, the causes of panic and anxiety, and the ways panic and anxiety are perpetuated by feedback loops among physical, cognitive, and behavioral response systems. In addition, specific descriptions of the psychophysiology of the fight-flight response are provided, as well as an explanation of the adaptive value of the various physiological changes that occur during panic and anxiety. The purpose of this education is to correct the common myths and misconceptions about panic symptoms (i.e., beliefs about going crazy, dying, or losing control) that contribute to panic and anxiety. The survival value of alarm reactions (i.e., panic attacks) is emphasized throughout.

Education also distinguishes between the state of anxiety and the emotion of fear/panic, both conceptually and in terms of its three response modes (subjective, physiological, and behavioral). This distinction is central to the model of panic disorder and to the remainder of the treatment. Anxiety is viewed as a state of preparation for future threat, whereas panic is the fight-flight emotion elicited by imminent threat. Panic/fear is characterized by perceptions of imminent threat, sudden autonomic discharge, and fight-flight behavior. In contrast, anxiety is characterized by perceptions of future threat and chronic tension, cautiousness, avoidance, and disruption of performance.

### **Self-Monitoring**

Self-monitoring is essential to the personal scientist model of cognitive-behavioral therapy. Self-monitoring is introduced as a way to enhance objective self-awareness and increase accuracy in self-observation. As noted earlier, patients are asked to keep at least two types of records. The first, the Panic Attack Record, is completed as soon after each panic attack as possible; this record provides a description of cues, maximal distress, symptoms, thoughts, and behaviors. The second, the Daily Mood Record, is completed at the end of each day to record overall or average levels of anxiety, de-

pression, and whatever else is considered important to record. Additionally, patients may keep a daily record of activities or situations completed or avoided.

### **Breathing Retraining and Capnometry-Assisted Respiratory Training**

Breathing retraining is a central component early on in the development of panic control treatments because many panic patients describe symptoms of hyperventilation as being very similar to their panic attack symptoms. It is noteworthy, however, that a hyperventilation symptom report does not always accurately represent hyperventilation physiology: Only 50% or fewer patients show actual reductions in end-tidal CO<sub>2</sub> values during panic attacks (Hibbert & Pilsbury, 1989; Holt & Andrews, 1989; Hornsvedt, Garssen, Fiedelij Dop, & van Spiegel, 1990).

In early conceptualizations, panic attacks were related to stress-induced respiratory changes that provoke fear either because they are perceived as threatening or they augment fear already elicited by other phobic stimuli (Clark, Salkovskis, & Chalkley, 1985). Several studies illustrated a positive effect of breathing retraining, involving slow abdominal breathing exercises (e.g., Kraft & Hoogduin, 1984). The value of breathing retraining was subsequently questioned. For example, several studies suggested that the addition of breathing retraining alone did not improve on *in vivo* exposure (e.g., de Beurs, van Balkom, Lange, Koele, & van Dyck, 1995). We found breathing retraining to be slightly less effective than interoceptive exposure when each was added to cognitive restructuring and *in vivo* exposure (Craske, Rowe, Lewin, & Noriega-Dimitri, 1997), and in another study, the inclusion of breathing retraining resulted in poorer outcomes than cognitive-behavioral therapy without breathing retraining, although the findings were not robust (Schmidt et al., 2000). From their review of efficacy and mechanisms of action, Garssen, de Ruiter, and van Dyck (1992) concluded that breathing retraining probably effects change not through breathing per se but through distraction and/or a sense of control. Thus, breathing retraining is no longer considered a central component of cognitive-behavioral therapy for panic disorder. Furthermore, to the extent that it might become misused as a means for avoiding physical symptoms, it may even be countertherapeutic. That being said, there may be occasions when breathing retraining is a useful tool, such as for the individual showing obvious signs of irregular breathing (e.g.,



rapid, shallow breathing, frequent deep breaths), as long as breathing retraining does not become a method of avoidance or safety seeking.

In contrast to traditional breathing retraining, capnometry-assisted respiratory training (CART) targets respiratory dysregulation, in particular hypocapnia (Meuret, Rosenfield, Seidel, Bhaskara, & Hofmann, 2010; Meuret, Wilhelm, Ritz, & Roth, 2008). CART is a brief, 4-week training that uses immediate feedback of end-tidal partial pressure CO<sub>2</sub> (pCO<sub>2</sub>) to teach patients how to raise their subnormal levels of pCO<sub>2</sub> (hyperventilation) and thereby gain control over dysfunctional respiratory patterns and associated panic symptoms (e.g., shortness of breath, dizziness). The device, a portable capnometer, offers breath-by-breath feedback of expired CO<sub>2</sub> and rate of breathing (both measured via a nasal canula). Due to the novelty of CART, randomized controlled trials are limited but promising. In a first randomized-controlled study, Meuret and colleagues (2008) tested the efficacy of 4 weeks of CART ( $N = 20$ ) compared to a delayed wait-list control group (WL,  $N = 17$ ). CART, but not WL, led to sustained increases in pCO<sub>2</sub> levels and reduced panic severity and frequency. Reductions in panic symptom severity (PDSS; Shear et al., 1997) were comparable to standard cognitive-behavioral therapy, and improvements were maintained at 12-month follow-up. In a second study, patients with panic disorder were randomly assigned to receive either 4 weeks of CART ( $N = 21$ ) or cognitive therapy ( $N = 20$ ). An initial 4 weeks of skills training was followed by three sessions of *in vivo* exposure and a fourth session at a 2-months follow-up. Respective skills acquisition trainings led to significant and comparable reductions in panic symptom severity and panic-related cognitions, irrespective of modality. However, only CART, not cognitive therapy, led to a correction of hypocapnic levels of pCO<sub>2</sub> (Meuret et al., 2010; Seidel, Rosenfield, Bhaskara, Hofmann, & Meuret, 2009). However, an evaluation of the degree to which CART augments exposure therapy (relative to exposure therapy alone) awaits testing.

### **Applied Relaxation**

A form of relaxation known as applied relaxation has shown good results as a treatment for panic attacks. Two studies by Öst (Öst & Westling, 1995; Öst, Westling, & Hellström, 1993) indicate that applied relaxation is as effective as *in vivo* exposure and cognitive therapy. In contrast, Barlow and colleagues (1989) found that ap-

plied progressive muscle relaxation (PMR) is relatively ineffective for panic attacks, although we excluded all forms of interoceptive exposure from the hierarchy of tasks to which PMR was applied, which was not necessarily the case in the studies by Öst. Clark and colleagues (1994) found cognitive therapy to be superior to applied PMR when conducted with equal amounts of *in vivo* exposure, whereas Beck, Stanley, Baldwin, Deagle, and Averill (1994) found very few differences between cognitive therapy and PMR when each was administered without exposure procedures.

### **Cognitive Restructuring**

Cognitive restructuring is a skills set in which patients learn to recognize cognitive errors and generate alternative, noncatastrophic explanations for the sensations that are feared during panic attacks. Cognitive therapy begins with a treatment rationale and discussion of the role of thoughts in generating emotions. Next, thoughts are recognized as hypotheses rather than as fact, and are therefore open to being questioned and challenged. Detailed self-monitoring of emotions and associated cognitions is instituted to identify specific beliefs, appraisals, and assumptions. Once identified, relevant cognitions are categorized into types of typical errors that occur during heightened emotion, such as overestimations of risk of negative events or catastrophization of meaning of events. The process of categorization, or labeling of thoughts, is consistent with a personal scientist model and facilitates an objective perspective by which the validity of the thoughts can be evaluated. Thus, in labeling the type of cognitive distortion, the patient is encouraged to use an empirical approach to examine the validity of his or her thoughts by considering all of the available evidence. Therapists use Socratic questioning to help patients make guided discoveries and question their anxious thoughts. Next, more evidence-based alternative hypotheses are generated. In addition to surface-level appraisals (e.g., "That person is frowning at me because I look foolish"), core-level beliefs or schemas (e.g., "I am not strong enough to withstand further distress" or "I am unlikable") are questioned in the same way. Importantly, cognitive restructuring is not intended as a direct means of minimizing fear, anxiety, or unpleasant symptoms. Instead, cognitive restructuring is intended to correct distorted thinking; eventually fear and anxiety are expected to subside, but their diminution is not the first goal of cognitive therapy.

Cognitive therapy is often intermingled with behavioral techniques (e.g., “behavioral experiments,” “hypothesis testing,” “instructions” involving exposure) that complicate direct testing of the efficacy of cognitive therapy in its “pure” form (e.g., Hoffart, Sexton, Hedley, & Martinsen, 2008; Hofmann et al., 2007; Öst et al., 1993; Teachman, Marker, & Smith-Janik, 2008). Nonetheless, there is some evidence that training in cognitive procedures in full isolation from exposure and behavioral procedures is efficacious in reducing aspects of panic (Beck et al., 1994; Meuret et al., 2010; Salkovskis, Clark, & Hackmann, 1991; van den Hout, Arntz, & Hoekstra, 1994). Similarly, in a study by Bouchard and colleagues (1996), cognitive restructuring was as effective as exposure therapy in reducing panic symptoms. However, the effects of cognitive therapy alone on agoraphobia are unclear. One study found that cognitive therapy was less effective than exposure therapy for agoraphobia (Williams & Falbo, 1996). Another study (Hoffart, 1995) found that cognitive therapy was as effective as guided mastery exposure delivered intensively over 6 weeks for individuals with moderate to severe agoraphobia, although some elements of exposure (e.g., hyperventilation tests to elicit sensations) were included in the cognitive therapy condition.

A few studies have evaluated the effects of cognitive therapy combined with exposure in comparison to exposure alone or in combination with other coping skills. Most often, cognitive therapy combined with exposure does not yield an additional benefit over *in vivo* exposure alone (Öst, Thulin, & Ramnero, 2004; van den Hout et al., 1994; see Murphy et al., 1998, for an exception).

### Exposure

Exposure is a critical phase of treatment and, once begun, is a major focus of treatment sessions as well as between-treatment session homework, since limited exposure practice is of small benefit and may even be detrimental. The exposure is designed to disconfirm misappraisals and extinguish conditional emotional responses to external situations and contexts, through *in vivo* exposure, as well as to bodily sensations, through interoceptive exposure. Growing evidence suggests that exposure represents the most powerful component of cognitive-behavioral therapy for panic disorder and agoraphobia, including meta-analyses that fail to show any additional benefit of either cognitive restructuring or somatic coping skills beyond exposure therapy alone

(Norton & Price, 2007). A large trial reported a dose-response relationship between exposure and improvement in agoraphobia (Gloster et al., 2011).

### In Vivo Exposure

*In vivo* exposure refers to repeated and systematic, real-life exposure, in this case, to agoraphobic situations. A long history of research has established the efficacy of *in vivo* exposure for agoraphobia.

Most often, *in vivo* exposure is conducted in a graduated manner, proceeding from the least to the most anxiety-provoking situations on an avoidance hierarchy. However, there is some evidence to suggest that intensive or ungraduated exposure may be effective. In a study by Feigenbaum (1988), treatment sessions were conducted in a massed format over the course of 6–10 consecutive days. One group received ungraded exposure ( $N = 25$ ), beginning with the most feared items from avoidance hierarchies. Another group received graded exposure ( $N = 23$ ), beginning with the least feared hierarchy items. Approximately one-third of this severely agoraphobic sample was housebound at initial assessment. At posttreatment and 8 months later, the conditions proved to be equally effective (although, intriguingly, the graded group reported the treatment to be more distressing). However, ungraded exposure was clearly superior at the 5-year follow-up assessment: 76% of the intensive group versus 35% of the graded group reported themselves to be completely free of symptoms. When 104 subjects were added to the intensive exposure format, the same results were obtained. Of 129 subjects, 78% were reportedly completely symptom-free 5 years later. This dramatic set of results suggests that an intensive approach, which is likely to produce higher levels of arousal than a graduated approach, can be very beneficial (at least when conducted in a massed format). Unfortunately, the validity of the outcome measures in this study is somewhat questionable, and replication by independent investigators has yet to be reported.

The amount of time devoted to *in vivo* exposure is very dependent on the patient’s agoraphobia profile. Obviously, more time is needed for patients with more severe agoraphobia.

### Interoceptive Exposure

In interoceptive exposure, the goal is deliberately to induce feared physical sensations a sufficient number of

times, and long enough each time, so that misappraisals about the sensations are disconfirmed and conditional anxiety responses are extinguished. A standard list of exercises, such as hyperventilating and spinning, is used to establish a hierarchy of interoceptive exposures. With a graduated approach, exposure begins with the less distressing physical exercises and continues with the more distressing exercises. It is essential that the patient endure the sensations beyond the point at which they are first noticed, for at least 30 seconds to 1 minute, because early termination of the task may eliminate the opportunity to learn that the sensations are not harmful and that the anxiety can be tolerated. The exercise is followed by a discussion of what the patient learned about the physical sensations. These interoceptive exercises are practiced daily outside of the therapy session to consolidate the process of learning. Interoceptive exposure extends to naturalistic activities that induce somatic sensations (e.g., caffeine consumption, exercise).

A series of studies reported on the effects of interoceptive exposure independent of other therapeutic strategies. Early on, Bonn, Harrison, and Rees (1971) and Haslam (1974) observed successful reduction in reactivity with repeated infusions of sodium lactate (a drug that produces panic-type bodily sensations). However, panic was not monitored in these investigations. Griez and van den Hout (1986) compared six sessions of graduated CO<sub>2</sub> inhalations to a treatment regimen of propranolol (a beta-blocker chosen because it suppresses symptoms induced by CO<sub>2</sub> inhalations), both conducted over the course of 2 weeks. CO<sub>2</sub> inhalation treatment resulted in a mean reduction from 12 to four panic attacks, which was superior to the results from propranolol. In addition, inhalation treatment resulted in significantly greater reductions in reported fear of sensations. A 6-month follow-up assessment suggested maintenance of treatment gains, although panic frequency was not reported. Beck and Shipherd (1997) similarly found a positive effect from repeated CO<sub>2</sub> inhalations, although it had little effect on agoraphobia (Beck, Shipherd, & Zebb, 1997). Broocks and colleagues (1998) tested the effects of exercise (with once-weekly supportive contact from a therapist) in comparison to clomipramine or drug placebo over 10 weeks. The exercise group was trained to run 4 miles, three times per week. Despite high attrition from exercise (31%), exercise was more effective than the drug placebo condition. However, clomipramine was superior to exercise.

In the first comparison to other cognitive and behavioral treatments, Barlow and colleagues (1989) compared applied PMR, interoceptive exposure plus breathing retraining and cognitive restructuring, their combination with applied PMR, and a waiting-list control, in a sample with panic disorder with limited agoraphobia. The two conditions involving interoceptive exposure, breathing retraining and cognitive restructuring, were significantly superior to applied PMR and wait-list conditions. The results were maintained 24 months following treatment completion for the group receiving interoceptive exposure, breathing retraining, and cognitive restructuring without PMR, whereas the combined group tended to deteriorate over follow-up (Craske, Brown, & Barlow, 1991). As already mentioned, we compared interoceptive exposure, cognitive therapy, and *in vivo* exposure to breathing retraining, cognitive therapy, and *in vivo* exposure for individuals with varying levels of agoraphobia. The condition that included interoceptive exposure was slightly superior to breathing retraining at posttreatment and 6 months later (Craske et al., 1997). Similarly, Ito, Noshirvani, Basoglu, and Marks (1996) found a trend for those who added interoceptive exposure to their self-directed *in vivo* exposure and breathing retraining to be more likely to achieve at least a 50% improvement in phobic fear and avoidance. However, the combination of breathing education, breathing retraining, and repeated interoceptive exposure to hyperventilation did not increase the effectiveness of *in vivo* exposure for agoraphobia (de Beurs, Lang, van Dyck, & Koele, 1995).

Interoceptive exposure is now a standard component of cognitive-behavioral therapy for panic disorder (e.g., Barlow et al., 2000; Craske, Lang, Aikins, & Mystkowski, 2005), although different groups give different emphases to interoceptive exposure, with some emphasizing it as a means for extinguishing fear responses (Barlow & Craske, 2006) and others, as a vehicle for disconfirming misappraisals (Clark, 1996).

### *Optimizing Learning during Exposure*

Our understanding of the mechanisms of exposure therapy has evolved over time. One of the most influential theories is emotional processing theory, which emphasized habituation of fear responding within an exposure trial as a necessary precursor to habituation across treatment sessions, that in turn leads to long-term corrective learning (Foa & Kozak, 1986; Foa & McNally, 1996). Most recently, we have emphasized

optimizing inhibitory learning and its retrieval in ways that are not necessarily dependent on reductions in fear throughout trials of exposure (Craske et al., 2008); we discuss this approach below.

Emotional processing theory emphasizes mechanisms of habituation as precursors to cognitive correction. Specifically, emotional processing theory purports that the effects of exposure therapy derive from activation of a “fear structure” and integration of information that is incompatible with it, resulting in the development of a non-fear structure that replaces or competes with the original one. Incompatible information derives first from within-session habituation, or reduction in fear responding with prolonged exposure to the fear stimulus. Within-session habituation is seen as a prerequisite for the second piece of incompatible information, which derives from between-session habituation over repeated occasions of exposure. Between-session habituation is purported to form the basis for long-term learning and to be mediated by changes in “meaning,” or lowered probability of harm (i.e., risk) and lessened negativity (i.e., valence) of the stimulus. Emotional processing theory guides clinicians to focus on the initial elevation of fear followed by within- and between-session reductions in fear as signs of treatment success. Although enticing in its face validity, support for the theory has been inconsistent at best (Craske et al., 2008; Craske, Liao, Brown, & Vervliet, 2012). Rather, the evidence suggests that the amount by which fear habituates from the beginning to the end of an exposure practice is not a good predictor of overall outcomes, and that evidence for between-session habituation is mixed (Craske et al., 2008, 2012).

A return to the science of fear learning and extinction may help to explain the effects of exposure therapy and thereby optimize its implementation. It is now thought that inhibitory learning is central to extinction (Bouton, 1993). Inhibitory pathways are also recognized in the neurobiology of fear extinction (see Sotres-Bayon, Cain, & LeDoux, 2006). Within a Pavlovian conditioning approach, inhibitory learning means that the original conditioned stimulus–unconditioned stimulus (CS-US) association learned during fear conditioning is not erased during extinction, but rather is left intact as a new, secondary learning about the CS-US develops (Bouton, 1993). The degree to which inhibitory associations shape fear responding at retest (the index of strength and stability of new “learning”) is independent of fear levels expressed throughout extinction and instead is dependent on factors such as context and time.

Based on the inhibitory retrieval model of extinction, outcomes may be enhanced by strategies that do not rely on fear reduction within a trial of exposure (Craske et al., 2008, 2012). Indeed, fear reduction may become a safety behavior for persons with panic disorder (since fear reduction eradicates the very thing that is feared), such that a more appropriate goal may be to maintain high levels of fear and anxiety in order to disconfirm the expectancy of negative consequences. One translational possibility is “deepened extinction” (Rescorla, 2006), in which multiple fear conditional stimuli are first extinguished separately before being combined during extinction, and in animal studies, decrease spontaneous recovery and reinstatement of fear. Indeed, this is what is essentially done when interoceptive exposure is conducted in feared agoraphobic situations (Barlow & Craske, 1994) and recent experimental data supports the beneficial effects of deepened extinction in human conditioning studies (Culver, Vervliet, & Craske, in press).

In addition, the effects of exposure therapy may be enhanced by the prevention or removal of “safety signals” or “safety behaviors.” Common safety signals and behaviors for clients with panic disorder are the presence of another person, therapists, medications, or food or drink. In the experimental literature, safety signals alleviate distress in the short term, but when they are no longer present, the fear returns (Lovibond, Davis, & O’Flaherty, 2000), an effect that may derive in part from interference with the development of inhibitory associations. In phobic samples, the availability and use of safety signals and behaviors has been shown to be detrimental to exposure therapy (Sloan & Telch, 2002), whereas instructions to refrain from using safety behaviors improved outcomes (Salkovskis, 1991). Similarly, the use of safety signals was associated with poorer outcomes for panic (Helbig-Lang & Petermann, 2010). However, recent data have presented contradictory findings (Rachman, Shafran, Radomsky, & Zysk, 2011).

Further options include stimulus variability throughout exposure, since variability has been shown to enhance the storage capacity of newly learned information. Two studies with clinical analogues have demonstrated positive benefits in terms of spontaneous recovery (Lang & Craske, 2000; Rowe & Craske, 1998), while a third showed trends only (Kircanski et al., 2011). In the treatment for panic disorder with agoraphobia, this implies conducting exposure for varying durations, at varying levels of intensity, rather than



continuing exposure in one situation until fear declines before moving to the next situation. Notably, such variability typically elicits higher levels of anxiety during exposure, but without detrimental effects and sometimes with beneficial effects in the long term.

Based on evidence for fear extinction to be weakened by antagonists of the glutamate receptors in the amygdala, Walker and Davis (2002) tested and demonstrated that drug agonists of the same receptors, and in particular, D-cycloserine, enhance extinction in animal studies. In a meta-analysis of the efficacy of D-cycloserine for anxiety disorders, Norberg, Krystal, and Tolin (2008) reported effect sizes of  $d = 0.60$  at posttreatment and  $0.47$  at follow-up in clinical anxiety samples. D-Cycloserine in combination with interoceptive exposure for panic clients has resulted in a greater reduction in symptom severity, and a greater likelihood of achieving a change in clinical status at posttreatment and 1-month follow-up compared to exposure plus placebo (Otto et al., 2010). Notably, D-cycloserine has been shown to have positive effects without influencing the level of fear during exposure per se.

A number of options for enhancing retrieval of the extinction memory have been tested. One option during extinction training is to include retrieval cues to be used in other contexts once extinction is over. This has been shown to be effective in animal studies and human conditioning studies (see Craske et al., 2012, for a review). In clinical analogue samples, the effects of a retrieval cue upon context renewal were very weak in one study (Culver et al., 2012), although instructions to reinstate what was learned mentally during exposure had more robust effects in reducing context renewal in another study (Mystkowski, Craske, Echiverri, & Labus, 2006). In the treatment of panic disorder, this approach simply suggests that clients carry with them cues (e.g., wristband) to remind them what they learned during exposure therapy (as long as the cues do not become safety signals), or are prompted to remind themselves of what they learned in exposure therapy each time they experience previously feared sensations or situations.

Another option is to provide multiple contexts in which extinction takes place. This approach has been shown to offset context renewal in rodent samples, and in a clinical analogue study of exposure therapy (Vansteenwegen et al., 2007) although the results are not always consistent (Neumann, Lipp & Cory, 2007). In the treatment of panic disorder and agoraphobia, this would mean asking clients to conduct their interoceptive and *in vivo* exposures in multiple different contexts,

such as when alone, in unfamiliar places, or at varying times of day or varying days of the week.

A recent (re-)discovery is that retrieving already stored memories induces a process of reconsolidation (Nader, Schafe, & Le Doux, 2000), since the memory is written into long-term memory again, requiring de novo neurochemical processes. Thus, it may be possible to change memories during the reconsolidation time frame upon retrieval. Propranolol, a beta-blocker, has been shown to block the reconsolidation of memories, and Debiec and Le Doux (2004) found that infusions of propranolol blocked the reconsolidation of a previously formed CS-US memory, and led to erasure of the fear response and resistance to reinstatement effects. This suggests that propranolol upon retrieval may be a useful clinical tool, and indeed, two fear conditioning studies in healthy humans (Kindt, Soeter, & Vervliet, 2009; Soeter & Kindt, 2010) have replicated the effects. However, the effects have not been tested in the context of exposure therapy for panic disorder.

### **Role of Acceptance during Exposure**

Cognitive and somatic coping skills are central to cognitive-behavioral therapy and are taught to facilitate and improve exposure therapy. Newer approaches that explore acceptance and cognitive defusion (e.g., acceptance and commitment therapy; Hayes, Strosahl, & Wilson, 1999) have been gaining interest, especially given evidence that experiential avoidance is a correlate of anxious psychopathology and acceptance increases willingness to experience and lessens emotional distress over induced anxiety symptoms in individuals with panic disorder (e.g., Campbell-Sills et al., 2006; Eifert & Heffner, 2003), including CO<sub>2</sub> inhalation challenges (Levitt et al., 2004). Interestingly, the acceptance approach is entirely consistent with our formulation of interoceptive exposure, in which patients are encouraged to experience the feared physical sensations without any attempt to lessen them or to think differently about them in the moment of exposure. We recently extended this model of acceptance during interoceptive exposure to acceptance during *in vivo* exposure in an open trial of 11 patients with panic disorder (Meuret, Twhig, Rosenfield, Hayes, & Craske, 2012). In general, the exposures were an opportunity for patients to behave *with* their panic-related thoughts, feelings, and bodily sensations; in other words, patients were encouraged to realize that they can drive for and reach life goals, even in the presence of unpleasant inner experiences. To that

end, it was explicitly stated that the level of anxiety or fear was not the determining factor. Rather, it was explained that “willingness can do surprising things to one’s inner experiences. If one is willing to experience anxiety it may or may not show up. Thus, we are not going to judge the success of these exposures on how high the anxiety gets, but instead in how open you are to what might show up.” To plan effectively for interoceptive (i.e., eliciting panic sensations such as a racing heart or shortness of breath) and *in vivo* exposures (i.e., seeking places and situations that one previously avoided because of the fear of panic sensations), a hierarchy of least to most anxiety-provoking items was created. Movement up the hierarchy was not based on reductions in anxiety at the preceding step but high willingness to experience panic-related inner experiences. During the exposures, patients were encouraged to maintain an open, nonjudgmental stance toward whatever thoughts, feelings, and bodily sensations arose in a given moment, experiencing them for what they were, and moving toward them while anxious. Treatment was associated with clinically significant improvements in panic symptom severity, willingness to allow inner experiences to occur, and reductions in avoidant behavior. In another study of a mixed anxiety disorder sample, we found very few differences in outcome between acceptance and commitment therapy (Hayes et al., 1999) and cognitive-behavioral therapy, although the treatments were matched on amount of time spent on exposure therapy, albeit framed differently within for each condition (Arch et al., 2012). Thus, the data to date suggest that both a cognitive therapy coping approach and an acceptance-based exposure approach are effective.

### OVERALL EFFICACY OF COGNITIVE-BEHAVIORAL THERAPY

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An extensive body of research has evaluated the efficacy of cognitive-behavioral therapy for panic disorder and agoraphobia. Cognitive-behavioral therapy, involving most or all of the components just listed, yields panic-free rates in the range of 70–80% and high end-state rates (i.e., within normative ranges of functioning) in the range of 50–70% for panic disorder with minimal agoraphobia (e.g., Barlow et al., 1989; Clark et al., 1994). Although agoraphobic avoidance is sometimes associated with less positive response (e.g., Dow et al., 2007), the overall within-group effect size for change in panic disorder and agoraphobia from pre- to post-

treatment is very large (e.g., effect size = 1.53; Norton & Price, 2007). Moreover, the between-group effect size is substantial in comparison to wait-list conditions (e.g., effect size = 0.64; Haby, Donnelly, Corry, & Vos, 2006). However, more research is needed comparing cognitive-behavioral therapy to alternative active treatment conditions.

The effectiveness extends to clients who experience nocturnal panic attacks (Craske, Lang, et al., 2005). Furthermore, cognitive-behavioral therapy results in improvements in rates of comorbid anxiety and mood disorders (e.g., Craske et al., 2007; Tsao, Mystkowski, Zucker, & Craske, 2005), although one study suggested that the benefits for comorbid conditions may lessen over time, when assessed 2 years later (Brown et al., 1995). Finally, applications of cognitive-behavioral therapy lower relapse rates upon discontinuation of high-potency benzodiazepines (e.g., Spiegel, Bruce, Gregg, & Nuzzarello, 1994). The effects of cognitive-behavioral therapy are sustained over time, as meta-analyses show little change (i.e., maintenance of treatment effects) from posttreatment to follow-up (effect size = 0.12; Norton & Price, 2007). From their review of meta-analyses for cognitive behavioral therapy across all disorders, Butler, Chapman, Forman, and Beck (2006) concluded that evidence for maintenance of treatment gains was particularly strong for panic disorder, where the rate of relapse was almost half the rate of relapse following pharmacotherapy. Continuing improvement after acute treatment is facilitated by involvement of significant others in every aspect of treatment for agoraphobia (e.g., Cerny et al., 1987). Also, booster sessions enhance long-term outcomes (Craske et al., 2006).

Efficacy data from research settings are now being complemented by effectiveness data from real-world, primary care settings. In a randomized controlled trial in primary care settings with novice therapists, cognitive-behavioral therapy combined with expert recommendations for medication regimens was more effective than treatment as usual (Roy-Byrne, Craske, et al., 2005). The effects appeared primarily to be due to cognitive-behavioral therapy rather than medication (Craske, Golinelli, et al., 2005). In the more recent CALM study (Craske et al., 2011), the effectiveness of cognitive-behavioral therapy for panic disorder in primary care settings was demonstrated in the hands of nonexperienced therapists with the aid of a computerized guide, combined with expert recommendations for medication, relative to treatment as usual.

Even though cognitive-behavioral therapy for panic disorder and agoraphobia is efficacious and effective, there is room for improvement. One study estimated that 30% of clients continue to function poorly at follow-up and only 48% reached high end-state status (Brown & Barlow, 1995). In a landmark study (Barlow et al., 2000), only 32% of clients with panic disorder assigned to cognitive-behavioral therapy alone demonstrated strong treatment response 12 months after acute treatment. Finally, of those who do start treatment, the mean dropout rate is 19%, with a range of 0–54% (Haby et al., 2006).

## TREATMENT DESCRIPTION: PROTOCOL

What follows is a description of a 12-session cognitive-behavioral therapy for panic disorder and agoraphobia tailored to Julie's presentation. Of course, the degree to which the various components of treatment are emphasized vary by the functional assessment conducted for each patient.

### Overview

The basic aim of the treatment protocol is to influence directly the catastrophic misappraisals and avoidance of bodily sensations and agoraphobic situations. This is done first through the provision of accurate information as to the nature of the fight–flight response. By provision of such information, patients are taught that they experience sensations that are normal and harmless. Second, treatment aims to teach a set of skills for developing evidence-based appraisals regarding bodily sensations and agoraphobic situations. At the same time, specific information concerning the effects of hyperventilation and its role in panic attacks is provided, with practice of breathing retraining if deemed appropriate. Then, the crux of the treatment involves repeated exposure to feared internal cues and agoraphobic situations.

### Session 1

The goals of Session 1 are to describe fear and anxiety; to help patients understand the cyclical influences among behavioral, physiological, and cognitive responses; to understand that panic attack symptoms are not harmful; and to begin self-monitoring, if it was not already begun with the initial assessment. Therapy begins with identifying anxiety patterns and the situa-

tions in which anxiety and panic attacks are likely to occur. Many patients have difficulty identifying specific antecedents, reporting that panic can occur at almost any time. Therapists help patients to identify internal triggers, specifically, negative verbal cognitions, catastrophic imagery, and physical sensations. The following interchange took place for Julie:

TERAPIST: In what situations are you most likely to panic?

JULIE: Crowded restaurants and when I'm driving on the freeway. But sometimes I am driving along, feeling OK, when all of a sudden it hits. And other times I can be sitting at home feeling quite relaxed and it just hits. That's when I really get scared because I can't explain it.

TERAPIST: So, when you are driving on the freeway, what is the very first thing you notice that tells you you're about to panic?

JULIE: Well, the other cars on the road look as if they are moving really slowly . . . it's as if I am in a dream.

TERAPIST: And what is the first thing you notice when you're at home?

JULIE: An unreal feeling, like I'm floating.

TERAPIST: So, what does that tell you? What is the common factor that started these two panic attacks?

JULIE: The feeling as if things are unreal? Wow, I always thought the physical feelings were the panic attack, but maybe they start the panic attack.

Next, the three-response system model for describing and understanding anxiety and panic is introduced. This model contributes to an objective self-awareness—to becoming a personal scientist—and provides the groundwork for an alternative conceptual framework for explaining panic and anxiety that replaces the patient's own misassumptions. Patients are asked to describe cognitive, physiological, and behavioral aspects to their responding: to identify the things that they *feel*, *think*, and *do* when they are anxious and panicky. As described earlier, differences between the response profiles of anxiety and panic are highlighted. After grasping the notion of three responses that are partially independent, interactions among the response systems are described. The patient is asked to describe the three-response system components in a recent panic attack and to identify ways in which they interacted to produce heightened distress. For example,

THERAPIST: How would you describe the three parts to the panic attack you had at home last week?

JULIE: Well, physically, my head felt really light, and my hands were clammy. I thought that I would either pass out or that I would somehow dissolve into nothingness. My behavior was to lie down and phone my husband.

THERAPIST: Ok that's a great description of your thoughts, physical feelings, and behaviors. Now let's look at the sequence of events. What was the very first thing you noticed?

JULIE: When I stood up, my head started to feel really weird, as if it was spinning inside.

THERAPIST: What was your very next reaction to that feeling?

JULIE: I held onto the chair. I thought something was wrong. I thought it could get worse and that I'd collapse.

THERAPIST: So it began with a physical sensation, and then you had some very specific thoughts about those sensations. What happened next?

JULIE: I felt very anxious.

THERAPIST: And what happened next?

JULIE: Well, the dizziness seemed to be getting worse and worse. I became really concerned that it was different from any other experience I had ever had. I was convinced that this was "it."

THERAPIST: So, as you became more anxious, the physical feelings and the thoughts that something bad was going to happen intensified. What did you do next?

JULIE: I called my husband and lay on the bed until he came home. It was horrible.

THERAPIST: Can you see how one thing fed off another, creating a cycle? That it began with a sensation, then some anxious thoughts, then feeling anxious, then more sensations and more thoughts, and more fear, and so on?

Next, the reasons why panic attacks first began are addressed briefly. Patients are informed that it is not necessary to understand the reasons why they began to panic to benefit from the treatment because factors involved in onset are not necessarily the same as the factors involved in the maintenance of a problem. Nev-

ertheless, the initial panic attack is described as a manifestation of anxiety/stress. The stressors surrounding the time of the first panic attack are explored with the patient, particularly in terms of how stressors may have increased levels of physical arousal and primed certain danger-laden cognitive schemas.

Also, the therapist briefly describes the physiology underlying anxiety and panic, and the myths about what the physical sensations might mean. The main concepts covered in this educational phase are (1) the survival value or protective function of anxiety and panic; (2) the physiological basis to the various sensations experienced during panic and anxiety, and the survival function of the underlying physiology; and (3) the role of specific learned and cognitively mediated fears of certain bodily sensations. The model of panic we described earlier in this chapter is explained. In particular, the concepts of misappraisals and interoceptive conditioning are explained as accounting for panic attacks that seem to occur from out of the blue—that are triggered by very subtle internal cues or physical sensations that may occur at any time. Not only does this information reduce anxiety by decreasing uncertainty about panic attacks but it also enhances the credibility of the subsequent treatment procedures. This information is detailed in a handout given to the patient to read over the next week (for the handout, see Barlow & Craske, 2006).

This information was very important for Julie because the inability to explain her panic attacks was a major source of distress. Here are some of the questions she asked in her attempt to understand more fully:

JULIE: So, if I understand you correctly, you're saying that my panic attacks are the same as the fear I experienced the time we found a burglar in our house. It doesn't feel the same at all.

THERAPIST: Yes, those two emotional states—an unexpected panic attack and fear when confronted with a burglar—are essentially the same. However, in the case of the burglar, where were you focusing your attention—on the burglar or on the way you were feeling?

JULIE: The burglar, of course, although I did notice my heart was going a mile a minute.

THERAPIST: And when you have a panic attack, where are you focusing your attention—on the people around you or on the way you are feeling?



JULIE: Well, mostly on the way I'm feeling, although it depends on where I am at the time.

THERAPIST: Being most concerned about what's going on inside can lead to a very different type of experience than being concerned about the burglar, even though basically the same physiological response is occurring. For example, remember our description of the way fear of sensations can intensify the sensations.

JULIE: I get that. But what about the feelings of unreality? How can they be protective or how can feeling unreal help me deal with a dangerous situation?

THERAPIST: OK, remember that it's the physiological events that are protective—not the sensations. The sensations are just the end result of those events. Now, feelings of unreality can be caused by changes in your blood flow to your brain (although not dangerously so), or from overbreathing, or from concentrating too intensely on what's going on inside you. So the unreality sensation may not be protective, but the changes in blood flow and overbreathing are.

JULIE: I understand how I can create a panic attack by being afraid of my physical feelings, like my heart racing or feeling unreal. But sometimes it happens so quickly that I don't have time to think.

THERAPIST: Yes, these reactions can occur very quickly, at times automatically. But remember, we are tuned to react instantaneously to things that we believe to be dangerous. Imagine yourself walking through a dark alley, and you have reason to believe that somewhere in the darkness lurks a killer. Under those conditions, you would be extremely attentive to any sign, any sound, or any sight of another person. If you were walking through the same alley and were sure there were no killers, you might not hear or detect the same signals you picked up on in the first case. Now let's translate this to panic; the killer in the dark alley is the panic attack, and the signs, sounds, and smells are the physical sensations you think signal the possibility of a panic attack. Given the acute degree of sensitivity to physical symptoms that signal a panic attack, it is likely that you are noticing normal "noises" in your body that you would otherwise not notice, and on occasion, immediately become fearful because of those "noises." In other words, the sensations are often noticeable because you attend to them.

Next, the method of self-monitoring was described and demonstrated with in-session practice of completing a Panic Attack Record. Julie was concerned that self-monitoring would only elevate her distress, by reminding of the very thing she was afraid of (panic and unreality). The therapist clarified the difference between objective and subjective self-monitoring, and explained that distress would subside as Julie persevered with self-monitoring.

The homework for this session was to self-monitor panic attacks, daily anxiety, and mood, and to read the handout. In fact, we encourage patients to reread the handout several times, and to actively engage in the material by circling or marking the most personally relevant sections or areas in need of clarification, because effort enhances long-term retention of the material learned. Of course, for some patients, reading the material draws their attention to things they fear (just as with self-monitoring). In this case, therapists can discuss the role of avoidance, and how, with repeated readings, distress levels will most likely subside.

At the end of the session, Julie suddenly became highly anxious. She felt unable to tolerate either the treatment procedures or her anticipation of them. She became very agitated in the office and reported feelings of unreality. She opened the office door to find her husband, who was waiting outside. The therapist helped Julie understand how the cycle of panic had emerged just at that moment: (1) The trigger was the treatment description—having to face eventually feared sensations and situations; (2) this was anxiety producing because Julie believed that she could not cope with the treatment demands, that the treatment would cause her so much anxiety that she would "flip out" and lose touch with reality permanently, or that she would never improve because she could not tolerate the treatment; (3) the current anxiety in the office elicited sensations of unreality and a racing heart; (4) Julie began to worry that she might panic and lose touch with reality permanently within the next few minutes; (5) the more anxious Julie felt, and the stronger her attempts to escape and find safety, the stronger the physical sensations became; and (6) she felt some relief upon finding her husband because his presence reassured her that she would be safe. Julie was reassured that treatment would progress at a pace with which she was comfortable, but at the same time she was helped to understand that her acute distress about the feeling of unreality would be the precise target of this type of treatment, therefore

attesting to the relevance of this treatment for her. She was also calmed by preliminary cognitive restructuring of the probability of permanently losing touch with reality. After a lengthy discussion, Julie became more receptive to treatment. A team approach to treatment planning and progress was agreed upon, so that Julie did not feel that she would be forced to do things she did not think she could do.

## Session 2

The goals of this session are to begin the development of a hierarchy of agoraphobic situations and coping skills of breathing retraining and cognitive restructuring. The individualized hierarchy comprises situations that range from mild to moderate anxiety, all the way up to extreme anxiety. These situations become the basis of graduated *in vivo* exposure. Although *in vivo* exposure exercises are not scheduled to take place until Session 4, the hierarchy is introduced now, so that cognitive restructuring skills can be practiced in relation to each situation on the hierarchy before *in vivo* exposure begins. Moreover, the hierarchy will be refined as a result of the cognitive restructuring practice because the latter highlights specific features of agoraphobic situations that are most anxiety provoking.

Julie was asked to develop a hierarchy over the following week. She expressed some doubt that she would ever be able to accomplish any, let alone all, of the items on her hierarchy. The therapist helped Julie by asking her to think of any situation in her lifetime that used to be difficult but became easier with practice. Julie remembered how anxious she used to be when she first started working with customers at her husband's office—and how that discomfort subsided over time. This was used to help Julie realize that the same might happen with the situations listed on her hierarchy. Julie's final hierarchy comprised the following situations: driving home from work alone; sitting in a crowded movie theater; spending 2 hours alone at home during the day; being alone at home as day turned to night; driving on surface streets to her brother's house (10 miles) alone; driving two exits on Freeway 444, with her husband following in the car behind; driving two exits on Freeway 444, alone; driving four exits on Freeway 444; and driving on the freeway to her brother's house alone. Then, Julie was to repeat all of these tasks without taking Klonopin, and without knowing the location of her husband.

Breathing retraining also is begun in this session. Patients are asked to hyperventilate voluntarily by standing and breathing fast and deep, as if blowing up a balloon, for 1½ minutes. With prompting and encouragement from the therapist, patients can often complete the full 1½ minutes, after which time they are asked to sit, close their eyes, and breathe very slowly, pausing at the end of each breath, until the symptoms have abated. The experience is then discussed in terms of the degree to which it produced symptoms similar to those that occur naturally during anxiety or panic. Approximately 50–60% of patients report that the symptoms of hyperventilation are very similar to their panic attack symptoms. Often, however, similarity of the symptoms is confused with similarity of the anxiety. Because the exercise is conducted in a safe environment and the symptoms have an obvious cause, most patients rate the experience as less anxiety provoking than if the same symptoms had occurred naturally. This distinction is important to make because it demonstrates the significance of perceived safety for the degree of anxiety experienced. Julie rated the hyperventilation exercise as very anxiety provoking (8 on a 0- to 10-point scale), and rated the symptoms as being quite similar to her panic symptoms (6 on a 0- to 10-point scale). She terminated the task after approximately 40 seconds, in anticipation of experiencing a full-blown panic attack. The therapist and Julie discussed this experience in terms of the three response systems, and the role of misappraisals and interoceptive conditioning described during the previous session.

Then, Julie was briefly educated about the physiological basis to hyperventilation (see Barlow & Craske, 2006). As before, the goal of the didactic presentation was to allay misinterpretations of the dangers of overbreathing, and to provide a factual information base on which to draw when actively challenging misinterpretations. The educational content is tailored to the patient's own educational level and covered only to the degree that it is relevant to the patient.

In the next step, the therapist teaches breathing retraining, which begins by teaching patients to rely more on the diaphragm (abdomen) than on chest muscles. In addition, patients are instructed to concentrate on their breathing by counting on their inhalations and thinking the word "relax" on exhalations. (Slow breathing is introduced in Session 3.) Therapists model the suggested breathing patterns, then provide corrective feedback to patients while they practice in the office setting.

(Note that CART uses a different method of breathing retraining that is based on raising levels of CO<sub>2</sub> in the blood through biofeedback.)

Initial reactions to the breathing exercise may be negative for patients who are afraid of respiratory sensations because the exercise directs their attention to breathing. It also can be difficult for patients who are chronic overbreathers, and patients for whom any interruption of habitual breathing patterns initially increases respiratory symptomatology. In both cases, continued practice is advisable, with reassurance that sensations such as shortness of breath are not harmful. The goal is to use breathing skills training to encourage continued approach toward anxiety and anxiety-producing situations. On occasion, patients mistakenly view breathing retraining as a way of relieving themselves of terrifying symptoms, thus falling into the trap of fearing dire consequences should they not succeed in correcting their breathing. This is what happened for Julie:

JULIE: So, all I have to do is to slow down my breathing, then everything will be OK?

THERAPIST: Certainly, slowing down your breathing will help to decrease the physical symptoms that you feel, but I am not sure what you mean when you ask whether everything will be OK.

JULIE: That proper breathing will prevent me from losing touch with reality—that I won't disappear.

THERAPIST: Breathing retraining will help you to regulate your breathing, which may lessen your physical symptoms, including the sense of unreality. Your question, though, is the reason for our next treatment skill of changing your thinking, so you can learn that the sense of unreality is not a sign of actual loss of touch with reality and disappearance.

The homework is to practice diaphragmatic breathing for at least 10 minutes, two times a day in relaxing environments.

Therapists introduce in this session cognitive restructuring, by explaining that everyone has errors in thinking when anxious, thus helping the patient to expect his or her thinking to be distorted. Patients are informed that these distortions have an adaptive function: Chances of survival are greater if we perceive danger as probable and worthy of attention rather than minimize it. Therefore, anxiety leads us to judge threatening events as being more likely and more threatening

than they really are. However, the cognitive distortions are unnecessary because there is no real threat in the case of panic disorder.

Then, patients are taught to treat their thoughts as hypotheses or guesses rather than as facts. The notions of automatic thinking and discrete predictions are also explained, to emphasize the need to become an astute observer of one's own habitual self-statements in each situation. This leads to a "downward arrow technique" to identify specific predictions made at any given moment, as shown with Julie.

THERAPIST: What is it that scared you about feeling detached in the movie theater last night?

JULIE: It is just such a horrible feeling.

THERAPIST: What makes it so horrible?

JULIE: I can't tolerate it.

THERAPIST: What makes you think you cannot tolerate it? What is the feeling of detachment going to do to you that makes you think it is horrible and intolerable?

JULIE: It might become so intense that it overwhelms me.

THERAPIST: And if it overwhelms you, what would happen?

JULIE: I could become so distressed that I lose touch with reality.

THERAPIST: What would it mean if you lost touch with reality?

JULIE: That I would be in a different mind state forever—I would never come back to reality. That I would be so crazy that I would have to be carted out of the movie theater to a mental hospital and locked away forever.

Overly general self-statements, such as "I feel terrible—something bad could happen," are insufficient, nontherapeutic, and may serve to intensify anxiety by virtue of their global and nondirective nature. Instead, detail in thought content, such as "I am afraid that if I get too anxious while driving, then I'll lose control of the wheel and drive off the side of the road and die," permits subsequent cognitive restructuring.

Analysis of anxious thought content yields two broad factors that are labeled as "risk" and "valence." These two main types of cognitive errors are described to pa-

tients. Risk translates to overestimation, or jumping to conclusions by viewing negative events as being probable events, when in fact they are unlikely to occur. The patient is asked to identify overestimations from the anxiety and panic incidents over the past couple of weeks: “Can you think of events that you felt sure were going to happen when you panicked, only to find out in the end that they did not happen at all?” Usually, patients can identify such events easily, but with protestations. For example,

JULIE: Well, several times I thought that I really was going to lose it this time . . . that I would flip out and never return to reality. It never actually happened, *but* it could still happen.

THERAPIST: Why do you think “it” could still happen?

JULIE: Part of me feels like I’ve always managed to escape it just in time, by either removing myself from the situation or by having my husband help me, or by holding on long enough for the feeling to pass. But what if I can’t hold on the next time?

THERAPIST: Knowing what we know about our thoughts when we are anxious, can you classify any of the ideas you just expressed, of “just holding on” or “just escaping in time,” as overestimations?

JULIE: I suppose you’re saying that I can hold on or I can always escape in time.

THERAPIST: More that you feel the need to hold on and the need to escape because you are overestimating the likelihood of flipping out and never returning to reality.

JULIE: But it really feels like I will.

THERAPIST: The confusion between what you think will happen and what actually happens is the very problem that we are addressing in this session.

The reasons why overestimations persist despite repeated disconfirmation are explored. Typically, patients misattribute the absence of danger to external safety signals or safety behaviors (e.g., “I only made it because I managed to find help in time,” “If I had not taken Xanax last week when I panicked in the store, I’m sure I would have passed out,” or “I wouldn’t have made it if I hadn’t pulled off the road in time”), or to “luck,” instead of realizing the inaccuracy of the original prediction. Similarly, patients may assume that the only reason they are still alive, sane, and safe is because the “big one” has not happened. In this case, patients err by

assuming that intensity of panic attacks increases the risk of catastrophic outcomes.

The method for countering overestimation errors is to question the evidence for probability judgments. The general format is to treat thoughts as hypotheses or guesses rather than as facts, and to examine the evidence and generate alternative, more realistic predictions. This is best done by the therapist using a Socratic style, so that patients learn the skill of examining the content of their statements and arrive at alternative statements or predictions after they have considered all of the evidence. Questioning of the logic (e.g., “How does a racing heart lead to heart attack?”), or the bases from which judgments are made (e.g., misinformation from others, unusual sensations) is useful in this regard. Continuing with the previous example from Julie, the questioning took the following course:

THERAPIST: One of the specific thoughts you have identified is that you will flip out and never return to reality. What specifically leads you to think that that is likely to happen?

JULIE: Well, I guess it really feels like that.

THERAPIST: Describe the feelings?

JULIE: Well, I feel spacey and unreal, like things around me are different and that I’m not connected.

THERAPIST: And why do you think those feelings mean that you have actually lost touch with reality?

JULIE: I don’t know—it feels as if I have.

THERAPIST: So, let’s examine that assumption. What is your behavior like when you feel unreal? For example, do you respond if someone asks you a question during those episodes?

JULIE: Well, I respond to you even though I feel that way sometimes in here.

THERAPIST: OK, and can you walk or write or drive when you feel that way?

JULIE: Yes, but it feels different.

THERAPIST: But you do perform those functions despite feeling detached. So, what does that tell you?

JULIE: Well, maybe I haven’t lost complete touch with reality. But what if I do?

THERAPIST: How many times have you felt detached?

JULIE: Hundreds and hundreds of times.

THERAPIST: And how many times have you lost touch with reality permanently?



JULIE: Never. But what if the feelings don't go away? Maybe I'll lose it then?

THERAPIST: So what else tells you that this is a possibility?

JULIE: Well, what about my second cousin? He lost it when he was about 25, and now he's just a mess. He can hardly function at all, and he is constantly in and out of psychiatric hospitals. They have him on a bunch of heavy-duty drugs. I'll never forget the time I saw him totally out of it. He was talking to himself in jibberish.

THERAPIST: So, do you make a connection between him and yourself?

JULIE: Yes.

THERAPIST: What are the similarities between the two of you?

JULIE: There are none really. It's just that he *is* what I think I will become.

THERAPIST: Did he ever feel the way you feel now?

JULIE: I don't know.

THERAPIST: And if another one of your cousins had severe back problems, would you be concerned that you would end up with severe back problems?

JULIE: No.

THERAPIST: Why not?

JULIE: Because it never crosses my mind. It is not something that I worry about.

THERAPIST: So, it sounds like you think you will end up like your cousin because you are afraid of ending up like him.

JULIE: I suppose so.

THERAPIST: So, let's look at all of the evidence and consider some alternatives. You have felt unreal hundreds of times, and you've never lost touch with reality because you've continued to function in the midst of those feelings, and they have never lasted. You are afraid of becoming like your cousin, but there are no data to show that you and he have the same problem. In fact, the data suggest otherwise because you function and he does not. So what is the realistic probability that you will lose touch with reality permanently? Use a scale of 0 to 100, where 0 = *No chance at all* and 100 = *Definitely will happen*.

JULIE: Well, maybe it is lower than I thought. Maybe 20%.

THERAPIST: So that would mean that you have actually lost touch with reality in a permanent way once every five times you have felt unreal.

JULIE: When it's put like that, I guess not. Maybe it's a very small possibility.

THERAPIST: Yes, so what is an alternative explanation?

JULIE: Perhaps the feelings of unreality are caused by feeling anxious or overbreathing, and having those feelings does not mean that I am actually losing touch with reality, and that I am not like my cousin at all.

For homework, in addition to continuation of self-monitoring and practice of diaphragmatic breathing, Julie was asked to identify her anxious thoughts in relation to every item on her agoraphobia hierarchy, and to use the in-session steps of examining the evidence and generating alternative evidence based interpretations for errors of overestimating the risk. She was to do the same for every panic attack that occurred over the next week.

### Session 3

The goals of this session are to develop breathing retraining and to continue active cognitive restructuring. The therapist reviews the patient's week of diaphragmatic breathing practice. Julie was disappointed with her attempts to practice.

JULIE: I just didn't seem to be able to do it the right way. Sometimes I would start off OK and then the more I tried, the more it felt like I was running out of air, and I'd have to take a big gulp between breaths. At other times, I felt dizzy and the unreal feelings would start, at which point I would stop and do "busy work" to keep my mind occupied.

THERAPIST: It sounds like quite a few things were going on. First of all, remember that this is a skill, just like learning to ride a bike, and you cannot expect it to be easy from the get-go. Second, it sounds like you experienced some uncomfortable physical symptoms that worried you. You said it felt like you were running out of air. Based on what we talked about last week, what do you think might have caused that feeling?

JULIE: Well, maybe I wasn't getting enough air into my

lungs because it's really hard for me to use my diaphragm muscle. I felt like I was suffocating myself.

THERAPIST: Possibly it's just a matter of learning to use the diaphragm muscle, but were you really suffocating or was it an interpretation that you might be suffocating?

JULIE: I don't know. I've had the feeling of suffocating before, especially when I'm trapped in a crowded room.

THERAPIST: So, how do you know you were suffocating?

JULIE: I don't know. It just felt that way.

THERAPIST: So, let's put the evidence together. You've had the feelings before and never suffocated. As we discussed last time, anxiety can sometimes create a sensation of shortness of breath even though you are getting plenty of air. Can you think of an alternative explanation?

JULIE: Well, maybe I wasn't suffocating. Maybe it just felt like that.

Julie's complaints represent typical concerns that should be addressed. The next step is to slow the rate of breathing until the patient can comfortably span a full inhalation and exhalation cycle of 6 seconds. Again, the therapist models slowed breathing, then provides corrective feedback on practice in the session. The patient is instructed to continue to practice slow breathing in "safe" or relaxing environments, and is discouraged from applying slow breathing when anxious or panicking, until fully skilled in its application.

Also, cognitive restructuring is continued by addressing the second cognitive error, which involves viewing an event as "dangerous," "insufferable," or "catastrophic." Typical examples of catastrophic errors are "If I faint, people will think that I'm weak, and that would be unbearable" or "Panic attacks are the worst thing I can imagine," and "The whole evening is ruined if I start to feel anxious." "Decatastrophizing" means to face the worst, to realize that the occurrences are not as "catastrophic" as stated, and to think about actual ways to cope with negative events rather than how "bad" they are. A key principle underlying decatastrophizing is that events can be endured even though they are uncomfortable. Recognition of the time-limited nature of discomfort contributes to the development of a sense of being able to cope. The critical distinction here is that although patients might prefer that these events not

occur, they can tolerate the discomfort, if necessary. Thus, for the person who states that negative judgments from others are unbearable, it is important to discuss what he or she would do to cope should someone else make a direct negative judgment. Similarly, for the person who states that the physical symptoms of panic are intolerably embarrassing, the following type of questioning is helpful:

JULIE: I am really worried that I might lose control and do something crazy, like yell and scream.

THERAPIST: Let's face the worst and find out what is so bad about it. What would be so horrible about yelling and screaming?

JULIE: I could never live it down.

THERAPIST: Well, let's think it through. What are the various things you could do in the situation? You have just yelled and screamed—now what?

JULIE: Well, I guess the yelling and screaming would eventually stop.

THERAPIST: That's right—at the very least you would eventually exhaust yourself. What else?

JULIE: Well, maybe I would explain to the people around me that I was having a really bad day but that I would be OK. In other words, reassure them.

THERAPIST: Good. What else?

JULIE: Maybe I would just get away—find someplace to calm down and reassure myself that the worst is over.

THERAPIST: Good.

JULIE: But what if the police came and took me away, locked me up in a mental ward?

THERAPIST: Again, let's face the worst. What if the police did come when you were yelling and screaming, and what if the police did take you away? As scary as that may sound to you, let's consider what actually would happen.

JULIE: I have this image of myself not being able to tell them what is really going on—that I am so out of it I don't have the ability to let them know I am just anxious.

THERAPIST: If you were so distraught that you could not clearly communicate, how long would that last?

JULIE: You're right. I would eventually exhaust myself and then I could speak more clearly. But what if they didn't believe me?

THERAPIST: What if they did not believe you at first? How long would it take before they would realize that you were not crazy?

JULIE: I guess that after a while they would see that I was OK, and maybe I could call a friend or my doctor to explain what was going on.

The homework for this session, in addition to continued self-monitoring, is to practice slow and diaphragmatic breathing in relaxing environments, and to identify errors of catastrophizing in relation to each item on the agoraphobia hierarchy, followed by practice of decatastrophizing and generation of ways to cope. In addition, Julie was to use the skill of decatastrophizing for panic attacks that occurred over the following week.

#### Session 4

The main goal of this session is to use breathing retraining skills as a coping tool, to review cognitive restructuring skills, and to begin *in vivo* exposure to the first item on the agoraphobia hierarchy.

Now that patients have practiced slow and diaphragmatic breathing sufficiently in relaxing environments, they are ready to use these methods in distracting environments and in anxious situations. Patients are encouraged to use breathing skills as a coping technique as they face fear, anxiety, and anxiety-provoking situations. Some patients use breathing skills as a safety signal or a safety behavior; in other words, they believe that they will be at risk for some mental, physical, or social calamity if they do not breathe correctly. This issue came up with Julie:

JULIE: When I panicked during the week, I tried to use the breathing. It didn't work. It made me feel worse.

THERAPIST: It sounds as if you might have attempted to use the breathing exercise as a desperate attempt to control the feelings you were experiencing.

JULIE: Yes, that's right.

THERAPIST: What did you think would have happened if you had not been able to control the feelings?

JULIE: I was really worried that I might not be able to handle the feelings.

THERAPIST: And if you weren't able to handle the feelings, what would happen?

JULIE: It just feels like I will lose it, permanently.

THERAPIST: So this is one of those thoughts that we were talking about last time. What does your evidence tell you about the likelihood of losing touch with reality permanently?

JULIE: So you mean even if I don't control my breathing, then I will be OK?

THERAPIST: Well, you had not lost touch with reality permanently before you learned the breathing exercise, so what does that tell you?

JULIE: OK, I get it.

THERAPIST: The breathing exercise is best thought of as a tool to help you face whatever is provoking anxiety. So, as you face situations and your anxiety increases, use the breathing exercise to help you to face rather than run away from anxiety.

Patients who consistently use the breathing skills as a safety behavior might be discouraged from using the breathing skills because they learn that what they are most worried about either does not happen or it can be managed without using the breathing skills.

In terms of the cognitive restructuring, therapists give corrective feedback to patients on the methods of questioning the evidence to generate realistic probabilities, facing the worst, and generating ways to cope with each item on the agoraphobia hierarchy and any panic attacks that occurred over the past week. Particular "corrective" feedback is given when patients lack specificity in their cognitive restructuring (e.g., patients who record that they are most worried about panicking should be encouraged to detail what it is about panicking that worries them) or rely on blanket reassurance (e.g., patients who record that "Everything will be OK" as their evidence and/or ways of coping should be encouraged to list the evidence and/or generate actual coping steps).

Next, attention is given to how to practice the first item on the agoraphobia hierarchy. If appropriate, reasons why previous attempts at *in vivo* exposure may have failed are reviewed. Typical reasons for patients' past failures at *in vivo* exposure include attempts that are too haphazard and/or brief, or spaced too far apart, and attempts conducted without a sense of mastery, or while maintaining beliefs that catastrophe is very possible. Julie had tried to face agoraphobic situations in the past, but each time she had escaped, feeling overwhelmed by panic and terrified of losing touch with reality permanently. The therapist helped Julie realize

how to approach the agoraphobic situations differently to benefit from the exposure. Julie's typical safety signals were the presence of her husband, or at least knowing his whereabouts, and Klonopin (which she carried but rarely used). The therapist discussed the importance of eventual weaning from those safety signals.

As mentioned earlier, the goal of exposure therapy is not immediate reduction in fear and anxiety; rather, the goal is for the patient to learn something new as a result of exposure. Clarification of what patients are most worried about as they face their feared situations and the conditions that best help them to learn that what worries them most never or rarely happens, and/or that they can cope with the situation and tolerate anxiety, is essential for effective exposure. If a patient is most worried that fear and anxiety will remain elevated for the duration of the practice, then corrective learning involves toleration of sustained anxiety. For Julie, the first situation on her hierarchy was to drive home from work, alone. She stated that what most worried her in that situation was that she would panic and lose touch with reality, and as a result, lose control of the car and die in an accident. She also stated that to drive at dusk was the condition under which she was most convinced of these eventualities. Thus, the task that the therapist considered most effective in teaching Julie that she would not lose touch with reality, or that she could cope with the sensations of unreality and panic, was to drive home from work at dusk.

Delineate the exposure task as concretely as possible, so that patients clearly understand exactly what the practice entails (e.g., "Walk around inside of mall for 10 minutes by myself"). Importantly, the practice should not be ended because of anxiety (e.g., "Continue driving on the freeway until I feel anxious") because the exposure practice would then reinforce avoidance of anxiety.

Julie was reminded to use her coping skills should she panic as she practiced the task; that is, in moments of fear, patients are encouraged to use their breathing and thinking skills to complete the assigned task; the coping skills are not intended as means to reduce fear and anxiety, but to tolerate it. Acceptance and nonjudgmental observation of physical sensations and thoughts can be another strategy to use in the midst of exposure therapy.

Patients are encouraged to maintain a regular schedule of repeated *in vivo* exposure practices at least three times per week, and to conduct these practices regardless of internal (e.g., having a "bad day," feeling ill) or

external (e.g., inclement weather, busy schedules) factors that may prompt postponement of practices. Julie expressed some concerns about being able to practice at least three times over the following week:

JULIE: I don't know if I can practice three times because more days than not I feel pretty worn down; maybe I can practice on just Monday and Tuesday because they are the days I typically feel better.

THERAPIST: What is it you are worried about happening if you practice on a day when you already feel worn down?

JULIE: I feel more fragile on those days.

THERAPIST: And if you feel more fragile, what might happen?

JULIE: I just don't think I could do it. It would be too hard. I might really freak out and lose touch with reality for ever.

THERAPIST: OK, so let's think about that thought. What does your experience tell you? How many times have you permanently lost touch with reality, including days when you were worn down?

JULIE: Well, never.

THERAPIST: So, what does that tell you?

JULIE: OK, but it still feels difficult to drive on those days.

THERAPIST: How about you start with Monday or Tuesday, but quickly move to the other days of the week when you are feeling worn down, so that you get a really good opportunity to learn whether you permanently lose touch with reality or not?

Julie's homework for this session involves continued self-monitoring, continued use of cognitive restructuring and breathing retraining in the event of elevated anxiety or panic, and practicing the first item on the agoraphobia hierarchy at least three times, with at least one of those times being without her husband Larry.

### Session 5

The goals of this session are to review the practice of *in vivo* exposure, to design another exposure task to be practiced over the next week, and to begin interoceptive exposure. Note that *in vivo* and interoceptive exposure can be done simultaneously or sequentially. For Julie, *in vivo* exposure was begun in Session 4, whereas in-



teroceptive exposure was begun in this session, but they could easily have been done in the opposite order.

It is essential to review the week's practice of *in vivo* exposure. An objective evaluation of performance is considered necessary to offset subjective and damaging self-evaluations. As demonstrated in experimental literature on learning and conditioning, appraisals of aversive events after they have occurred can influence anxiety about future encounters with the same types of aversive events. Any practice that is terminated prematurely is to be reviewed carefully for contributing factors that can then be incorporated into subsequent trials of *in vivo* exposure. Recognition of the precipitant to escape is very important because the urge to escape is usually based on the prediction that continued endurance would result in some kind of danger. For example, patients may predict that the sensations will become intense and lead to an out-of-control reaction. This prediction can be discussed in terms of jumping to conclusions and blowing things out of proportion. At the same time, escape itself need not be viewed catastrophically (i.e., as embarrassing, or as a sign of failure). In addition, therapists reinforce the use of breathing and cognitive skills (or acceptance skills) to help patients remain in the situation until the specified duration or task has been completed, despite uncomfortable sensations.

Again, it is important for patients to recognize that the goal is repeatedly to face situations despite anxiety, not to achieve a total absence of anxiety. Tolerant of fear rather than immediate fear reduction is the goal for each exposure practice; this approach leads to an eventual fear reduction over time. Anxiety that does not decline over repeated days of *in vivo* exposure may result from too much emphasis on immediate fear and anxiety reduction; that is, trying too hard or wishing too much for anxiety to decline typically maintains anxiety.

Julie had success with her first *in vivo* exposure practice; she managed to drive home from work at dusk, alone, four different times. She noted that the first time was easier than she had expected; the second was harder, and the one time she pulled off to the side of the road. The therapist helped Julie identify the thoughts and sensations that led her to "escape" from the situation: the sensations of unreality and fears of losing touch with reality. Julie had waited for a few minutes, then continued driving home—an action that was highly reinforced by the therapist. The third and fourth times were easier.

Julie's husband, Larry, attended Session 5, so that he could learn how to help Julie overcome her panic and agoraphobia. He was supportive and eager to help in any way possible, expressing frustration at having had no idea how to help in the past.

There are general principles for involvement of significant others in treatment. First, a treatment conceptualization is provided to the significant other to reduce his or her frustration and/or negative attributions about the patient's emotional functioning (e.g., "Oh, she's just making it up. There's nothing really wrong with her" or "He has been like this since before we were married, and he'll never change"). The way in which the agoraphobic problem has disrupted daily routines and distribution of home responsibilities is explored and discussed also. Examples might include social activities, leisure activities, and household chores. The therapist explains that family activities may be structured around the agoraphobic fear and avoidance to help the patient function without intense anxiety. At the same time, reassignment of the patient's tasks to the significant other may actually reinforce the agoraphobic pattern of behavior. Consequently, the importance of complying with *in vivo* exposure homework instructions, even though the patient may experience some distress initially, is emphasized.

The significant other is encouraged to become an active participant by providing his or her perception of the patient's behavior and fearfulness, and the impact on the home environment. Sometimes the significant other provides information of which the patient is not fully aware, or did not report, particularly in relation to how the patient's behavior affects his or her own daily functioning. Larry, for example, described how he felt restricted at home in the evenings; whereas, before, he occasionally played basketball with his friends at the local gym, he now stays at home because he feels guilty if he leaves Julie alone.

The next step is to describe the role of the significant other regarding *in vivo* exposure tasks. The significant other is viewed as a coach, and the couple is encouraged to approach the tasks as a problem-solving team. This includes deciding exactly where and when to practice *in vivo* exposure. In preparation for practices, the patient identifies his or her misappraisals about the task and generates cognitive alternatives. The significant other is encouraged to help the patient question his or her own "anxious" thoughts. Role plays of this type of questioning of the patient by the significant other may be conducted in the session, so that the

therapist can provide corrective feedback to each partner. Throughout *in vivo* exposure, the significant other reminds the patient to apply coping skills, whether it be cognitive challenges, breathing skills, or acceptance skills. Because the significant other is usually a safety signal, tasks are less anxiety provoking. However, the patient must be weaned from the safety signal eventually. Therefore, initial attempts at facing agoraphobic situations are conducted with the significant other, and later trials are conducted alone. Weaning from the significant other may be graduated, as in the case of Julie (1) driving first with Larry in the car, (2) with him in a car behind, (3) meeting him at a destination point, and (4) driving alone.

Very important to the success of this collaboration is style of communication. On the one hand, the significant other is discouraged from magnifying the experience of panic and encouraged to help the patient apply coping statements when anxious. On the other hand, the significant other is encouraged to be patient given the fact that progress for the patient may be erratic. The patient and the significant other are instructed to use a 0- to 10-point rating scale to communicate with each other about the patient's current level of anxiety or distress, as a way of diminishing the awkwardness associated with discussion of anxiety, especially in public situations. The patient is warned about the potential motivation to avoid discussing his or her feelings with the significant other, due to embarrassment or an attempt to avoid the anxiety for fear that such discussion and concentration on anxiety may intensify his or her distress level. Avoidance of feelings is discouraged because distraction is viewed as less beneficial in the long term than objectively facing whatever is distressing and learning that predicted catastrophes do not occur. The patient is reassured that the initial discomfort and embarrassment will most likely diminish as the partners become more familiar with discussing anxiety levels and their management. Furthermore, the patient's concerns about the significant other being insensitive or too pushy are addressed. For example, a significant other may presume to know the patient's level of anxiety and anxious thoughts without confirmation from the patient, or the significant other may become angry at the patient for avoiding or escaping from situations, or being fearful. All of these issues are described as relatively common and understandable patterns of communication that are nevertheless in need of correction. In-session role playing of more adaptive communication styles during episodes of heightened anxiety is a

useful learning technique. On occasion, more specific communications training may be beneficial, especially if the partners frequently argue in their attempts to generate items or methods for conducting *in vivo* exposure.

The next *in vivo* exposure task for Julie was to sit in a crowded movie theater, gradually moving away from the aisle, toward the middle of the row, because that was the condition in which she was most concerned that she would lose control and draw attention to herself. Julie and Larry rehearsed their approach to the *in vivo* exposure task in session, while the therapist provided corrective feedback using the principles of communication and coping described earlier. They were instructed to practice this task at least three times over the next week. On at least one occasion, Julie was to practice the task alone.

Next, interoceptive exposure was introduced. As with *in vivo* exposure, through repeated exposures to feared sensations, patients learn that they are not harmed by the sensations, and they achieve increased confidence in their ability to tolerate symptoms of anxiety. The procedure begins with assessment of the patient's response to a series of standardized exercises. The therapist models each exercise first. Then, after the patient has completed the exercise, the therapist records the sensations, anxiety level (0 to 10), sensation intensity (0 to 10), and similarity to naturally occurring panic sensations (0 to 10). The exercises include shaking the head from side to side for 30 seconds; placing the head between the legs for 30 seconds and lifting the head to an upright position quickly; running in place or using steps for 1 minute; holding one's breath for as long as possible; complete body muscle tension for 1 minute or holding a push-up position for as long as possible; spinning in a swivel chair for 1 minute; hyperventilating for 1 minute; breathing through a narrow straw (with closed nasal passages) or breathing as slowly as possible for 2 minutes; and staring at a spot on the wall or at one's mirror image for 90 seconds. If none of these exercises produce sensations at least moderately similar to those that occur naturally, other, individually tailored exercises are generated. For example, tightness around the chest may be induced by a deep breath before hyperventilating; heat may be induced by wearing heavy clothing in a heated room; choking sensations may be induced by a tongue depressor, a high-collared sweater, or a necktie; and startle may be induced by an abrupt, loud noise in the midst of relaxation. For Julie, the sensations produced by hyperventilating, spinning, and staring at a spot on the wall were most anxiety provoking.

Patients who report little or no fear because they feel safe in the presence of the therapist are asked to attempt each exercise alone, either at home or with the therapist out of the office. At the same time, discussing the influence of perceived safety as a moderating factor in the amount of fear experienced reinforces the value of cognitive restructuring. For a minority of patients, the known cause and course of the sensations override the fear response; that is, because the sensations are predictably related to a clear cause (the interoceptive exercise), and because the sensations can be relatively easily controlled by simply terminating the interoceptive exercise, fear is minimal. Under these conditions, discussion can productively center on the misassumptions that render naturally occurring sensations more frightening than the ones produced by the interoceptive exercises. Typically, these misassumptions are that naturally occurring sensations are unpredictable; that unpredictable sensations are more harmful; and that if naturally occurring sensations are not controlled, then they pose a potential threat. The majority of patients fear at least several of the interoceptive exercises despite knowing the cause of the sensations and their controllability.

Interoceptive exercises rated as producing at least somewhat similar sensations to naturally occurring panic (at least 3 on the 0- to 10-point scale) are selected for repeated exposure. A graduated approach is used for interoceptive exposure, beginning with the lowest item on the hierarchy established in Session 4. For each trial of exposure, the patient is asked to begin the induction, to indicate when the sensations are first experienced (e.g., by raising a hand), and to continue the induction for at least 30 seconds longer to permit corrective learning. After terminating the induction, anxiety is rated, and the patient is given time to apply cognitive and breathing coping skills. Finally, the therapist reviews the induction experience and the application of management strategies with the patient. During this review, the therapist emphasizes the importance of experiencing the sensations fully during the induction, of concentrating objectively on the sensations versus distracting from them, and the importance of identifying specific cognitions and challenging them by considering all of the evidence. In addition, the therapist asks key questions to help the patient realize his or her safety (e.g., "What would have happened if you had continued spinning for another 60 seconds?"), and to generalize to naturally occurring experiences (e.g., "How is this different from when you feel dizzy at work?"). In other

words, cognitive restructuring extends the cognitive reprocessing already taking place implicitly as a result of repeated interoceptive exposure.

Specific, previously unrecognized cognitions sometimes become apparent during repeated exposure. For example, when Julie began to conduct repeated exposures to hyperventilation and spinning, she became more aware of her implicit assumption that sensations of spaciness or lightheadedness would lead her to lose control of her limbs. This related to her concern about causing an accident when driving. During repeated hyperventilation exercises, and with prompting of "what ifs" from the therapist, Julie discovered her fear of not being able to move her arms or legs. The therapist then behaviorally challenged this assumption by having Julie overbreathe for longer periods of time, followed immediately by walking, picking up objects, and so on.

Homework practice is very important because safety signals present in the clinic setting or that derive from the therapist per se may, again, prevent generalizability to the natural setting. Patients are instructed to practice the interoceptive items conducted in session on a daily basis, three times each day. Julie was to practice hyperventilation over the following week. She expressed some concern at doing the exercises alone, so the therapist helped Julie to use her cognitive restructuring skills in relation to being alone. In addition, more graduation of homework was suggested, so that Julie would practice hyperventilating when her husband was at home the first couple of days, then when he was not at home the rest of the time.

### **Sessions 6 and 7**

The primary goal of these sessions is to review the past week of *in vivo* exposure practices, design new exposures, review between-session practices of interoceptive exposure, conduct repeated interoceptive exposure in session, and assign those as homework for the next week.

The *in vivo* exposure is reviewed, as in the previous session. In this case, Julie and Larry had done well with the movie theater practice. Julie even practiced going to the movies on her own. On that occasion she reported higher anxiety than when she was with Larry for fear of having to get up and leave the theater and worries about bothering others in the audience. The therapist helped Julie to identify what worry led her to think about leaving in the first place; in other words, what did she think might happen if she could not leave? When

Julie indicated that she had thoughts of losing control and causing a scene, she was then prompted to apply her cognitive restructuring skills of evidence-based analyses and decatastrophizing. She was ready to move to the next items on her hierarchy: to spend 2 hours alone at home during the day and to stay alone at home as day turned to night. As with every *in vivo* exposure task, Julie identified what she most feared happening in those situations, and the best practice conditions under which to learn that either those eventualities would not happen and/or she could cope with the worst.

The past week of interoceptive exposure practice is reviewed in session with a mind toward avoidance: either overt failure to practice or covert avoidance by minimizing the intensity or duration of the sensations induced, or by limiting practice to the presence of a safety signal (e.g., a significant other) or times when background anxiety is minimal. Reasons for avoidance may include continued misinterpretation of the dangers of bodily sensations (i.e., “I don’t want to hyperventilate because I’m afraid that I won’t be able to stop overbreathing and no one will be there to help me”) or the belief that anxiety will not reduce with repetition of the task.

For the first week, Julie practiced interoceptive exposure exercises about half of the days between sessions. The therapist used a “downward arrow” method to explore Julie’s reasons for not practicing every day.

JULIE: I tried hyperventilating on my own. However, I wasn’t very successful because I felt too scared and I stopped it as soon as I noticed the strange feelings.

THERAPIST: What did you think would happen if the sensations became more intense?

JULIE: I thought the feelings would get worse and worse and worse, and just overwhelm me. I didn’t want to have that feeling of panic again.

THERAPIST: If you did become overwhelmed, then what would happen to you?

JULIE: Then I’d feel really terrible.

THERAPIST: And if you felt really terrible?

JULIE: Well, nothing. I’d just feel terrible.

THERAPIST: The word “terrible” carries a lot of meaning. Let’s see if we can pin down your anxious thoughts that make the feelings so terrible.

JULIE: I just can’t tolerate the feeling.

THERAPIST: What tells you that you cannot tolerate it? How do you know you can’t tolerate it?

And the discussion continued, so that Julie realized what was most important for her to learn by the repeated hyperventilation: She could tolerate the sensations and anxiety. However, after the subsequent week of repeated practice, Julie remained cautious for fear that the exercises would cause her to revert to her state of several weeks earlier; that is, she was concerned that the inductions would leave her in a persistent symptomatic state. Furthermore, she was particularly reluctant to practice interoceptive exposure at the end of the day, when she was more likely to feel unreal, or on a day when an important social event was scheduled. Again, these avoidance patterns were related to fears that the symptoms would become too intense or result in some type of mental or social catastrophe. These types of avoidance patterns are addressed in the following vignette:

THERAPIST: When did you practice deliberately spinning and hyperventilating?

JULIE: Usually in the mornings. One day I left it until the end of the day, and that turned out to be a bad idea. I felt terrible.

THERAPIST: Let’s think about that a bit more. What made it terrible when you practiced at the end of the day?

JULIE: Well, I was already feeling pretty unreal—I usually do around that time of the day. So I was much more anxious about the symptoms.

THERAPIST: Being more anxious implies that you thought the symptoms were more harmful. Is that what happened on the day that you practiced interoceptive exposure when you were already feeling unreal?

JULIE: Yes, I felt that because I was already feeling unreal, I was on the edge, and that I might push myself over the edge if I tried to increase the feelings of unreality.

THERAPIST: What do you mean by “push myself over the edge”?

JULIE: That I would make the feelings so intense that I really would lose it—go crazy.

THERAPIST: So there is one of those hypotheses: to feel more intense unreality means to be closer to going crazy. Let’s examine the evidence. Is it necessarily the case that more intense unreality means you are closer to craziness?



In sessions, the therapist continued practice of interoceptive exposure with the next item on Julie's hierarchy, which was to stare at a spot on the wall and to spin around.

The homework from this session is to continue self-monitoring, *in vivo* exposure to an item from the agoraphobia hierarchy at least three times, and daily practice of interoceptive exposure.

### Sessions 8 and 9

The primary goals of these sessions are to continue *in vivo* exposure, as described in the prior sessions, and to extend interoceptive exposure to natural activities. Julie had practiced staying at home for 2 hours alone during the day and as daylight turned to dusk, with good results. In particular, despite experiencing a couple of panic attacks during these *in vivo* exposure practices, she continued with the assigned practice. This was critical for Julie because it allowed her to learn that she could survive the feeling of panic; it was the first time she had remained in a situation despite panicking.

In reviewing the week's practice of interoceptive exposure, it became apparent that Julie was separating the practices from real-life experiences of bodily sensations in a way that would limit generalization. This was addressed as follows:

JULIE: After spinning and hyperventilating several times, I really do feel much less anxious. I was terrified at the start, but now I am only mildly anxious, if at all. But this is different than what happens to me when I'm on the freeway or at home.

THERAPIST: How is it different?

JULIE: I don't know when the feelings of dizziness and unreality are going to hit.

THERAPIST: From our previous discussions, let's think of potential reasons why you might feel dizzy or unreal at a particular time?

JULIE: I know. I have to keep remembering that it could be my breathing, or just feeling anxious, or tired, or a bunch of different things.

THERAPIST: OK. And why is it so important to know when those feelings will occur?

JULIE: Because I don't want them to be there at all.

THERAPIST: And why not . . . what are you afraid of?

JULIE: I guess it's the same old thing . . . that I'll lose it somehow?

THERAPIST: So let's go back to the cognitive restructuring that you have been doing. What specifically are you afraid of? How likely is it to happen? What are the alternatives?

JULIE: I understand.

THERAPIST: So, now you see that whether the sensations of dizziness or unreality are produced by anxiety, overbreathing, diet, or the exercises we do here, they're all the same—they are just uncomfortable physical sensations. The only reason they perturb you more when you are driving or at home is because of the meaning you still give to them in those situations.

"Naturalistic" interoceptive exposure refers to exposure to daily tasks or activities that have been avoided or endured with dread because of the associated sensations. Typical examples include aerobic exercise or vigorous physical activity, running up flights of stairs, eating foods that create a sensation of fullness or are associated with sensations of choking, saunas or steamy showers, driving with the windows rolled up and the heater on, caffeine consumption, and so on. (Of course, these exercises may be modified in the event of actual medical complications, such as asthma or high blood pressure.) From a list of typically feared activities and generation of items specific to the individual's own experience, a hierarchy is established. Each item is ranked in terms of anxiety ratings (0–10). Julie's hierarchy was as follows: looking out through venetian blinds (anxiety = 3); watching *One Flew over the Cuckoo's Nest* (anxiety = 4); playing tennis (anxiety = 4); scanning labels on a supermarket shelf (anxiety = 5); concentrating on needlework for an hour (anxiety = 6); driving with windows closed and heater on (anxiety = 7); a nightclub with strobe lights (anxiety = 8); and rides at Disneyland (anxiety = 10).

Like the symptom exercises, the activity exercises are designed to be systematically graduated and repetitive. Patients may apply the breathing and cognitive skills while the activity is ongoing. This is in contrast to the symptom induction exercises, in which coping skills are used only after completion of the symptom exercise, because the activities often are considerably longer than the symptom induction exercises. Nevertheless, patients are encouraged to focus on the sensations and experience them fully throughout the activity, and not use the coping skills to prevent or remove the sensations.

Patients are instructed to identify maladaptive cognitions and rehearse cognitive restructuring before beginning each activity. In-session rehearsal of the cognitive preparation allows therapists to provide corrective feedback. Julie did this with her therapist for her first two naturalistic activities, which were to look at venetian blinds and to watch *One Flew over the Cuckoo's Nest*. Julie realized that she was most worried about sensations of unreality and fears of going crazy, although, as a result of her various exposure exercises up to this point, she quickly was able to recognize that such sensations were harmless and that she could tolerate them, and that such fears were unrealistic based on the evidence.

As with all exposures, it is important to identify and remove (gradually, if necessary) safety signals or protective behaviors, such as portable phones, lucky charms, walking slowly, standing slowly, and staying in close proximity to medical facilities. These safety signals and behaviors reinforce catastrophic misappraisals about bodily sensations. Julie's safety behaviors were identified as checking the time on the clock (as a reassurance that she was in touch with reality) and pinching herself (again, to feel reality). She was asked to practice the two naturalistic interoceptive exposures at least three times each before the next treatment session, without the safety behaviors.

### Sessions 10 and 11

The primary goals of these sessions are to review the *in vivo* and naturalistic exposure exercises over the past week, and to combine exposure to feared and avoided agoraphobic situations with deliberate induction of feared sensations into those situations. As with earlier interoceptive exposure homework assignments, it is important to evaluate and correct tendencies to avoid naturalistic interoceptive exposure tasks, mainly by considering the underlying misassumptions that lead to avoidance. Remember also that a form of avoidance is to rely on safety signals or safety behaviors, so careful questioning of the way in which the naturalistic exposure was conducted, and under what conditions, may help to identify inadvertent reliance on these unnecessary precautions. Julie reported that she was successful in looking at the venetian blinds, even though she experienced sensations of unreality. She had more difficulty watching *One Flew over the Cuckoo's Nest* because it tapped directly into her worst fears of losing touch with reality permanently; she tried but terminated the film

early. The second time, she watched it with Larry, who prompted Julie to remember her cognitive and breathing skills, and she was able to watch the entire film. She watched the film one more time on her own. Two new naturalistic exposure items were selected for the coming week, with special attention to weaning or removing safety signals and safety behaviors, and rehearsal of cognitive restructuring in session. For Julie, these were playing tennis (something she had avoided for years) and scanning items on supermarket shelves.

The notion of deliberately inducing feared bodily symptoms within the context of feared agoraphobic situations derives from the evidence that compound relationships between external and internal cues can be the most potent anxiogenic agent (i.e., deepened extinction, as reviewed in earlier sections); that is, neither just the situation nor just the bodily sensation triggers distress. It is the combination of the bodily sensation and the situation that is most distressing. Thus, effective exposure targets both types of cues. Otherwise, patients run the risk of later return of fear. For example, repeated practice walking through a shopping mall without feeling dizzy does not adequately prepare patients for occasions on which they feel dizzy walking through a shopping mall, and without such preparation, patients may be likely to panic and escape should they feel dizzy in this or similar situations in the future. Wearing heavy clothing in a restaurant helps patients to learn to be less afraid of not only the restaurant but also of feeling hot in a restaurant. Other examples include drinking coffee before any of the agoraphobic tasks, turning off the air-conditioning or turning on the heater while driving, breathing very slowly in a crowded area, and so on.

Patients choose an item from their hierarchy of agoraphobia situations, either one already completed or a new item, and also choose which symptom to induce and ways of inducing that symptom in that situation. Julie's task was to drink coffee as she went to a movie. She expressed the following concerns:

JULIE: Do you really think I am ready to drink coffee and go to the movie?

THERAPIST: What worries you about the combination of coffee and the movie theater?

JULIE: Well, I've practiced in the movie theaters a lot, so that feels pretty good, but the coffee is going to make me feel very anxious.

THERAPIST: And if you feel very anxious in the movie theater, then what?

JULIE: Then, I don't know what. Maybe I will get those old feelings again, like I have to get out.

THERAPIST: Based on everything you have learned, how can you manage those feelings?

JULIE: Well, I guess my number one rule is never to leave a situation because I am feeling anxious. I will stick it out, no matter what.

THERAPIST: That sounds great. It means you are accepting the anxiety and taking the opportunity to learn that you can tolerate it. What else?

JULIE: I can ask myself what is the worst that can happen. I know I am not going to die or go crazy. I will probably feel my heart rate going pretty fast because of the coffee.

THERAPIST: And if your heart rate goes fast, what does that mean?

JULIE: I guess it just means that my heart rate will go fast.

THERAPIST: This will be a really good way for you to learn that you can tolerate the anxiety and the symptoms of a racing heart.

The homework for this session is to continue self-monitoring, to practice *in vivo* exposure combined with interoceptive exposure, and to continue naturalistic interoceptive exposure.

### Session 12

The last treatment session reviews the principles and skills learned and provides the patient with a template of coping techniques for potentially high-risk situations in the future. Julie finished the program after 12 sessions, by which time she had not panicked in 8 weeks, rarely experienced dizziness or feelings of unreality, and was driving further distances. There were some situations still in need of exposure practices (e.g., driving very long distances away from home and on the freeway at dusk). However, Julie and Larry agreed to continue *in vivo* exposure practices over the next few months to consolidate her learning and to continue her improvement.

### CONCLUSION

As noted earlier in this chapter, cognitive-behavioral treatments for panic disorder and agoraphobia are

highly effective and represent one of the success stories of psychotherapy. Between 80 and 100% of patients undergoing these treatments will be panic free at the end of treatment and maintain these gains for up to 2 years. These results reflect substantially more durability than medication treatments. Furthermore, between 50 and 80% of these patients reach a point of "high end state," which means their symptoms and functioning are within normative realms, and many of the remainder have only residual symptomatology. Nevertheless, major difficulties remain.

First, these treatments are not foolproof. As many as 50% of patients retain substantial symptomatology despite improvement from baseline, and this is particularly likely for those with more severe agoraphobia. Further research must determine how treatments can be improved or better individualized to alleviate continued suffering. For example, one of us (D. H. B.) saw a patient several years ago who had completed an initial course of treatment but required continued periodic visits for over 4 years. This patient was essentially improved for approximately 9 months but found himself relapsing during a particularly stressful time at work. A few booster sessions restored his functioning, but he was back in the office 6 months later with reemerging symptomatology. This pattern essentially continued for 4 years and was characterized by symptom-free periods followed by (seemingly) stress-related relapses. Furthermore, the reemerging panic disorder would sometimes last from 3 to 6 months before disappearing again, perhaps with the help of a booster session.

Although this case was somewhat unusual in our experience, there was no easy explanation for this pattern of relapses and remissions. The patient, who has a graduate degree, understood and accepted the treatment model and fully implemented the treatment program. There was also no question that he fully comprehended the nature of anxiety and panic, and the intricacies of the therapeutic strategies. While in the office, he could recite chapter and verse on the nature of these emotional states, as well as the detailed process of his own reaction while in these states. Nevertheless, away from the office, the patient found himself repeatedly hoping that he would not "go over the brink" during a panic attack, despite verbalizing very clearly the irrationality of this concept while in the office. In addition, he continued to attempt to reduce minor physiological symptoms associated with anxiety and panic, despite a full rational understanding of the nature of these symptoms (including the fact that they are the same symptoms he experi-

enced during a state of excitement, which he enjoyed). His limited tolerance of these physical sensations was also puzzling in view of his tremendous capacity to endure pain.

Any number of factors might account for what seemed to be “overvalued ideation” or very strongly held irrational ideas during periods of anxiety, including the fact that the patient has several relatives who have repeatedly been hospitalized for emotional disorders (seemingly mood disorders or schizoaffective disorder). Nevertheless, the fact remains that we do not know why this patient did not respond as quickly as most people. Eventually he made a full recovery, received several promotions at work, and considered treatment to be the turning point in his life. But it took 5 years.

Other patients, as noted earlier, seem uninterested in engaging in treatment, preferring to conceptualize their problems as chemical imbalances. Still others have difficulty grasping some of the cognitive strategies, and further attempts are necessary to make these treatments more “user-friendly.”

It also may seem that this structured, protocol-driven treatment is applied in a very standard fashion across individuals. Nothing could be further from the truth. The clinical art involved in this, and in all treatments described in this book, requires a careful adaptation of these treatment strategies to the individual case. Many of Julie’s symptoms revolved around feelings of unreality (derealization and depersonalization). Emphasizing rational explanations for the production of such feelings, as well as adapting cognitive and exposure exercises to maximize these sensations, is an important part of this treatment program. Although standard interoceptive provocation exercises seemed sufficient to produce relevant symptomatology in Julie’s case, we have had to develop new procedures to deal with people with more idiosyncratic symptoms and fears, particularly those involving feelings of unreality or dissociation. Other innovations in both cognitive and behavioral procedures will be required by individual therapists as they apply these procedures.

Although these new treatments seem highly successful when applied by trained therapists, treatment is not readily available to individuals with these disorders. In fact, these treatments, although brief and structured, are far more difficult to deliver than, for example, pharmacological treatments (which are also often misapplied). Furthermore, few people are currently skilled in the application of these treatments. What seems to

be needed for these and other successful psychosocial treatments is a new method of disseminating them, so that they reach the maximum number of patients. Modification of these treatment protocols into more user-friendly formats, as well as brief periods of training for qualified therapists to a point of certification, would be important steps in successfully delivering these treatments. This may be difficult to accomplish.

## NOTE

1. Specific phobias were not assessed, but by being most circumscribed, they would be hypothesized to load the least on negative affectivity.

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