PANIC DISORDER, PHOBIAS, AND GENERALIZED ANXIETY DISORDER

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Abstract This chapter provides a review of recent empirical developments, current controversies, and areas in need of further research in relation to factors that are common as well as specific to the etiology and maintenance of panic disorder, phobias, and generalized anxiety disorder. The relative contribution of broad risk factors to these disorders is discussed, including temperament, genetics, biological influences, cognition, and familial variables. In addition, the role that specific learning experiences play in relation to each disorder is reviewed. In an overarching hierarchical model, it is proposed that generalized anxiety disorder, and to some extent panic disorder, loads most heavily on broad underlying factors, whereas specific life history contributes most strongly to circumscribed phobias.

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INTRODUCTION

The purpose of this chapter is to review recent empirical developments, controversies in the literature, and areas in need of future research in relation to panic disorder (PD), phobias, and generalized anxiety disorder (GAD). The factors in common as well as the factors that are unique to the etiology and maintenance of these anxiety disorders are presented.

FEATURES OF PANIC DISORDER, PHOBIAS, AND GENERALIZED ANXIETY DISORDER

As with all the anxiety disorders, PD, phobias, and GAD share features of threat-relevant responding (i.e., anxious apprehension, fear, and avoidance), but differ in the object and breadth of threat. The broadest threat-responding occurs in GAD, which is defined as excessive and uncontrollable worry about a number of different life events and accompanying symptoms of motor tension and vigilance (American Psychiatric Association 1994). The onset of GAD tends to be insidious, with many patients reporting having been generally anxious since childhood (Anderson et al. 1984).

Panic disorder is characterized by recurrent unexpected panic attacks accompanied by persistent apprehension over their recurrence or consequences, which may occur with or without agoraphobia (American Psychiatric Association 1994). Relative to GAD, the object of threat is narrower and pertains to bodily sensations and their associated contexts (internal and external), and onset is usually defined by an initial unexpected panic attack (Barlow 1988), most typically in the mid 20s (Brown et al. 2001).

Social phobia [or social anxiety disorder (SAD)], the most prevalent anxiety disorder (13.3% lifetime; Kessler et al. 1994), represents excessive fear of social or performance situations in which embarrassment or negative judgments from others might occur. Nongeneralized SAD entails a much narrower threat base (usually performance situations) than generalized SAD, and like GAD, is more likely to emerge throughout childhood and adolescence (Öst & Treffers 2001). Very narrowly defined threat responding occurs in specific phobias (SPs), or, marked and persistent fear of clearly discernible and circumscribed objects or situations, estimated to occur in 11.3% of the population (Kessler et al. 1994). In adults, animal phobias, blood/injury/injection phobias, and natural environment phobias (possibly excepting height phobias) reportedly develop during childhood in contrast to a later onset (20s) for situational phobias (Öst & Treffers 2001).

Specific anxiety symptom clusters shift, and many anxiety disorders remit, throughout childhood and adolescence (Olford et al. 1992), even within a
six-month interval (Beidel et al. 1996). Social fears may be more stable throughout childhood than fears of animals, situations, or places (Achenbach & Edelbrock 1981). Moreover, some youths are likely to retain a syndrome of anxiety, in one form or another, since anywhere from 30% to the majority of treated youths develop additional anxiety/mood disorders three to four years after initial evaluation, despite mostly successful treatment of their entrance anxiety disorder (e.g., Last et al. 1996).

Childhood anxiety disorders are neither necessary nor sufficient for adult anxiety disorders, but anxiety disorders become more stable over development. Hence, substantially more anxiety disorders at 21 years of age were preceded by an anxiety disorder during adolescence than was the case for adolescent anxiety disorders and their childhood precedents (McGee et al. 1992). Also, anxiety disorders during adolescence pose a greater (twofold) risk for adult anxiety disorders than do childhood anxiety disorders (Pine et al. 1998). By adulthood, prospective evaluation indicates that, albeit waxing and waning in severity, anxiety disorders are mostly enduring, with remission rates as low as 12% to 30% over extended periods of time (e.g., Angst & Vollrath 1991). Phobic symptoms may be more stable than other anxiety symptoms (e.g., Tyrer et al. 1987). With the exception of GAD, rates for most anxiety disorders decrease in late life (Beekman et al. 1998).

BROAD RISK FACTORS AND COROLLARIES

Temperament

The temperament most associated with anxiety disorders is Neuroticism/Emotional Stability (Eysenck 1967), or, as it was later termed, “negative affectivity” (Watson & Clark 1984). Gray (1987) attributed proneness to anxiety to a lowered threshold for behavioral inhibition system activation (a defensive motivational state to which neuroticism, and to a lesser degree extraversion, contribute) in response to signals of punishment, frustrative nonreward (i.e., expected positive reinforcement is not received), extreme novelty, and intense and innate fear stimuli. Additionally, low extraversion may have a special affinity with SAD, although the findings are limited to cross-sectional comparisons (e.g., Trull & Sher 1994).

Converging with these models of motivational state are personality theories of negative affectivity, or the tendency to experience a variety of negative emotions across a variety of situations, even in the absence of an objective stressor (Watson & Clark 1984). Heightened negative affect is common to anxiety and depression, whereas low positive affect or anhedonia is relatively specific to depression (e.g., Watson & Clark 1984). Structural analyses confirm one higher-order factor, negative affect, which distinguishes each anxiety disorder and depression from controls with no mental disorder. In addition, lower-order factors discriminate among anxiety disorders: fear of fear, social anxiety, generalized dysphoria, obsessions and compulsions, agoraphobia, and simple fears (Brown et al. 1996). Hence, a hierarchical model has been proposed in which a broad trait vulnerability
of neuroticism/negative affectivity is common across anxiety disorders (and depression) and is responsible for the overlap among anxiety disorders (described below), whereas specific, unique factors contribute to the discrimination among anxiety disorders (Zinbarg & Barlow 1996). The anxiety disorders load differentially on negative affectivity, with more pervasive anxiety disorders, such as GAD, loading more heavily, PD loading at an intermediate level, and SAD loading the least (Brown et al. 1998). Specific phobias were not assessed, but by being most circumscribed, SPs would be hypothesized to load the least on negative affectivity.

The contributory role of neuroticism/negative affectivity is demonstrated by positive relationships between measures of negative affectivity/neuroticism and subsequent symptoms of anxiety and depression across all ages (e.g., Hayward et al. 2000, Jorm et al. 2000). Also, emotional reactivity at age 3 was a significant variable in the classification of PD in 18- to 21-year-old males (Craske et al. 2000), and anxiety sensitivity, a second-order facet of trait anxiety related to a specific tendency to react anxiously to one’s own anxiety and related sensations, predicted panic attacks (e.g., Hayward et al. 2000) and worry about panic (Schmidt et al. 1997). Finally, stress reactivity at age 18 was elevated in those with anxiety disorders as well as affective disorders at age 21, especially in individuals with co-occurring forms of distress (Krueger et al. 1996). However, there are no longitudinal data regarding neuroticism and the subsequent development of PD, SAD, SP, or GAD in particular.

Other support derives from research on behavioral inhibition, operationalized as restriction of exploration and withdrawal from novelty (Kagan et al. 1989), and conceptualized as a behavioral manifestation of neuroticism (Turner et al. 1996). Several prospective studies indicate that behaviorally inhibited youth more often develop multiple anxiety disorders than do uninhibited peers (Biederman et al. 1990, 1993; Hirshfeld et al. 1992). Especially telling is that the probability for each anxiety disorder to be occurring three years later in children who were “well” (nondisordered) at baseline was greater for inhibited children (Biederman et al. 1993). A particular affinity may exist between behavioral inhibition and social-evaluative anxiety disorders (Turner et al. 1996). Social anxiety disorder was related to earlier behavioral inhibition in one study (Biederman et al. 1993) although not in another, albeit smaller, study (Hirshfeld et al. 1992). More recently, Schwartz et al. (1999) reported that behaviorally inhibited 2-year-olds were more likely to exhibit generalized social anxiety at age 13 than were uninhibited peers, but were not more likely to exhibit specific fears, separation anxiety, or performance anxiety, consistent with the notion that more-pervasive anxiety disorders load more heavily on the general disposition of negative affectivity (Brown et al. 1998). Yet, the anxiety disorder that loads most heavily on negative affectivity (i.e., GAD) was not more evident in behaviorally inhibited youths in two studies (Biederman et al. 1993, Hirshfeld et al. 1992) and was not assessed in the third (Schwartz et al. 1999). Small sample sizes may thwart attempts to establish risk relations for specific anxiety disorders. Also, the overlap in samples across these three
studies is not well delineated, and the only independent prospective study found that behaviorally inhibited children were at greater risk for major depression in early adulthood but not for anxiety disorders (Caspì et al. 1998). Thus, further independent research is needed on the relationship between behavioral inhibition and subsequent anxiety disorders, and interactions of behavioral inhibition with other risk factors, since the majority of inhibited children (e.g., 70%; Biederman et al. 1993) remain free of any anxiety disorder.

Genetic Influences

Strong genetic contributions are found for animal traits, such as high reactivity in rhesus monkeys, which appears similar to the human trait of neuroticism (Suomi et al. 1981). Also, emotional reactivity (i.e., aroused and reduced activity in novel environments) can be bred in rats and mice (Gray 1987). Moreover, numerous multivariate genetic analyses of human twin samples consistently attribute approximately 50% of variance in neuroticism to additive genetic factors (Lake et al. 2000). The observed phenotypic covariation among anxious symptoms, depression symptoms, and neuroticism is due largely to a single common genetic factor (Kendler et al. 1987). That is, anxiety and depression appear to be variable expressions of the heritable tendency toward neuroticism. Symptoms of fear (e.g., 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 et al. 1988).

Even though heritability studies of anxiety disorders rely on poorly validated lifetime diagnostic instruments (e.g., Diagnostic Interview Schedule), two broad but distinct genetic factors have been identified. The first is defined by high loadings for GAD and major depression, and moderate loadings for PD (Mineka et al. 1998). In fact, major depression and GAD are considered genetically indistinguishable (Roy et al. 1995). Some of this unity may be due to overlapping diagnostic criteria and diagnostic unreliability, since rates of diagnostic agreement for GAD are among the lowest for the anxiety disorders, and use of one-month duration versus the usual six-month duration criterion for GAD increases the likelihood of diagnostic error. However, other findings described below bolster the strong association between major depression and GAD. Agoraphobia, SAD, and animal phobias were found to share lesser but still moderate amounts of genetic influence with major depression (Kendler et al. 1993), although results may differ when diagnostic error is taken into account, since accounting for such error changed the overall heritability estimates for these phobias (Kendler et al. 1999).

As mentioned, the evidence suggests two broad genetic sources of variance in the anxiety disorders. The first is the genetic diathesis on which GAD and depression load most heavily. It is viewed as distinguishable from a second, separate broad genetic diathesis on which PD and phobias load most heavily (Kendler et al. 1995). Support for these two broad diatheses exists in separate analyses of the Vietnam Era Twin Registry (Scherrer et al. 2000).
Conceivably, the genetic factor most relevant to GAD and major depression, and less so to PD and phobias, represents the same genetic diathesis that is common to neuroticism and symptoms of anxiety and depressed mood. The second genetic factor most relevant to PD and phobias may represent the separate genetic influences that pertain to fear and panic, especially since fears of milder manifestation are on the same genetic liability dimension as fears of clinical severity, at least in men (Kendler et al. 2001). Shared diathesis across all of the anxiety disorders may explain features of familial aggregation and co-occurrence among the anxiety disorders.

Familial Aggregation

Risk for anxiety disorders among offspring of parents with anxiety disorders averages 3.5 (range 1.3 to 13.3) times greater than the risk for healthy controls (e.g., Merikangas et al. 1999). Paternal anxiety may confer the same risk as maternal anxiety (e.g., Connell & Goodman 2002), although more research is needed. Children of parents who both suffer from psychopathology may be at incremental risk for anxiety disorders (Merikangas et al. 1999), but incremental risk is not always demonstrated (Biederman et al. 2001). A shared diathesis explanation of familial aggregation for anxiety disorders would predict a low degree of specificity in familial transmission and highest risk in the offspring of parents with the highest loadings on that diathesis (i.e., GAD). Unfortunately, no study to date has evaluated risk associated with parental GAD. Comparisons across highly select, nonrepresentative samples of parents with isolated phobias indicate that offspring were at increased risk only for the disorder exhibited by the parent (e.g., Fyer et al. 1995). However, parents with isolated phobic disorders may possess lower vulnerabilities toward anxiety disorders in general; higher parental loadings on predisposing traits may enhance offspring vulnerability for all anxiety disorders (Craske 1999). In accord, when other parental anxiety disorders were not a source of exclusion, offspring of parents with PD had increased rates of separation anxiety and multiple anxiety disorders as well as PD (Biederman et al. 2001).

Co-Occurrence of Anxiety Disorders

The broad vulnerability conferred by neuroticism to all anxiety disorders and depression most likely contributes to their high rates of co-occurrence (Mineka et al. 1998). In a large sample (N = 1127) of adults seeking help for anxiety disorders, current and lifetime rates of co-occurrence with other anxiety disorders ranged from 27% to 62% and from 37% to 71%, respectively (Brown et al. 2001). Although differential patterns of clustering existed among the disorders (Brown et al. 2001), specific interrelations are dependent on the sample studied, the diagnoses assessed, and the diagnostic method. Hence, different clusters were observed in the National Comorbidity Study data set (Kessler et al. 1998). Nonetheless, a consistent finding is for GAD to have higher co-occurrence with other disorders (Brown et al. 2001), possibly reflecting a higher loading on negative affectivity.
In a complication-type model, manifestation of a disorder increases the likelihood of other manifestations of shared vulnerability. In support, aside from the high rates of co-occurrence already described, anxiety disorders typically precede and statistically predict major depression in treatment-seeking and non-treatment-seeking adults (e.g., Brown et al. 2001, Kessler et al. 1998) and youths (Kovacs et al. 1989). [However, the reverse is true for dysthymia (Brown et al. 2001, Kovacs et al. 1989).] The pervasive distress of GAD may be particularly likely to enhance other manifestations of shared vulnerability. In accord, whereas adolescent SP predicted only SP in adulthood, and adolescent SAD predicted both SAD and SP in adulthood, adolescent GAD had the broadest influence, predicting adult SAD, PD, GAD, and depression (Pine et al. 1998). Similarly, a trend (albeit nonsignificant) existed for GAD in 5- to 18-year-olds to be associated with higher rates of new anxiety disorders over the subsequent three to four years in comparison with every other anxiety disorder (Last et al. 1996). In contrast, SPs often are more stable than other anxiety disorders (Tyrer et al. 1987) but confer limited risk for other types of anxiety disorders. Thus, as stated, adolescent SP predicted adult SP only (Pine et al. 1998), and SP at age 15 was not associated with higher rates of disorder (including depression, anxiety, conduct, and substance abuse) at age 18 relative to a no-disorder group. The reverse was true for other anxiety disorders (excluding obsessive-compulsive disorder) at age 15 (Feehan et al. 1993). That youths with GAD are at greater risk for future anxiety disorders than are youths with SP may be explained by both higher loadings on a broad diathesis of neuroticism/negative affectivity and by the distress of pervasive anxiousness strengthening the diathesis and potentiating subsequent manifestations.

**Biological Corollaries**

Consideration of the biological features of anxiety disorders introduces another trait, referred to as "emotion regulation," or the propensity to soothe emotional reactivity. Some argue that negative affectivity is insufficient and that the style of coping with negative affect is essential for explaining emotional disorders (Lonigan & Phillips 2001). Thus, anxiety disorders may entail both a defensive motivational state of heightened negative reactivity and self-regulatory processes that interfere with effective modulation of negative affect. The physiology corresponding to these two traits is reviewed below.

**CARDIAC VAGAL TONE** The parasympathetic branch of the autonomic nervous system, and in particular the vagus nerve, is considered critical to self-regulatory processes because it inhibits the output of sympathetic activation and is central to attentional processing and flexible responding to environmental stimuli. Cardiac vagal tone is assessed via the measurement of respiratory sinus arrhythmia, or beat-to-beat changes in heart rate during respiration, that indexes solely the extent to which the vagus nerve mediates parasympathetic influence on the heart through a constant neural firing, or tonus (Porges 1995). Thus, vagal influence can be indexed by the extent of variability in heart rate.
Tonic heart rate variability (HRV) is thought to "index the ability to organize physiological resources and respond adaptively" (Thayer et al. 2000, p. 362). Individuals with chronically low cardiac vagal tone (i.e., attenuated HRV due to respiratory sinus arrhythmia) are presumed to lack flexibility, whereas those with higher levels of HRV possess more adaptive behavioral and emotional responses to stressful events (Porges 1995). Higher tonic cardiac vagal tone facilitates orienting to discrete environmental stimuli that is required for responsive engagement with the environment, and lower tonic cardiac vagal tone is indicative of nonresponsiveness characterized by poorer attention to and discrimination among environmental cues (Friedman & Thayer 1998b, Thayer et al. 2000).

Attention to discrete cues and discrimination among stimuli, which are necessary for recognition of cause-effect relationships, may be central to generalization of conditional fear responding and pervasiveness of anxiety. Support derives mostly from conditioning studies involving unpredictable versus predictable aversive stimuli, since unpredictable aversive stimuli mimic the effects of impaired attention and limited discrimination among stimuli. For example, predictable shock elicited stronger conditioning to discrete stimuli, whereas unpredictable shock elicited stronger conditioning to surrounding contextual cues (Grillon 2002b), and predictable shock led to explicit fear-potentiated startle, whereas random shock resulted in greater startle potentiation in the anticipatory baseline phase of a second laboratory recording (Baas et al. 2004). In other words, predictable aversive stimuli resulted in more circumscribed conditioned responding, whereas unpredictable aversive stimuli resulted in more generalized conditioned responding. Also, awareness of the contingency between a shock and a conditional stimulus was associated with better conditioning to explicit conditional stimuli, whereas failure to recognize the contingency led to enhanced reactivity across the board, including to a stimulus that was never paired with shock (Grillon 2002b). That is, impaired attention to and discernment of cause-effect relationships was associated with more generalized anxious responding. Contingency awareness relates negatively to trait anxiety (Chan & Lovibond 1996), suggesting that individuals who are more anxious have poorer contingency awareness, which potentially contributes to their general anxiety. In summary, initial attentional processing of stimuli gives rise to an orienting response necessary for perceiving environmental changes, discriminating among stimuli, and learning appropriate conditional responses. Impaired orienting (vagally mediated) is expected to parallel the effects of unsignaled random shock or noncontingency awareness. Orienting deficits may contribute to anxiety because impaired discernment of relations among events in the environment contributes to overgeneralized (versus explicit-cue) responding to environmental threats.

Evidence for this set of relations exists in regard to GAD. In comparison with nonanxious controls, participants with GAD had lower tonic cardiac vagal tone, smaller cardiac orienting responses, impaired habituation of cardiac orienting to neutral words, and sustained anticipatory responding to threat words (e.g., Thayer et al. 2000). In addition, patients with dental anxiety with low cardiac vagal tone
were less able to regulate attentional processes for threat words in an emotional Stroop task in comparison with patients with high cardiac vagal tone (Johnsen et al. 2003). However, in absence of a control group, it remains unclear to what extent low cardiac vagal tone contributes uniquely to dental anxiety.

In fact, generalized vagally mediated orienting deficits may be less characteristic of SP than of PD or GAD. Relative to nonanxious controls, low tonic cardiac vagal tone is observed in adults with high trait anxiety (e.g., Yeragani et al. 1998), PD (e.g., D.E. Atkins & M.G. Craske, manuscript in submission), and GAD (e.g., Thayer et al. 2000), but certain phobia groups (blood phobia) display higher HRV than other anxiety disorders (e.g., Friedman & Thayer 1998a). Furthermore, studies have shown relative sympathetic dominance and lower cardiac vagal control of heart rate in individuals with PD (consistent with the sympathetic activity and vagal withdrawal that underlies panic attacks) compared with more vagally mediated HRV in individuals with blood phobias (consistent with the sympathetic hyperarousal followed by sympathetic inhibition and overcompensatory parasympathetic rebound that underlies blood phobic reactions) (e.g., Friedman et al. 1993). Moreover, nonanxious control participants exhibited more HRV and cardiac vagal tone than either anxious group (e.g., Friedman & Thayer 1998a). These findings do not necessarily generalize to all SPs, since preliminary findings indicate differences in cardiac vagal tone between individuals with blood phobia and spider phobia (Sarlo et al. 2002). Nonetheless, all SPs would be hypothesized to exhibit higher tonic cardiac vagal tone than PD, GAD, or generalized SAD, because by way of the narrower and highly specific set of stimuli that trigger specific phobic reactions, affected individuals are capable of greater emotional flexibility than the broader, overgeneralized anxious responding in PD (Friedman & Thayer 1998a) and GAD (Friedman & Thayer 1998b). However, direct comparisons among PD, GAD, and phobias are yet to be conducted.

As stated, chronically low cardiac vagal tone is posited to contribute to overgeneralization of anxious responding, but there is no direct evidence in relation to anxiety disorders. Only indirect evidence exists in that cardiac vagal tone during infancy and childhood correlates with concurrent and subsequent emotionality and behavioral responding. For example, infants with high tonic cardiac vagal tone were more reactive to both positive and negative events at 5 months and more sociable at 14 months (Fox 1989). Also, infants who displayed more negative emotional expressions (i.e., anger) when frustrated (e.g., arm restraint) also were more highly active, less fearful of novelty, and displayed higher levels of cardiac vagal tone (Stifter & Fox 1991). Further, infant regulation of cardiac vagal tone is associated with more responsivity toward an experimenter, more positive affect, greater endurance, and less fear and irritability (e.g., Stifter & Corey 2001). Conversely, low cardiac vagal tone correlates with behavioral inhibition in toddlers (Rubin et al. 1997), and behavioral inhibition in the first six weeks of commencing school (Fox & Field 1989). Thus, lower tonic cardiac vagal tone and weak vagal regulation are related to poor emotion regulation and to individual differences in temperamental constructs, such as behavioral inhibition early
in development, but there is no direct evidence for a contributory role for anxiety disorders.

Friedman & Thayer (1998b) suggest an opposite pathway of influence: instead of vagal tone contributing to anxiety, worry and anxiety are posited to attenuate vagal tone, and restrictions occurring at the level of cardiovascular functioning parallel restrictions in affective experiences and behavior in an effort to suppress or avoid anxiety symptoms. The positive effect of treatment for anxiety on cardiac vagal tone (Craske et al. 2004) supports the notion that negative affectivity influences emotion regulation processes. However, whether cardiac vagal tone is fully independent of level of emotional reactivity and whether it contributes to the development of anxiety disorders is not yet known.

**ANTICIPATORY AROUSAL** Physiological arousal refers to a variety of processes incorporating sympathetic adrenal medullary and hypothalamic pituitary axis outputs as well as startle reactivity, all of which are presumed to support the heightened vigilance and attention to threat that are characteristic of anxious individuals (Craske 2003). The collective evidence indicates that individuals with PD differ from controls in physiological responses occurring at baseline rather than in response to acute stressors. In fact, when baseline differences in heart rate and skin conductance are taken into account, much of the physiological difference between PD and nonanxious groups in response to acute stressors disappears, even with highly anxiogenic procedures (e.g., Roth et al. 1992). Exemplary of this effect is a study of the time course of startle eye-blink responding after a threat cue indicated that a 50-second countdown had begun, at the end of which a shock was delivered: Baseline startle was enhanced in participants with PD relative to controls, but the groups showed otherwise equivalent patterns of responding to the approaching shock (Grillon et al. 1994). Since “baseline” represents a state of anticipation about upcoming experimental procedures, the results are interpreted as elevated physiological reactivity to stressful conditions in general versus exaggerated responding to explicit threat cues, thereby paralleling results pertaining to lowered cardiac vagal tone and reactivity to surrounding contexts versus explicit threat cues.

In contrast to PD, responses to specific threat cues are exaggerated in SPs (e.g., de Jong et al. 1996) and there is little evidence of anticipatory baseline differences between SPs and nonanxious controls. For example, phobic stimulus potentiation of startle reactivity does not generalize to anticipatory or contextual cues as much as occurs for other anxiety disorders (Grillon 2002a). Results pertaining to SAD are more complex. Heart rate during baselines prior to laboratory stressors did not differ between individuals with generalized SAD and nonanxious controls (Stein et al. 1994). On the other hand, individuals with nongeneralized SAD exhibited elevated baseline responding in comparison with generalized socially anxious individuals in anticipation of a public speaking task (Levin et al. 1993), which raises the possibility that the specificity of the match between anxiety focus and laboratory stressor may yield anticipatory reactions. Moreover, effects may be moderated
by severity of anxiety, since clinically severe socially anxious individuals showed elevated heart rates during baseline before impromptu speeches (e.g., Davidson et al. 2000), whereas high trait social-anxious individuals were no different from controls (e.g., Mauss et al. 2003).

Like PD, GAD is not characterized by elevated physiological reactivity to explicit threat cues, and in fact, nonanxious individuals sometimes have autonomic responses to acute stressors that are stronger than those of individuals with GAD (e.g., Thayer et al. 1996). However, evidence for elevated anticipatory baseline arousal is equivocal. Baseline heart rates did not differ between GAD and nonanxious groups in some studies (Hoehn-Saric et al. 1989), whereas individuals with GAD had faster heart rates than those of controls across all experimental conditions, including baseline, in another study (Thayer et al. 1996).

Overall, SPs are characterized by explicit threat cue responding in absence of overgeneralized anticipatory responding. PD and GAD are characterized by lack of explicit threat cue responding and overgeneralized anticipatory responding (although it is less robust in GAD). The match between the laboratory task and the focus of anxious concern (a factor that does not apply to PD) and severity of anxiety may influence anticipatory responding in SAD. Consequently, indices of physiological responding for SAD appear to lie intermediate between PD/GAD and SP.

Parenting Influences

The degree of “coordination” in the way parents and infants respond to each other’s affective and behavioral displays is important for the development of emotion regulation (Schore 2001). Coordination is defined as the caregiver’s behavior being guided by the infant’s expressive displays—gaze, facial expressions, gestures, and vocalizations—and in turn the infant’s behavior being affected by the expressive displays of the caregiver (Tronick 1989). Coordinated interactions facilitate the development of sustained attention, orienting, and attentional control within the infant (Kochanska et al. 2000). Also, affectively synchronized play interactions may strengthen infant cardiac vagal tone (Schore 2001), and hence, the processes underlying emotion regulation. Parental monitoring of the infant’s state and the use of calming and soothing behaviors helps infants regulate arousal, develop greater tolerance of higher arousal states (Ruff & Rothbart 1996), and develop resilience to emotional fluctuation (Schore 2001), all of which contribute to early self-regulation within the infant.

Moreover, a relative amount of parent-infant coordination may contribute to a sense of prediction and control for the infant (Craske 2003)—two factors that are central to anxiety and its management (Barlow 1988). That is, by observing their caregiver’s responses to their own cues, infants learn associations between response and outcome, how to influence their caregiver’s behavior, and principles of instrumental learning as well as expectations about the behavior of others (Rochat & Striano 1999). Emerging awareness of these contingent relations promotes
predictability in the infant’s environment that eventually transfers to awareness of contingency between the infant’s own behavior and emotional state, or a sense of control over emotional responses (Tronick 1989). Control and mastery immunize the effects of subsequent stressful experiences, at least in lab-reared rhesus monkeys (Mineka & Cook 1986), and thus are considered crucial in buffering reactivity to stressors. However, no studies have directly evaluated the relationship between early parent-infant synchronicity and the development of anxiety disorders. This is a particularly important area to study, especially in light of the likely negative effects of parental anxiety and rumination upon parent-infant synchronicity (Craske 2003). Such anxiety may be exacerbated by irritable or inconsolable infants (Lowinger 1999) who possess elevated negative affectivity and/or poorer emotion regulation processes, possibly due to chronically low vagal tone, the latter having been shown to moderate restrictive parenting practices over time (e.g., Kennedy et al. 2004).

At later stages of development, data from self-report and observational studies consistently show that parents of anxious children are more likely to be controlling, less granting of autonomy, and less likely to suggest positive consequences than are parents of controls (e.g., Siqueland et al. 1996). Hudson & Rapee (2001) proposed that an intrusive parenting style emerges through a bidirectional relationship between the parent and the anxious child: Overinvolvement stems from parental efforts to reduce and/or prevent the child’s distress (and possibly the parent’s own anxiety), which in turn reinforces the child’s anxious behaviors by promoting the perception that the world is an unsafe place from which the child requires protection and over which the child has no control.

An overcontrolling parenting style is thought to be influenced by both child and parental psychopathology. An abundance of research demonstrates a link between an overinvolved, controlling parenting style and anxiety in children, but much of this research relies on retrospective questionnaire methods and/or comparisons of anxiety-disordered groups with nondisordered controls. Also, overcontrolling and rejecting parenting is linked to many other forms of child psychopathology (e.g., Schwartz et al. 1990), and in studies comparing parents of anxious children with parents of other clinically disordered (e.g., oppositional children) and nondisordered children, parents of both clinical groups displayed more intrusive involvement than did mothers of control children (e.g., Hudson & Rapee 2001). Thus, overinvolvement may be a parenting style common to child psychopathology, with parents becoming more involved whenever their child experiences problems.

In an evaluation of the role of parental psychopathology, anxious mothers catastrophized and criticized more, were less granting of autonomy, and displayed less warmth than did nonanxious mothers (e.g., Whaley et al. 1999). Also, parenting behaviors predicted offspring anxiety, offspring anxiety predicted maternal granting of autonomy, and when child anxiety was covaried, the relationship between maternal anxiety and parenting behaviors remained. Thus, anxious mothers may have lower perceived control as a caregiver, resulting in a tendency to react poorly to their child’s responses—reactions that may be exacerbated by a temperamentally
difficult child (Hudson & Rapee 2001). To demonstrate that overinvolved parenting contributes to anxiety disorders, it will be necessary to compare the parenting styles of anxious parents with those of parents with other forms of psychopathology and to examine the extent to which parenting style is related to anxiety disorders in children versus other forms of child psychopathology.

Parental overcontrol and intrusiveness are likely to interfere with the child’s development of a sense of control and acquisition of effective strategies for coping and managing distress (Rapee 2001). Early experiences with diminished control may lead to perceptions of low control when encountering new situations, and a generalized tendency to perceive events as not within one’s control, which, in turn, increases proneness to anxiety (Chorpita & Barlow 1998). In addition, opportunities for attaining competencies are likely to be fewer for children of overprotective and controlling parents, but with fewer areas of competency come higher ratings of anxiety and depression in children (Cole et al. 1999). Child temperament, parent-infant coordination, and style of parenting are best construed as broad, nonspecific risk factors for anxiety disorders. More specific mechanisms through which parental influence may impact the development of anxiety disorders are information transmission and modeling, described in the Specific Risk Factors: Associative Learning section below.

Cognitive Biases

Cognitive biases, predominantly hypervigilance for threat cues and danger-laden judgments, both characterize and contribute to the maintenance of anxiousness (e.g., Williams et al. 1996). Whereas cognitive biases can be conceptualized as an anxious process common to all anxiety disorders, the content of these biases becomes relatively specific, through past history and learning experiences as described earlier, to stimuli of significance to each disorder.

An anxiety-related attentional bias toward threat stimuli has been demonstrated in individuals with PD (e.g., Maidenberg et al. 1996), GAD (e.g., MacLeod et al. 1986), SAD (e.g., Mogg et al. 2004b), and SP (e.g., Lavy et al. 1993). Moreover, anxiety-linked preferential processing of threat stimuli has been observed across a variety of experimental paradigms (presumed to measure different components of attentional processing), including the probe-detection task (e.g., Mogg et al. 2004b), the emotional Stroop task (e.g., Maidenberg et al. 1996), visual search tasks (Öhman et al. 2001), and spatial-orienting tasks (e.g., Yiend & Mathews 2001). Whereas anxious individuals overly attend to threat, nonanxious adults direct attention away from innocuous threat stimuli, such as threat words and low-threat pictures (e.g., Wilson & MacLeod 2003), but display an attentional bias toward stimuli with high objective stimulus threat value, such as high-threat scenes (e.g., Mogg et al. 2000, Wilson & MacLeod 2003) and evolutionarily prepared threat stimuli (e.g., Öhman et al. 2001).

Given enhanced processing of threat stimuli by anxious adults, a memory bias for threat cues might also be expected. However, no consistent evidence exists for
implicit biases in memory in high trait anxiety or GAD (e.g., Nugent & Mineka 1994), and some studies suggest poorer explicit memory of threat-related material (e.g., Watts et al. 1986). Consequently, some have argued that following initial rapid orienting of attention toward threat, anxious individuals direct attention away from threat to avoid anxiety-provoking situations and to reduce subjective distress and/or perceived danger (e.g., Mogg & Bradley 1998). Such a “vigilance-avoidance” pattern is viewed as a maladaptive attempt to regulate negative emotion because it may potentiate sensitization and interfere with habituation, thereby maintaining anxiety in the long term (Mogg & Bradley 1998). However, whereas relatively robust evidence is documented for an anxiety-related attentional bias toward threat during initial stages of stimulus processing, evidence for anxiety-related avoidance at later stages is mixed (e.g., Mogg et al. 1997, 2004b versus Hermans et al. 1999). Contradictory results may arise from limitations of the probe-detection task, which permits several shifts of attention toward and away from the threat stimulus before probe onset and provides only a “snapshot view of the attentional bias” (Mogg et al. 2004b, p. 163). Alternative paradigms, such as monitoring eye movements throughout attentional tasks, may be more effective for indexing a vigilance-avoidance profile in anxious individuals (Mogg et al. 2004b).

Moreover, avoidance of threat cues may be less evident in high trait-anxious and GAD samples than in individuals with specific phobias. That is, whereas high trait-anxious individuals showed no evidence of avoidance subsequent to initial vigilance, participants with high-blood-injury fear showed significant avoidance of high-threat scenes compared with low- and medium-fear groups (Mogg et al. 2004a). Perhaps more generalized anxiety reflects a “defensive-approach” state of ongoing vigilance that conflicts with avoidant responding (Mogg et al. 2004a). By contrast, attentional avoidance shown by high-blood-injury fearful participants may reflect activation of a specific fear state characterized by predominant avoidance and escape (Mogg et al. 2004a).

Specific components of attention that underlie initial biased responding to threat stimuli in anxious individuals remain under investigation. Yiend & Mathews (2001) recently utilized a spatial orienting task to demonstrate that biased attention to threat in high trait-anxious individuals reflected difficulty with attentional disengagement. On the other hand, visual search tasks demonstrate that adults with SPs were faster than controls to detect their feared stimulus, but were no different from controls in locating nonfear-relevant stimuli or neutral stimuli, all from among arrays of neutral distracters (Öhman et al. 2001). These findings suggest that the vigilance portion of attentional bias in at least some SPs is not explained entirely by slowed disengagement (Craske 2003). Finally, individual differences in attentional control—the ability to shift attention away from unpleasant stimuli and focus on given tasks in order to regulate attention allocation—can moderate attentional bias effects (Derryberry & Reed 2002). Thus, difficulty with effortless attentional control maybe another factor underlying attentional processing.

Whereas some studies found that anxious children, like anxious adults, attend preferentially to threat (e.g., Taghavi et al. 2003), a similar number of studies found
that bias toward threat was common to both anxious children and controls (e.g., Kindt et al. 2000, Waters et al. 2004). Inconsistencies may relate to age and developmental level, since evidence for a general threat bias mostly comes from studies with younger children (8–12 years; e.g., Waters et al. 2004), whereas anxiety-specific effects were observed in studies of 9- to 19-year-olds (e.g., Taghavi et al. 2003). Thus, attentional bias toward threat seems stronger in older anxious youths.

Many more “normative fears” are experienced during childhood than in adulthood (see Gullone 2000 for a review)—fears that are thought to be developmentally appropriate to help protect children from danger and harm (King 1993). Children also have had less learning experience with threat-related stimuli in comparison with adults. Thus, enhanced attentiveness to threat stimuli may be an important component of an adaptive response to fearful stimuli (i.e., adaptive emotion regulation) in young children. At the same time, young anxious children are likely to be much closer to the onset of their disorder than are older anxious youths and adults, and anxiety disorder diagnoses are relatively unstable and highly comorbid during childhood (e.g., Last et al. 1996). Therefore, attentional processes may not be as selectively sensitized to stimuli depicting anxious concerns (Mayer et al. 1999).

The magnitude of attentional bias appears to persist in anxious children but to subside in nonanxious children with advancing age, possibly because with increasing development, nonanxious children learn to inhibit the processing of threat information, whereas anxious children do not (Kindt et al. 2000). Controlled studies of younger and older youths are required to track the developmental progression of this bias as a function of anxiety status and to determine whether failure to learn to inhibit the allocation of attention to emotional stimuli during childhood plays a role in the continuation of anxiety from childhood through adolescence and adulthood.

Whether attentional biases play a causal or maintaining role in anxiety remains unclear, although most researchers posit both pathways of influence. The strongest support for a contributory role of attentional biases comes from experimental induction. MacLeod and colleagues (MacLeod et al. 2002, Mathews & MacLeod 2002) demonstrated stronger negative reactivity to a stressor following training of attentional bias in a negative direction in mid-range trait-anxious adults. However, whether such a bias is sufficient for the development of chronic anxiety disorder and to what extent this bias translates specifically to one anxiety disorder over another remains to be investigated. Further, the evidence that an attentional bias is common in younger children in general and becomes more crystallized in anxious children with increasing age suggests that the causal role of an attentional bias depends on the acquisition of skills thought to moderate adaptive initial orienting to threat, such as attentional control (e.g., Derryberry & Reed 2002) and inhibitory processes (e.g., Kindt et al. 2000). However, assertions about the developmental progression of an anxiety-linked attentional bias toward threat remain speculative in the absence of direct investigation at this time.

Studies of judgment biases indicate that high trait-anxious individuals (Butler & Mathews 1987) and anxiety-disorder groups (Foa et al. 1996) overestimate
subject personal risk for negative events compared with controls. These findings also are true for anxious children who expect a larger number of negative outcomes (Chorpita et al. 1996) and anticipate that more negative events are likely to happen to them (Suarez & Bell Dolan 2001). Similarly, both clinically anxious and high trait-anxious adults and children are more likely to make threatening interpretations of ambiguous information (e.g., Taghavi et al. 2000), and recent studies have demonstrated that these biases occur at the time ambiguous information is encountered (e.g., Hirsch & Mathews 2000). Indeed, threat-related judgment biases seem more stable than biased attentional processes in anxious children, and may be affected by parental influence (e.g., Barrett et al. 1996).

SPECIFIC RISK FACTORS: ASSOCIATIVE LEARNING

Direct traumatic conditioning, vicarious observation (i.e., observing a model respond fearfully or be traumatized), and informational transmission (i.e., conveyance of threatening information) (Rachman 1978) represent the types of individually unique life experiences believed to contribute to specific anxiety disorders, accounting for more of the variance for PD and phobias than for GAD. Laboratory studies that validate these associative learning pathways include many examples of direct aversive conditioning of electrodermal and startle blink response (e.g., Grillon & Morgan 1999), and vicarious fear acquisition in laboratory-reared rhesus monkeys who, not previously exposed to snakes, observed unrelated, wild-reared monkeys react fearfully in the presence of live and toy snakes (Mineka et al. 1984). However, it is unethical to conduct the type of human experimental research necessary to demonstrate the causal role of these associative pathways in the development of excessive and chronic anxiety. Thus, aside from recordings before and after naturally occurring traumas, we are relegated to indirect evidence, much of which involves youth samples and therefore may not generalize to adults.

Self-reported reasons for phobia onset are often presented as evidence for the associative pathways of fear acquisition (e.g., de Jongh et al. 1995), but such recollections are fraught with imprecision and unreliability (Henry et al. 1994). Prospective longitudinal research is rare (e.g., Craske et al. 2001) and beset with its own sources of error in the absence of verifications of surrounding contexts and third-variable explanations. Moreover, it is overly simplistic to assume that an aversive association alone explains phobic responding, because a myriad of constitutional, life history, contextual, and postevent factors both mediate and moderate the impact of an aversive experience (Mineka & Zinbarg 1995). For example, neuroticism enhances aversive conditioning (Mineka & Zinbarg 1995). Also, history of positive experience (direct or indirect) with a stimulus buffers the development of an aversive association (Mineka & Cook 1986), a finding that may explain why familial concordance rates are not higher (Mineka & Zinbarg 1995) and that provides further reason for the negative effects of an overcontrolling parenting style that limits a child's breadth of experiences.
Contextual factors (intensity, controllability, and preparedness) at the time of the aversive experience are important determinants of the conditions under which an individual is more vulnerable to developing conditioned reactions, and preparedness explains the nonrandomness of phobias (de Silva et al. 1977). Debate continues regarding the automaticity (versus cognitive) and innate (versus cultural) accounts of preparedness (e.g., Bond & Siddle 1996 versus Öhman & Mineka 2001). The persistence of aversive associations following conditioning is influenced by expectancies for aversive outcomes and avoidant responding, which in turn are likely to be enhanced by high levels of negative affectivity and poorer emotion-regulation skills. Although direct evidence for associative pathways of acquisition for PD, SAD, and SP is lacking, associative models that take into account interactive pathways with constitutional and postconditioning variables are reviewed for each disorder in turn.

**Panic Disorder**

Consistent with a trauma-learning history, individuals with PD report more medical illnesses, particularly respiratory illnesses, than do individuals with other anxiety disorders (e.g., Verburg et al. 1995). In addition, respiratory disturbance at age 3 was a significant classification variable for PD at age 18 or 21 (Craske et al. 2001). Vicarious and informational transmission pathways are implicated in the finding that individuals with PD and with high anxiety sensitivity (a trait especially elevated in PD) (Zinbarg & Barlow 1996) are more likely to report that their parents suffered from chronic illnesses and physical symptoms of anxiety and modeled more sick-role behaviors related to panic symptoms than are individuals with other anxiety disorders and controls (e.g., Ehlers 1993).

Perhaps most important is that panic attacks themselves are aversive and form the basis for acquiring a learned fear of signals of panic, at least in vulnerable individuals. This is posited to occur through a process of interoceptive conditioning, whereby low-level somatic sensations of arousal or anxiety become conditional stimuli (Razran 1961) so that early somatic components of the anxiety response come to elicit anxiety or panic (Bouton et al. 2001). An extensive body of experimental literature attests to the robustness of interoceptive conditioning (e.g., Sokolowska et al. 2002). In addition, interoceptive conditional responses are not dependent on conscious awareness of triggering cues (Razran 1961), such that, once acquired, these responses can be elicited under anesthesia, even in humans (e.g., Block et al. 1987). Consequently, changes in relevant bodily functions that are not consciously recognized may elicit conditional fear due to previous pairings with panic, thereby accounting for the apparent spontaneity of panic attacks (Barlow 1988). The close proximity between initial signals of panic and the panic attack results in panic attacks themselves becoming conditional responses (Bouton et al. 2001): The conditional response that occurs to a more distal reminder of an aversive event (such as situations or places associated with panic attacks) is more preparatory than actively defensive in nature, and is quite distinct from the
unconditional response of fight or flight. Because the experimental literature indicates that conditional anxiety enhances conditional and unconditional responding to other stimuli, anxiety to distal/situational reminders of panic attacks is posited to lower the threshold for subsequent panic attacks in a self-perpetuating type of model (Bouton et al. 2001). Furthermore, consistent with the evidence pertaining to unsignaled or noncontingent shock, the unexpectedness of panic attacks is likely to contribute to generalized anxious responding (Craske et al. 1995).

The interoceptive conditioning model contrasts with the catastrophic appraisal model (Clark 1986), in which misappraisals of bodily sensations (e.g., imminent death, loss of control) are viewed as central and necessary. Misappraisals are posited to operate at both conscious and subconscious levels of awareness, such that individuals may automatically judge bodily sensations in a catastrophic manner without being aware of doing so, and thus experience “out-of-the-blue” panic attacks. Bouton et al. (2001) argue against the notion that panic and anxiety inevitably involve propositional, declarative knowledge as is implied by the cognitive theory of panic. Öhman & Mineka (2001) and LeDoux (1996) have argued persuasively that aversive emotional learning can occur without conscious representation of learning (although others disagree with respect to initial fear acquisition; Lovibond & Shanks 2002), and that implicit emotional memories can activate amygdala-based fear systems without individuals being aware of the reasons. In fact, there is abundant evidence for conditional fear responding to masked presentations of previously conditional “prepared” stimuli (e.g., Katkin et al. 2001), and unusual or novel bodily sensations are presumed to represent an evolutionarily prepared stimulus (Rachman 1991).

On the other hand, catastrophic misappraisals may accompany panic attacks because they have been encouraged and reinforced, much like sick-role behaviors (Bouton et al. 2001). In addition, misappraisals may become conditional stimuli that trigger anxiety and panic, as demonstrated via panic induction through presentation of pairs of words denoting sensations and catastrophic outcomes (Clark et al. 1988). In this case, catastrophic cognitions may well be sufficient (albeit not necessary) to elicit panic attacks. Furthermore, catastrophic cognitions probably enhance the emotional intensity of panic attacks, thus contributing to strength of conditioning. In addition, expectancies for aversive outcomes and inflation effects through mental rehearsal (Davey & Matchett 1994) following panic attacks (as a postconditioning factor) are likely to contribute to the persistence of PD. Similarly, catastrophic appraisals and expectancies also predict avoidance behavior and reliance on safety signals that in turn contribute to the maintenance of the disorder (e.g., Salkovskis et al. 1996).

Social Anxiety Disorder

Angry faces are viewed as prepotent stimuli that can elicit a conditional emotional response even when presented in a masked fashion (e.g., Öhman & Soares 1998). Also, repeated social defeat produces many of the effects seen with inescapable
shock, including escape deficits in the face of aversive stimuli and potentiated conditional fear responses (Mineka & Zinbarg 1995). Thus, direct experience with being ridiculed or rejected is naturally aversive, particularly when repeated, and possibly especially for emotionally vulnerable individuals. However, aside from retrospective self-report, there is no direct empirical evidence for the role of such experiences in the onset of SAD. Vicarious and informational pathways are indirectly implicated in the finding that adults with SAD are more likely to report that their parents placed greater emphasis on the opinion of others than are adults with agoraphobia or controls (Rapee 1997). More telling is that parents of socially anxious children expected their children to avoid as a way of coping with socially threatening situations, and that the children’s avoidant responses increased after a family discussion about those social situations (Barrett et al. 1996).

Specific maladaptive beliefs may enhance learning to fear social situations by influencing the intensity of the emotional response and/or the subsequent appraisals and reactions to an ambiguous or negative social event. Such beliefs have been proposed to incorporate rigid rules for governing social behavior (e.g., “I must always sound fluent and intelligent”), conditional assumptions about the consequences of one’s social behavior (e.g., “If people see me shake they will think I am stupid”), and core beliefs concerning self as a social object (e.g., “I am boring”) (Wells & Clark 1997). In support, expectancies for aversive outcomes in social situations characterize socially anxious individuals (e.g., Alden & Wallace 1995) and are hypothesized to generate a dysfunctional awareness of how one appears to others, an observer perspective that in turn generates more distress (e.g., Wells & Clark 1997). Whether appraisals are necessary for socially anxious responding has not yet been fully debated, although the evidence for persistence of conditional fear responding to masked presentations of angry faces suggests not (Öhman & Soares 1998).

Specific Phobias

Relative to GAD and PD, less variance in SP is explained by the diathesis shared between neuroticism and anxiousness, and more variance is explained by unique factors. Thus, experiences involving traumatic, vicarious, and informational transmission of fear are likely to play a prominent role in SP. Again, supportive evidence is mostly limited to retrospective report of etiological factors, although in a prospective longitudinal study, late onset dental fear was associated with more aversive experiences due to tooth decays and tooth loss (Poulton et al. 2001). Indirect (vicarious, informational) acquisition is implicated in the finding that children’s fears vary as a function of the extent to which mothers express their fears in the presence of their children (e.g., Muris et al. 1996). Also, toddlers express more negative affect and avoidance of a toy toward which the mother expressed a negative versus a positive reaction (Gerull & Rapee 2001), although generalizability to chronic phobias is not known. Finally, parents of children with SP expected their children to be avoidant in physically threatening situations, and subsequent to a discussion
with the parents, the child’s avoidance increased (Barrett et al. 1996). However, relevance of data from youth samples to adult phobias is not known.

Traumatic events are not necessarily a distinguishing feature of phobias. That is, phobic individuals do not differ from controls with respect to the number of re-membered aversive encounters with the phobic stimulus (e.g., Ehlers et al. 1994). Mineka & Cook (1986) point out that nonphobic individuals have more opportunities for aversive experiences because they are less avoidant, but at the same time, they are less likely to develop phobias from those experiences due to latent inhibition and immunization. In support, individuals who had a history of painful dental treatments but did not develop dental anxiety reported a number of relatively painless treatments prior to the painful experiences (Davey 1989), and those who had always been fearful of dentists had relatively short durations between their first dental treatment and their first painful treatment. This finding suggests that positive experiences provided a buffer in the development of long-lasting fear when a painful treatment occurred (de Jongh et al. 1995). Again, however, these data are based on verbal retrospection.

Because many individuals with SP (0% to 77%, 25.3% on average) are unable to recall events related to the onset of their fears, and instead report being fearful upon their first encounter with the phobic stimulus in the absence of independent aversive events, Menzies & Clarke (1993) concluded that fears have nonassociative, Darwinian origins; evolutionary pressures have innately endowed certain stimulus configurations (i.e., conspecific threat in primates, separation from caregivers, heights, odors, and novelty) with fear-evoking qualities. In contrast to preparedness notions, however, the expression of fear in relation to these stimuli is not dependent on aversive learning or information. Individual differences in fearfulness are hypothesized to lie not in the acquisition of fear but in the genetic readiness to fear and in the elimination of fear (Menzies & Clarke 1993). However, as already stated, retrospective recall of etiological factors is highly biased, and just because conditioning factors cannot be recalled does not mean they did not exist (Mineka & Öhman 2002). In addition, the assumption of genetic readiness is refuted by the evidence for only moderate heritability of SPs (Kendler et al. 1999).

Just as with PD and SAD, expectancies for aversive outcomes are likely to enhance the acquisition and persistence of learned fear of circumscribed stimuli. There is abundant evidence for elevated estimates of danger and panic in relation to phobic stimuli (e.g., Menzies & Clarke 1995) and for overestimates of negative outcomes in relation to phobic stimuli in studies of covariation bias (e.g., Tomarken et al. 1989). Furthermore, such expectancies are presumed to generate more avoidance behavior and thereby persistence of phobic responding, and indeed catastrophizing thoughts were the strongest predictor of avoidance behavior in individuals with acrophobia (Marshall et al. 1992). Again, however, the necessity of appraisals for phobic responding has been questioned in light of evidence for responding to masked conditional stimuli (Öhman & Soares 1998) and an implicit fear activation pathway that bypasses higher cortical functioning (Öhman & Mineka 2001).
Generalized Anxiety Disorder

GAD is the disorder for which fear cues are the least circumscribed, or the most diffuse, and it is the disorder that loads most highly on neuroticism; conversely, it is the disorder for which unique influences account for the least variance (Mineka et al. 1998). Hence, the associative model of fear acquisition is less relevant to GAD than to phobias and PD. Moreover, when aversive events do occur, they may lead to threat associations with a broad array of surrounding stimuli rather than to explicit threat cues. Such a process may be due to the impairing effects of low cardiac vagal tone upon orienting to discrete cues along with the generalized anxious responding effects of unpredictable and uncontrollable emotional responding because of high loadings on negative affectivity (Craske 2003).

SUMMARY

In this chapter, we have highlighted the similarities and differences between GAD, PD, and the phobias. In addition, we have pointed out areas that remain speculative and in need of future research. We have attempted to draw together empirical and theoretical developments from areas of personality and temperament, psychophysiology, learning, and cognition. An overarching hierarchical model of anxiety disorders is presented in which broad vulnerability factors toward neuroticism/negative affectivity combine with specific life history factors to explain the onset of anxiety disorders, with GAD and, to a lesser extent, PD loading more heavily on broad vulnerability factors and circumscribed phobias loading more heavily on life history factors. However, additional research is needed because the findings to date regarding negative affectivity derive from cross-sectional and longitudinal studies with insufficient sample sizes. Moreover, data regarding specific life experiences that contribute to PD and phobias are mostly analog in nature, albeit complemented by extrapolation from clinical samples. The genetic and parenting influences upon negative affectivity and emotion regulation appear to be substantial.

The breadth of anxiousness in GAD and PD is associated with lower tonic cardiac vagal tone, which is important to the degree that low cardiac vagal tone impairs orienting to discrete stimuli and discernment of cause-effect relations, and thereby is posited to contribute to overgeneralized anxious responding. In contrast, the circumscribed nature of SP (and perhaps nongeneralized SAD) is associated with higher tonic cardiac vagal tone in comparison with other anxiety disorders. Notably, early parenting may be a critical factor in cardiac vagal tone and emotion regulation. Moreover, individuals with PD (and possibly GAD) exhibit elevated anticipatory responding to threat-relevant contexts in the absence of magnified acute stress responding to explicit threat cues. In contrast, individuals with SP exhibit magnified responding to explicit threat cues but do not show evidence for elevated anticipatory responding. Recent developments from the study of information processing yield parallel results, with high trait anxiety and GAD characterized by
attentional vigilance, and SP possibly more likely to exhibit initial vigilance followed by avoidance or diversion of attention from explicit threat cues. However, many of these findings require further empirical investigation.

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