Functional Consequences of Panic Attacks

In the context of co-occurring mental disorders, including anxiety disorders, depressive disorders, bipolar disorder, substance use disorders, psychotic disorders, and personality disorders, panic attacks are associated with increased symptom severity, higher rates of comorbidity and suicidality, and poorer treatment response. Also, full-symptom panic attacks typically are associated with greater morbidity (e.g., greater health care utilization, more disability, poorer quality of life) than limited-symptom attacks.

Differential Diagnosis

Other paroxysmal episodes (e.g., "anger attacks"). Panic attacks should not be diagnosed if the episodes do not involve the essential feature of an abrupt surge of intense fear or intense discomfort, but rather other emotional states (e.g., anger, grief).

Anxiety disorder due to another medical condition. Medical conditions that can cause or be misdiagnosed as panic attacks include hyperthyroidism, hyperparathyroidism, pheochromocytoma, vestibular dysfunctions, seizure disorders, and cardiopulmonary conditions (e.g., arrhythmias, supraventricular tachycardia, asthma, chronic obstructive pulmonary disease). Appropriate laboratory tests (e.g., serum calcium levels for hyperparathyroidism; Holter monitor for arrhythmias) or physical examinations (e.g., for cardiac conditions) may be helpful in determining the etiological role of another medical condition.

Substance/medication-induced anxiety disorder. Intoxication with central nervous system stimulants (e.g., cocaine, amphetamines, caffeine) or cannabis and withdrawal from central nervous system depressants (e.g., alcohol, barbiturates) can precipitate a panic attack. A detailed history should be taken to determine if the individual had panic attacks prior to excessive substance use. Features such as onset after age 45 years or the presence of atypical symptoms during a panic attack (e.g., vertigo, loss of consciousness, loss of bladder or bowel control, slurred speech, or amnesia) suggest the possibility that a medical condition or a substance may be causing the panic attack symptoms.

Panic disorder. Repeated unexpected panic attacks are required but are not sufficient for the diagnosis of panic disorder (i.e., full diagnostic criteria for panic disorder must be met).

Comorbidity

Panic attacks are associated with increased likelihood of various comorbid mental disorders, including anxiety disorders, depressive disorders, bipolar disorders, impulse-control disorders, and substance use disorders. Panic attacks are associated with increased likelihood of later developing anxiety disorders, depressive disorders, bipolar disorders, and possibly other disorders.

Agoraphobia

Diagnostic Criteria **300.22 (F40.00)**

A. Marked fear or anxiety about two (or more) of the following five situations:
   1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).
   2. Being in open spaces (e.g., parking lots, marketplaces, bridges).
   3. Being in enclosed places (e.g., shops, theaters, cinemas).
   4. Standing in line or being in a crowd.
   5. Being outside of the home alone.

B. The individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symp-

toms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).

C. The agoraphobic situations almost always provoke fear or anxiety.
D. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.
E. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.
F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
H. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.
I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in social anxiety disorder); and are not related exclusively to obsessions (as in obsessive-compulsive disorder), perceived defects or flaws in physical appearance (as in body dysmorphic disorder), reminders of traumatic events (as in posttraumatic stress disorder), or fear of separation (as in separation anxiety disorder).

Note: Agoraphobia is diagnosed irrespective of the presence of panic disorder. If an individual's presentation meets criteria for panic disorder and agoraphobia, both diagnoses should be assigned.

Diagnostic Features

The essential feature of agoraphobia is marked, or intense, fear or anxiety triggered by the real or anticipated exposure to a wide range of situations (Criterion A). The diagnosis requires endorsement of symptoms occurring in at least two of the following five situations: 1) using public transporation, such as automobiles, buses, trains, ships, or planes; 2) being in open spaces, such as parking lots, marketplaces, or bridges; 3) being in enclosed spaces, such as shops, theaters, or cinemas; 4) standing in line or being in a crowd; or 5) being outside of the home alone. The examples for each situation are not exhaustive; other situations may be feared. When experiencing fear and anxiety cued by such situations, individuals typically experience thoughts that something terrible might happen (Criterion B). Individuals frequently believe that escape from such situations might be difficult (e.g., "can't get out of here") or that help might be unavailable (e.g., "there is nobody to help me") when panic-like symptoms or other incapacitating or embarrassing symptoms occur. "Panic-like symptoms" refer to any of the 13 symptoms included in the criteria for panic attack, such as dizziness, faintness, and fear of dying. "Other incapacitating or embarrassing symptoms" include symptoms such as vomiting and inflammatory bowel symptoms, as well as, in older adults, a fear of falling or, in children, a sense of disorientation and getting lost.

The amount of fear experienced may vary with proximity to the feared situation and may occur in anticipation of or in the actual presence of the agoraphobic situation. Also, the fear or anxiety may take the form of a full- or limited-symptom panic attack (i.e., an expected panic attack). Fear or anxiety is evoked nearly every time the individual comes into contact with the feared situation (Criterion C). Thus, an individual who becomes anxious only occasionally in an agoraphobic situation (e.g., becomes anxious when standing in line on only one out of every five occasions) would not be diagnosed with agoraphobia. The individual actively avoids the situation or, if he or she either is unable or decides not to avoid it, the situation evokes intense fear or anxiety (Criterion D). *Active avoidance* means the individual is currently behaving in ways that are intentionally designed to prevent or minimize contact with agoraphobic situations. Avoidance can be behavioral (e.g., changing

daily routines, choosing a job nearby to avoid using public transportation, arranging for food delivery to avoid entering shops and supermarkets) as well as cognitive (e.g., using distraction to get through agoraphobic situations) in nature. The avoidance can become so severe that the person is completely homebound. Often, an individual is better able to confront a feared situation when accompanied by a companion, such as a partner, friend, or health professional.

The fear, anxiety, or avoidance must be out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context (Criterion E). Differentiating clinically significant agoraphobic fears from reasonable fears (e.g., leaving the house during a bad storm) or from situations that are deemed dangerous (e.g., walking in a parking lot or using public transportation in a high-crime area) is important for a number of reasons. First, what constitutes avoidance may be difficult to judge across cultures and sociocultural contexts (e.g., it is socioculturally appropriate for orthodox Muslim women in certain parts of the world to avoid leaving the house alone, and thus such avoidance would not be considered indicative of agoraphobia). Second, older adults are likely to overattribute their fears to age-related constraints and are less likely to judge their fears as being out of proportion to the actual risk. Third, individuals with agoraphobia are likely to overestimate danger in relation to panic-like or other bodily symptoms. Agoraphobia should be diagnosed only if the fear, anxiety, or avoidance persists (Criterion F) and if it causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion G). The duration of "typically lasting for 6 months or more" is meant to exclude individuals with short-lived, transient problems. However, the duration criterion should be used as a general guide, with allowance for some degree of flexibility.

Associated Features Supporting Diagnosis

In its most severe forms, agoraphobia can cause individuals to become completely homebound, unable to leave their home and dependent on others for services or assistance to provide even for basic needs. Demoralization and depressive symptoms, as well as abuse of alcohol and sedative medication as inappropriate self-medication strategies, are common.

Prevalence

Every year approximately 1.7% of adolescents and adults have a diagnosis of agoraphobia. Females are twice as likely as males to experience agoraphobia. Agoraphobia may occur in childhood, but incidence peaks in late adolescence and early adulthood. Twelve-month prevalence in individuals older than 65 years is 0.4%. Prevalence rates do not appear to vary systematically across cultural/racial groups.

Development and Course

The percentage of individuals with agoraphobia reporting panic attacks or panic disorder preceding the onset of agoraphobia ranges from 30% in community samples to more than 50% in clinic samples. The majority of individuals with panic disorder show signs of anxiety and agoraphobia before the onset of panic disorder.

In two-thirds of all cases of agoraphobia, initial onset is before age 35 years. There is a substantial incidence risk in late adolescence and early adulthood, with indications for a second high incidence risk phase after age 40 years. First onset in childhood is rare. The overall mean age at onset for agoraphobia is 17 years, although the age at onset without preceding panic attacks or panic disorder is 25–29 years.

The course of agoraphobia is typically persistent and chronic. Complete remission is rare (10%), unless the agoraphobia is treated. With more severe agoraphobia, rates of full remission decrease, whereas rates of relapse and chronicity increase. A range of other disorders, in particular other anxiety disorders, depressive disorders, substance use disorders, and personality disorders, may complicate the course of agoraphobia. The long-term

course and outcome of agoraphobia are associated with substantially elevated risk of secondary major depressive disorder, persistent depressive disorder (dysthymia), and substance use disorders.

The clinical features of agoraphobia are relatively consistent across the lifespan, although the type of agoraphobic situations triggering fear, anxiety, or avoidance, as well as the type of cognitions, may vary. For example, in children, being outside of the home alone is the most frequent situation feared, whereas in older adults, being in shops, standing in line, and being in open spaces are most often feared. Also, cognitions often pertain to becoming lost (in children), to experiencing panic-like symptoms (in adults), to falling (in older adults).

The low prevalence of agoraphobia in children could reflect difficulties in symptom reporting, and thus assessments in young children may require solicitation of information from multiple sources, including parents or teachers. Adolescents, particularly males, may be less willing than adults to openly discuss agoraphobic fears and avoidance; however, agoraphobia can occur prior to adulthood and should be assessed in children and adolescents. In older adults, comorbid somatic symptom disorders, as well as motor disturbances (e.g., sense of falling or having medical complications), are frequently mentioned by individuals as the reason for their fear and avoidance. In these instances, care is to be taken in evaluating whether the fear and avoidance are out of proportion to the real danger involved.

Risk and Prognostic Factors

Temperamental. Behavioral inhibition and neurotic disposition (i.e., negative affectivity [neuroticism] and anxiety sensitivity) are closely associated with agoraphobia but are relevant to most anxiety disorders (phobic disorders, panic disorder, generalized anxiety disorder). Anxiety sensitivity (the disposition to believe that symptoms of anxiety are harmful) is also characteristic of individuals with agoraphobia.

Environmental. Negative events in childhood (e.g., separation, death of parent) and other stressful events, such as being attacked or mugged, are associated with the onset of agoraphobia. Furthermore, individuals with agoraphobia describe the family climate and child-rearing behavior as being characterized by reduced warmth and increased overprotection.

Genetic and physiological. Heritability for agoraphobia is 61%. Of the various phobias, agoraphobia has the strongest and most specific association with the genetic factor that represents proneness to phobias.

Gender-Related Diagnostic Issues

Females have different patterns of comorbid disorders than males. Consistent with gender differences in the prevalence of mental disorders, males have higher rates of comorbid substance use disorders.

Functional Consequences of Agoraphobia

Agoraphobia is associated with considerable impairment and disability in terms of role functioning, work productivity, and disability days. Agoraphobia severity is a strong determinant of the degree of disability, irrespective of the presence of comorbid panic disorder, panic attacks, and other comorbid conditions. More than one-third of individuals with agoraphobia are completely homebound and unable to work.

Differential Diagnosis

When diagnostic criteria for agoraphobia and another disorder are fully met, both diagnoses should be assigned, unless the fear, anxiety, or avoidance of agoraphobia is attributable to the other disorder. Weighting of criteria and clinical judgment may be helpful in some cases.

Specific phobia, situational type. Differentiating agoraphobia from situational specific phobia can be challenging in some cases, because these conditions share several symptom characteristics and criteria. Specific phobia, situational type, should be diagnosed versus agoraphobia if the fear, anxiety, or avoidance is limited to one of the agoraphobic situations. Requiring fears from two or more of the agoraphobic situations is a robust means for differentiating agoraphobia from specific phobias, particularly the situational subtype. Additional differentiating features include the cognitive ideation. Thus, if the situation is feared for reasons other than panic-like symptoms or other incapacitating or embarrassing symptoms (e.g., fears of being directly harmed by the situation itself, such as fear of the plane crashing for individuals who fear flying), then a diagnosis of specific phobia may be more appropriate.

Separation anxiety disorder. Separation anxiety disorder can be best differentiated from agoraphobia by examining cognitive ideation. In separation anxiety disorder, the thoughts are about detachment from significant others and the home environment (i.e., parents or other attachment figures), whereas in agoraphobia the focus is on panic-like symptoms or other incapacitating or embarrassing symptoms in the feared situations.

Social anxiety disorder (social phobia). Agoraphobia should be differentiated from social anxiety disorder based primarily on the situational clusters that trigger fear, anxiety, or avoidance and the cognitive ideation. In social anxiety disorder, the focus is on fear of being negatively evaluated.

Panic disorder. When criteria for panic disorder are met, agoraphobia should not be diagnosed if the avoidance behaviors associated with the panic attacks do not extend to avoidance of two or more agoraphobic situations.

Acute stress disorder and posttraumatic stress disorder. Acute stress disorder and posttraumatic stress disorder (PTSD) can be differentiated from agoraphobia by examining whether the fear, anxiety, or avoidance is related only to situations that remind the individual of a traumatic event. If the fear, anxiety, or avoidance is restricted to trauma reminders, and if the avoidance behavior does not extend to two or more agoraphobic situations, then a diagnosis of agoraphobia is not warranted.

Major depressive disorder. In major depressive disorder, the individual may avoid leaving home because of apathy, loss of energy, low self-esteem, and anhedonia. If the avoidance is unrelated to fears of panic-like or other incapacitating or embarrassing symptoms, then agoraphobia should not be diagnosed.

Other medical conditions. Agoraphobia is not diagnosed if the avoidance of situations is judged to be a physiological consequence of a medical condition. This determination is based on history, laboratory findings, and a physical examination. Other relevant medical conditions may include neurodegenerative disorders with associated motor disturbances (e.g., Parkinson's disease, multiple sclerosis), as well as cardiovascular disorders. Individuals with certain medical conditions may avoid situations because of realistic concerns about being incapacitated (e.g., fainting in an individual with transient ischemic attacks) or being embarrassed (e.g., diarrhea in an individual with Crohn's disease). The diagnosis of agoraphobia should be given only when the fear or avoidance is clearly in excess of that usually associated with these medical conditions.

Comorbidity

The majority of individuals with agoraphobia also have other mental disorders. The most frequent additional diagnoses are other anxiety disorders (e.g., specific phobias, panic disorder, social anxiety disorder), depressive disorders (major depressive disorder), PTSD, and alcohol use disorder. Whereas other anxiety disorders (e.g., separation anxiety disorder, specific phobias, panic disorder) frequently precede onset of agoraphobia, depressive disorders and substance use disorders typically occur secondary to agoraphobia.

Generalized Anxiety Disorder

Diagnostic Criteria **300.02 (F41.1)**

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
B. The individual finds it difficult to control the worry.
C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

   Note: Only one item is required in children.

   1. Restlessness or feeling keyed up or on edge.
   2. Being easily fatigued.
   3. Difficulty concentrating or mind going blank.
   4. Irritability.
   5. Muscle tension.
   6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).
F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

Diagnostic Features

The essential feature of generalized anxiety disorder is excessive anxiety and worry (apprehensive expectation) about a number of events or activities. The intensity, duration, or frequency of the anxiety and worry is out of proportion to the actual likelihood or impact of the anticipated event. The individual finds it difficult to control the worry and to keep worrisome thoughts from interfering with attention to tasks at hand. Adults with generalized anxiety disorder often worry about everyday, routine life circumstances, such as possible job responsibilities, health and finances, the health of family members, misfortune to their children, or minor matters (e.g., doing household chores or being late for appointments). Children with generalized anxiety disorder tend to worry excessively about their competence or the quality of their performance. During the course of the disorder, the focus of worry may shift from one concern to another.

Several features distinguish generalized anxiety disorder from nonpathological anxiety. First, the worries associated with generalized anxiety disorder are excessive and typically interfere significantly with psychosocial functioning, whereas the worries of everyday life are not excessive and are perceived as more manageable and may be put off when more pressing matters arise. Second, the worries associated with generalized anxiety disorder are

more pervasive, pronounced, and distressing; have longer duration; and frequently occur without precipitants. The greater the range of life circumstances about which a person worries (e.g., finances, children's safety, job performance), the more likely his or her symptoms are to meet criteria for generalized anxiety disorder. Third, everyday worries are much less likely to be accompanied by physical symptoms (e.g., restlessness or feeling keyed up or on edge). Individuals with generalized anxiety disorder report subjective distress due to constant worry and related impairment in social, occupational, or other important areas of functioning.

The anxiety and worry are accompanied by at least three of the following additional symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and disturbed sleep, although only one additional symptom is required in children.

Associated Features Supporting Diagnosis

Associated with muscle tension, there may be trembling, twitching, feeling shaky, and muscle aches or soreness. Many individuals with generalized anxiety disorder also experience somatic symptoms (e.g., sweating, nausea, diarrhea) and an exaggerated startle response. Symptoms of autonomic hyperarousal (e.g., accelerated heart rate, shortness of breath, dizziness) are less prominent in generalized anxiety disorder than in other anxiety disorders, such as panic disorder. Other conditions that may be associated with stress (e.g., irritable bowel syndrome, headaches) frequently accompany generalized anxiety disorder.

Prevalence

The 12-month prevalence of generalized anxiety disorder is 0.9% among adolescents and 2.9% among adults in the general community of the United States. The 12-month prevalence for the disorder in other countries ranges from 0.4% to 3.6%. The lifetime morbid risk is 9.0%. Females are twice as likely as males to experience generalized anxiety disorder. The prevalence of the diagnosis peaks in middle age and declines across the later years of life.

Individuals of European descent tend to experience generalized anxiety disorder more frequently than do individuals of non-European descent (i.e., Asian, African, Native American and Pacific Islander). Furthermore, individuals from developed countries are more likely than individuals from nondeveloped countries to report that they have experienced symptoms that meet criteria for generalized anxiety disorder in their lifetime.

Development and Course

Many individuals with generalized anxiety disorder report that they have felt anxious and nervous all of their lives. The median age at onset for generalized anxiety disorder is 30 years; however, age at onset is spread over a very broad range. The median age at onset is later than that for the other anxiety disorders. The symptoms of excessive worry and anxiety may occur early in life but are then manifested as an anxious temperament. Onset of the disorder rarely occurs prior to adolescence. The symptoms of generalized anxiety disorder tend to be chronic and wax and wane across the lifespan, fluctuating between syndromal and subsyndromal forms of the disorder. Rates of full remission are very low.

The clinical expression of generalized anxiety disorder is relatively consistent across the lifespan. The primary difference across age groups is in the content of the individual's worry. Children and adolescents tend to worry more about school and sporting performance, whereas older adults report greater concern about the well-being of family or their own physical heath. Thus, the content of an individual's worry tends to be age appropriate. Younger adults experience greater severity of symptoms than do older adults.

The earlier in life individuals have symptoms that meet criteria for generalized anxiety disorder, the more comorbidity they tend to have and the more impaired they are likely to