Psychopathology of panic disorder

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Abstract
Panic disorder is a common, debilitating and often chronic clinical condition. It is characterized by recurrent, unexpected panic attacks, and is commonly associated with agoraphobia and other psychiatric disorders such as mood disorders. Although the precise aetiology is currently unknown, a growing body of research supports a cognitive model in which panic attacks are said to arise from the catastrophic misinterpretation of benign, arousal-related bodily sensations (e.g. misinterpreting exertion-induced palpitations as an indication that one is about to have a heart attack). The role of catastrophic misinterpretations has also been incorporated into leading biological and contemporary psychodynamic models. Accumulating research also suggests that genetic factors play a role, with numerous genes each making a small contribution to the person's risk for developing the disorder. The cognitive and biological models are each associated with empirically supported treatments, such as cognitive–behaviour therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs). Before initiating any form of treatment, however, it is important to conduct a thorough diagnostic evaluation, including a general medical evaluation, in order to accurately diagnose panic disorder and to rule out general medical conditions that can mimic the disorder.

Keywords agoraphobia; catastrophic misinterpretation; fear network; panic attacks; panic disorder

What's new?

- Research continues to provide support for the cognitive model of panic, which proposes that the tendency to catastrophically misinterpret benign bodily sensations plays an important role in the disorder.[1–3]
- Research into the psychobiology of panic disorder has increasingly focused on genetic factors. Genetic variants of several candidate genes of neurotransmitter or neurohormonal systems, each with a small individual effect, may contribute to the susceptibility to panic disorder.[4–6]
- In other developments, theorists have attempted to integrate models of panic disorder, such as neurobiological and psychodynamic approaches,[7] but the merits of such efforts have been debated.[8]

Classification and defining features

Types of panic attack

Panic disorder is characterized by recurrent, unexpected panic attacks.[9] Full-blown attacks are defined by four or more of the symptoms in Table 1, whereas limited-symptom attacks are defined by three or fewer symptoms. The frequency and severity of panic attacks vary widely among patients. Table 2 describes the three types of panic attacks found in panic disorder (and, less commonly, in other anxiety disorders). Such panic attacks can also occur in the general population; these are often referred to as non-clinical panic.

Panic attack symptoms

A panic attack is a discrete period of intense fear or discomfort in the absence of real danger that develops abruptly, reaches a peak within 10 minutes, and is accompanied by four or more of the following symptoms:

- palpitations, pounding heart or accelerated heart rate
- sweating
- trembling or shaking
- sensations of shortness of breath or smothering
- feeling of choking
- chest pain or discomfort
- nausea or abdominal distress
- feeling dizzy, unsteady, light-headed or faint
- derealization (feelings of unreality) or depersonalization (feeling of being detached from oneself)
- fear of losing control or going crazy
- fear of dying
- paraesthesiae (numbness or tingling sensations)
- chills or hot flushes

(Adapted from American Psychiatric Association, 2000.[9])

Table 1

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Major types of panic attack

Type of attack	Defining features	Example	Diagnostic significance
Situationally bound (cued) panic	Almost always occurs immediately upon encountering, or in anticipation of, a situational cue	A patient who always panics when in a crowded shopping mall	Frequent in panic disorder. Experienced by the majority of patients with social and specific phobias
Situationally predisposed panic	Often, but not always, occurs in response to a situational cue	A patient who is more likely to panic when standing in a supermarket line	Frequent in panic disorder. Experienced by many patients with generalized anxiety disorder and post-traumatic stress disorder
Unexpected panic	Appears (to the patient) to occur spontaneously or 'out of the blue'	A patient who panics but can't identify any trigger for the attack	Necessary for diagnosis of panic disorder

(Adapted from American Psychiatric Association, 2000.[9])

Table 2

Panic disorder

Table 3 shows the DSM-IV diagnostic criteria for panic disorder. The attacks must not stem solely from the direct effects of a psychoactive substance (intoxication or withdrawal), medication or a general medical condition (e.g. hyperthyroidism, vestibular dysfunction). Panic disorder is not diagnosed if the panic attacks are better accounted for by another psychiatric disorder.

Agoraphobia

Panic disorder commonly co-occurs with agoraphobia. The latter typically develops as a consequence of full-blown or limited-symptom panic attacks.[9,10] In clinical settings over 95% of patients with agoraphobia also have a current or past history of panic disorder.[9] The diagnostic criteria for agoraphobia appear in Table 3.

Associated features

Prevalence

Estimates of the lifetime prevalence of panic disorder range between 1% and 4.7%.[9,11] Women are diagnosed with the disorder twice as often as men.[11] Panic disorder has been identified across many different cultures, although the expression of the disorder may vary from culture to culture (e.g. people with panic disorder in some cultures may be more likely to emphasize the somatic symptoms of their panic attacks, while being reluctant to report cognitive symptoms such as fears of going mad or of losing control).

Onset and course

The age of onset for panic disorder is bimodally distributed, typically developing between 15 and 19 years or between 25 and 30 years.[9] The disorder is often chronic in the absence of treatment, following a fluctuating course of exacerbation (often in the context of stressful life events) and remission.[9] Developmental factors (e.g. adverse childhood events such as separation from a parent; sexual and physical abuse), learning experiences (e.g. observing other people becoming alarmed by bodily sensations) and genetic vulnerability factors have all been implicated in the aetiology of panic disorder.[5,12,13]

Comorbidity

Panic disorder is often comorbid with other anxiety disorders, mood disorders, somatoform and pain-related disorders, substance use disorders (particularly alcohol abuse and dependence) and personality disorders.[11]

Diagnostic criteria for panic disorder and agoraphobia

Panic disorder

- One or more full-blown panic attacks, occurring in the absence of real danger
- The attacks are not due to a general medical condition
- Attacks are followed by a month or more of any of the following:
  - persistent concern about having more attacks
  - worry about the implications or consequences of the attacks (e.g. 'I could go crazy')
  - behavioural changes as a result of the attacks (e.g. avoidance of work or school activities)

Agoraphobia

- Anxiety about being in places or situations from which escape might be difficult or embarrassing, or in which help might not be available in the event of a panic attack or panic-like symptoms
- Avoidance of a wide range of situations, including:
  - being outside the home
  - being alone at home
  - crowds
  - bridges
  - elevators
  - travelling by car, train, bus or aeroplane
- Often, the person is better able to endure these situations while accompanied by a trusted companion such as a parent or spouse

(Adapted from American Psychiatric Association, 2000.[9])

Table 3

Theories of panic disorder

Aetiology

The precise aetiology of panic disorder is unknown. However, accumulated evidence supports the view that panic attacks arise from, or are worsened by, the catastrophic misinterpretation of bodily sensations. This premise is found in various theories of panic disorder, including cognitive approaches, in contemporary psychodynamic formulations and in Gorman's neuroanatomical model of panic.

Cognitive models

Vicious circle of panic: Clark[14] proposed that panic attacks arise from a tendency to catastrophically misinterpret arousal-related sensations (e.g. misinterpreting dizziness as a sign that one is about to go mad). The model is illustrated in Figure 1. Other contemporary cognitive models similarly emphasize the importance of the misinterpretation or excessive fear of bodily sensations.[15] Clark's model and similar approaches are supported by a good deal of empirical research and have led to a highly effective form of treatment.[13]

In support of Clark's model, research shows that people with panic disorder, compared to control groups, are more likely to hold dysfunctional beliefs about the dangerousness of bodily sensations. Longitudinal research shows that such beliefs predict the further occurrence of panic attacks. Experimental studies show that when such beliefs are reduced in strength (by the provision of corrective information), the probability is reduced that panic patients will panic in response to agents such as sodium lactate and carbon dioxide (which induce intense bodily sensations). These and other findings in support of the cognitive model are reviewed elsewhere.[13,14]

Importance of misinterpretations: Clark's model is based on several propositions, which have been generally supported by empirical research.

- While recognizing that a person's initial panic attack may be caused by various factors (e.g. drug-related autonomic surges), the model proposes that people prone to panic disorder have an enduring tendency to catastrophically misinterpret benign arousal-related sensations.
- Misinterpretations can occur at the conscious and unconscious level.
- The vicious circle of panic can be entered at any point. The cycle can be initiated by a contextual trigger (e.g. derealization induced by fatigue or fluorescent lighting), or simply by having catastrophic thoughts about bodily sensations.
- Physiological changes are viewed as one of several components in a process, rather than as a core pathogenic mechanism.

As predicted by the cognitive model, people with panic disorder, compared with control groups, display various forms of cognitive bias such as the tendency to be vigilant for bodily sensations, especially sensations that they believe to be dangerous, such as palpitations or derealization.[13] This increases the chances that the person will detect, and become alarmed by, bodily sensations. The cognitive approach also predicts that panic disorder should be effectively treated by reducing the patient's tendency to catastrophically misinterpret bodily sensations. Research findings support this conclusion.[13]

Agoraphobia: cognitive models can also account for agoraphobia. Panic attacks typically occur in particular situations that are often inherently arousing (e.g. crowded trains or supermarkets). The attacks serve to motivate the person to avoid or escape these situations. Avoidance and escape behaviours are reinforced by the

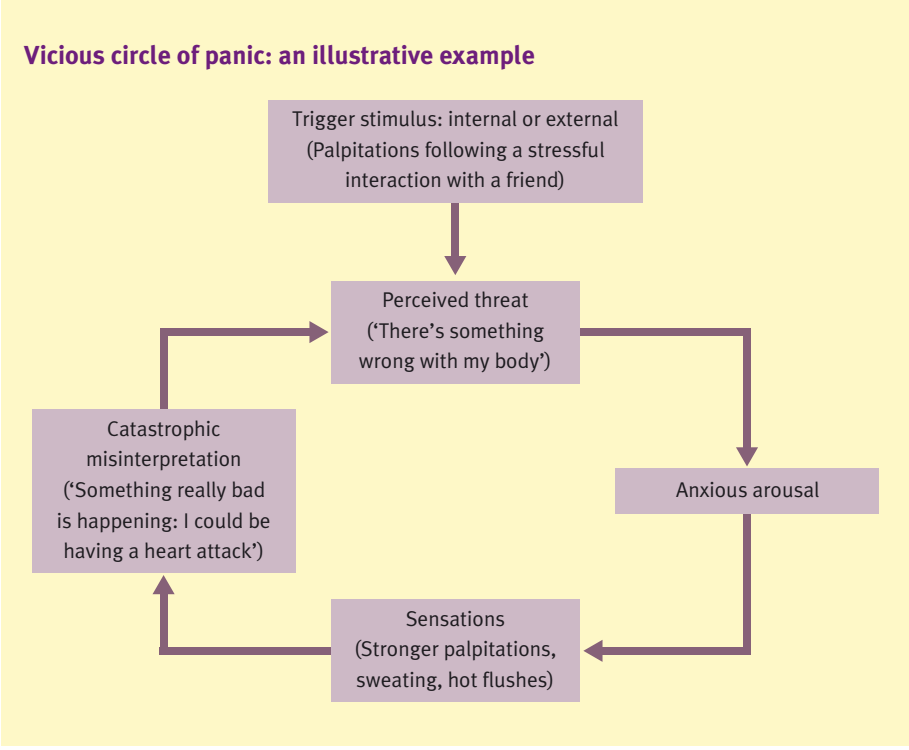

Figure 1

escape from panic attacks. Cognitive factors, such as expectations that an attack with be imminent and harmful and that coping will be ineffective, play a significant role by influencing and maintaining avoidance behaviour.[13] Specific types of catastrophic cognitions appear to have differential roles in the genesis and clinical course of particular panic disorder features (e.g., catastrophic social concerns involving fears of being embarrassed by publicly observable anxiety symptoms may contribute to greater agoraphobic avoidance) as well as treatment outcome.[16,17]

Psychodynamic models

Contemporary approaches: the most promising psychodynamic models for understanding panic disorder are those that focus specifically on this disorder, as exemplified by the model developed in the USA by the Cornell Panic-Anxiety Study Group.[18,19] This model has led to a promising treatment for panic disorder, although it is too early to recommend this treatment for routine clinical practice; current guidelines are that other treatments such as CBT and SSRIs should be used.[20] According to the Cornell group, people at risk of panic disorder have a neurophysiological vulnerability to panic attacks and/or multiple experiences of developmental trauma. These factors lead the child to become frightened of unfamiliar situations, and to become excessively dependent on the primary caregiver to provide a sense of safety. The caregiver is unable always to provide support, so the child develops a fearful dependency.

Role of conflicts and misinterpretations: the childhood experiences lead to the development of unconscious conflicts about dependency (independence versus reliance on others) and anger (expression versus inhibition). The dependency conflict is said to express itself in a number of ways. Some panic-vulnerable individuals are sensitive to separation and overly reliant on other people, while others are sensitive to suffocation and overly reliant on a sense of independence. These conflicts can activate conscious or unconscious fantasies of catastrophic danger, which can trigger panic attacks. The conflicts also evoke aversive emotions such as anxiety, anger and guilt. The otherwise benign arousal sensations accompanying these emotions can become the focus of conscious as well as unconscious cognitive catastrophizing, thereby leading to panic attacks.[17]

Biological models

Neurotransmitter systems: evidence suggests that several neurotransmitter systems, involving neurotransmitters or neuromodulators such as serotonin, noradrenaline, adenosine, γ-aminobutyric acid (GABA) and cholecystokinin-4, play a role in panic disorder.[21,22] For example, PET imaging data reveals evidence of reduced benzodiazepine receptor and 5-HT_{1A} receptor binding, which might contribute to brain vulnerability to panic attacks.[23,24] Contemporary biological models emphasize the amygdala and associated brain regions.[21]

Neuroanatomical hypothesis: among the most promising biological models is Gorman's neuroanatomical hypothesis.[21] Gorman and colleagues noted similarities between the physiological and behavioural consequences of panic attacks in humans and the conditioned fear responses in animals. Similarities include:

- autonomic arousal
- fear evoked by specific cues (contextual fear)
- avoidance of these cues.

Animal research suggests that conditioned fear responses are mediated by a 'fear network' in the brain, consisting of the amygdala and its afferent and efferent projections, particularly its connections with the hippocampus, medial prefrontal cortex, thalamus, hypothalamus and brainstem. Animal studies show that activation of this network produces biological and behavioural reactions that are similar to those associated with panic attacks in humans. Gorman and colleagues posit that a similar network is involved in panic disorder, in that panic attacks arise from excessive activation of the fear network. The network in panic disorder is said to be sensitized (conditioned) to respond to noxious stimuli such as internal stimuli (bodily sensations) and external stimuli (contexts or situations) that the person associates with panic. Sensitization of the network may be manifested by the strengthening of various projections from the central nucleus of the amygdala to brainstem sites (such as the locus ceruleus, periaqueductal grey region and hypothalamus). The neuroanatomical hypothesis proposes that dysregulations in cortico-amygdala pathways could be the biological correlate of the tendency to catastrophically misinterpret bodily sensations in panic disorder; such misinterpretations lead to inappropriate activation of the fear network. This hypothesis integrates the cognitive model and places it in a neuroanatomical context.

The neuroanatomical model accounts for much of the treatment outcome data. According to guidelines from the National Institute for Health and Clinical Excellence,[20] the interventions with the most enduring treatment effects include cognitive–behavioural therapy and particular pharmacotherapies (selective serotonin reuptake inhibitors, imipramine and clomipramine). Benzodiazepines are less effective in producing long-term remission of panic disorder.[21]

Conclusion

Panic disorder is a common and disabling condition that tends to follow a chronic course if left untreated. It arises from multiple pathogenic processes, and recent research has led to a better understanding of the underlying mechanisms. Particular cognitive, biological and psychodynamic approaches are promising for understanding this disorder, and each approach has led to useful treatments. However, much remains to be learned about the genesis, expression and course of panic disorder. ◆

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Practice points

- A thorough diagnostic evaluation, including a general medical evaluation, is important for the accurate diagnosis and treatment of panic disorder
- Panic disorder commonly co-occurs with other psychiatric disorders, particularly agoraphobia
- Although the precise aetiology is unknown, contemporary models of panic disorder, in particular cognitive models and some biological models, are supported by a good deal of research and have led to effective treatments
- Contemporary cognitive models and some influential biological models emphasize the role of the person's beliefs about the meaning of bodily sensations: that is, panic attacks can be triggered or worsened when the person catastrophically misinterprets the significance of bodily sensations (e.g. misinterpreting benign, fatigue-induced derealization as evidence that one is about to go mad)
- An important step in treating panic disorder is to show the patient how his or her panic attacks can be understood in terms of catastrophic misinterpretations and the vicious circle of panic