Chapter

Panic Attacks and Panic Disorder

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Abstract

A panic attack is an intense wave of fear characterized by its unexpectedness and debilitating, immobilizing intensity. Regardless of the cause, panic attacks are treatable. The signs and symptoms of a panic attack develop abruptly and usually reach their peak within 10 min. Panic attack symptoms may include hyperventilation, heart racing, chest pain, and trembling, sweating, and dizziness, with a fear of losing control, going crazy, or dying. Although the exact causes of panic attacks and panic disorder are unclear, the tendency to have panic attacks runs in families. There also appears to be a connection with major life transitions and severe stress. Treatment for panic attacks and panic disorder include psychotherapy and medication.

Keywords: panic attacks, panic disorder, symptoms, causes, treatment

1. Introduction

A panic attack is an intensive fear characterized by unexpectedness and immobilizing intensity. Often strikes without any warning, very often with no clear trigger, and also may occur when the person is relaxed or even when is asleep. Panic attacks are common. A panic attack can be a one-time occurrence, but usually many people experience repeat episodes, in a longer lifetime period. Among persons that ever had a PA, the majority had recurrent PAs (66.5, s.e. 0.5%). Most people recover without treatment, only a few of them from panic attacks develop panic disorder. Lifetime prevalence of PAs is 13.2% (s.e. 0.1%) [18].

Sometimes recurrent panic attacks are often triggered by a specific situation, in which the person felt endangered before. A panic attack may also occur as part of another disorder, such as panic disorder, social phobia, or depression.

Depending on the relationship between the occurrence of the attack and absence or presence of situational triggers, panic attacks can be divided into the following:

- Unexpected (untested) panic attacks in which the occurrence of a panic attack is not related to a situation trigger (occurs spontaneously as a lightning strike) and is the most common type of attack in the PD [44].

- Situational-induced (triggered) panic attacks, which almost invariably occur immediately after exposure, or the anticipation of a trigger situation (e.g., seeing a snake or dog always triggers an immediate panic attack).

- Situational predisposed panic attacks, which is highly expected to occur when exposed to the trigger situation but are not inseparably linked to the trigger, and it is not necessary to occur immediately after exposure (e.g., panic attacks

are more likely to occur during the ride, but sometimes individuals they can drive and have no panic attacks, or they happen half an hour after the ride).

- Other types of attacks are those that occur in a special emotional context those involving limited symptoms as well night attacks.

- Situational-induced attacks are more characteristic of social and specific phobias. Situationally predisposed panic attacks are particularly common in panic disorder, but can also occur in specific and social phobias.

The onset of unexpected panic attacks is necessary for the diagnosis of panic disorder with or without agoraphobia.

The frequency and severity of panic attacks vary widely. For example, some individuals have intermediate frequency attacks (e.g., once a week), which occur constantly for months. Others report frequent attacks in a short period (day, week) that are separated for a long period (weeks or months) without seizures or with rare attacks (two per month) over a long period of time. Attacks with limited symptoms (e.g., identical to full panic attacks, but with fewer associated symptoms) are very common in panic disorder.

2. Manifestation and diagnosis of panic disorder

2.1 The signs and symptoms of a panic attack

The signs and symptoms of a panic attack may include hyperventilation, heart racing, chest pain, and trembling, sweating, and dizziness, with a fear of losing control, going crazy, or dying.

2.2 The signs and symptoms of panic disorder

Among persons that ever had a PA only 12.8% fulfilled DSM-5 criteria for PD. In comparison with panic attacks, panic disorder is characterized by repeated panic attacks. Panic disorder (PD) is a chronic mental disorder with essential features such as recurrent panic attacks, persisting concern about the attacks, and a change in behavior as a result of the attacks [17].

The lifetime prevalence of PD is two times more likely to occur in women than in men [32]. Age of onset for PD is a wide range between 25 and 53 years regardless of gender. Alongside the variation in age, the most probable period is the late adolescence and the middle of the 1930s. A certain number of PD cases begin in childhood or after 45 years of age [33]. Panic disorder usually begins in late adolescence or early adulthood and affects women about two times more often than men. The median age of onset is 32. Cross-national lifetime prevalence estimates is 1.7% for PD [18].

Individuals with PD show distinctive concern about the consequences of panic attacks. Some fear that attacks indicate the presence of an undetected life-threatening disease (e.g., heart disease), and others fear that panic attacks indicate that they are causing, losing control, or being emotionally weak. However, patients with PD do not necessarily show deterioration in the quality of their lives by becoming prisoners of panic attacks [17]. Some individuals with PD significantly change their behavior (e.g., they leave work). Concerns about the next attack or its consequences are often associated with avoiding behavior. Hence, PD is defined as an experience of having panic attacks and as emotional and behavioral consequences from it.

2.3 Diagnosis of panic disorder

To help pinpoint a diagnosis it is necessary to do:

- Complete physical exam.
- Blood tests to check the thyroid and other possible conditions and tests on heart, such as an electrocardiogram (ECG or EKG).
- Psychological evaluation about symptoms, fears or concerns, stressful situations, relationship problems, situations that are avoided, and family history. Fill out a psychological self-assessment or questionnaire.
- Check alcohol or other substance use.

Criteria for diagnosis of panic disorder according to ICD-10 are:

- At least 1 month many attacks with vegetative anxiety which occur in circumstances where there is no objective danger;
- Panic attacks are without restrictions on known and predictable situations
- There is no symptoms of anxiety between seizures (although anxiety may be common)
- Psychological or vegetative symptoms are primary manifestations of anxiety, and not secondary to other symptoms, such as crazy ideas or obsessive thoughts;
- Anxiety must be limited to at least two of the following situations (or mainly to occur only in them): crowds, public places, travel from home, or unaccompanied travel by another person;
- Avoiding the phobic situation

A single panic attack may only last a few minutes, up to 20–30 min, but can cause serious problems in the everyday life. This can also lead to:

- Anticipatory anxiety in between panic attacks, the patient feels anxiety and tension, because of a fear of having future panic attacks. This "fear of fear" is present most of the time, and can be extremely disabling in everyday life.
- Phobic avoidance of certain situations or environments. This avoidance may be based on the belief that the situation that is avoided caused the previous panic attack, or is a place where the escape is difficult or the help is unavailable in case of a panic attack. Taken to its extreme, phobic avoidance becomes agoraphobia.

3. Causes of panic attacks and panic disorder

The causes have not been fully illuminated, although there are a number of theories.

3.1 Biological theories and pathophysiology of panic attacks and panic disorder

From biological theories, there is a genetic predisposition and disturbance in the functioning of certain neurotransmitter systems in the brain (noradrenergic, serotonergic, dopaminergic, GABA). During panic attack an excessive vegetative reaction, with an increased tonus of sympathetic system is present, and also with increased catecholamine release [20].

The exact pathophysiology of PD is currently unknown. There are theories that functioning of serotonin, norepinephrine, dopamine and gamma-aminobutyric acid (GABA) neurotransmitter systems play a role [42].

- The noradrenergic theory assumes that in PD presynaptic norepinephrine auto-receptors are hypersensitive to stimulation by norepinephrine [31].

- Other clinical studies demonstrate that medications increasing the synaptic availability of 5-HT, are effective in the treatment of PD. Rival theories of 5-HT deficiency vs. excess attempt to explain the impact of 5-HT function in PD [41].

- Researches are indicating that GABA may play a role—PD is a result of a lack of central inhibition and decreased GABA concentrations, leading to uncontrolled anxiety during panic attacks [24, 26].

3.2 Psychological theories

As a special predisposing characteristic of people who are prone to the development of panic disorder, the existence of anxiety character is emphasized, which is manifest in childhood as a tendency to shame, cold and wet palms, fear of illness, constant need for support, hypersensitivity to the opinions of others, constant fear not to commit mistake, incompetence to accept responsibility, tranquility, scrupulousness, too high expectations of oneself.

Psychological theories speak of separation fears, the austerity of the release of sexual energy, the traumatized trauma, various misconceptions, or irrational thoughts, etc.

- Psychodynamic theory of panic attacks describes a state of regression in which a complete collapse of the defense defeats, anxiety overwhelms the person and is “empty” through panic states.

- Behavioral theory stresses that anxiety can be learned through the identification of the parent behavior model, then anxiety that develops after experiencing frightening stimuli, such as accidents, that are transmitted to other stimuli, as well as anxiety due to frustration that becomes a conditioned response to other stressful situations.

3.3 Researches: causes for panic attack and panic disorder

3.3.1 Genetic

Several studies have shown that the risk of PD is eight times higher in those with first-degree relatives with PD compared to those with no family history [40, 55]. Recent studies examine twins and estimate that the heritability of panic disorder is 30–40%.

A review of family and twin studies shows the highly familial nature of panic disorder and suggests evidence for a genetic etiology. The population-based lifetime rates of panic disorder cross-nationally range between 1.2/100 and 2.4/100, whereas, the lifetime rates in first-degree relatives of panic probands range between 7.7/100 and 20.5/100 [66].

3.3.2 Environmental

Combination of genetic and environment interactions can produce panic disorder [60]. Major stress and temperament that is more sensitive to stress or prone to negative emotions are connected with a onset of PD including major life transitions such (graduating from college and entering the workplace, getting married, or having a baby), and other severe stress (death of a loved one, divorce, or job loss) [21]. The aversive childhood events such as physical or sexual abuse have been associated with an increased risk of PD in adulthood [9, 10, 25].

3.3.3 Other

Asthma and smoking also have been associated with an increased risk of PD [13, 28]. Panic attacks can also be caused by medical conditions and other physical causes like mitral valve prolapse or hyperthyroidism [2, 34]. Substance abuse, especially stimulants (amphetamines, cocaine, and caffeine), may also be connected with the onset of panic attacks and PD.

4. Complications of panic attacks and panic disorder

Complications that panic attacks and panic disorders may cause avoidance of social situations, problems at work or school, depression with suicidal thoughts, substance abuse.

5. Treatment for panic disorder

The first contact of patient with PD usually is with a family physician. Due to the presence of numerous physical symptoms of panic attack, many people initially perform different somatic tests, from routine, to more complex, to internal and neurological examinations, and fail to timely initiate treatment. This is why the role of a family physician is important in recognizing and treating the disorder, or referring to a psychiatrist. Unfortunately only a minority of patients with panic disorder receive adequate care. One of the reasons is that about 50% of patients seek help [27, 36, 43].

Treatment of panic disorder should in no way be limited to providing first aid during panic attacks (usually by injection of diazepam intramuscularly as an emergency) without planning a targeted and ongoing treatment. The main treatment options are psychotherapy and medications. Combination of them is considered as the most effective [3].

5.1 Psychotherapy

Psychotherapy can help to understand panic attacks and panic disorder and learn how to cope with them.

- Individual therapy: That is, the most usual form of psychotherapy when dealing with panic disorder, but also other form of psychotherapy can be applied.

- Group therapy: Group therapy has positive sides because by sharing the experiences with others, people are creating opportunities for reinforcement by the others and decreasing their shame.

- Couples and family therapy: Symptoms of panic disorder usually affect the relations among the members in the family. Family and couple therapy helps them to improve the communication and to support the person with panic attack or disorder in an appropriate way.

5.1.1 Psychoanalysis and psychodynamic therapy

Psychoanalysis and psychodynamic therapy deals with problematic behavior, feeling, or thought by finding their unconscious meaning. When focused on panic deal with core conflicts in the person which are involving aggression and fearful dependency, or other intrapsychic conflicts that can also contribute to panic symptomatology [45].

5.1.2 Cognitive behavioral therapy

Cognitive-behavioral therapy involves teaching patients to recognize their distorted thinking. The goal is to clarify the patient's misinterpretation of the physical symptoms of panic attack and act on avoiding behavior by gradually exposing the situations that led to the attack. Useful relaxation exercises as well as regular breathing exercises, with moderate physical activity, are also useful.

In cognitive-behavioral treatment of panic disorder patients learn useful information about how and why anxiety, fear and panic occur, learn to apply various relaxation techniques, go through a gradual exposure to situations that create fear when are prepared, learn how their thoughts, assumptions and beliefs about anxiety and panic and their consequences worsen their problem and how they can deal with them, along with the therapy they go through various experiments to test their beliefs about fear and panic, and find out what to do in case of panic attacks [14].

Research shows that CBT efficacy is between 85 and 90% for treatment consisting of 12–15 meetings. In addition, most of the participants maintained this progress a year after treatment when monitored. Some studies have shown that CBT is at least as successful in the treatment of panic disorder as pharmacotherapy, but that treatment has been more prolonged by CBT. Namely, in CBT, an individual learns strategies to efficiently cope with his anxiety that is the skill he can use for his entire life [1, 49, 51, 67].

5.1.3 Humanistic therapy

Humanistic therapy (client-centered therapy, gestalt therapy, and existential therapy) is focused on people's capacities to make rational choices to use their potential and to accept the responsibility for themselves. It helps people to understand what is happening with them and to focus on the present by making new, more functional choices [65].

5.1.4 Self-help tips for panic attacks

The following self-help techniques can make a difference to overcome panic:

- Learn about panic and anxiety.
- Learn how to control your breathing. Deep breathing can relieve the symptoms of panic.
- Practice relaxation techniques—yoga, meditation, muscle relaxation to increase feelings of joy and equanimity.
- Exercise regularly. At least 30 min on most days (three 10-min sessions is just as good) like walking, running, swimming, or dancing can be especially effective.
- Connect face-to-face with family and friends. Symptoms of anxiety can become worse when you feel isolated, so building supportive friendships can help.
- Avoid smoking, alcohol, and caffeine.
- Get enough restful sleep [4].

5.2 Pharmacotherapy

There are a large number of drugs that have been studied in patients with panic disorder, but no drug has proven superior to other drugs used in the treatment of patients with panic disorder. Pharmacological agents with sufficient evidence to support their use in the treatment of panic disorder include:

- Antidepressants—selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitor (SNRI), tricyclic antidepressants (TCAs) and
- Benzodiazepines [8, 37].

5.2.1 Antidepressants

The modern treatment of panic disorder is based on the use of antidepressants from the selective serotonin reuptake inhibitor (SSRI) and antidepressants from the serotonin and noradrenaline reuptake inhibitor (SNRI). Use of these drugs has less danger of creating addiction and abuse than benzodiazepines. The disadvantage of these antidepressants is delayed by the onset of the positive effect and adverse effects that occur during treatment.

Clinical studies have demonstrated the significant efficacy of SSRI/SNRI drugs in the treatment of panic disorder. Certain differences in medication do not occur in terms of efficacy, but can be observed in terms of side effects, drug delivery methods during their use, and the occurrence of deterioration in dose reduction and upon discontinuation of the drug. Therefore, it is important to pay attention to these factors in the individual selection of medicines. The dosage of antidepressants effective in panic disorder is shown in **Table 1**.

5.2.1.1 Efficacy of antidepressants in acute phase treatment of panic disorder

Antidepressants acting on the serotonergic system—citalopram, fluvoxamine, fluoxetine, paroxetine, sertraline [8, 16, 46, 61], the SNRIs venlafaxine and duloxetine [15, 35, 38, 58], and the TCAs imipramine and clomipramine [5, 39] are effective in treating acute phase of panic disorder.

Drug name	Start	Recommended	Maximum
Antidepressants SSRIs (mg/day)			
Citalopram	10	20–40	40
Escitalopram	5	10–20	20
Fluoxetine	10	20–40	60
Paroxetine	10	20–40	60
Sertraline	50	50–100	150
SNRIs			
Venlafaxine	37.5	75–225	300
Duloxetine	30	60–120	120
TCAs			
Clomipramine	25	100–150	250
Imipramine	25	100–150	300

Table 1.
Dosage of antidepressants effective in panic disorder.

5.2.1.2 Efficacy of antidepressants in long-term treatment of panic disorder

The SSRIs i.e., citalopram, fluvoxamine, paroxetine, the SNRIs venlafaxine and duloxetine and the TCAs, all remain effective in the treatment of panic disorder over the long-term [5, 15, 22, 52].

5.2.1.3 Side effects of antidepressants

In order to avoid or at least alleviate adverse effects, it is recommended that the starting daily dose of antidepressant drugs be lower than the recommended effective dose, and that the daily dose increase will be gradual in the first weeks of treatment. Psycho-education of patients with panic disorder about side effects and slow onset of action of antidepressants is very important. The assessment of outcome should be made only after several weeks of treatment.

5.2.1.4 Dropout rates in treatment of panic disorder with antidepressants

During pharmacological treatment of panic disorder 18% of patients treated with SSRIs, 1–12% of patients treated with venlafaxine and about 30% of patients treated with TCAs dropout prematurely [5, 50, 64].

5.2.2 Benzodiazepines

There are a number of clinical studies, with many years of experience, which indicated that benzodiazepines are effective in treating patients with panic disorders. The benzodiazepines are superior to placebo in the acute phase treatment of panic disorder [11, 63]. They have strong effects on somatic symptoms of anxiety and sleep problems. In addition, Benzodiazepines have a fast onset of action, i.e., they produce effects as soon as an effective dose is administered. For half an hour to an hour after taking benzodiazepine, panic symptoms are reduced, and patients feel easier. No other drug can do this [11]. The correct dosage of benzodiazepine involves a gradual increase in dose to a dose that removes symptoms and does not

cause significant adverse effects, with regular taking more than once a day. Dosage of benzodiazepines effective in panic disorder is shown in **Table 2**.

5.2.2.1 Length of treatment with benzodiazepines

Due to the possible occurrence of dependence and abstinence syndrome, the duration of therapy with benzodiazepines should be short, for several weeks. However, because of the chronic character of the disease, sometimes they should be administered for several months, even for a year with continuous monitoring of the patient [47].

5.2.2.2 Side effects and risks involved in treatment with benzodiazepines

When benzodiazepines are prescribed for long-term use, dependence may occur manifested by dose escalation and problems withdrawing the medication [47, 63].

5.2.2.3 Dropout rates in treatment with benzodiazepines

In panic disorder trials, dropout rates due to side effects are about 15% for benzodiazepines [47].

5.2.3 First-line pharmacotherapy of panic disorder

SSRIs and venlafaxine should both be considered first-line agents for treatment of panic disorder. SSRIs and venlafaxine are effective in acute and long-term treatment, have an acceptable side effect profile and acceptable dropout rate [16, 48, 57].

TCAs may have a slower onset than SSRIs. In addition, TCAs have a less tolerable side effect profile than SSRIs given that they have more anticholinergic effects, and are generally less safe than SSRIs. Finally, reported dropout rates are higher for TCAs compared to SSRIs [5, 6, 62].

In summary, benzodiazepines as monotherapy should not be regarded as a first-line treatment in view of their side effect profile and in view of their lack of efficacy in treating comorbid conditions.

5.2.4 Optimal duration of pharmacotherapy of panic disorder

Studies reported that more than half of the patients interrupt treatment within several months to years [62, 64]. But considering, often relapsing course of panic disorder long-term treatment is recommended [3, 7, 12, 22, 43]. Most guidelines refer to expert consensus and suggest pharmacotherapy for at least a year [6].

Benzodiazepines			
Drug name	**Start**	**Recommended**	**Maximum**
Alprazolam	1	2–4	6
Clonazepam	0.25–0.5	1.5–3	6
Diazepam	5–10	40–50	50
Lorazepam	1–3	2.5–7.5	10
Bromazepam	3	3–9	15

Table 2.
Dosage of benzodiazepines effective in panic disorder.

Providing psychotherapy to panic disorder patients is also beneficial in enhancing the long-term outcome. Some evidence indicates that a CBT relapse-prevention program prevents relapse in patients with panic disorder [23, 59].

5.2.5 Pharmacotherapy in treatment-refractory patients with panic disorder

Some panic disorder patients do not respond, or only respond partially to pharmacotherapy. The treatment of refractory patients should consist of optimizing the current treatment, switching to another agent, or augmentation. Optimizing the current pharmacotherapy may be useful but some studies reported that an increased dosage of a SSRI is no more effective [8, 43].

Switching within or between classes of pharmacological agents, or to another treatment modality with proven efficacy in treating panic disorder, such as CBT, may be effective [23, 29, 53, 57].

Augmentation of antidepressants with an antipsychotic has been suggested for refractory panic disorder patients [30, 54, 56].

6. Conclusion

Panic disorder is a prevalent and disabling disorder with unknown etiology. Panic disorder should be diagnosed as soon as possible and to start the treatment which can be effective. The main treatment for panic disorder is psychotherapy and medication. One or both types of treatment may be recommended, depending of the patient preference, his history and the severity of the panic. The first-line treatment of panic disorder usually is CBT and pharmacotherapy with SSRIs. The recommendations are at least a year of antidepressant treatment. Management of treatment-refractory panic disorder includes a range of switching and augmentation strategies. Psychotherapy helps patients to overcome their fears usually within several months, but occasional visits afterward can help them to ensure that panic attacks are under control.

Conflict of interest

The authors declare that there is no conflict of interest.

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