

TREATMENT OF PANIC DISORDER IN THE REAL WORLD

Panic disorder is classified as an anxiety disorder in the DSM-IV.¹ It affects between 2% and 4% of the general population and is more common in females than in males. It usually manifests itself in young adult life, but may be present in all age groups.



Piet Oosthuizen

*MB ChB, MMed (Psych), PhD
Associate Professor
Department of Psychiatry
Stellenbosch University*

Piet Oosthuizen works in academic practice at Tygerberg Hospital as well as in part-time private practice. His special interests are early psychoses, treatment-resistant mood disorders and anxiety disorders.



D J H Niehaus

*MB ChB, MMed (Psych)
Consultant
Psychiatrist*

*Department of Psychiatry
Stellenbosch University and
MRC Unit for Anxiety and
Stress Disorders
Tygerberg*

Dr Niehaus is a consultant psychiatrist in the Department of Psychiatry at Stellenbosch University. He spent 3 years researching in the genetic basis of obsessive compulsive disorder (OCD) and has a special interest in the treatment of this condition. He currently heads the Ngaphakathi workgroup that focuses on susceptibility factors in schizophrenia.



Dan J Stein

*MB ChB, PhD, FRCPC
Professor and Director
MRC Unit on Anxiety and
Stress Disorders
Department of Psychiatry
Stellenbosch University*

Dan Stein did medicine at UCT, then psychiatry and psychopharmacology at Columbia University. He has edited or authored more than a dozen books, including the American Psychiatric Press Textbook of Anxiety Disorders. The MRC Unit does extensive research on anxiety disorders and offers evaluations to appropriate patients (call 021-938-9229).

DEFINING THE PROBLEM

Panic disorder is marked by recurrent panic attacks. These can be spontaneous or cued, expected or unexpected, nocturnal or diurnal, and can occur with or without agoraphobia.

Panic attacks occur in panic disorder, but may also be present in a number of other psychiatric or general medical conditions (Table I).

Agoraphobia is an irrational fear of places or situations where help may not be readily available, or from which escape may be difficult. Agoraphobia will often lead to avoidance of the feared situations, such as supermarkets, going to church, driving on the freeway and/or attending large gatherings. This may impair the sufferer's functioning on many different levels, including work and social functioning.

WHERE DOES PANIC DISORDER COME FROM?

Neurobiology

Genetics

There is a definite genetic component to panic disorder. First-degree family members have a four-fold to eight-fold increased risk of developing this condition. There is also a fairly high concordance in monozygotic twins.

Functional neuroanatomy

- Neurocircuitry. Two sets of brain areas (neurocircuits) seem to be involved in the experience and processing of anxiety. The first involves the anterior cingulate gyrus, the amygdala, parahippocampal gyrus, orbitofrontal cortex, insulae, cerebellum and superior colliculi. The major-

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Panic disorder will often be comorbid with major depressive disorder. Panic-depression is the most common form of co-morbid anxiety-mood disorder.

ity of these areas are involved in the evaluation of noxious stimuli. The second set involves the sensory and polymodal association areas, which are involved in the processing of anxiogenic stimuli.

- Neurochemistry. Serotonergic, noradrenergic and GABA-ergic neurons all contribute to the amygdala-hippocampal circuits that underlie fear conditioning and extinction.

Psychological factors

The cognitive model of anxiety suggests that irrational cognitions are at the centre of the disorder. According to this model, an innocuous stimulus is followed by negative automatic thoughts (which are often unconscious). Physical and emotional responses to the automatic thoughts are interpreted by the sufferer to be indicative of threat or danger, which leads to further escalation of anxiety.

HOW DOES PANIC DISORDER PRESENT CLINICALLY?

The first panic attack is usually spontaneous, although it may occur after exercise or emotional stress such as separation or loss.

Table I. Medical disorders that may mimic panic disorder

Cardiovascular	Neurological	Substances	Other
Anaemia	Transient ischaemic attacks	Amphetamines	Anaphylaxis
Angina	Cerebrovascular accident	Cocaine	Electrolyte disturbance
Heart failure	Epilepsy	Hallucinogens	
Supraventricular tachycardia	Ménière's disease	Cannabis	
	Migraine	Nicotine	
		Theophylline	
Pulmonary	Endocrine	Withdrawal	
Asthma	Addison's disease	Alcohol	
Hyperventilation	Carcinoid	Benzodiazepine	
Pulmonary embolism	Hypoglycaemia	Opiate	
	Hyperthyroidism		
	Phaeochromocytoma		

Table II. Physical symptoms commonly experienced during a panic attack

Shortness of breath
Tachycardia
Dizziness, light-headedness
Paraesthesia
Chest pain or discomfort
Feeling of choking
Fainting, unsteadiness
Sweating
Tremor
Hot or cold flushes
Derealisation/depersonalisation
Urge to urinate/defaecate
Dry mouth
Nausea
Muscle tension
Visual disturbances
The person feels he or she is going to die/is losing control/'is going crazy'

During a panic attack, there is a rapid escalation of symptoms over approximately 10 minutes. The psychological symptoms are severe, intense anxiety and a feeling that something terrible will happen. This is accompanied by multiple physical symptoms, which may include some, or all, of the symptoms listed in Table II (all of which are mediated by amygdala efferents).

As the panic worsens, most people will try to escape from the situation or get help, hoping that this will cause the panic to stop. It is a frightening experience and although after suffering multiple panic attacks patients realise that they won't die, panic

attacks continue to be extremely unpleasant.

Agoraphobia

People with this condition anticipate the possibility that they may have another panic attack, and therefore avoid situations where it is difficult to escape or to get help. They also prefer to be accompanied by family and friends when they visit places like the church, shopping centres, confined places like lifts and even when travelling in a car on a freeway. Some patients become totally housebound.

Other symptoms

Panic disorder will often be co-morbid with major depressive disorder. Panic-depression is the most common form of co-morbid anxiety-mood disorder. Also, the consequences of panic disorder disrupt a patient's life on various levels, which include social and work functioning, as well as the risk of drug abuse through patients trying to medicate themselves.

COURSE

Panic disorder typically begins in early adulthood, but can start at any age. It is usually a chronic condition, although the course is variable. The condition may be complicated by co-morbid major depressive disorder (between 40% and 80% of patients). In cases with co-morbid agoraphobia, the outcome is worse. The course may be complicated further by alcohol abuse as patients try to self-medicate.²

DIFFERENTIAL DIAGNOSES

There are a number of psychiatric conditions that may present with panic attacks (Table III). These need to be differentiated from panic disorder, as the treatment may be different. Also, there are various medical disorders that may mimic panic disorder (Table I). These need to be considered before a diagnosis of panic disorder is made. Clinicians should be aware of the medical factors that may complicate panic and investigate these as appropriate (Table IV).

Table III. **Psychiatric disorders that may present with panic attacks**

Common

- Major depressive disorder
- Social phobia
- Specific phobias
- Post-traumatic stress disorder

Less common

- Obsessive-compulsive disorder
- Hypochondriasis
- Factitious disorder

Table IV. **Medical workup for patients with symptoms of panic disorder⁶**

- Medical, psychiatric and social history
- Physical and neurological evaluation
- Family history
- Medication and drug history
- ECG (patients > 40 years)
- Laboratory tests
- Full blood count
- Blood chemistry
- Thyroid function test
- Others specifically indicated

Table V. **Dosing schedule with SSRIs in panic disorder**

Medication	Starting dose per day (mg)	Mean daily dose (mg)	Maximum daily dose (mg)
Fluoxetine	2.5	20 - 40	60
Citalopram	10	20 - 40	60
Sertraline	50	50 - 100	200
Paroxetine	10	20 - 40	60
Fluvoxamine	50	100	300

TREATMENT

Treatment of panic disorder may consist of pharmacotherapy, psychotherapy or a combination of the two. Of these, medications have a more rapid onset of effect; however cognitive behaviour therapy (CBT) may have the advantage of preventing relapse once medication is discontinued. Many clinicians prefer to use a combination of treatments.³

PSYCHOLOGICAL TREATMENTS

Psychoeducation

Patients with panic disorder often fear that they may have a life-threatening medical disorder such as ischaemic heart disease or epilepsy. Other patients fear that the attacks may themselves be fatal or may damage them in some way. It is of utmost importance that patients with panic disorder understand the illness, its symptoms and treatment very well. The doctor has a crucial role in educating both the patient and his/her carers, but other resources such as other mental health workers, information leaflets,

the Internet and support groups such as the Depression and Anxiety Support Group of SA may also be of great help.

Psychotherapies

The best evidence for treatment success exists for cognitive-behavioural approaches.⁴ A trained therapist, who may be a clinical psychologist or a psychiatrist who has had training in these treatment modalities, can do this. However, the general principles are straightforward and can be incorporated into general practice.

The aim of the cognitive part of the therapy is to eliminate or modify thought patterns that may cause or contribute to the patient's symptoms. The behavioural part of the therapy may consist of relaxation training, breathing exercises and various forms of exposure, including interoceptive exposure and systematic desensitisation. The principle of behaviour therapy is to encourage the patient to face up to feared situations and not to avoid anxiety-provoking stimuli.

Pharmacological treatment

Although there are a variety of medications that may be effective in the treatment of panic disorder, the selective serotonin reuptake inhibitors (SSRIs) are widely accepted as the first-line pharmacological treatment.⁵ Other pharmacological agents that may be effective are some of the older tricyclic antidepressants (particularly imipramine and clomipramine), high-potency benzodiazepines (such as alprazolam and clonazepam) and monoamine oxidase inhibitors. Use of medications from one or more of the last three groups may be complex and

require high levels of vigilance on the part of the clinician. These second-line and third-line treatments should only be commenced under the supervision of a psychiatrist. The most important principle in the pharmacological treatment of panic disorder is: 'start low, go slow, end high'.

Patients with panic disorder are usually extremely sensitive to medication and may often find that the initiation of pharmacotherapy worsens their symptoms before improving them. Hence the principle of initiating medication at very low doses. Paradoxically, however, patients with panic disorder may ultimately need fairly high doses of antidepressants to control their symptoms.

When starting a patient on an SSRI, recommended starting doses are in the order of 2.5 mg of fluoxetine per day, 5 mg of escitalopram, 10 mg of citalopram/paroxetine per day, and 25 - 50 mg of sertraline/fluvoxamine per day (Table V).

Patients should be warned that their anxiety might increase over the first few days of taking an SSRI. To counteract this, a course of treatment with benzodiazepines is often prescribed in the first 2 weeks. Medications that are commonly used for this purpose include clonazepam and alprazolam. Patients should be warned about the side-effects of benzodiazepines and should be advised not to drive a car or operate dangerous machinery while on a benzodiazepine. After 2 - 3 weeks, the benzodiazepine may be tapered and discontinued.

Patients should also be informed about the other potential side-effects of the SSRIs, such as headaches, nausea and sexual dysfunction. It is important for patients to realise that side-effects are 'normal' and transient, to avoid non-compliance should unexpected side-effects occur.

The dose of the SSRI should be increased slowly over a period of weeks and should be titrated against the patient's symptoms and side-effect

burden. As mentioned before, patients with panic disorder may often require doses of antipanic medications that are higher than the doses prescribed in major depressive disorder. A therapeutic trial with an antipanic agent should last for at least 6 - 8 weeks before efficacy can be assessed.

Failure of an SSRI to relieve symptoms should prompt the clinician to re-evaluate the diagnosis, differential diagnosis and non-pharmacological treatment, before a new medication is started. It is common practice to change to a medication from a different class after a failed trial. However, there is anecdotal evidence that failure of one SSRI is not necessarily indicative of a class effect and that another SSRI or a serotonin noradrenaline reuptake inhibitor (SNRI) may be effective for a given patient. If the patient fails to respond to a second agent, he/she should be referred for a specialist opinion.

Once the patient has been stabilised, treatment should continue at the same dose until the patient has been totally symptom-free for at least 12 months. Even mild, limited symptoms may suggest a need for continued or additional treatment. Discontinuation of pharmacological treatment should be a gradual, supervised process during which the physician is available for support.

Panic disorder tends to be chronic and some patients will need on mainte-

nance treatment. CBT may allow for an earlier discontinuation of medication and prevent relapse. Patients should be made aware that chronic treatment with an antidepressant may be necessary and that this will not lead to physiological dependency.

References available on request.

IN A NUTSHELL

Panic disorder is a common condition.

Panic disorder is often accompanied by agoraphobia, where patients will avoid situations where help is not readily available or from which it may be difficult to escape.

Panic disorder often co-exists with major depressive disorder.

Medical disorders which may mimic panic attacks should be ruled out before a final diagnosis is made.

Treatment consists of a combination of medication and psychotherapy. SSRIs are the first line of pharmacological treatment.

The most important principle in the pharmacological treatment of panic disorder is: 'Start low, go slow, end high'.

Patients should be treated until they are symptom-free for at least a year.

Psychoeducation forms an integral part of the treatment of panic disorder.

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