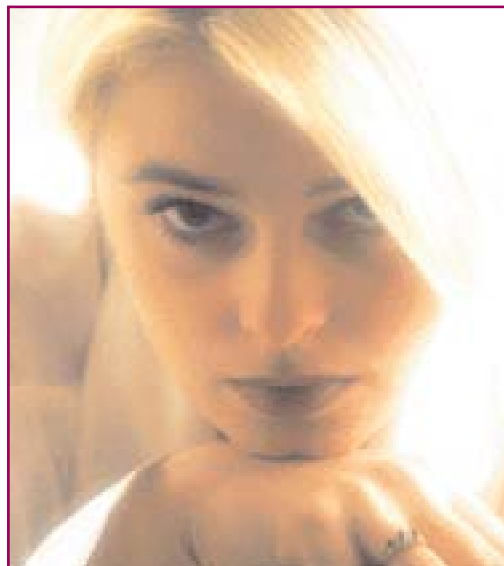

Anxiety Disorders: From Diagnosis to Treatment

Physicians are often called upon to diagnose anxiety disorders. It is important to be familiar with these common psychiatric disorders and their treatment modalities.

By Pierre Bleau B.Sc., MD, CSPQ, FRCPC

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Anxiety and fear are consequences of a complex mechanism that help us to adapt to danger and prepare for appropriate behaviors (flight, fight or freeze) (Figure 1).[1] Anxiety is a fear-like emotion that can be defined through cognitive, somatic and behavioral components. Anxiety could be viewed in a general sense as part of a problem-solving process—an attempt to counteract an obstacle. On the other hand, when anxiety loses its adaptational character, the individual becomes dysfunctional. He/she is then in emotional pain and unable to function normally. At this point, simple anxiety becomes anxiety disorder (AD).

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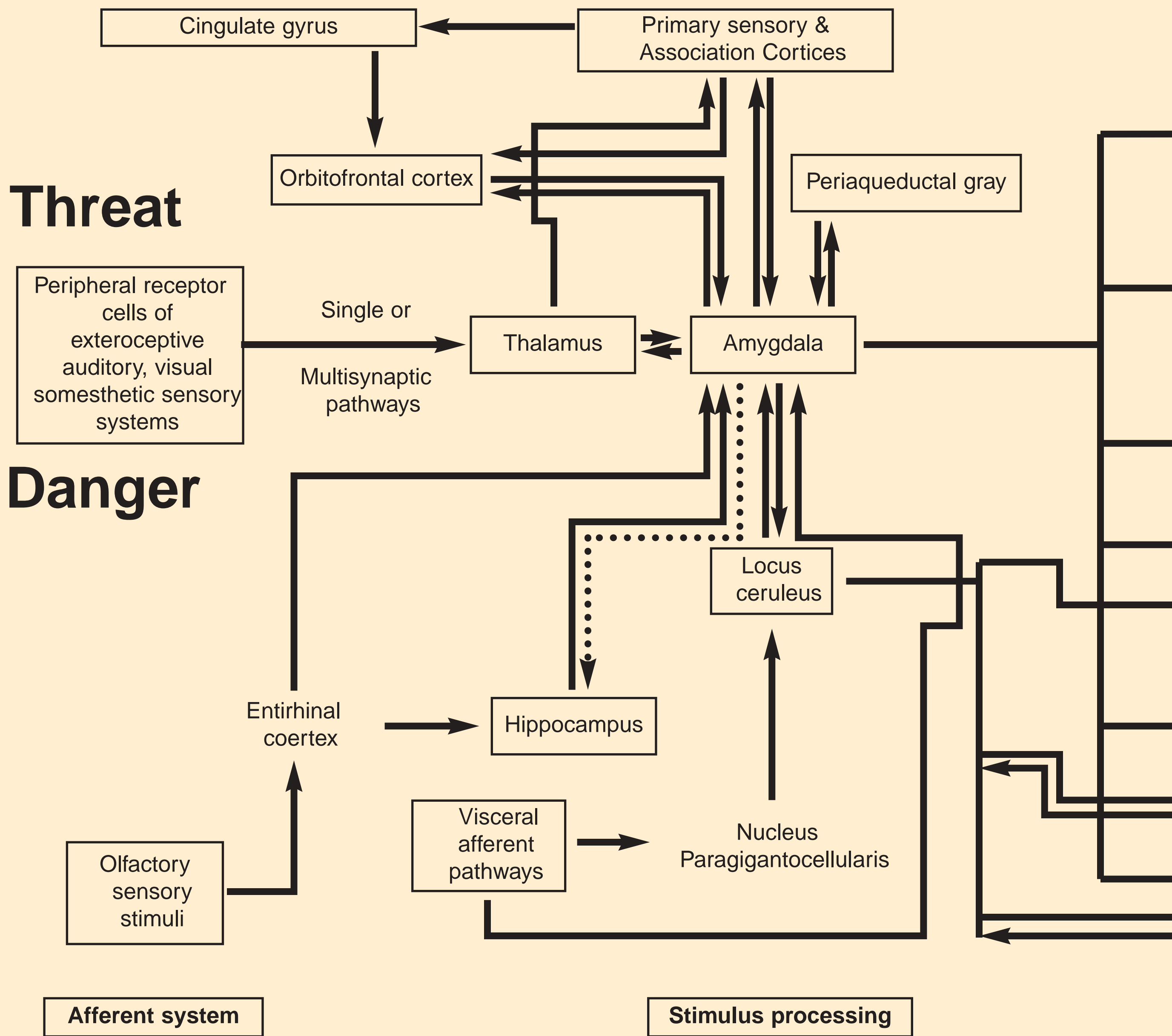
Over the last 20 years, ADs have been the subject of many intense research studies. We now have a better semiologic definition, and a different understanding of the neurobiological processes implicated in AD, as well as of the development of a wider range of treatment modalities. AD represents 50% of all psychiatric disorders. According to the National Comorbidity Survey (NCS), AD is prevalent in 25% of the general population (Table 1).[2]

Table 1

Functional Neuroanatomy of Fear and Anxiety



Adapted from Charney & Deutsch, 1996.[1]

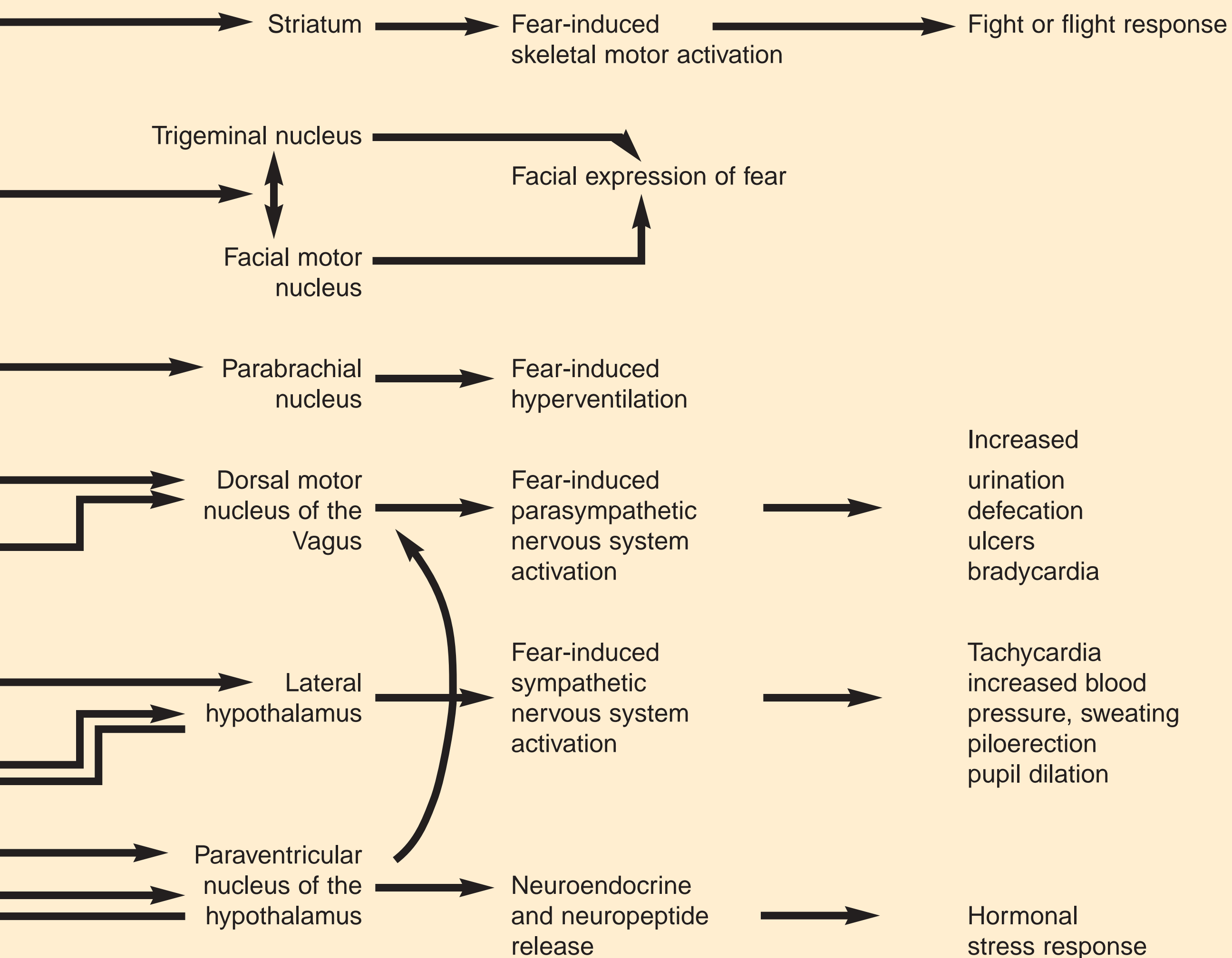

Fear and Anxiety
Response Patterns
Striatum
Fear-induced
skeletal motor activation
Fight or flight response
Trigeminal nucleus
Facial expression of fear
Facial motor
nucleus
Parabrachial
nucleus
Fear-induced
hyperventilation
Dorsal motor
nucleus of the
Vagus
Fear-induced
parasympathetic
nervous system
activation
Increased
urination
defecation
ulcers
bradycardia
Lateral
hypothalamus
Fear-induced
sympathetic
nervous system
activation
Tachycardia
increased blood
pressure, sweating
piloerection
pupil dilation
Paraventricular
nucleus of the
hypothalamus
Neuroendocrine
and neuropeptide
release
Hormonal
stress response
Efferent system

Table 1

Anxiety Disorders (DSM-IV TR)*

- Panic Disorder
- Agoraphobia
- Specific Phobia
- Social Anxiety Disorder
- OCD
- Acute Stress Disorder
- Post-traumatic Stress Disorder
- Generalized Anxiety Disorder
- Adjustment Disorder (Not in AD, but often with anxiety)

Adapted from *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition, Text Revision. American Psychiatric Association, Washington, DC, 2000.

Table 2

Physical Symptoms

Physical Symptoms

- Panic attacks
- Difficulty falling or staying asleep
- Hypervigilance
- Startled response
- Exaggerated startle response
- Restlessness or feeling "keyed up" (on edge)
- Fatigue
- Muscle tension

Cognitive Symptoms

- Irritability
- Has difficulty concentrating
- Worries
- Responsiveness
- Depersonalization } Interpretation from psychosensory modification
- Derealization }

Behavioral Symptoms

- Avoidance
- Rituals
- Alcoholism
- Addictive behavior (with others, with substance)

Far away from an acute reaction, researchers have demonstrated the chronicity and morbidity of AD. Often pervasive, ADs are comorbid with each other, with affective disorders and with substance-abuse disorders.

Get the Diagnosis Right

Without getting into a detailed description of all diagnostic criteria contained in the DSM-IV-TR, certain aspects should be noted. Indeed, the ADs are classified according to certain constants:

1. Each disorder manifests itself with physical, psychological or cognitive and behavioral symptoms (Table 2).
2. Before diagnosing AD, physicians must eliminate all medical conditions, as well as toxic states that could be responsible for the symptoms.
3. Each disorder represents a nosological entity because the patient is in pain and dysfunctional.
4. The fearful object, the content of cognitive aspects of the fear, represent the differential criteria.

Even though all behavioral signs or physical symptoms (*e.g.,* panic attacks) can be part of any AD, physicians can ask questions that will help clarify the diagnosis. Some questions to ask include:

- What is the worst that could happen to you?
- What are you thinking about while enduring your anxiety?

The cognitive thematic also will be the main focus for cognitive behavioral treatment.

Panic disorder (PD) patients have a sharp interoceptive focus. They fear everything they feel inside their bodies. Everything new or unexpected is believed to have a possible catastrophic outcome (catastrophic interpretations). Anticipation of imminent danger could lead to avoidance of places where the patient fears becoming helpless (agoraphobia).

Social anxiety disorder (SAD). Patients who suffer from SAD have dysfunctional beliefs concerning the judgment of others. Patients are unable to tolerate being observed or embarrassed, and humiliation is perceived to be the worst thing that could happen to them.

Obsessive compulsive disorder (OCD). Even though the rituals and the compulsiveness of patients with OCD are seen as characteristic of this disorder, the diagnosis cannot be based solely on the presence of these behaviors. The presence of obsessions (imposed thoughts) create anxiety. Then, rituals begin in order to alleviate the anxiety. Patients are often afraid that their obsessions will become real, or that their anxiety might lead to "insanity."

Generalized anxiety disorder (GAD). In this disorder, patients experience thoughts as an inner speech. Patients are intolerant of the "unknown," and uncertainty leads them to excessive planning, anticipation or exaggerated problem solving. They consider everyday occurrences in the worst regard.

Post-traumatic stress disorder (PTSD). Traumatic events are the main cause of worry in these patients. The trauma is played back in thoughts, images or dreams. The patient tries to stop or avoid the painful images, which results in panic attacks, sadness, isolation and hypervigilance.

Panic attacks occur in most anxiety disorders. They should be explored to ensure a correct diagnosis of the particular psychiatric disorder (AD, affective disorder).

Treating Anxiety Disorders

When in doubt, treat an AD as if it was depressive disorder. Cognitive-behavioral therapy (CBT) and

When you see genital herpes, think Famvir.

It has been estimated that 7 out of 10 genital herpes sufferers go undiagnosed.[1]

Famvir is indicated to treat or suppress recurrent episodes of genital herpes in immune-competent adults. Therapy should be initiated during the prodome or as soon as possible after the onset of lesions.

Most common adverse reactions reported with Famvir in clinical trials were headache and nausea. In patients with moderately or severely reduced renal function, dosage reduction is recommended.

See prescribing information for more information.

1. Catotti DN *et al.* Herpes Revisited: Still a cause for concern. *Sex Trans Dis* 1993; 20 (2):77-80.
* Registered trademark of Novartis AG.

Episodic 125 mg BID for 5 days, suppression 250 mg BID

Table 3

Pharmacotherapy of Anxiety Disorders

Class of Drugs	Name	Dosage (mg)	Comments
SSRI	Paroxetine	10-60	Wait until 8-10 wks for PD, 12-16 for SAD,PTSD
	Sertraline	25-200	Start low, go slow
	Citalopram	10-60	For ocd, aim highest dosage, for PD intermediate
	Fluvoxamine	25-300	
	Fluoxetine	10-80	
SNRI	Venlafaxine XR	37.5-300	Good for GAD, watch PA in PD when >75 mg
MAOI	Phenelzine	15-90	Watch for hypertensive crisis
RIMA	Moclobemide	150-600	Used with higher dosage in Europe for SAD, PD
NaSSA	Mirtazapine	15-45	Consider as alternative in PD, PTSD
TCAs	Clomipramine	25-300	Clomipramine=SRI used in OCD
	Desipramine	25-200	
	Nortryptiline	10-60	
BZD*	Alprazolam	0,25-3000	Alprazolam: used in PD
	Clonazepam	0,5-4	Clonazepam: used in PD, SAD (Could be used in GAD, but consider addiction)
Anticonvulsivant	Valproate	250-1500	Useful for treating PTSD,PD,OCD as augmentation therapy.
	Gabapentine	600-3600	Gabapentine described as first line for SAD in a recent study
5-HT$_2$ blocker	Nefazodone**	50-600	Useful for GAD, PD, PTSD
	Trazodone**		Given as sedative
5-HT$_{1a}$ action	Buspirone (agonist)	15-60	Could be useful as augmentation
	*Pindolol (antagonist)	2,5 tid	Used mainly in OCD
Neuroleptic	Risperidone	0,5-2	Augmentation in OCD and PTSD
	Olanzapine		in study
Others	Ondansetron (5-HT$_3$ blocker)	0,25 bid.	Could be used in GAD & SAD
	Pramipexole	0,125 tid.	Augmentation in SAD
	Clonidine	0,1 bid	In PD & SAD Early in PTSD 0,05 B.I.D. in OCD

SSRI=Selective serotonin reuptake inhibitor; SNR=Serotonin/noradrenalin reuptake inhibitor; MAOI=Monoamine oxydase inhibitor; TCA=Tricyclic antidepressant; RIMA=Reversible inhibitors of monoamine oxydase; NaSSA=Noradrenergic/specific serotonin antidepressant; BZD=Benzodiazepine; 5-HT$_{1,2,3}$=serotonin receptors; PD=Panic disorders; SAD=Social anxiety disorders; GAD=Generalized anxiety disorders; OCD=Obsessive-compulsive disorders; PTSD=Post traumatic stress disorders;
*Pindolol=antihypertensive medication.
**MCPP as metabolite, could create anxiety.

psychopharmacotherapy are the gold standards for treating AD. Although sometimes offered together, it may be necessary to get sequential treatment in order to achieve better results (Table 3). Over the past few years, selective serotonin reuptake inhibitors (SSRI) have become the first line of action. Because of their side-effect profiles, benzodiazepines (BZD) and tricyclics antidepressants (TA) are second-line modalities, while monoamine-oxydase-inhibitors are a third choice.

Cognitive behavioral therapy (CBT) involves exposure to the fear and thought restructuring. Medication desensitizes the whole limbic apparatus of fear, and may play a specific role in the prefrontal lobe in OCD, and in the brainstem in PD. This could be obtained while modulating the serotonin, the noradrenalin and the gamma-aminobutyric acid (GABA) systems.

Because of their prevalence, chronicity and comorbidity, ADs are important psychiatric disorders that should receive close attention. CME

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Suggested Readings
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Put Your Knowledge to the Test

Answer the questions in our quiz found on page 207 and send the response card to the University of Calgary for CME credits.