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.

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Presented as part of McGill University’s Thursday Evening Lecture Series, Montreal, Quebec, November 2000.

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). 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).

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).
Table 1

Functional Neuroanatomy of Fear and Anxiety

Adapted from Charney & Deutsch, 1996.¹
Anxiety Disorders

Fear and Anxiety Response Patterns

- Striatum → Fear-induced skeletal motor activation → Fight or flight response
- Trigeminal nucleus
- Facial motor nucleus → Facial expression of fear
- Parabrachial nucleus → Fear-induced hyperventilation
- Dorsal motor nucleus of the Vagus → Fear-induced parasympathetic nervous system activation
- Lateral hypothalamus → Fear-induced sympathetic nervous system activation
- Paraventricular nucleus of the hypothalamus → Neuroendocrine and neuropeptide release

Increased
- urination
- defecation
- ulcers
- bradycardia

Tachycardia
- increased blood pressure
- sweating
- piloerrection
- pupil dilation

Hormonal
- stress response

Efferent system
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?

### 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)


### Table 2

**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
- Derealization

**Behavioral Symptoms**

- Avoidance
- Rituals
- Alcoholism
- Addictive behavior (with others, with substance)
The cognitive thematic also will be the main focus for cognitive behavioral treatment.

Panic disorder (PD) patients have a sharp introspective 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).

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

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**When you see genital herpes, think Famvir.**

It has been estimated that 7 out of 10 genital herpes sufferers go undiagnosed:

Famvir is indicated to treat or suppress recurrent episodes of genital herpes in immune-competent adults. Therapy should be initiated during the prodrome 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.


* Registered trademark of Novartis AG.

Episodic 125 mg BID for 5 days, suppression 250 mg BID
### Table 3

**Pharmacotherapy of Anxiety Disorders**

<table>
<thead>
<tr>
<th>Class of Drugs</th>
<th>Name</th>
<th>Dosage (mg)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRI</strong></td>
<td>Paroxetine</td>
<td>10-60</td>
<td>Wait until 8-10 wks for PD, 12-16 for SAD, PTSD</td>
</tr>
<tr>
<td></td>
<td>Sertraline</td>
<td>25-200</td>
<td>Start low, go slow</td>
</tr>
<tr>
<td></td>
<td>Citalopram</td>
<td>10-60</td>
<td>For ocd, aim highest dosage, for PD intermediate</td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine</td>
<td>25-300</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoxetine</td>
<td>10-80</td>
<td></td>
</tr>
<tr>
<td><strong>SNRI</strong></td>
<td>Venlafaxine XR</td>
<td>37.5-300</td>
<td>Good for GAD, watch PA in PD when &gt;75 mg</td>
</tr>
<tr>
<td><strong>MAOI</strong></td>
<td>Phenelzine</td>
<td>15-90</td>
<td>Watch for hypertensive crisis</td>
</tr>
<tr>
<td><strong>RIMA</strong></td>
<td>Moclobemide</td>
<td>150-600</td>
<td>Used with higher dosage in Europe for SAD, PD</td>
</tr>
<tr>
<td><strong>NaSSA</strong></td>
<td>Mirtazapine</td>
<td>15-45</td>
<td>Consider as alternative in PD, PTSD</td>
</tr>
<tr>
<td><strong>TCAs</strong></td>
<td>Clomipramine</td>
<td>25-300</td>
<td>Clomipramine=SRI used in OCD</td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td>25-200</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nortryptiline</td>
<td>10-60</td>
<td></td>
</tr>
<tr>
<td><strong>BZD</strong></td>
<td>Alprazolam</td>
<td>0.25-3000</td>
<td>Alprazolam: used in PD</td>
</tr>
<tr>
<td></td>
<td>Clonazepam</td>
<td>0.5-4</td>
<td>Clonazepam: used in PD, SAD (Could be used in GAD, but consider addiction)</td>
</tr>
<tr>
<td><strong>Anticonvulsivant</strong></td>
<td>Valproate</td>
<td>250-1500</td>
<td>Useful for treating PTSD, PD, OCD as augmentation therapy. Gabapentine described as first line for SAD in a recent study</td>
</tr>
<tr>
<td></td>
<td>Gabapentine</td>
<td>600-3600</td>
<td></td>
</tr>
<tr>
<td><strong>5-HT2 blocker</strong></td>
<td>Nefazodone**</td>
<td>50-600</td>
<td>Useful for GAD, PD, PTSD</td>
</tr>
<tr>
<td></td>
<td>Trazodone**</td>
<td></td>
<td>Given as sedative</td>
</tr>
<tr>
<td><strong>5-HT1a action</strong></td>
<td>Buspirone (agonist)</td>
<td>15-60</td>
<td>Could be useful as augmentation</td>
</tr>
<tr>
<td></td>
<td>*Pindolol (antagonist)</td>
<td>2,5 tid</td>
<td>Used mainly in OCD</td>
</tr>
<tr>
<td><strong>Neuroleptic</strong></td>
<td>Risperidone</td>
<td>0.5-2</td>
<td>Augmentation in OCD and PTSD in study</td>
</tr>
<tr>
<td></td>
<td>Olanzapine</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Ondansetron (5-HT3 blocker)</td>
<td>0.25 bid.</td>
<td>Could be used in GAD &amp; SAD</td>
</tr>
<tr>
<td></td>
<td>Pramipexole</td>
<td>0.125 bid.</td>
<td>Augmentation in SAD</td>
</tr>
<tr>
<td></td>
<td>Clonidine</td>
<td>0.1 bid</td>
<td>In PD &amp; SAD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Early in PTSD, 0.05 B.I.D. in OCD</td>
</tr>
</tbody>
</table>

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-HT1,2,3=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-oxidase-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.

Suggested Readings

References