Anxiety Disorders: Diagnosis and Treatment

John J. Miller, M.D.
Medical Director,
Center for Health and Well-Being
Exeter, NH

Objectives

• Define the Anxiety Disorders that are classified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

• Describe the FDA approved medications indicated for each of the Anxiety Disorders

• Discuss the epidemiology of Anxiety Disorders, including the lifetime prevalence of each anxiety disorder, as well as the co-morbidity with Major Depression
Anxiety Disorders

DSM-IV Anxiety Disorders

- Panic disorder
- Generalized anxiety disorder
- Social anxiety disorder
- Obsessive-compulsive disorder
- Post-traumatic stress disorder
- Acute stress disorder
- Agoraphobia
- Specific phobia
- Anxiety disorder due to medical condition
- Substance-induced anxiety disorder
- Anxiety disorder not otherwise specified
Anxiety Disorders: Largely Untreated

Characteristics of PTSD, Panic Disorder, OCD and GAD

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Traumatic Stress Disorder</td>
<td>Intrusive reexperiencing of the trauma – flashbacks and/or nightmares, avoidance of the trauma, numbing, anhedonia, withdrawal, and hyperarousal</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>Recurrent, unexplained panic attacks associated with sweating, palpitations, and trembling along with dyspnea, choking, derealization, and fear of dying</td>
</tr>
<tr>
<td>Obsessive-Compulsive Disorder</td>
<td>Fear of contamination, perseveration at counting behaviors, and recurrent compulsive rechecking of tasks AND/OR severe obsessing</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder</td>
<td>Excessive and uncontrollable worry, edginess, fatigue, poor concentration, irritability, muscle tension, insomnia</td>
</tr>
</tbody>
</table>
Social Anxiety Disorder

- Fear of embarrassment or humiliation in social situations
  - Typical situations include public speaking, eating, conversing with others, using public restrooms
- Blushing, sweating, tremor, and palpitations
- Common comorbidities: dysthymia, obsessive-compulsive disorder, panic disorder, depression, and alcohol abuse
- Interference with functioning
- Anticipatory anxiety

Demographics of Anxiety Disorders

<table>
<thead>
<tr>
<th>Anxiety Disorder</th>
<th>Lifetime Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized Anxiety</td>
<td>5%</td>
</tr>
<tr>
<td>Obsessive Compulsive</td>
<td>3%</td>
</tr>
<tr>
<td>Panic</td>
<td>2-3%</td>
</tr>
<tr>
<td>Post Traumatic Stress</td>
<td>8%</td>
</tr>
<tr>
<td>Social Anxiety</td>
<td>13%</td>
</tr>
</tbody>
</table>
Pharmacotherapy for Obsessive-Compulsive Disorder

**FDA Approved Treatments**

- Clomipramine (Anafranil)
- Sertraline (Zoloft)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)

**Pharmacotherapy for Obsessive-Compulsive Disorder**

**Traditional Treatment**

- Clomipramine
- Sertraline
- Fluoxetine
- Fluvoxamine
- Paroxetine
- Citalopram

**Adjunctive Treatment With:**

- Clonazepam
- Atypical Antipsychotics
Pharmacotherapy for Panic Disorder

FDA Approved Treatments

- SSRIs
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)
  - Fluoxetine (Prozac)
- Benzodiazepines
  - Alprazolam (Xanax)
  - Clonazepam (Klonopin)

Pharmacotherapy for Panic Disorder

Traditional Treatment

- Antidepressants
  - SSRIs
  - TCAs
  - MAOIs
- Benzodiazepines
  - Alprazolam
  - Clonazepam

Treatment With Anticonvulsants

- Valproate
- Carbamazepine
- Gabapentin
FDA Approved Pharmacotherapy for Generalized Anxiety Disorder

- Alprazolam (Xanax)
- Buspirone (BuSpar)
- Venlafaxine (Effexor XR)
- Paroxetine (Paxil)
- Escitalopram (Lexapro)

Pharmacotherapy for Generalized Anxiety Disorder

- Benzodiazepines
- BuSpar
- Effexor XR
- SSRIs
- Anticonvulsants?
FDA Approved Pharmacotherapy for Social Anxiety Disorder

- Venlafaxine  (Effexor)
- Sertraline  (Zoloft)
- Paroxetine  (Paxil)

Pharmacotherapy for Social Anxiety Disorder

- Paroxetine
- Sertraline
- Fluvoxamine
- Fluoxetine
- Citalopram
- Venlafaxine
- Phenelzine
- Clonazepam
- Beta blockers
- Gabapentin
FDA Approved Pharmacotherapy for Post-Traumatic Stress Disorder

- Sertraline (Zoloft)
- Paroxetine (Paxil)

Pharmacotherapy for Post-Traumatic Stress Disorder

Treatments with evidence for efficacy include
- SSRIs (sertraline & paroxetine = FDA approved)
- Antidepressants
- Divalproex
- Lamotrigine
- Carbamazepine
- Adrenergic agonists
- Adrenergic antagonists
- Atypical antipsychotics
Comorbid Mood & Anxiety Disorders...

Generalized Anxiety Disorder
8%-39% 5

Panic disorder
50%-65% 1

Social Anxiety Disorder
70% 2

PTSD
48% 4

Depression

OCD
67% 3

1. American Psychiatric Association DSM IV 1994
2. Van Ameringen M. J Affect Disord. 1991
5. American Psychiatric Association DSM IV 1994

Response Time Varies

- Major Depression: 2-4 weeks
- Panic Disorder: 6-8 weeks
- Obsessive Compulsive Disorder: 10-12 wk
- Premenstrual Dysphoric Disorder: days
Three Important Neurotransmitters

Dopamine
- Attention
- Motivation
- Pleasure
- Cognition
- Energy
- Drive

Norepinephrine
- Alertness
- Attention
- Pain
- Modulation

Serotonin
- We All Treat Depression
- Female Specific Mood Disorders
- Decreases anxiety
- Pain Modulation

Serotonin Selective Reuptake Inhibitors
- Are Currently Considered First Line Medication
- Treatment For Most Anxiety Disorders
Serotonin Reuptake Inhibitors*

- fluoxetine (Prozac, Sarafem)
- clomipramine (Anafranil, a TCA)
- sertraline (Zoloft)
- paroxetine (Paxil, Paxil CR)
- fluvoxamine (Luvox)
- venlafaxine (Effexor, IR XR)
- citalopram (Celexa, Lexapro)
- duloxetine (Cymbalta)

*In order of U.S.A. market entry.

SRI FDA Approvals

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Prozac</th>
<th>Zoloft</th>
<th>Paxil</th>
<th>Effexor</th>
<th>Celexa</th>
<th>Lexapro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression</td>
<td>+*</td>
<td>+*</td>
<td>+*</td>
<td>+*</td>
<td>+</td>
<td>+*</td>
</tr>
<tr>
<td>OCD</td>
<td>+</td>
<td>+*</td>
<td>+*</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>+</td>
<td>+*</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>GAD</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Social Anxiety</td>
<td>-</td>
<td>+*</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PTSD</td>
<td>-</td>
<td>+*</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PMDD</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bulimia nervosa</td>
<td>+*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*FDA approved for both acute and chronic treatment (longer than 44 weeks)
(FDA approvals in children: Zoloft age 6; Prozac age 7; Luvox age 8)
SRI FDA Approvals
Relapse free in weeks

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Prozac</th>
<th>Zoloft</th>
<th>Paxil</th>
<th>Effexor</th>
<th>Celexa</th>
<th>Lexapro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression</td>
<td>50</td>
<td>52</td>
<td>60</td>
<td>60</td>
<td>34</td>
<td>44</td>
</tr>
<tr>
<td>OCD</td>
<td>13</td>
<td>80</td>
<td>52</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>12</td>
<td>80</td>
<td>36</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>GAD</td>
<td>-</td>
<td>-</td>
<td>32</td>
<td>26</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>Social Anxiety</td>
<td>-</td>
<td>44</td>
<td>12</td>
<td>12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PTSD</td>
<td>-</td>
<td>52</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PMDD</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bulimia nervosa</td>
<td>52</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

If At First You Don’t Succeed:

- Add a second medication
- Change to a different medication
  - Same class
  - Different class
- Re-think the differential diagnoses
- Role of psychotherapy
- Motivation of patient
But What About Us??

Other Important Contributors to Anxiety & Depression

- Genetic Predisposition
- Metabolic/Biological Factors
- Personality Structure
- Environmental Factors
- Developmental Factors
- Cultural Factors
- Spiritual Factors

Conclusions

- Most clinically relevant anxiety disorders are treated in the primary care setting.

- Many pharmacological options exist, with significant differences in mechanism of action, kinetics and secondary binding properties.

- SSRIs have proven to be a safe and effective first-line treatment for all anxiety disorders.