Anxiety Disorders

- Separation Anxiety Disorder
- Selective Mutism
- Specific Phobia
- Social Anxiety Disorder (social phobia)
- Panic Disorder
- Agoraphobia
- Generalized Anxiety Disorder
- Substance/Medication-Induced Anxiety Disorder
- Anxiety Disorder Due to Another Medical Condition
- Other Specified Anxiety Disorder
- Unspecified Anxiety Disorder
Obsessive–Compulsive Disorder
Obsessive–Compulsive Disorder and Related Disorders

- Obsessive–Compulsive Disorder
- Body Dysmorphic Disorder
- Hoarding Disorder
- Trichotillomania
- Excoriation Disorder
- Substance/Medication–Induced Obsessive–Compulsive and Related Disorder
- Obsessive–Compulsive and Related Disorder Due to Another Medical Condition
- Other Specified Obsessive–Compulsive and Related Disorder
- Unspecified Obsessive–Compulsive and Related Disorder

All characterized by preoccupations and by repetitive behaviors or mental acts in response to the preoccupations.
A) Presence of obsessions, compulsions, or both:
   ◦ Obsessions:
     • Recurrent and persistent thoughts, urges, or images that are experienced, as intrusive and unwanted, and cause marked anxiety or distress.
     • The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action
     • Not pleasurable or voluntary
   ◦ Compulsions:
     • Repetitive behaviors or mental acts that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
     • The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation
     • Not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.
DSM–V Review: Diagnostic Criteria

- B) The obsessions or compulsions are **time-consuming** or cause clinically **significant distress or impairment** in social, occupational, or other important areas of functioning.

- C) The obsessive–compulsive symptoms are **not attributable** to the physiological effects of a substance or another medical condition.

- D) Not better explained by the symptoms of another mental disorder.

Specify if:
- With good or fair insight
- With poor insight
- With absent insight/delusional beliefs
- Tic-related
### DSM–V: Diagnostic Criteria Examples

<table>
<thead>
<tr>
<th>Obsessions</th>
<th>Compulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent thoughts of contamination</td>
<td>Ritualizing</td>
</tr>
<tr>
<td>Ruminations</td>
<td>Washing</td>
</tr>
<tr>
<td>Images of violent or horrific scenes</td>
<td>Checking</td>
</tr>
<tr>
<td>Urges to stab someone</td>
<td>Counting</td>
</tr>
<tr>
<td></td>
<td>Repeating words silently</td>
</tr>
<tr>
<td></td>
<td>Hoarding</td>
</tr>
</tbody>
</table>
DSM–V Review: Diagnostic Criteria Themes

- Including:
  - Cleaning
    - contamination obsessions and cleaning compulsions
  - Symmetry
    - Symmetry obsessions and repeating, ordering, and counting compulsions
  - Forbidden or taboo thoughts
    - Aggressive, sexual, or religious obsessions and related compulsions and
  - Harm
    - Fears of harm to oneself or others and checking compulsions

- Occur across different cultures
- Relatively consistent over time in adults with the disorder
- May be associated with different neural substrates
**DSM–V Review: Diagnostic Issues**

- **Culture-Related Diagnostic Issues:**
  - OCD occurs across the world.
  - Similarity across cultures in the *gender distribution, age at onset, and comorbidity* (Lewis–Fernández et al. 2010).
  - Similar symptom structure involving *cleaning, symmetry, hoarding, taboo thoughts, or fear of harm* (Bloch et al. 2008).
  - Regional variation in symptom expression
  - *Cultural* factors may shape the content of obsessions and compulsions.

- **Gender-Related Diagnostic Issues:**
  - Males have an *earlier* age at onset & are more likely to have *comorbid* tic disorders.
  - Females more likely to have symptoms in the *cleaning* dimension
  - Males more likely to have symptoms in the *forbidden thoughts and symmetry dimensions*.
  - Onset or exacerbation of OCD & symptoms that can interfere with the *mother–infant relationship*
DSM–V: Associated and Secondary Features

- Cleaning
- Symmetry
- Taboo thoughts
- Harming self or others
- Hoarding

- Increased suicide risks
- Panic attacks
- Agoraphobia
- Distress
- Avoid:
  - people,
  - places, and
  - things that trigger obsessions and compulsions
DSM-V: Prevalence

- United States: 1.2%
- Internationally: 1.1%–1.8%
- Females are affected at a slightly higher rate than males in adulthood,
- Males are more commonly affected in childhood (Ruscio et al., 2010; Weissman et al., 1994)
DSM–V: Onset

- United States, mean onset: 19.5 years
  - 25% start by age 14 years (Kessler et al. 2005; Ruscio et al. 2010)

- Onset after age 35 years is unusual

- Males have an earlier age at onset than females
  - nearly 25% of males have onset before age 10 years (Ruscio et al. 2010).

- Onset of symptoms is typically gradual.
  - Acute onset has also been reported.
DSM–V: Course

- Usually **chronic**
  - Often with **waxing** and **waning** symptoms (Ravizza et al., 1997; Skoog & Skoog 1999)

- Onset in childhood or adolescence can lead to a **lifetime** OCD

- **40%** of individuals with onset of OCD in **childhood or adolescence** may experience **remission** by early adulthood (Stewart et al. 2004)

- Pattern of symptoms in adults can be **stable** over time, but it is more **variable** in children (Mataix–Cols et al. 2002; Swedo et al. 1989).

- May be based on developmental stage
Greater internalizing symptoms

Higher negative emotionality, and

Behavioral inhibition in childhood
  ◦ (Coles et al. 2006; Grisham et al. 2011).
Physical and sexual abuse and other stressful or traumatic events (Grisham et al., 2011)

Sudden onset of symptoms associated with different environmental factors
  ◦ Infectious agents and a post–infectious autoimmune syndrome (Singer et al., 2012; Swedo et al., 2004).
Rate of OCD among first-degree relatives of adults with OCD is approximately two times that among first-degree relatives of those without the disorder.

Among first-degree relatives → increased 10-fold onset (Pauls 2010)

Familial transmission
- 0.57 for monozygotic
- 0.22 for dizygotic (Pauls 2010)

Dysfunction
- Orbitofrontal cortex,
- Anterior cingulate cortex, and
- Striatum (Millad and Rauch 2012).
DSM–V: Comorbidity

- Anxiety disorder: 76%
- Depressive or bipolar disorder: 63%
- Major depressive disorder: 41%
- Obsessive–compulsive personality disorder: 23%–32%
- Body dysmorphic disorder
- Trichotillomania
- Excoriation disorder
- ODD
- Tic Disorder
DSM– V Model:

Risk and Prognostic Features

Temperament:
- Greater internalizing 
- Higher negative emotionality
- Behavioral inhibition

Environmental:
- Physical/Sexual abuse
- Trauma
- Infectious disease
- Autoimmune syndrome

Genetics/Physiology:
- Familial transmission
- Dysfunction in OFC, ACC, and striatum

Diagnostic Criteria
- Obsessions
- Compulsions
- Secondary and associated features

Anxiety Disorder
- Depressive or Bipolar
- OCD Personality

ODD, Excoriation, Body dysmorphic, Trichotillomania
Components of OCD

As per extant literature
Diagnostic Criteria:

- Presence of distressing **intrusive**, unwanted, thoughts, impulses, fears or images (obsessions), and/or **repetitive** behaviors or mental rituals (compulsions)

- Knowledge that the thoughts and actions are **senseless** and **unreasonable** (Turner et al., 1985)

- Rituals usually serve an **anxiety-reducing** function (Turner et al., 1985)
## Diagnostic Criteria

<table>
<thead>
<tr>
<th>Obsessions</th>
<th>Compulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>‣ Fear of germs</td>
<td>‣ Washing</td>
</tr>
<tr>
<td>‣ Fear of harm befalling self or others</td>
<td>‣ Cleaning</td>
</tr>
<tr>
<td>‣ Need for order or symmetry</td>
<td>‣ Checking</td>
</tr>
<tr>
<td></td>
<td>‣ Counting</td>
</tr>
<tr>
<td></td>
<td>‣ Repeating</td>
</tr>
<tr>
<td></td>
<td>‣ Touching</td>
</tr>
<tr>
<td></td>
<td>‣ Straightening</td>
</tr>
</tbody>
</table>

(March et al., 2004)
Diagnosis Criteria: 4 Symptom Dimensions

- Cleaning and contamination
  - Checking
- Hoarding
- Symmetry and ordering
  - Repeating and counting
- Sexual and religious obsessions
  - Aggression, somatic issues, and checking
## Diagnostic Criteria: Symptom Prevalence

### TABLE 2
Lifetime Frequencies (%) of the Major Symptom Categories of the CYBOCS Symptom Checklist, Coded as Present/Absent

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Total</th>
<th>Boys</th>
<th>Girls</th>
<th>Boys vs. Girls</th>
<th>χ² (df = 1); p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obsessions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggressive</td>
<td>192 (81.4)</td>
<td>117 (78.5)</td>
<td>75 (86.8)</td>
<td>2.13; .14</td>
<td></td>
</tr>
<tr>
<td>Contamination</td>
<td>184 (78.0)</td>
<td>112 (75.2)</td>
<td>72 (82.8)</td>
<td>1.84; .17</td>
<td></td>
</tr>
<tr>
<td>Sexual</td>
<td>66 (28.0)</td>
<td>50 (33.6)</td>
<td>16 (18.4)</td>
<td>6.27; .01</td>
<td></td>
</tr>
<tr>
<td>Hoarding</td>
<td>75 (31.8)</td>
<td>45 (30.2)</td>
<td>30 (34.5)</td>
<td>0.46; .49</td>
<td></td>
</tr>
<tr>
<td>Religious</td>
<td>96 (40.7)</td>
<td>66 (44.3)</td>
<td>30 (34.5)</td>
<td>2.19; .13</td>
<td></td>
</tr>
<tr>
<td>Symmetry*</td>
<td>99 (41.9)</td>
<td>64 (43.0)</td>
<td>35 (40.2)</td>
<td>0.16; .68</td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>95 (40.3)</td>
<td>56 (37.6)</td>
<td>39 (44.8)</td>
<td>1.19; .27</td>
<td></td>
</tr>
<tr>
<td>Compulsions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning</td>
<td>187 (79.2)</td>
<td>121 (81.2)</td>
<td>66 (75.9)</td>
<td>0.95; .32</td>
<td></td>
</tr>
<tr>
<td>Checking</td>
<td>189 (80.1)</td>
<td>120 (80.5)</td>
<td>69 (79.3)</td>
<td>0.05; .82</td>
<td></td>
</tr>
<tr>
<td>Repeating</td>
<td>179 (75.8)</td>
<td>116 (77.9)</td>
<td>63 (72.4)</td>
<td>0.88; .34</td>
<td></td>
</tr>
<tr>
<td>Counting</td>
<td>116 (49.2)</td>
<td>67 (45.0)</td>
<td>49 (56.3)</td>
<td>2.83; .09</td>
<td></td>
</tr>
<tr>
<td>Ordering</td>
<td>140 (59.3)</td>
<td>88 (59.1)</td>
<td>52 (59.8)</td>
<td>0.01; .91</td>
<td></td>
</tr>
<tr>
<td>Hoarding</td>
<td>99 (41.9)</td>
<td>53 (35.6)</td>
<td>46 (52.9)</td>
<td>6.75; .009</td>
<td></td>
</tr>
</tbody>
</table>

*Note: CYBOCS = Children’s Yale-Brown Obsessive Compulsive

(Mataix–Cols et al., 2008)
Diagnostic Criteria: Obsession–Compulsion Relationship

**Obsessions**
- Symmetry
- Religious
- Sexual
- Aggressive
- Somatic
- Contamination
- Hoarding

**Compulsions**
- Ordering
- Repeating
- Checking
- Counting
- Cleaning
- Hoarding

F1 (25.2%)
- Symmetry
- Ordering
- Repeating
- Checking

F2 (15.3%)
- Contamination
- Aggression
- Somatic
- Cleaning

F3 (11.1%)
- Hoarding
- Sexual

F4 (8.2%)
- Religious
Diagnosing in Children

- Must occur before puberty

- Difficult to diagnose in children
  - Lack insight to realize obsessions are irrational (Kalra et al., 2009)
  - Prognosis is worse for children with poor insight
  - Lack of insight militates against the benefits of cognitive–behavioral therapy (CBT)

- 40% of children deny compulsions are driven by obsessive thoughts
OCD Differences in Children

- **Symptom presentation**
  - Change of obsessions/compulsions over time (Weiss, 2008)
  - Obsessions/compulsions vague, magical, or superstitious (Franklin, 2004)
  - Children have trouble describing their obsessions (Weis, 2008)
  - Fear that stating obsessions aloud will make them come true (Weis, 2008)
  - More likely to have tic-like compulsions

- **Patterns of comorbidity**
  - ADHD
  - Tics: 2/3 children
    - Boys more likely to have comorbid
  - Tourette's syndrome: 20–80%
    - Compulsions may be less severe

- **Sex distribution**
  - Boys more likely: 2–3:1
  - At or after puberty: 1:1.35 (m:f)

- **Degree insight**
  - Etiopathogenesis
1%–4% of children and adolescents

At least 1/3 of adult OCD subjects had the onset of symptoms in childhood (Rasmussen & Eisen, 1992).

Children and adolescents share similar features with the exception of age at onset and OCD symptom expression. (Mancebo, 2008)

Consistent across lifespan (Stewart, 2007)
Adult patients with EOCD were characterized by
- (1) male gender predominance,
- (2) greater number of clinically significant obsessions and compulsions,
- (3) higher frequency of rituals repetition,
- (4) an increased severity of obsessive–compulsive symptoms at baseline, and
- (5) greater number of required therapeutic trials during the follow-up
Diagnostic Onset: EOCD v.s LOCD

EOCD:
- More premature onset.
- More aggressive course.
- More obsessions and compulsions.
- May represent a more severe variety of the disorder.
- Higher frequency of tic–like compulsions.
- Higher frequency sensory phenomena.
- Higher frequency comorbid tic disorders.
- Worse short–term therapeutic response to SSRIs.
| Table 1 | Clinical variables in early- and late-onset obsessive-compulsive disorder (OCD) |
|---|---|---|---|
| | Early-onset OCD patients (N = 33) | Late-onset OCD patients (N = 33) | t-Value | p-Value |
| Age (years ±3) | 28.03 ± 7.73 | 41.73 ± 13.18 | −5.15*** |
| Gender | 6.15* |
| Male | 60.6% | 27.3% | |
| Female | 39.4% | 72.7% | |
| Age of onset (years) | 11.18 ± 3.00 | 32.58 ± 13.26 | −9.04*** |
| Mode of onset | 3.51 NS |
| Insidious | 81.8% | 57.6% | |
| Sudden | 18.2% | 42.4% | |
| Duration of illness (years) | 17.06 ± 9.13 | 9.24 ± 9.12 | 3.48*** |
| Course | 0.16 NS |
| Chronic | 87.9% | 90.9% | |
| Episodic | 12.1% | 9.1% | |
| Subtype (ICD-10)^* | 5.84 NS |
| Mixed | 87.9% | 63.6% | |
| Compulsive | 9.1% | 21.2% | |
| Obsessive | 3.0% | 15.2% | |
| No. of obsessions | 2.61 ± 1.41 | 1.48 ± 1.06 | 3.64 *** |
| No. of compulsions | 2.67 ± 1.14 | 1.01 ± 1.28 | 2.57 * |
| Type of OCD symptoms | 7.59*** |
| Ruminative repetition | 60.6% | 24.2% | |
| Comorbidity | |
| Mood disorders | 51.51% | 39.39% | 0.55 NS |
| Anxiety disorders | 30.30% | 15.12% | 1.38 NS |
| Tic disorders | 18.20% | 9.10% | 0.51 NS |
| Initial scores | |
| YBOCS^b | 27.22 ± 8.01 | 21.66 ± 8.13 | 2.80 ** |
| CGI | 5.49±0.93 | 5.15±1.03 | 1.41 NS |
| HDRS-21^d | 17.30 ± 7.55 | 18.69 ± 5.46 | −0.85 NS |
| BOD | 22.17 ± 7.77 | 24.62 ± 5.17 | −1.50 NS |
| GAF | 49.21 ± 7.79 | 48.78 ± 7.06 | 0.23 NS |
Prevalence

- Lifetime prevalence: 1%–3% (Pauls, 2010)

- Juveniles more likely to be males

- Males: earlier onset (Mancebo, 2008)
  - At puberty, the sex ratio of affected individuals switches from pre-dominantly males to predominantly females (Kalra et al., 2009)
Associated & Secondary Features

- Higher suicide attempts
- Depression
- Anxiety

- **Celibacy rates:** 72% (Coryell, 1981)
  - Especially in men
  - Proportional to severity of the illness.
- Marry later (Turner & Michelson, 1984).
- Lower rates of fertility (Turner & Michelson, 1984)
- Higher parental stress (Coles et al., 2006)
- Interference in school, social, work, and family (Placentini & Bergman, 2000)
  - Doing assigned chores at home: 61%
  - Getting ready for bed: 56%
  - Concentrating at school: 62%
  - Getting along with parents: 56%
  - Getting along with siblings: 53%
Comorbidity

- Tic Disorder: 26%
- Anxiety Disorder
- Tourette’s disorder: 18–25%
- ADHD: 34–51%
- Major depression: 33–39%
- ODD: 17–51%
- Overanxious disorder: 16%
- Specific development: 24%
- Simple phobias: 17%
- Adjustment disorder w/depressed mood: 13%
- CD: 7%
- Separation anxiety: 7%
- Enuresis: 4%

- Juveniles: lower rates of mood, substance use and eating disorders compared to adults.
Comorbidity: OCD overlap with Tic Disorder

(Franklin et al., 2012)
Risk and Prognostic Features
Environmental Factors

- 45% variance for younger sample (Hudziak et al., 2004)

- **Prenatal** (Santangelo et al., 1994):
  - Labor complications
  - Maternal smoking
  - Excessive caffeine or alcohol
  - Difficulty getting pregnant: 53% (Vasconcelos et al., 2007)
  - Preexisting medical problems: 51% (Vasconcelos et al., 2007)

- **Parenting style** (Albano, 2004):
  - Over controlling parents
  - Low parental acceptance

- **Aversive reaction to change** (Zohar & Felz, 2001):
  - child tries to enforce consistency on objects and significant others

- **Family Size** (Guerrero et al., 2003)

- **Substance abuse** (Fontenelle & Hasler, 2007)
Risk and Prognostic Features
Temperament

- **Behavioral Inhibition**
  - Over-protective parenting (Coles et al., 2006)
  - Significantly predicted levels of OCD (Coles et al., 2006)
  - High levels of restraint, withdrawal, and avoidance of novel stimuli, of both a social and nonsocial nature (García-Coll et al., 1984)

- **Higher internalizing problems** (Zohar & Felz, 2001)
  - More Shy
  - More emotional
  - More fearful
Risk and Prognostic Features
Genetic Factors

- Twin studies
  - **Bolton et al., 2007:**
    - 57% variance in MZ twins
    - 22% in DZ twins
  - **Van Grootheest et al., 2005:**
    - 45–65% genetic influences

- Ritual repetition may represent a behavioral marker for a specific genotype.

- 10–25% youths have at least 1 parent w/OCD
Risk and Prognostic Features

Neurochemical Factors

- **Serotonergic systems**
  - Central role
  - Only discovered by administering treatment and observing effects

- **Dopaminergic systems**
  - Reported by adult patients with basal ganglia disorders
  - OCD, TS, Sydenham Chorea, Huntington Chorea

- **Glutamatergic system**
  - Primary excitatory neurotransmitter
  - Key role in the functioning of the fronto–striato–thalamo–cortical circuit (CSTC Circuit)
Risk and Prognostic Features Neuroimmune Dysfunction

- Can be triggered by infections
  - Group A β-hemolytic streptococci (GABHS) are the most studied initial autoimmune response-inciting event
  - Viruses
  - Mycoplasma pneumonia
  - Borrelia burgdorferi
  - Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections—PANDAS

- Parallels between:
  - Sydenham chorea,
  - Neurological manifestation of rheumatic fever, and childhood-onset OCD

- Dysfunction in orbitofrontal–striatal circuit
  - Involved in the mediation of emotional responses to biologically significant stimuli
Risk and Prognostic Features
Neurobiological Substrates

- Fronto–striato–thalamo–cortical circuit
  - Explains behavioral loop

- fMRI studies:
  - Global and local deviant topological properties
    - Disturbances in brain network balance
    - Reduced small world efficacy @ baseline
    - Changes in modular structure
    - Basis of the inability to disengage from reverberating internal stimuli (Shin et al., 2013)
  - Reduced volume:
    - Left putamen (Hoexter et al., 2012)
    - Left medial orbitofrontal cortex (Hoexter et al., 2012)
    - Right medial orbitofrontal cortex (Hoexter et al., 2012)
    - Right anterior cingulate cortex (Hoexter et al., 2012)
    - Caudate (Saxena et al., 1999)
    - Thalamus (Saxena et al., 1999)
**Literature Based Model**

- **EOCD** leads to Obsessions and Compulsions.
- **OCD** is reinforced due to escape/avoidance processes involving GABA.
- **Error Processing** promotes Rumination of Obsessions.
- **Anxiety** prompts Action and Compulsion.
- **Reward Processing** reinforces compulsion due to escape/avoidance.

Genetic Predisposition, Neuroimmune Dysfunction, and Parenting Style influence neural substrates.

Excitatory glutamatergic output is increased, leading to more excitatory glutamatergic output.

INCR Inhibition of GABA leads to increased excitatory output.