Obsessive-Compulsive Disorder (OCD): Summary

Core Symptoms:
- Obsessions
  - recurrent, unwanted and unpleasant thoughts or images causing marked anxiety or distress
- Compulsions
  - repetitive, ritualistic behaviors that a person feels driven to perform
- Obsessive & compulsive subtypes fall along specific dimensions
- Mood & Anxiety disorder comorbidity in the majority of cases
- Familial, usually early-onset (often childhood, most by age 18)
- Causes [c] remain unknown
- Consistently associated with functional neuroimaging abnormalities
- Occasionally associated with focal brain injury
- Behavior therapies & medications are effective
- Highly refractory (“intractable”) cases can improve with neurosurgery
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OCD is Relatively Common around the World

That, plus early onset, made OCD the 10th Leading Cause of Disability in Developed Countries (WHO, 1997).

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OCD can be Disabling

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Slide 6

Other Common OCD Symptoms

<table>
<thead>
<tr>
<th>Harm-related thoughts or images</th>
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<tbody>
<tr>
<td>- Lead to avoidance, washing, checking, reassurance-seeking</td>
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<tr>
<td>Disturbing aggressive, sexual or religious thoughts or images (&quot;Taboo Thoughts&quot;)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Symmetry/Exactness</th>
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<tr>
<td>- Leads to ordering/arranging</td>
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<table>
<thead>
<tr>
<th>Compulsive Hoarding</th>
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<tr>
<td>Incompleteness</td>
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<tr>
<td>- Not based in fear of &quot;something bad happening.&quot;</td>
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<tr>
<td>- Things don't feel done; rituals continue until patient &quot;feels right.&quot;</td>
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</table>
A man will not go to public places because he fears he will have intolerable sexual thoughts or falsely accuse someone of committing a crime.

A woman's persistent urge to shout out an obscenity or blasphemy in church can be suppressed only by counting slowly backward from 100 to one.

A man feels a drop in his eye as he looks up while passing a building and cannot dismiss the thought that someone with AIDS has spit out of a window. To reassure himself, he proceeds to knock on the door of every office in the 10-story building.
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For eight years a man spends an hour a day washing his hands, showering, and dressing. He has stopped grooming and changing his clothes because the rituals required are too long. He stays in his room, eating only a few carefully selected foods and constantly checking to see that furniture is in exactly the “right” place.

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Contamination & Excessive Cleaning
“Must be ‘just right’”
Symmetry, Order, Arranging
“Incompleteness”
Must be “just right”
Co-occurring Disorders

90% - 1 or more Axis I dx (lifetime)
75% - Mood disorder
53% - Other anxiety disorder
26% - Substance use disorder
15% - Impulse Control disorder
10% - Eating disorder
38% - 1 or more Personality Disorders

Pinto et al., 2006
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**Exposure & Ritual Prevention**
- Patients actively confront feared things & situations.
- Person is encouraged not to carry out compulsive rituals after being exposed.
- Repeated exposures without the feared consequence happening result in extinction of the anxiety response, i.e., compulsive rituals. Extinction is a kind of learning.
- Very effective in people who agree to do it
  - may be as little as half the patients in some studies.
- Availability is limited by time needed; availability of expert therapists; insurance restrictions.

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**CBT in the "Real World"**
- 55% attended at least one session with a CBT therapist ($M=37$ sessions, $SD=45$)
- 38% received at least 13 sessions of CBT lifetime
- 24% received a continuous course of at least 13 sessions of CBT
- 6% received intensive (3x or more per week)
- All but 4 participants were also taking medications

Mancebo et al. 2006

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**Medications for OCD**
- Serotonin Reuptake Inhibitors (SRIs)
  - Clomipramine (Anafranil)
  - Fluvoxamine (Luvox)
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Venlafaxine (Effexor)
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
- SRIs are used before clomipramine due to less side effects and better safety profile; but some data suggest clomipramine is more effective.
- Medication combinations:
  - SRI + Antipsychotics (1st or 2nd generation)
  - SRI + Benzodiazepine anxiolytics
### Long-Term Treatment Options

- Combined Therapy (meds plus CBT) is recommended for many, especially if getting off medication is a goal.
- OCD is usually chronic
- Relapse Rates for treatments when used alone:
  - 24% of E/RP alone
  - 70-90% of SSRI alone
- Significant numbers of patients do not benefit meaningfully from existing treatments (20-35% of the total). Some of them are disabled by OCD, others can manage, but with a degraded quality of life.

### Genetics

(natural history and family patterns of illness)

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### OCD Runs in Families:

Compared to relatives of healthy controls, relatives of people with OCD were 3-5 times more likely to have OC symptoms or OCD.

Disorders were more familial than compulsions.

Tics or OC personality did not increase “familiarity” of OCD.

Disorders co-occur with OCD, esp. mood (Anx. Dos vary by study)

The earlier someone developed OCD, the more likely relatives were to have OCD too (Only OCD with age of onset < 18 was familial).

And people with OCD were less likely to marry
And even less likely to have children (makes genetic studies hard)

(Nestadt et al., 2003)
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OCD Inheritance Within Families

- "Segregation analysis" looks for patterns that hint at how OCD may be inherited:
  - Is there a single gene? (No)
  - Multiple genes? (Probably)
  - Could there be a gene with a "major effect" - which increases risk for illness substantially? (studies suggest this)
- Genetic Risk Prob. Differs by Symptom Subtypes

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"Candidate Genes"

- Genes coding for proteins possibly involved in OCD have variants (alleles) with different effects on brain function. So, people with some of these forms might be at greater risk. e.g., Serotonin (synthesis, transport, receptors, metabolism)
- Some evidence that gene variants are associated with OCD.
- Promising, but results generally not well-replicated.
- Better "phenotypes" (symptom dimensions) & whole genome association might lead to better understanding of OCD genetics.
- Current whole genome association study underway at Butler/Brown

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Towards "Natural Kinds" of OCD

Better phenotypes should get us better genetic data
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What goes on in the Brain in OCD?

High metabolism in fronto-basal regions (before treatment)

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Blood flow increases during OC symptoms in cortico-basal-thalamic circuits

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Metabolic Decreases in OCD Patients after Paroxetine (Paxil) Treatment

Saxena et al, 2001
Stereotactic Lesion Procedures for OCD and MDD

Effectiveness in Open Studies: 30 - 70% (Greenberg et al., 2003)

Neurosurgery for OCD: Collaborators & Disclosures

- Butler/RI Hosp/Brown
- Linda Carpenter
- Gerhard Friehs
- Paul Malloy
- Richard Marsland
- Georg Noren
- Lawrence Price
- Steven Rasmussen
- Stephen Salloway
- Audrey Tyrka
- Paul Cosyns
- Louis Gabriels
- Bart Nuttin
- MGH
- Darin Dougherty
- Scott Rauch
- Cleveland Clinic
- Kenneth Baker
- Cynthia Kubu
- Donald Malone
- Ali Rezai
- Rochester
- Suzanne Haber
- (Anatomy)
- Pittsburgh
- Anthony Grace
- (Physiology)
- Univ. of Florida
- Wayne Goodman
- Kelly Foote
- Michael Okun
- N. A. Shapira
- Cornell
- Joseph Fins
- (Ethics)
- Medtronic
- Keith Mullett
- Mark Rose
- Paul Stypulkowski
- Roy Testerman

Funding (US sites):
- NARSAD; Medtronic, Inc.; NIMH

DBS: Off Label for OCD
FDA Humanitarian Device Application Submitted

What are the risks, and how do we minimize them?
**Patient Selection: Principles**

- Accurate diagnosis (longitudinal perspective, multiple informants)
- Sufficient severity and chronicity
- Nonresponse to adequate conventional treatments, documented
- Capacity to consent (monitored)
- Capacity for close, long-term followup

*The treatment team is fully committed to provide that follow-up.*
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QuickTime™ and a decompressor are needed to see this picture.

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Before

After

Gamma Capsulotomy
(1 year post-shots 3 and 4)

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Behavior therapy can become possible after neurosurgery

QuickTime™ and a decompressor are needed to see this picture.
Systems-Level Overlap of Targets for Subcaudate Tractotomy, Capsulotomy, & DBS – procedures used for both OCD & MDD.

One Potential Overlap in Targets of SRI Antidepressants & Surgery

DBS Target - Lead Tip (on right)

DBS Acutely Changed Affective State in OCD (+ Comorbid MDD)

DBS OFF

DBS ON
Before & After VC/VS DBS for OCD

QuickTime™ and a H.263 decompressor are needed to see this picture.

After DBS x 2 years

OCD Severity During Chronic DBS

Depressive & Anxiety Symptoms
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Anterior-Posterior Lead Site in Early, Middle, and Most Recent Patient Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>L-AP Coordinate</th>
<th>R-AP Coordinate</th>
</tr>
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<tbody>
<tr>
<td>1st</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2nd</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3rd</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

AP coordinate is at the Anterior Commissure

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DBS for OCD: Adverse Effects

- **Surgical**
  - Small hemorrhage without symptoms or sequelae (1/10)
  - Superficial infection (1/10)
  - Single intraoperative seizure (1/10)
- **Stimulation**
  - Mood Elevation/Hypomania (1/5, 2/5 in 3 pts, lasted 2/4/19)
  - Sensorimotor (eg, facial “hemi-smile,” paresthesias)
  - Exsomnia
  - Autonomic
  - Memory flashbacks
  - Anxiety and/or Panic (2/10)
- **OFF effects**
  - Symptom return (worsening in mood > OCD Sx)
- No AEs were persistent

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DBS for OCD: Neuropsychological Performance

Multiple cognitive domains tested before & after DBS x 10 mo., using practice corrected change scores.

- No pattern of pervasive worsening in any patient.
- Improvements in immediate ($t(9)=4.39$, $p<.01$, $d=1.4$) and delayed ($t(9)=2.55$, $p<.05$, $d=0.8$) prose passage recall
- No other significant changes.
- Effect size ($d=0.5$) suggests visuospatial skills ($t(9)=1.66$, $p>.05$), might have shown improvement in a larger sample.

C. Kibu et al., under review
OCD Resources

- OC Foundation (www.ocfoundation.org)

- Treatment manuals for professionals
  - Kozak & Foa (1997) – Mastery of OCD
  - Steketee & Frost (2007) – Compulsive Hoarding and Acquiring

- Self-Help manuals
  - Brain Lock
  - OCD Workbook
  - Stop Obsessing!
  - Compulsive Hoarding and Acquiring
  - Buried Treasures