

## Overview of OCD

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## Obsessive-Compulsive Disorder: DSM-IV Criteria

### Obsessions

- Recurrent thoughts, images, or impulses that are intrusive and cause marked distress
  - Aggressive, Contamination, Sexual, Religious, Somatic, Symmetry/Order, Hoarding
- Obsessions are not simply excessive worries
- Person tries to suppress or neutralize them
- Obsessions are initially recognized as part of one's mind - not inserted

## The Problem

- OCD is a common disorder associated with significant disability and chronicity
  - W.H.O.: OCD is one of the world's top ten causes of illness related disability
  - Lifetime prevalence of 2-3%
- Approximately 10-30% of patients are not helped at all or are inadequately helped by current pharmacotherapies.

## Obsessive-Compulsive Disorder: DSM-IV Criteria

### Compulsions

- Repetitive behaviors (handwashing, ordering, checking) or mental acts (praying, counting, repeating words silently) that the person is driven to perform
- Compulsions are aimed at reducing distress or preventing some dreaded consequence

## Patient #1

- 54 year old married woman
- OCD since childhood but not diagnosed until age 43
  - Childhood: get up at night to check homework, erase work and restart
  - Young adult: bumps in road when in car would make her fear she ran someone over
  - Numerous meds & behavior therapy were not helpful (prior to seeing us)

## Obsessive-Compulsive Disorder: DSM-IV Criteria

- B. Obsessions are recognized at some point as excessive or unreasonable (excludes children).
- C. Causes marked distress, is time consuming, or interferes with normal functioning
- D. Content is not limited to other Axis I disorders, such as Anorexia, Trichotillomania, Body Dysmorphic Disorder, Hypochondria, Paraphilia, Major Depression

### Epidemiology of OCD: Cross-National Collaborative Study (1994)

- U.S. Lifetime prevalence of 2.3 per 100 (ECA)
- Similar prevalence in 7 other countries
- Mean age of onset: 22 - 35
- 12-60% have comorbid major depression and 35-70% had another anxiety disorder
- Female to male ratio of 6:4
- Symptom profiles vary per country. In the U.S., 50% had obsessions only, 34% had compulsions only, and only 16% had both.

### Tic-related OCD

- Earlier age of onset (prepubertal)
- Affects males more than females
- Certain OCD symptoms more common:
  - Tic-like compulsions (touch, tap, or rub)
  - Intrusive violent or aggressive thoughts
  - Worries about symmetry and exactness
  - (Contamination, cleaning, checking were independent of pt's tic status)
- Rituals done until "Just right"
- Responds less well to SSRIs....OCD improves with dopamine D2 receptor antagonists

### Related Features of OCD

- Pathological Uncertainty
  - "How can I be sure?"
- Pathological Sense of Responsibility
  - "Why did I let that happen?"
- Pervasive Avoidance
  - From avoiding public restrooms or shaking hands to avoidance of all contact with the outside world
- Magical Thinking
  - Omnipotence of thought. Merely thinking a thought can cause it to occur

### Phenomenology Summary

- OCD is a phenomenologically heterogeneous disorder
- Subtypes of OCD may have differing pathophysiology & therapeutic response
- Identification of biologically homogenous subtypes will enhance genetic & neuroimaging studies, early detection & therapeutic intervention

### Why propose a corticostriatal model for OCD?

- Neuroimaging Studies
  - Hyperactivity in OFC, Cingulum, Caudate
- Neuropsychologic Studies
  - Subtle fronto-striatal functional deficits
- Neurosurgical approaches target CS tracts
- Other diseases with known striatal pathology have high frequencies of OC features
  - Sydenham's chorea
  - Huntington's disease
  - Tourette's syndrome

### *First-Line Treatments for OCD:*

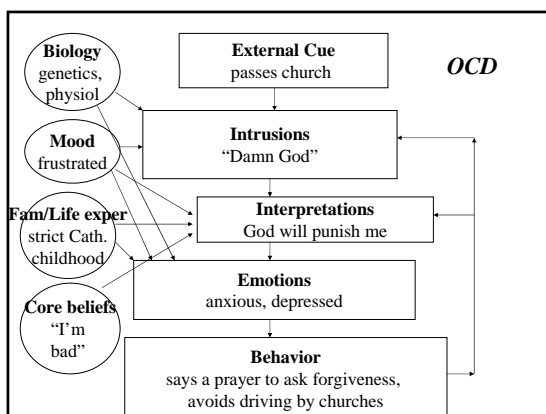
- Pharmacotherapy with serotonin reuptake inhibitors (SRIs):
  - clomipramine
  - selective serotonin reuptake inhibitors (SSRIs--fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram)
- Cognitive-Behavioral Therapy consisting of exposure and response (or ritual) prevention (EX/RP)

## Cognitive Behavioral Model of OCD

- Common types of interpretations/beliefs that influence the development of OCD (OCCWG, 1997)
  - responsibility for harm
  - overestimation of threat
  - perfectionism
  - intolerance of uncertainty
  - over-importance of thoughts
  - need to control thoughts

## How is behavior therapy done?

- Varies in intensity: 15-25 individual sessions, each lasting 1-2 hours, 1-5 times per week, home visits.
- Initial sessions: review the treatment rationale, constructing a hierarchy of feared stimuli, planning how and when to confront feared stimuli
- EX/RP sessions: therapist-supervised exposures starting with stimuli that generate moderate fear and continuing until the most feared stimuli are faced without ritualizing
- Homework: exposure practice and ritual prevention
  - (Simpson slide)



## Explanation for efficacy of BT?

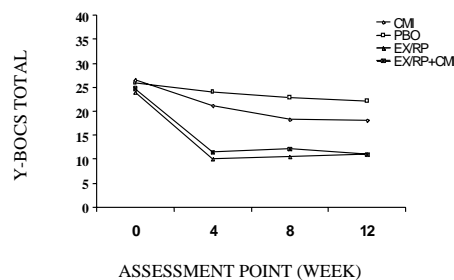
- Habituation. By facing real and imagined fears for a prolonged period without ritualizing, the initial anxiety/discomfort dissipates on its own ("habituation")
  - Breaks the connection between feared stimuli and anxiety
  - Breaks the connection between rituals and anxiety relief
  - Corrects mistaken beliefs (e.g., that harm is likely, that thoughts are the same as actions, that anxiety/discomfort will persist forever, that rituals protect against harm)

## What Is behavioral therapy?

- Live confrontations with feared situations or objects ("in-vivo exposure")
- Imaginal confrontations with feared consequences ("imaginal exposure")
- Ritual prevention (i.e., patient refrains from compulsions and avoidance)

## Y-BOCS in CMI BT OCD Trial:

Treatment completers (Liebowitz, Foa, Simpson, Kozak)



## Factors Associated with Poor Response to SRIs

- Inadequate duration of trial, inadequate dosing
- Incorrect diagnosis (e.g., OCPD vs OCD)
- Clinical features
  - Hoarders
  - Comorbid tic disorder
  - Comorbid schizotypal features
- Continuous Clinical course (rather than episodic)
- Early Age of Onset
- Poor insight
- Greater severity of neurologic soft signs

## Meta-Analyses of CMI vs SSRIs

- Effect size > for CMI than for SSRIs
  - EF CMI > fluoxetine (Jenike 1990)
  - EF CMI > sertraline and fluvoxamine (Davis 1991)
  - EF CMI > fluoxetine, sertraline, fluvoxamine (Greist 1995)
    - SSRIs comparable to one another:
      - Proportion of pts improved (43%-44%)
      - Percentage decrease in Y-BOCS (20-27%)
    - Patients treated with CMI had significantly better results
      - Proportion of pts improved (60%)
      - Percentage decrease in Y-BOCS (39%)
- Critique of Meta-analyses:
  - Cohort effect: pts treated with CMI had not had prior SSRI exposure

## Clomipramine

- Clomipramine:
  - Potent 5-HT (CMI) and NE (DCMI) reuptake blockade
  - Average symptom improvement of 36%-46%
  - Ciba-Geigy: dosing up to 300 mg/d
    - much improvement in 60-61% on CMI vs 5-9% on placebo
    - Many AEs, but <10% dropped from studies
    - Improvement starts early (2wks) & increases with time
  - No dose finding studies exist
  - 1980s: CMI > placebo, desipramine, amitriptyline
  - Range in studies: 150-250mg/day, but some studies allow lower dosing of 75-150 mg/d

## Double-blind Comparisons of CMI vs SRIs

- Fluvoxamine similar to CMI (Freeman 1994, Koran 1996)
  - F: Flex dose, n=66, similar in AE also
  - K: Flex dose, n=79, fl:100-300mg v cmi: 100-250 mg
- Fluoxetine similar to CMI (Lopez-Ibor 1996)
  - Fixed dose, n=55, 8 wk, fl: 40 mg v cmi:150 mg
- Sertraline similar to CMI (Bisserbe 1997)
  - Flex, n=86, 16 wks, mean ser: 129mg, cmi: 90mg/d
- Paroxetine similar to CMI and better than placebo (Zohar 1996)
  - Flex dose, n=399, 12 wks. Range: Paroxetine 10-60, CMI 25-250
  - Mean dose: Parox 37.5 mg/d, CMI 113 mg/d
  - CMI associated with more AE than placebo and than paroxetine

## Dosing Trials of SSRIs: % Change in Y-BOCS from baseline

- Fluoxetine: 13-wk Fixed Dose Study, n=355 (Tolefsen)
  - Y-B: 20 mg (20%), 40 mg (22%), 60 mg (27%), Pbo (3%)
  - A.E.: nausea, dry mouth, tremor
- Sertraline: 12 wk Fixed Dose Study, n=324 (Greist)
  - Y-B: 50 mg (24%), [100 mg (19%)], 200 mg (28%), pbo (15%)
  - A.E.: diarrhea, insomnia, decreased libido, nausea, anorexia
- Fluvoxamine: 10 wk Flexible Dose Study, n=300 (Rasmussen)
  - Y-B: mean dose 249 mg/d (change 20%), pbo (5%)
  - A.E.: insomnia, nausea, somnolence, dry mouth
- Paroxetine: 12 wk Fixed Dose Study, n=263 (Wheadon)
  - Y-B: [20 mg (19%)], 40 mg (25%), 60 mg (29%), pbo (13%)
- Citalopram: 12 wk Fixed Dose Study, n=401 (Montgomery 2001)
  - Y-B: 20 mg (34%), 40 mg (34%), 60 mg (40%) or pbo (22%)

## Augmentation Strategies

- Many agents helpful in case reports or small series, but few have either been studied at all or shown to be effective when subjected to a randomized, placebo-controlled design.
  - Tryptophan, d-fenfluramine, gabapentin, donepezil, clonazepam, pindolol, lithium, buspirone, inositol, bromocriptine, oxytocin, morphine, naltrexone
- Multiple studies support use of adjunctive typical or atypical neuroleptics

### Controlled trials of conjoint SRI-neuroleptic Treatment in refractory OCD

- Haloperidol (~6mg) + Fluvoxamine (McDougle, 1994) (RPCT)
  - 34 pts with partial or no response to 8 wks of Fluv were given 4 weeks of either Pbo or haloperidol adjunctively.
  - 11 of 17 (65%) given H responded vs 0 of 17 given Pbo
  - 8 of 8 pts with comorbid tic disorders responded (with a 47% decrease in YBOCS) compared to 3 of 9 pts without tic disorder.
- Risperidone + SSRI (McDougle 2000) (RPCT)
  - Effective among pts with and without tics
  - 50% given Risperidone + SRI responded vs 0% given Pbo + SRI
  - Y-BOCS improved 31% over baseline in Risperidone group
- Olanzapine + SSRI (Bystritsky)
  - Effective with a 20% reduction in Y-BOCS
- No placebo-controlled trials yet of quetiapine, ziprasidone or aripiprazole, although numerous case reports and small series report favorable results for the use of quetiapine as an augmentor.

### Corticostriatal Circuitry & Corticostriatal Hypothesis of OCD

- **Striatum:** caudate, putamen, nucleus accumbens (a.k.a. ventral striatum). Functions to modulate motor, cognitive, and affective processes.
- **"Direct" and "Indirect" Corticostriatal Collaterals**
  - **Direct:** direct projections from striatum to globus pallidus interna (substance P) with net excitatory effect on thalamus, overdriving the corticothalamic branch
  - **Indirect:** indirect projections from striatum to globus pallidus externa (enkephalin) to GP interna with net inhibitory effect on thalamus.
  - A dominant direct collateral may lead to a reverberating corticothalamic "worry circuit"

### Reports on Atypical Antipsychotics for adjunctive SRI therapy for OCD

Table 1. Decrease in Yale-Brown Obsessive Compulsive Scale (YBOCS) Scores in Trials in Which Atypical Antipsychotics Were Added to Serotonin Reuptake Inhibitors\*

Study	Drug	Type of Trial	Patients (N)	Decrease in YBOCS Score, %		
				Mean	Median	SD
McDougle et al <sup>2</sup>	Risperidone	Open	3	54	56	10
Saxena et al <sup>3</sup>	Risperidone	Open	21	NA <sup>a</sup>	NA <sup>a</sup>	NA <sup>a</sup>
Stein et al <sup>4</sup>	Risperidone	Open	8	22	10	29
Pfanner et al <sup>6</sup>	Risperidone	Open	20	30	32	9
McDougle et al <sup>7</sup>	Risperidone	Double-blind	20	31	30	27
Weiss et al <sup>8</sup>	Olanzapine	Open	10	40	42	25
Koran et al <sup>9</sup>	Olanzapine	Open	10	16	9	22
Bogetto et al <sup>10</sup>	Olanzapine	Open	23	30	NA <sup>a</sup>	NA <sup>a</sup>
Francobandiera <sup>11</sup>	Olanzapine	Open	9	37	42	25
Bystritsky <sup>12</sup>	Olanzapine	Double-blind	13	20	NA <sup>a</sup>	NA <sup>a</sup>

\*Individual YBOCS scores were not available.

### Deep Brain Stimulation for OCD

- Case reports suggest effectiveness
- Lead follows anterior limb of internal capsule (similar to capsulotomy). Pulse generator is implanted in abdomen or chest.
- Reversible...improvement may occur rapidly
- Risks (due to tissue displacement and damage to vasculature): seizure (1-3%), hemorrhage (1-5%), infection (2-25%)
- Mechanisms of action unclear: inhibits transmission via depolarization blockade or neural jamming

### Bilateral Neurosurgery

- **Anterior Cingulotomy:** success rate of 56%
  - Interrupts fibers in the cingulate bundle
- **Subcaudate tractotomy:** success rate of 50%
  - Lesions in rostral part of orbitofrontal cortex ventral to head of the caudate
- **Limbic Leukotomy:** success rate of 61%
  - Lesions in cingulate & orbitomedial frontal areas which contain a segment of the fronto-caudate-thalamic tract
- **Anterior Capsulotomy:** success rate of ~50-67%
  - Lesions in the anterior limb of the internal capsule
  - Fibers of fronto-striatal-pallidal-thalamic-frontal loops are believed to pass through anterior limb of the internal capsule.

### DBS for 3 Pts with Treatment

Refractory OCD Gabriels et al, Acta Psychiatrica Scand 2003

- Quadripolar electrode implants in anterior limb of int capsule bilaterally
- Stimulation parameters optimized over 2 weeks based on mood/anxiety reduction...then continuous bilat stim.
- Outcome 1 year later: personality, OCD, & frontal lobe tests.

## Treatment Summary

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- Treatment strategies:
  - SSRIs or clomipramine
  - Behavioral therapy
  - Combo of Drug and behavioral therapy
  - Then if patient is not responding well
    - Reassess diagnosis
    - Neuroleptic augmentation
    - Address comorbid conditions
    - Consider anticonvulsant trial
    - Consider neurosurgery or deep brain stimulation
  - Efficacy of Yoga? Of Transcranial Magnetic Stimulation?