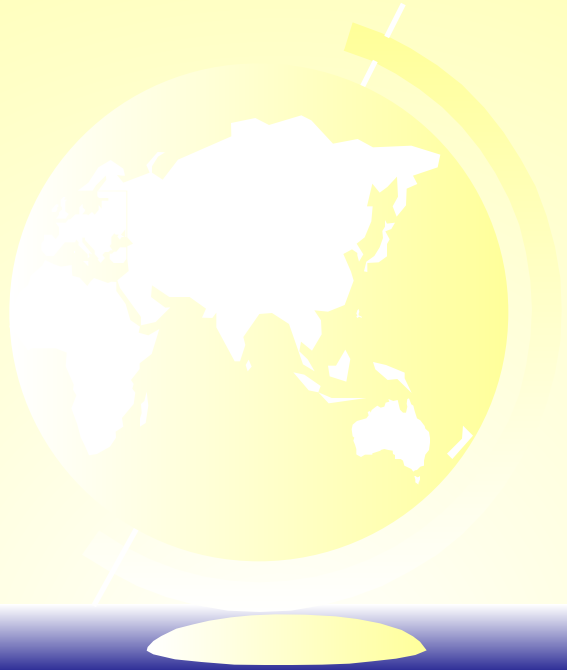


Obsessive-Compulsive Disorder

Why Discuss OCD?

- Underdiagnosed (4th most common psychiatric diagnosis)
- More common than previously recognized
  (mental compulsions or rituals)
- May be very disabling:
  - suicide risk
  - 40% of patients unable to work for 2 years

Why is OCD Underdiagnosed?

- Symptoms are embarrassing
- Lack of insight into problems with the illness
- Average patient visits 3 to 4 physicians for 9 years - *before correct diagnosis made*

OCD – a secretive disorder

- 62% - ignorance of illness
- 35% - fear to be considered as foolish

The Problem...

- **The average patient does not receive appropriate treatment for 17 years *after* OCD diagnosed!!!**

Epidemiology

- **Lifetime prevalence** 2-3%
- **U.S.A.** 5-7 million adults
  1 million kids
- **Mean age of onset** 20 years old
  <5% after age 40
  1/3 onset as child
- **Sex ratio** males = females (adult)
  males > females (teens)

Etiology

- Genetic factors
- Biologic factors
- Behavioral theory
- Psychodynamic theory

Genetic Factors

- Inheritance most evident in childhood onset OCD
- 10% of 1st degree relatives of OCD patients also have OCD (but different symptoms)
- 8% have “subthreshold” OCD
- 30% have OCPD
- Genetic relation to TS

Neuroanatomy: *striatal disorders*

- **Tourette's syndrome**
- **Sydenham's chorea**
- **Huntington's disease**
- **Parkinson's disease**
- **Encephalitis Economo**

OCD: brain disorder

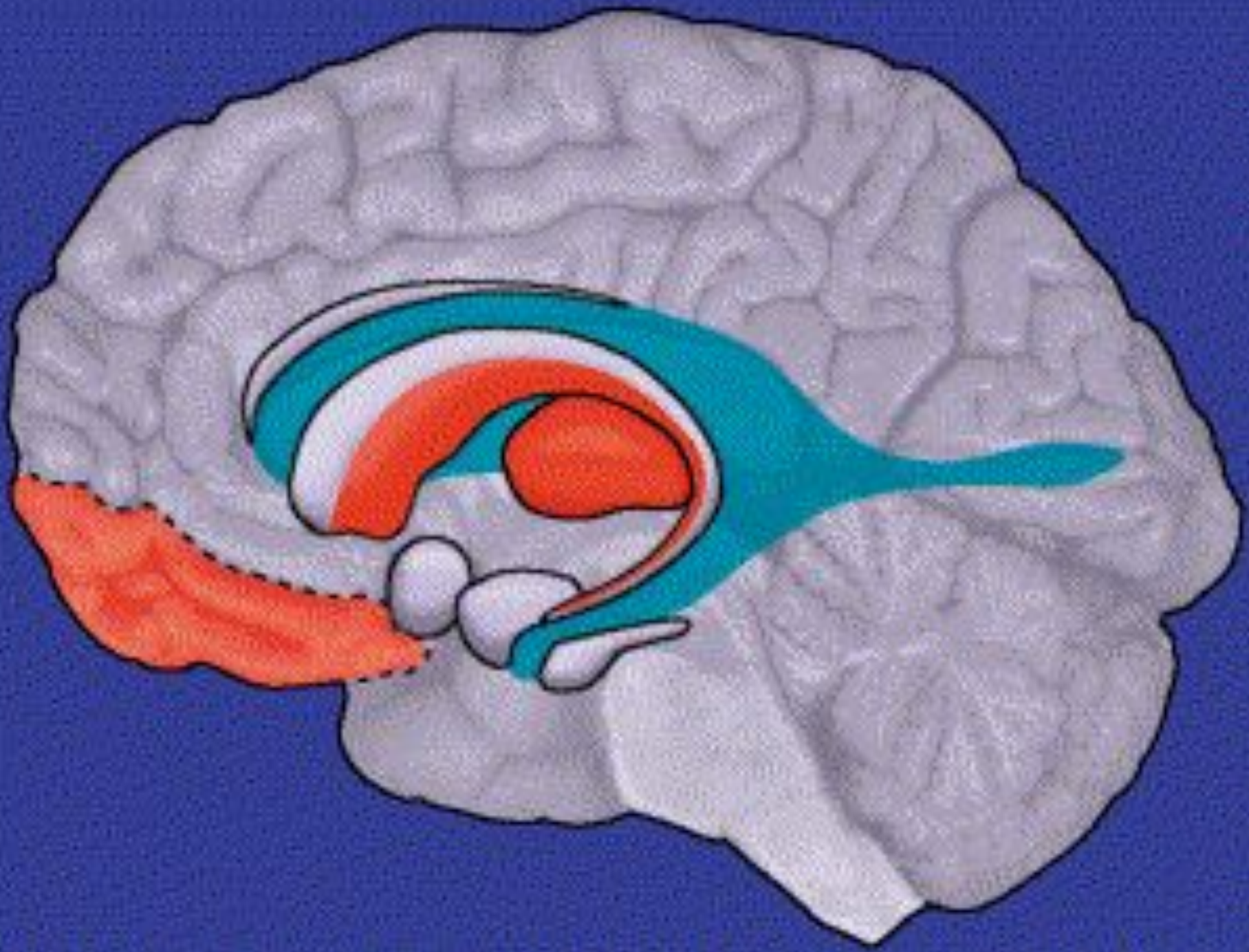
(*Cortico-striatal-thalamo-cortical circuit)*

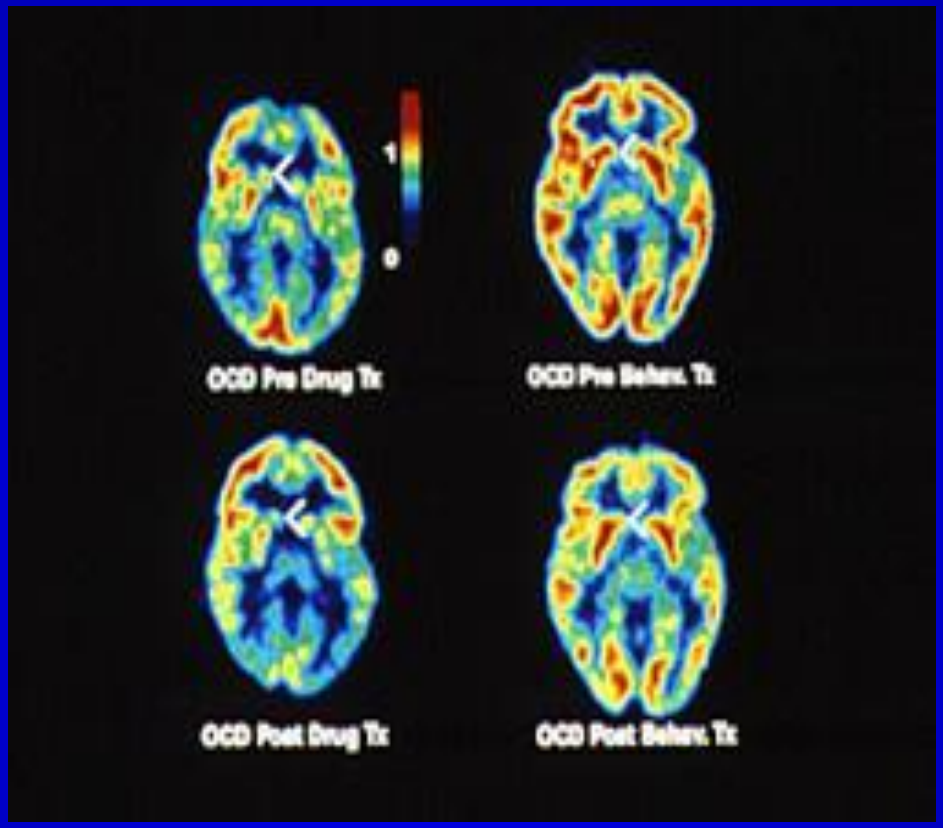
- **Neurological soft signs**
- **Evoked potentials**
- **Prepulse inhibition**
- **Executive function**
- **TMS**

Conclusion: OCD – impaired cortical inhibition

OCD: *brain disorder*

- **Frontal lobe**
  basal ganglia
  anterior/posterior cingulate
- **PET scan**: > metabolic activity in:
  - frontal lobes (orbital frontal cortex)
  - caudate of the basal ganglia
  - cingulum
- **Treatment decreases this activity** (even cognitive-behavioral therapy!)

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OCD Pre Drug Tx
OCD Pre Behav. Tx
OCD Post Drug Tx
OCD Post Behav. Tx

Neurochemistry: 5HT system

- **Neurotransmitter dysregulation**
- **Serotonin**
  - SRI drugs work
  - > CSF 5-HIAA suggests higher rate of serotonin turnover
  - lower density of serotonin receptors

5HT1D-receptors (sumatriptan, imaging, genetic polymorphism)

5HT2C-receptors

Neurochemistry: dopamine

- **Dopamine agonists –** induced OCD (cocaine, methylphenidate)
- **Dopamine antagonists** – effective in some types of OCD (haloperidol, risperidone, olanzapine,quetiapine)

Neurochemistry: *other than 5HT/DA systems*

- **Glutamate**
- **Neuropeptides**
- **Gonadal steroids**
- **Second/third messengers (protein kinase C)**
- **Opiates**

Diagnosis (DSM-5)

- **Must have either obsessions or compulsions**
- **Obsessions** - increase anxiety
- **Compulsions** - decrease anxiety
- **Obsessions:**
  - recurrent thoughts or urges
  - intrusive, inappropriate
  - cause significant anxiety
  - unwanted

Diagnosis (cont.)

- **Compulsions:**
  - repetitive behaviors or thoughts
  - patient feels compelled to perform to reduce anxiety caused by the obsession
- **Compulsions:**
  - excessive
  - unrealistic (ex., washing)

Diagnosis (cont.)

- Patient realizes that the obsessions and compulsions are excessive and unreasonable
- Obsessions and compulsions:
  - marked distress
  - time-consuming (> 1 hour)
  - significant interference with life (ex., late for work, family upset)
- No organic etiology (ex., brain trauma)
- Specifier: OCD with poor insight (frontal lesion?)

Clinical Presentation

- OCD patients often *first* seen by clinician *other* than psychiatrist/psychologist
- 75-85% have both obsessions and compulsions (15% have only obsessions)
- Most patients have several obsessions and compulsions simultaneously
- Symptoms may change over time in the same patient

Clinical Presentation (cont.)

- 50-75% onset after stressful event (ex., move/ new school story)
- Chronic course – wax and waining
- Acute onset: dopamine agonists
  post-streptococcal infection
  postpartum

Contamination Obsession (cont.)

- Lengthy shower
- Family collusion (father/garage)

Pathological Doubt Obsession

- How many times do you check your locked door, or the coffee pot?
- Obsession often involves concern about not performing an action - that could result in a dangerous situation (ex., coffee pot - fire)
- Compulsive ritual may involve checking or asking (repeatedly) for reassurance

Pathological Doubt Cases

- Front door checking/staring (20 min.)
- Jack Nicholson (door) in “As Good as It Gets”

Aggressive Thoughts Obsession

- Religious theme suggests harsh, punitive superego
- Urge to shout obscenities in church
- Sexual thoughts in church
- Urge to shout “damn” whenever “God” is mentioned
- Urge to stab passenger in car

Obsession about Symmetry/Precision

- Compulsive ritual involves slow and meticulous behavior
- Jack Nicholson avoiding sidewalk cracks
- Shaving for hours/count razor strokes
- Case - aligning shoes, books
  - counting steps to ensure equality

Other Presentations

- **Touching**
- **Religious obsessions** (hypermorality)
- **Pathological fear** of voiding in public (planning and searching for restrooms)
- **Compulsive hoarding** (floor covered in papers)

Rituals vs Compulsions

- ***Rituals***
  Calming
  Socializing function

  Compulsions
  Suffering
  Aggravation of anxiety

OCD dimensions

- Symmetry / ordering, counting, repeating
- Hoarding obsessions / compulsions
- Contamination obsessions / cleaning rituals
- Aggressive obsessions / checking rituals
- Sexual/religious obsessions / related rituals

OCD dimensions

- Stability over time
- Differential treatment response
- Neural correlates
- Possible differential genetic underprint

Early-onset OCD

- Anger attacks
- Continuous compulsive questions “Mom, you won’t due tonight?”
- Tyrannical orders :”Mom, give me a last kiss, otherwise …”
- Ineffective at school – “slow child” (continuous verifications)
- Perception of OC as normal behavior

Neural Correlates

- **Striatal/thalamic** *I. Checking compulsions / sexual, aggressive obsessions*

  II. Symmetry obsessions / ordering, repeating, counting

- **Orbitofrontal cortex / anterior cingulate** III.*Contamination obsessions / cleaning/washing compulsions*

Differential Diagnosis - Organic

- **Tics** - less complex than compulsion
  - not preceded by obsessive thought
- **Complex-partial seizure**
- **CNS insult** (trauma, tumor, CVA, infection, toxin - CO poisoning)
- **Huntington's chorea**
- **Sydenham's chorea** - autoimmune response in basal ganglia from antistreptococcal antibodies
- **Tourette's syndrome**

PANDAS

- Pediatric Autoimmune Neuropsychiatric Disorders Associated with group A beta-haemolytic streptococcus (GABHS)
- Some kids may develop OCD or tics after Group A beta-hemolytic streptococcal infection
- Suspect - in child with sudden onset of severe OCD

PANDAS:clinical phenotypes

- **Psychiatric disorders**: OCD, ADHD, anxiety,depression, emotional instability
- **Movement disorders**: Sydenham's chorea, tic disorder, dystonia

PANDAS:Pathogenesis

- Molecular mimicry: M protein amino acid sequence on streptococcal cell wall share homology with host basal ganglia antigen
- **BBB** – penetrable for antibodies/lymphocytes (Archelos&Hartung,2000)
- **Presence** of ***universal*** serum antibodies that bind to basal ganglia proteins in PANDAS and Sydenham's chorea (Dale et al, 2001).
- Anti-basal ganglia antibodies are ***rarely*** found in *uncomplicated GABHS infection/neurological controls* *(Dale et al,2001)*– may be a specific marker and diagnostic tool for PANDAS
- High incidence of B-lymphocyte marker **D8/17** in patients with Sydenham's chorea/PANDAS (present also in a sign. proportion of general population)
- MRI – enlargement of the basal ganglia, which resolves on symptom remission (Giedd et al, 2000)

PANDAS:Pathogenesis (con't)

- ***Five*** **criteria for** ***autoimmune*** **neurological disease:**

  a/ presence of autoantibody

  b/ immunoglobulins at target structure

  c/ response to plasma exchange

  d/ transfer of disease to animals

  e/ disease induction with antigen

PANDAS/Sydenham's chorea meet ***three*** **criteria:**

a/ presence of autoantibody

c/ plasma exchange and immunoglobulin treatment was associated with symptoms' amelioration (Perlmutter et al,1999)

d/ serum from children with PANDAS infused into rats induced tics

(Hallett et al,2000)

Differential Diagnosis - Psychiatric

- **Schizophrenia** - delusional belief is "fixed" (overvalued idea in OCD)
- **Major Depressive Disorder** - ruminations
- **Hypochondriasis**
- **Body Dysmorphic Disorder**
- **Eating Disorders**
- **Generalized Anxiety Disorder**
- **Simple Phobia** - worry more specific than in OCD

Differential Diagnosis - Psychiatric

- **Obsessive-Compulsive Personality Disorder** (ego syntonic vs. dystonic in OCD)
- **Pervasive Developmental Disorder** (autism)
- **Mental Retardation** (stereotypy)

Differential Diagnosis -Psychiatric/Veterinary

- Canine Acral Lick Syndrome in patient with Lycanthropy
- Veterinarians treat acral lick with Prozac

Comorbid Diagnoses

- **Major Depressive Disorder** - most common (1/3 to 2/3 of OCD patients have MDD)
- **Social Phobia** - in 1/4 of OCD patients
- **Alcohol and drug abuse** - to cope with OCD
- **Eating Disorders**
- **Tics** - in 20% of OCD patients

Comorbid Diagnoses (cont.)

- **Tourette's Syndrome** - 1/3 to 2/3 have OCD
- **Attention-Deficit/Hyperactivity Disorder**
- **Classic triad**: ADHD + OCD + Tics (or Tourette's)
- **Obsessive-Compulsive Personality Disorder** (in 25% of OCD patients)
- **Other Personality Disorders** (dependent, compulsive, avoidant)

Treatment

- **Combination (*pharmacotherapy/psychotherapy*) treatment best**
- **Serotinergic antidepressants (SRIs)**
- **Behavioral therapy**
- **Cognitive therapy**
- **Group therapy**
- **Family/marital therapy**

Pharmacotherapy - SRIs

- **SSRIs** fluoxetine (60-80mg) sertraline (150-200mg)
  paroxetine (40-60mg) fluvoxamine (200-300mg)
  citalopram (40-60gm)
- **All equally effective**
- **Adequate trial** 8-12 weeks, max dose
- **TCA** clomipramine (200-300mg/day)
- **Clomipramine** - may be more effective than SSRIs, but more side effects
- **Use SSRIs before clomipramine**

Resistant OCD: Switch/Augmentation

- **First, try a second SSRI, venlafaxine or clomipramine**
- **Neuroleptic -tics, TS, schizoid**
- **IV clomipramine**

- ***Lithium - mood***
- ***TCA - depression***
- ***T3***
- ***Buspirone, clonazepam - anxiety***

OCD: experimental approaches

- **5HT$_{1D}$** *receptor agonists –sumatriptan, zolmitriptan*
- **Inositol** – *membrane stabilization*
- **Clonidine** – *alpha2 –adrenergic agonist (with Toutette's syndrome)*
- **Gabapentin** –*GABA modulator: OCD-related increased excitatory responses*
- **Oral morphine/tramadol**
- **Anti-androgen therapy** – *cyproterone acetate*

Behavioral Treatment

- More effective for compulsions
- As effective as medications
- Improvement lasts longer than medications
- Exposure (graduated) to feared situations
- Response prevention - resist the compulsive ritual
- Flooding

Example of exposure hierarchy for a obsessional fear of cancer

- **Read an article about cancer**
- **Watch a TV show about cancer**
- **Talk with a person who has had cancer**
- **Shake hands with a person who has had cancer**
- **Share a meal with a person who has had cancer**
- **Visit a cancer treatment facility**
- **Wear a shirt that was handled by a person who has had cancer**
- **Wear a shirt was worn by a person who has had cancer**

Cognitive psychotherapy

- Inflated responsibility
- Overimportance of thoughts
- Excessive concern about controlling thoughts
- Overestimation of threat

Salkovskis, Behav Res Ther1999

Behavioral observations that suggest OCD

- **Raw or reddened hands skin from excessive washing**
- **Questions from the patient about germs or contamination**
- **Complaints of quirky or repetitive habits from family members**
- **Excessive requests for medical reassurance or visits by the patient**
- **Inordinate number or intensity of health concerns**

“Heroic” Treatments

- **Electroconvulsive therapy** - case studies
- **Psychosurgery** - 25-65% success
  - stereotactic cingulotomy
  - limbic leucotomy
  - anterior capsulotomy
  - tractotomy
  - gamma knife

Therapeutic brain stimulation TMS, DBS, VNS

- ***TMS-transcranial magnetic stimulation***

  Single session of right prefrontal rTMS (20Hz)decrease compulsive urges for 8h (Greenberg et al, Am J Psychiatry, 1997)

- ***DBS- deep brain stimulation***

  Uses a brain lead 1.27mm in diameter and is implanted stereotactically into specific brain areas. The stimulating leads are connected via an extension wire to pulse generators placed in the chest. The devices sometimes called "brain pacemakers".

  Rational: the identification of surgical lesions with therapeutic effects was followed by the discovery that DBS, applied to the same structures at high frequencies, also had therapeutic effect.

  FDA approval - Parkinson's disease and essential tremor.

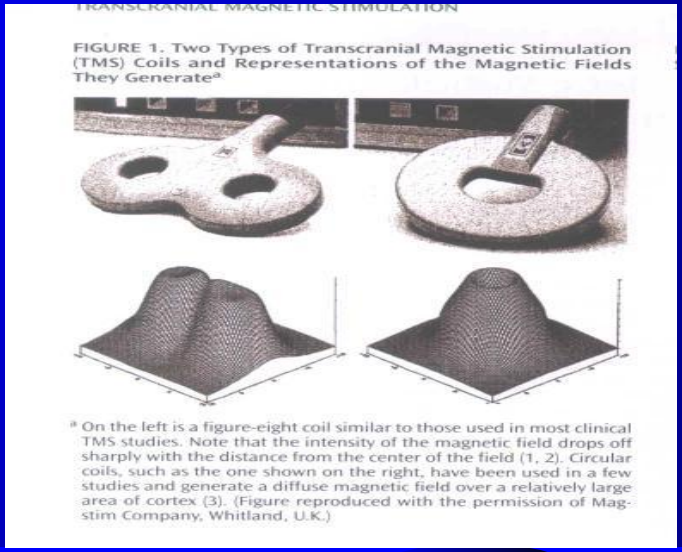
  Investigational uses – epilepsy, pain, dystonia, brain injury.

  OCD – anterior limb of the internal capsule in intractable OCD patient (Nuttin et al, Lancet 1999)

VNS – vagus nerve stimulation ?

TMS

- ***TMS***-noninvasive focal brain stimulation
- ***TMS***-high-intensity current is rapidly turned on and off in the electromagnetic coil through the discharge of capacitors
- ***TMS***-brief magnetic fields (microseconds) induce electrical currents in the brain
- ***rTMS***-if pulses are delivered repetitively and rhythmically (1Hz vs 20-30Hz)



TRANSCRANIAL MAGNETIC STIMULATION

FIGURE 1. Two Types of Transcranial Magnetic Stimulation (TMS) Coils and Representations of the Magnetic Fields They Generate[a]

[a] On the left is a figure-eight coil similar to those used in most clinical TMS studies. Note that the intensity of the magnetic field drops off sharply with the distance from the center of the field (1, 2). Circular coils, such as the one shown on the right, have been used in a few studies and generate a diffuse magnetic field over a relatively large area of cortex (3). (Figure reproduced with the permission of Magstim Company, Whitland, U.K.)

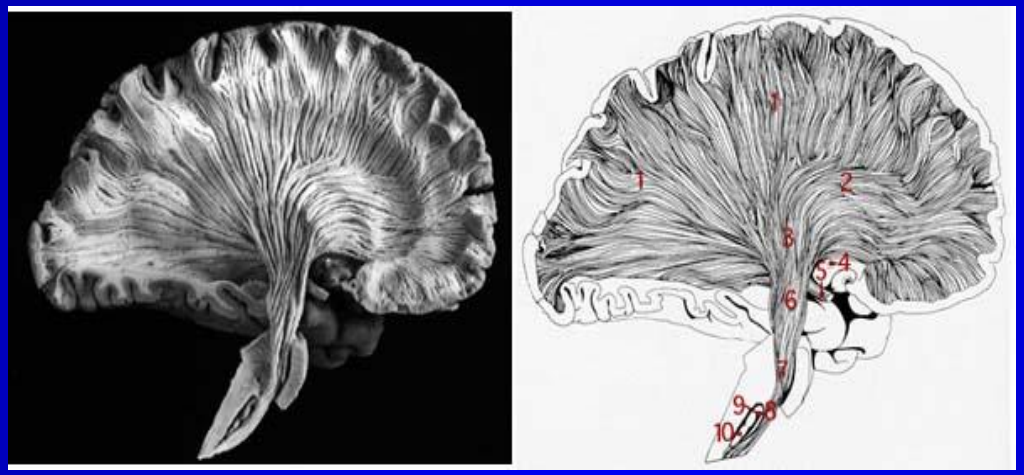
TMS

- ***TMS - MDD***
- ***TMS***-side effects: seizures

FIGURE 2. A Subject Undergoing Transcranial Magnetic Stimulation (TMS)[a]

[a] Most investigators perform TMS with the operator holding the coil flat over the target brain region. In this illustration, the coil is mounted and the electrodes are in place to allow continuous EEG monitoring. Mounted coils and head supports might play a role in future strategies for anatomically precise stimulation. (Photograph reproduced with the permission of Dubravko Kicic, BioMag Laboratory, Helsinki University Central Hospital, Finland.)

DBS in intractable OCD: anterior limb of the internal capsule



- *The internal capsule and corona radiata have been exposed by removal of the corpus callosum, caudate nucleus, and diencephalon. The most striking feature of this preparation is the convergence of great masses of corticofugal fibers from extensive areas of cerebral cortex into the relatively narrow, but thick, basis pedunculi.*

Treatment response

- **25%** significant improvement
  50% moderate improvement
  25% unchanged or worse

Poor Prognosis

- yield to compulsive rituals
- severe symptoms + functional impairment
- comorbid diagnoses
- childhood onset
- poor insight

Most Common Presentations

- **Contamination** - cleaning
  - avoid touching
- **Doubt/incompleteness** - checking
- **Agressive thought** - mental ritual
  - prayer
- **Symmetry/precision** - slowness

Good Prognosis

- precipitating event
- episodic symptoms
- good premorbid functioning
- shorter duration
- comorbid additional anxiety disorder diagnosis

Obsessive-Compulsive Spectrum Disorders

- **Similar symptoms** (repetitive thoughts and/or behaviors)
- **Similar features:**
  - age of onset
  - clinical course
  - family history
  - comorbidity
- **Common etiology** ?(serotonin, frontal lobe activity)
- **Respond to similar treatments** (SSRIs, behavioral therapy)

OC Spectrum Disorders

- **Focus on body appearence and sensations**: Somatoform Disorders:
  - Hypochondriasis
  - Body Dysmorphic Disorder

Eating Disorders:

- Anorexia Nervosa
- Bulimia Nervosa

Psychodynamic Theory

- Obsessions and compulsions involve regression from the oedipal to the anal stage of development
- Anal stage conflicts are managed with defenses like “undoing”
- The compulsive ritual represents this “undoing”

- Sounds like “psychobabble” to me

OC Spectrum Disorders

- **Neurological Disorders**:
  - Tourette's Syndrome
  - Sydenham's Chorea
  - Torticollis
- **Impulse Control Disorders:**
  - Trichotillomania
  - Paraphilias
  - Kleptomania
  - Pathological Gambling
  - Compulsive Shopping
  - Self-injury

OC Spectrum Disorders

- **"Mall Disorder":**

  Kleptomania

  + Compulsive Shopping

  + Binge Eating

Compulsive / impulsive subspectrum

- *BDD,OCD, anorexia, hypochondriasis*
- **High harm avoidance**
- **Risk aversion**
- **Resistance**
- **Anticipatory anxiety**
- **Lack of gratification**

- *Pathological gambling, kleptomania*
- **Low harm avoidance**
- **Risk seeking**
- **Lack of resistance**
- **Low anticipatory anxiety**
- **Gratification**

Similarities between OCD and selected OCD-spectrum disorders

Domain	*BDD*	*Tourette's*	*Hypochondriasis*	*Trichotillomania*
Symptoms	+++	++	++	++
Comorbidity with OCD	+++	+++	+	+
Familial relationship	++	+++	+	+
Treatment response	++	0	+	+

K.Phillips/Psychiatr Clin N Am / 2002; 25: 791-809

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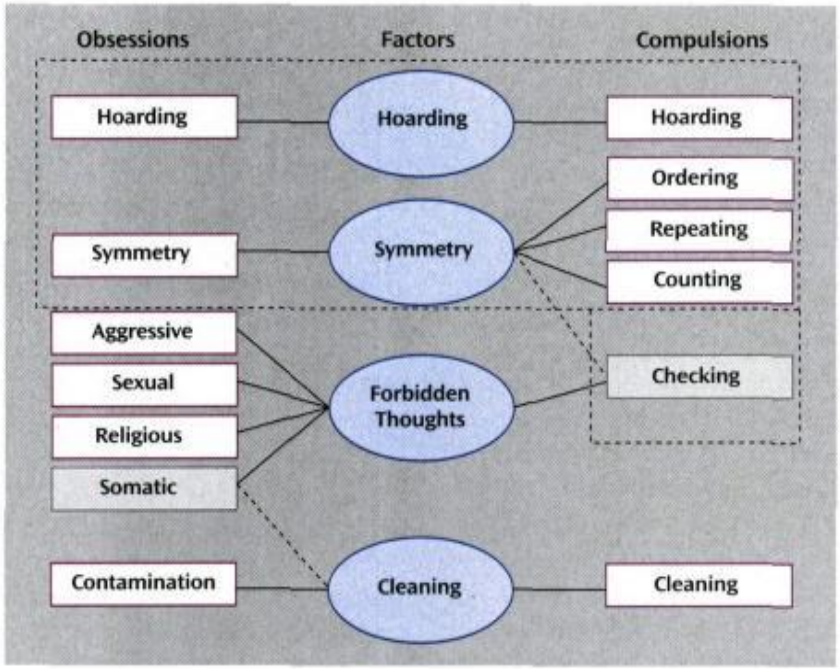
FIGURE 1. Factor Structure of the Yale-Brown Obsessive-Compulsive Scale Symptom Checklist Across the Lifespan[a]



[a] Symptom categories shaded in white are associated with the same factor across the lifespan. Symptom categories shaded in gray are associated with different factors in adults and children. Solid lines indicate that a symptom category is associated with a particular factor in adults. Dashed lines indicate that the symptom category is associated with a particular factor in children only. The hoarding and symmetry factors that are surrounded by a dashed box were collapsed into the same factor in some subgroup analyses, including when studies included non-English-speaking subjects or when ratings of symptom severity were used. The forbidden thoughts factor split into two separate factors in subgroup analyses involving non-English-speaking subjects and when only studies using item-level data were considered.

Outline

- Epidemiology
- Etiology
- Diagnostic Criteria
- Clinical Presentation
- Differential Diagnosis
- Comorbidity
- Treatment
- Prognosis
- Obsessive-Compulsive Spectrum Disorders

Images in Neurology

How long does it take for putting on sneakers? An obsessive-compuls

The ritual takes 1 minute and 25 seconds to put on each foot sneaker, a task usually expected to be accomplished in less than 5 seconds. The ritual includes: 1/fingers repetitive movements (A to F), 2/the need to hear the pounding of feet on the ground (G, H), and 3/marching in the same place for sixteen steps (I to L).

Behavioral Theory

- Obsession is a conditioned stimulus
- A neutral stimulus is paired with an event that is anxiety-provoking - to thus become a stimulus that also causes anxiety

Integration

- Ventral cortico-striatal-thalamo-cortical circuit
  - recognition of behaviorally significant stimuli and in error detection
  - regulation of autonomic and goal-directed behavior

OCD: inability to inhibit procedural strategies mediated by this circuit from intruding into consciousness

Contamination Obsession

- Fear of contamination with germs, HIV virus
- Compulsive ritual involves cleaning, avoiding contaminated surfaces
- Lady Macbeth (handwashing)
- Howard Hughes (tissue, windows)
- Expectoration (shower)