DEFINITION, CHARACTERISTICS, AND EPIDEMIOLOGY:

Definition and characteristics: Obsessive-compulsive disorder (OCD) is **an anxiety disorder** characterized by intrusive obsessions and repetitive compulsions, which cause distress or are a significant burden to the patient. **Obsessions are recurrent and persistent thoughts that are experienced as intrusive and inappropriate, causing marked anxiety. Compulsions, on the other hand, are repetitive behaviors or mental acts carried out in response to an obsession and are aimed at preventing or reducing anxiety.** At some point during the course of the disorder, a patient has recognized that the obsessions or compulsions are excessive or unreasonable. These characteristic symptoms of OCD often interfere with a person's normal routine, occupation, or social activities and relationships.

Typical Obsessions:
Fear of getting dirty or contaminated by people or the environment
Fear of infection, including AIDS or other illness
Disgust with bodily waste or secretions
Recurring thoughts of harming oneself or others
Fear that a disaster will occur
Fear of committing a crime
Recurring distressing sexual thoughts or images
Fear of thinking sinful or blasphemous thoughts
Fear of blurting out obscenities or insults
Extreme concern with order, symmetry or exactness
Recurrent intrusive thoughts of certain sounds, images, words or numbers
Intense need to know or remember
Fear of losing/discarding something important

Typical Compulsions:
Excessive or ritualized hand washing
Prolonged or ritualized showering, brushing teeth, or toilet

routine
Repeated dressing and undressing
Repeated cleaning of household objects
Intense need to order or arrange things in a particular way
Repeatedly checking locks, switches, faucets, appliances
Checking to see no one has been harmed by the patient's actions
Need to tell, ask, confess
Repeating certain actions (e.g. going through doors)
Checking that the patient did not make a mistake
Constant seeking of approval or reassurance
Touching certain objects in a particular way
Repeated counting to a certain number or a multiple of that number
Hoarding useless objects

Associated Diagnoses: OCD is often associated with other disorders such as depression (>50%), dsythymia, anxiety disorders such as social phobia and panic disorder, hypochondriasis, and eating disorders. Obsessive-compulsive symptoms are often seen in schizophrenia as well. There is a great deal of overlap with other repetitive behaviors such as **Tourette's Syndrome** (<50% have OCD, but 25% with OCD have tics).

Obsessive-Compulsive Personality Disorder (OCPD) is characterized by rigid overconcern with rules, sometimes so much that individuals lose the point of an activity. OCPD is usually seen without OCD in individuals and vice-versa, but OCD and OCPD may run together in families.

Epidemiology: OCD has a lifetime prevalence of 2-3% in the United States. There is bimodal pattern of onset of OCD, occurring in childhood and late adolesence/early adulthood. Two-thirds of cases have their onset earlier than age 25, and only 15% occur after age 35. About one-third of cases have onset in childhood or early adolescence. Males tend to have earlier onset and undergo a more malignant course.

Symptoms may be present for years before treatment is sought and those affected often suffer in silence. The disease follows a chronic waxing and waning course where 15% of patients have deterioration and 5% have episodes with interepisode recovery.

ETIOLOGY:

Familial/Genetic Theories: Twin studies have shown that concordance rates for monozygotic twins is higher than that of dizygotic twins. OCD prevalence is higher if a 1st degree relative has OCD or Tourette's. There is also evidence that in some families with Tourette's syndrome, rates of both OCD and Tourette's are increased in biological relatives, which suggests that in these families, OCD and Tourette's may be alternative phenotypic expressions of the same underlying genetic defect.

Behavioral Theories: Two-stage classical instrumental conditioning model of OCD: Obsessions result from pairing mental stimuli with anxiety-provoking thoughts. Compulsions are neutral behaviors that have been associated with anxiety reduction and therefore reinforced.

Neurobiological Theories: Converging evidence from imaging, pharmacological and behavioral studies implicates **hyperactivity in frontal-subcortical thalamic circuits in the pathogenesis of OCD**. This theory holds that hyperactivity in these circuits leads to excess activity in frontal-subcortical systems giving rise to the behavioral disturbance in OCD.

prefrontal cortex (orbitofrontal and anterior cingulate)→ basal ganglia→ globus pallidus→ thalamus→ prefrontal cortex

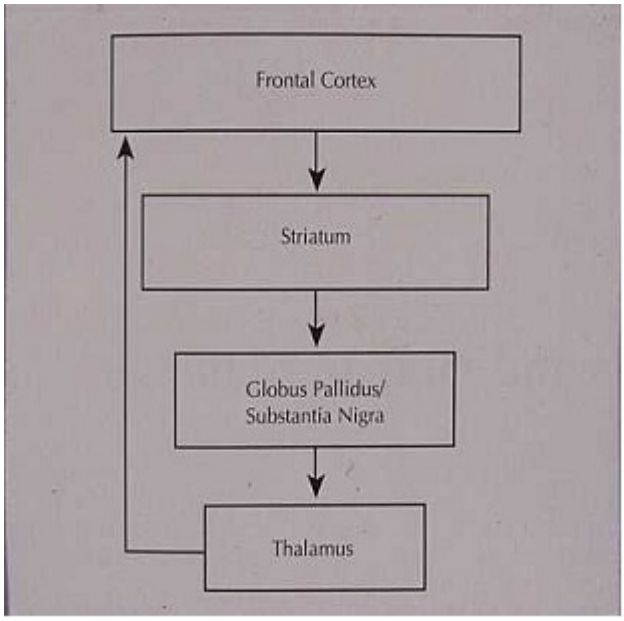

Figure 1

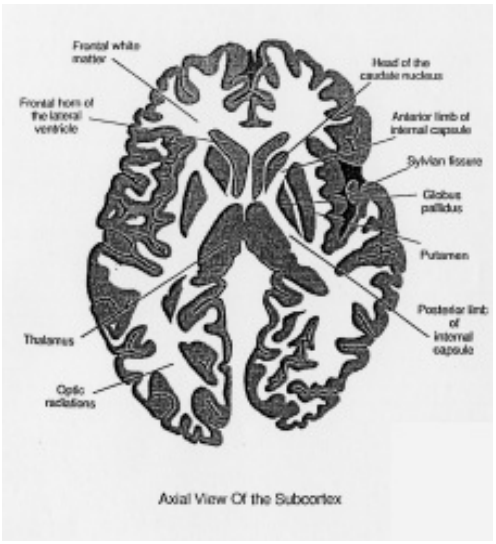

Figure 2

A series of functional imaging studies (PET, SPECT, fMRI) have demonstrated **increased perfusion and metabolism in the orbital frontal cortex, anterior cingulated gyrus and head of the caudate nucleus (Figure 60) in patients with active OCD** Some studies have suggested that the hypermetabolism may have a right-sided predominance. **The hypermetabolism in these circuits can be reversed following successful medication, behavioral or surgical treatment of the OC symptoms.**

Cognitive functions of frontal-subcortical structures involved in the development of a "worry circuit" in OCD

- Response inhibition,

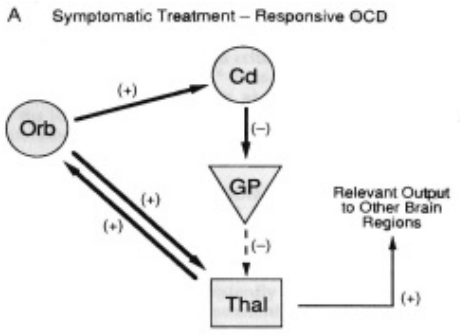

Figure 3. Schematic diagram of OCD "worry circuit." Orb= orbitofrontal cortex
Cd= caudate nucleus, GP= globus pallidus
Thal= thalamus

planning, error detection and mood regulation-prefrontal cortex
- Integrating external stimuli with emotional states and modulation of arousal and intense emotion-paralimbic cortex, orbitofrontal and amygdala
- Automatic filtering of stimuli and mediation of stereotyped behaviors-basal ganglia
- Gating of transmission of stimuli and refined information back to the cortex-thalamus

Several findings implicate the serotonergic system in modulation of OCD symptoms:

Serotonin Reuptake Inhibitors (SRIs) are uniquely effective in OCD.
Serotonin partial agonists (mCPP) can acutely worsen OCD.
Serotonin antagonists (metergoline, ritanserin) can provoke OCD symptoms in SRI responders.
There is a tentative association between some variants in genes coding for serotonin system components and OCD.

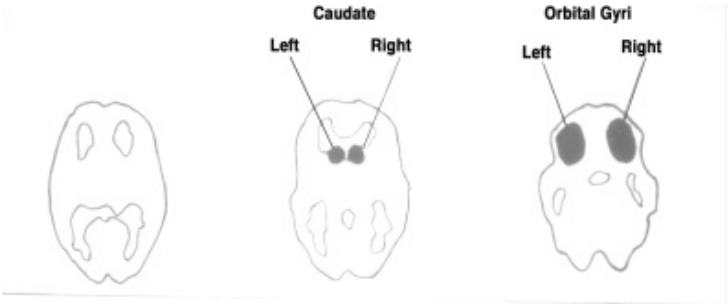

Figure 4. PET studies of a patient with OCD shows hyperactivity of orbitofrontal cortex and caudate nucleus (gray areas). (Baxter, 1999)

TREATMENT:

OCD can be treated with medication, behavioral therapy, and even surgical procedures**. Serotonin reuptake inhibitors (SRI) are the only medications currently**

approved for the treatment of OCD. Some SRI's used to treat OCD include the following:

Clomipramine is found to be most effective although it has some side effects which include: sedation, anticholinergic effects, decreased sex drive, and weight gain. *Very rarely* produces orgasm when yawning.

Fluoxetine has similar side effects as clomipramine.

Fluvoxamine has similar side effects, but "rebound" symptoms may occur if patients are taken off the drug too quickly.

Paroxetine and sertaline are characterized by sedation and "rebound" symptoms similar to fluvoxamine.

Citalopram is normally well-tolerated but may have side effects such as nausea and anticholinergic effects.

Benzodiazapines may help blunt initial anxiety problems and insomnia. Tricyclics and trazodone may also help alleviate the insomnia. It appears that combination treatments may work best in treating OCD.

In general, combining medications and behavior therapy may work best, especially for patients who are unable to tolerate behavioral therapy due to severe anxiety (more than 25% in some series). Behavioral therapy involves exposing the patient to symptom-triggering situations and not allowing them to perform compulsive or avoidance responses. This gradual desensitization allows the patient to build up the ability to handle everyday situations.

Neurosurgery (anterior cingulotomy, capsulotomy, limbic leucotomy) should be considered a last resort. Recent analysis from Mass. Gen. Hospital found about 30% of patients with severe, refractory OCD benefited from cingulotomy. Anterior capsulotomy, especially with the "double-shot" gamma-knife technique looks promising for

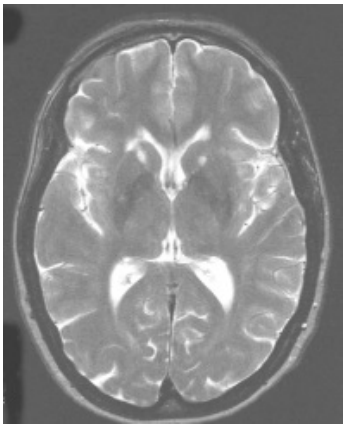

Figure 5. Axial T2 MRI image of patient 6 months after bilateral "double-shot" gamma-knife capsulotomy.

In this view, two lesions are visible in the right internal capsule, and one lesion is discernable in the left internal capsule.

patients with intractable and disabling OCD. 40% of patients were very much improved on the clinical global impression scale at 12 months after the procedure. There is often a delay after the procedure before symptoms improve.

Deep brain stimulation is a new approach described in a recent Lancet article (Nuttin et al., 1999), which is still early in development. It has markedly improved symptoms in a small number of severely-affected patients who would otherwise be candidates for neurosurgery. Potential advantages over neurosurgery is that no brain tissue is destroyed, it can be titrated for maximum individual benefit, and is reversible.