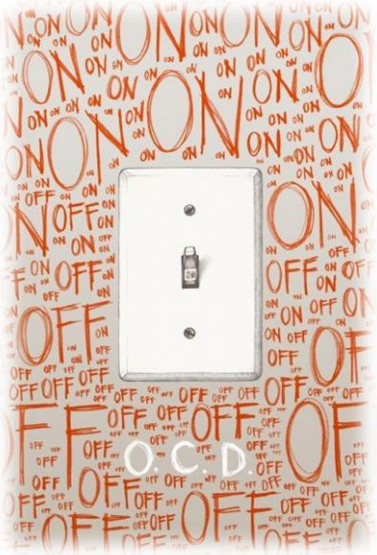
Obsessive-Compulsive Disorder

from Cell to Clinic…



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NeuroMaPC
Center for Neuromodulation and Pain

دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کاشان

Definition

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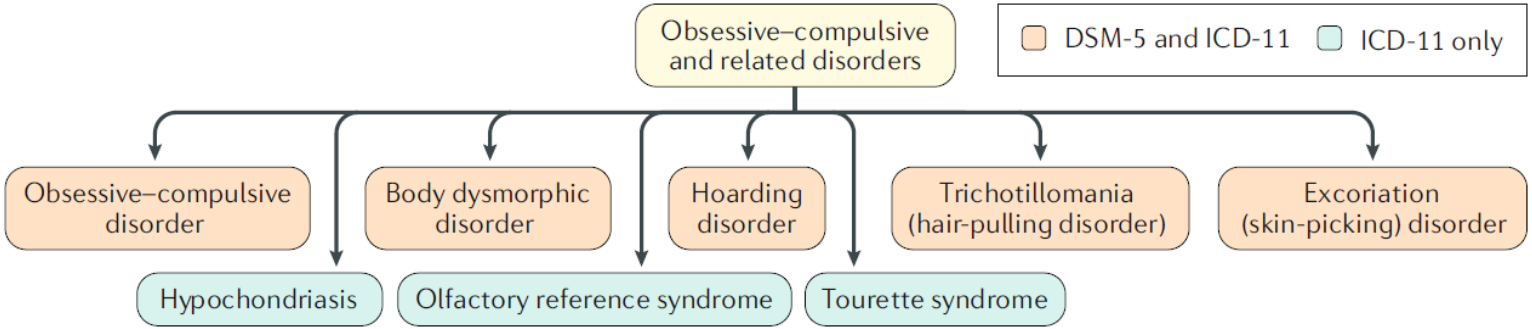
Obsessive-Compulsive Disorder

- A mental disorder characterized by the presence of
  - **Obsessions**
    - **Repetitive** and **persistent** thoughts, images, impulses or urges
    - **Intrusive** and **unwanted**
    - Commonly associated with **anxiety**
  - **Compulsions**
    - **Repetitive** behaviors or mental acts
    - Individual feels **driven to** perform
      - **In response** to an obsession according to rigid rules
      - To achieve a sense of **completeness**

Classification



Epidemiology

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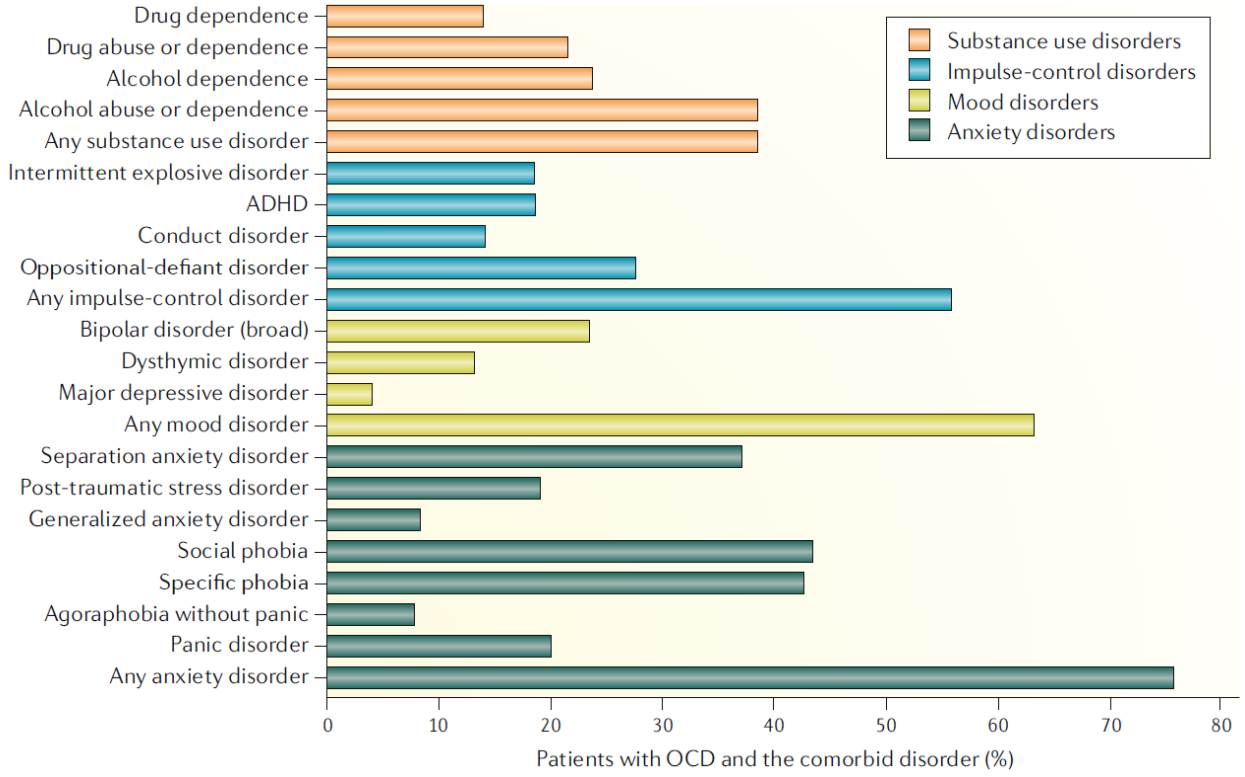
- OCD has a lifetime prevalence of **2–3%**
- More common in **females** than in males
- **Starts early** in life and has a **long duration**
  - Highest rate: **18-29** years of age

- **Comorbidities**
  - Anxiety disorders
  - Mood disorders
  - Impulse-control disorders
  - Substance use disorder

Comorbidities



Ruscio, A. M., Stein, D. J., Chiu, W. T. & Kessler, R. C. The epidemiology of obsessive- compulsive disorder in the National Comorbidity Survey Replication. *Mol. Psychiatry* **15**, 53–63 (2008). **This community survey provides data on the prevalence and comorbidity of OCD in the general population**.

Genetic vs. Environment

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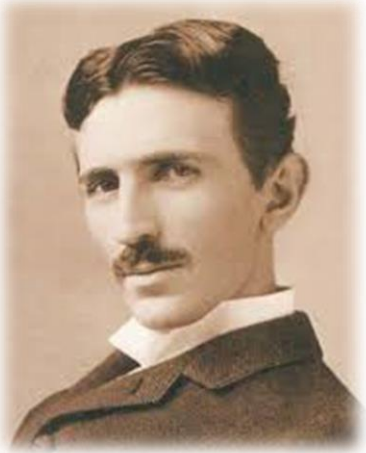
- OCD is a **polygenic disorder** with many identified risk loci of small effect
  - Variants in **glutamatergic** genes (16p13.11)

- A broad range of environmental factors identified as potential risk factors for OCD
  - **Adverse perinatal events** such as birth complications
  - **Stressful** or **traumatic** events



OCD Symptom Dimensions

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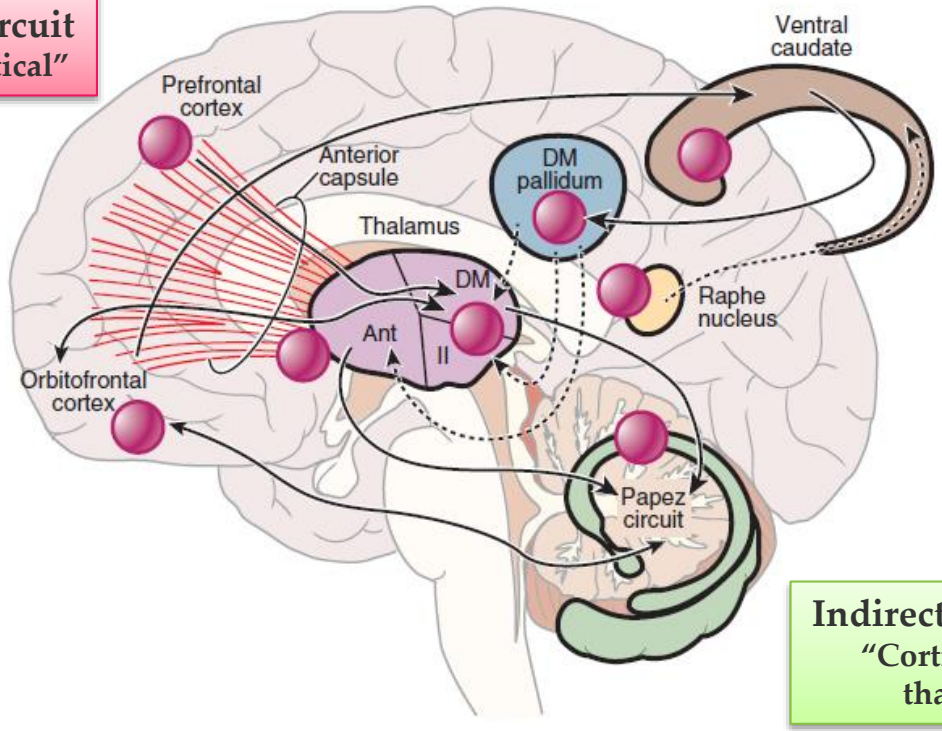
Dimension	Obsessions	Compulsions
Contamination symptoms	Concerns about dirt and germs	Washing, showering or cleaning
Harm-related symptoms	Concerns about harm (self or others)	Checking
Unacceptability symptoms	Intrusive aggressive, sexual or religious thoughts	Mental rituals or praying
Symmetry symptoms	Symmetry concerns	Ordering, straightening, repeating or counting
Hoarding symptoms	Hoarding concerns	Hoarding behaviors

* Studies evaluating sex differences in symptom dimensions have **not** reported consistent differences

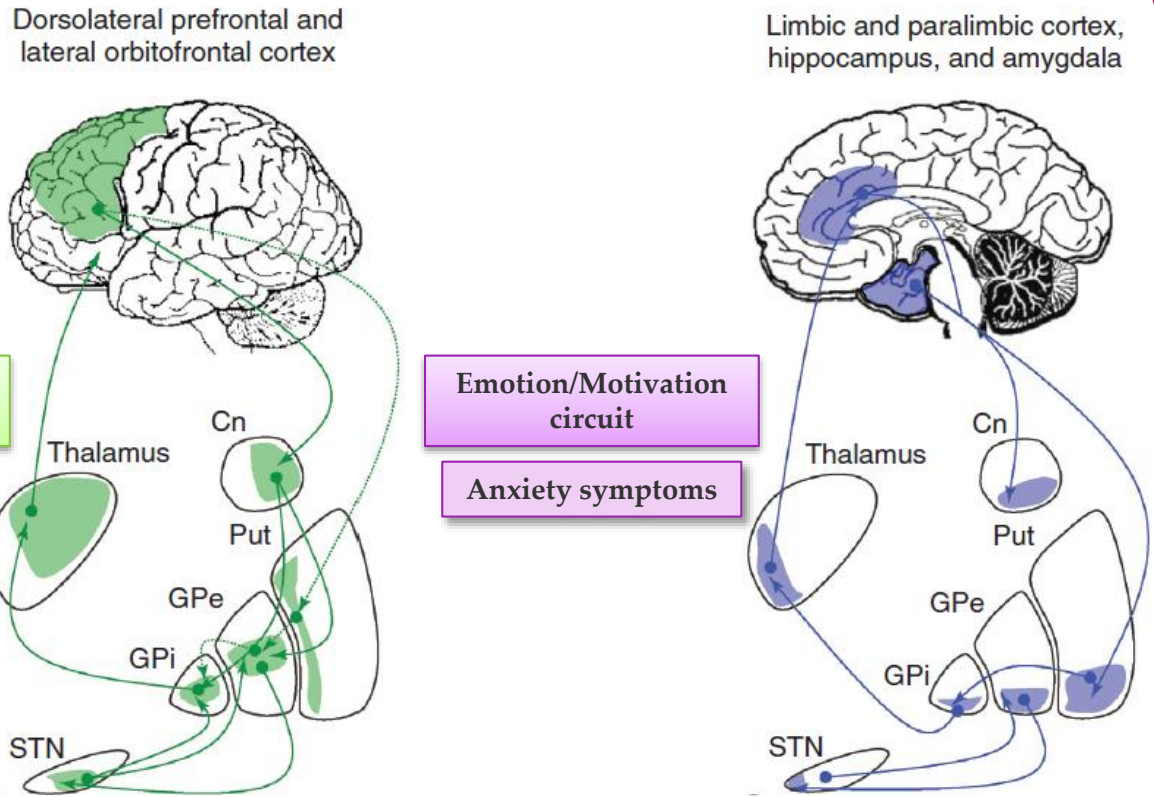
Pathophysiologic Model

Direct excitatory circuit
"Cortico-thalamo-cortical"



Indirect inhibitory circuit
"Cortico-basal ganglia-thalamo-cortical"

Pathophysiologic Model



Pathophysiologic Model

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1- "Lateral Orbitofrontal (LOFC) – Ventromedial Caudate" loop

- **Normal function**:
  - Response to emotionally salient stimuli
- **In OCD:**
  - **Overactivity** of "**Direct** corticothalamic pathway"
  - **Exaggerated attention** to perceived threat >>> "**Obsessions"**

Pathophysiologic Model

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2- "Dorsolateral Prefrontal Cortex (dlPFC) and Dorsolateral caudate" loop

- **Normal function**:
  - Executive function and facilitation of cognitive flexibility

- **In OCD:**
  - **Hypoactive >>> Cognitive inflexibility**
  - Unable to deviate from ritualistic compulsions
  - Lack of flexibility needed to abandon these rigid behavioral patterns

Pathophysiologic Model

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3- Anterior Cingulate Cortex (dACC)

- A **hub** for **cognitive control functions** through **integration** with various frontal regions
  - **With the dlPFC:**
    - **Modulating** cognitive flexibility and executive function
  - **The primary, premotor, and supplementary motor cortices:**
    - **Govern** behavior **execution** and **cessation**
- **In OCD:**
  - **Abnormal activity** in both resting-state and symptom-provocation studies

Molecular Mechanisms

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- Key neurotransmitter systems involved
  - **Serotonin**
  - **Dopamine**
  - **Glutamate**

- **Serotonin**
  - **Selective efficacy** of the **SRIs** in patients with OCD
  - Surprisingly **little evidence** of an underlying serotonin deficit that has a **primary causal role** in OCD

Molecular Mechanisms

- **Dopamine**
  - ▼ in **striatal D2 receptors** in molecular imaging studies on OCD
  - **Good response** to augmentation of SRIs with dopamine **D2 receptor antagonists**
  - Association between variants in catecholaminergic genes (including COMT) and OCD
- **Glutamate**
  - **CSF** and **MRS studies**: alterations in glutamatergic metabolites
  - Association between variants in glutamatergic genes (such as ***SLC1A1*** and ***GRIN2B***) and OCD

Diagnosis

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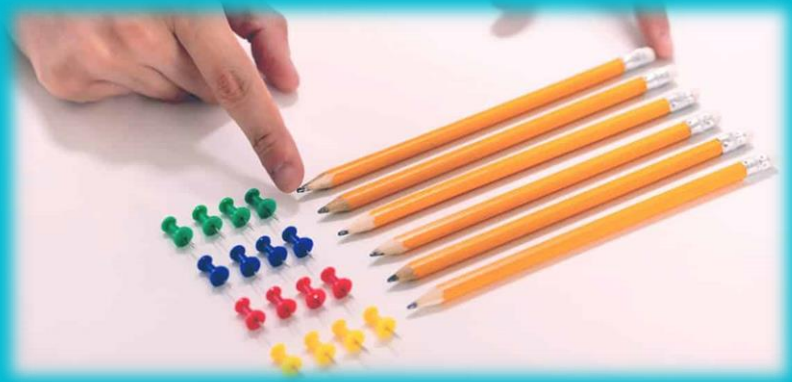
- **Presence of obsessions, compulsions, or both + :**
  - Time-consuming (**>1 hour per day**)
  - Significant **distress** or **impairment** in social, occupational, or other important areas of functioning.

- **Specifiers:**
  - **Insight:**
    - **Good** or fair insight
    - **Poor** insight
    - **Absent** insight/**delusional** beliefs
  - **Tic- relation**



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Treatment

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- **Psychoeducation and psychotherapy**
  - Cognitive-behavioral therapy
- **Pharmaco-therapy**
  - **SRIs (first line): at least** for **12-24 months**
  - **Augmentation in resistant cases**
    - Antipsychotics
    - Clomipramine
    - Glutamatergic drugs

Treatment

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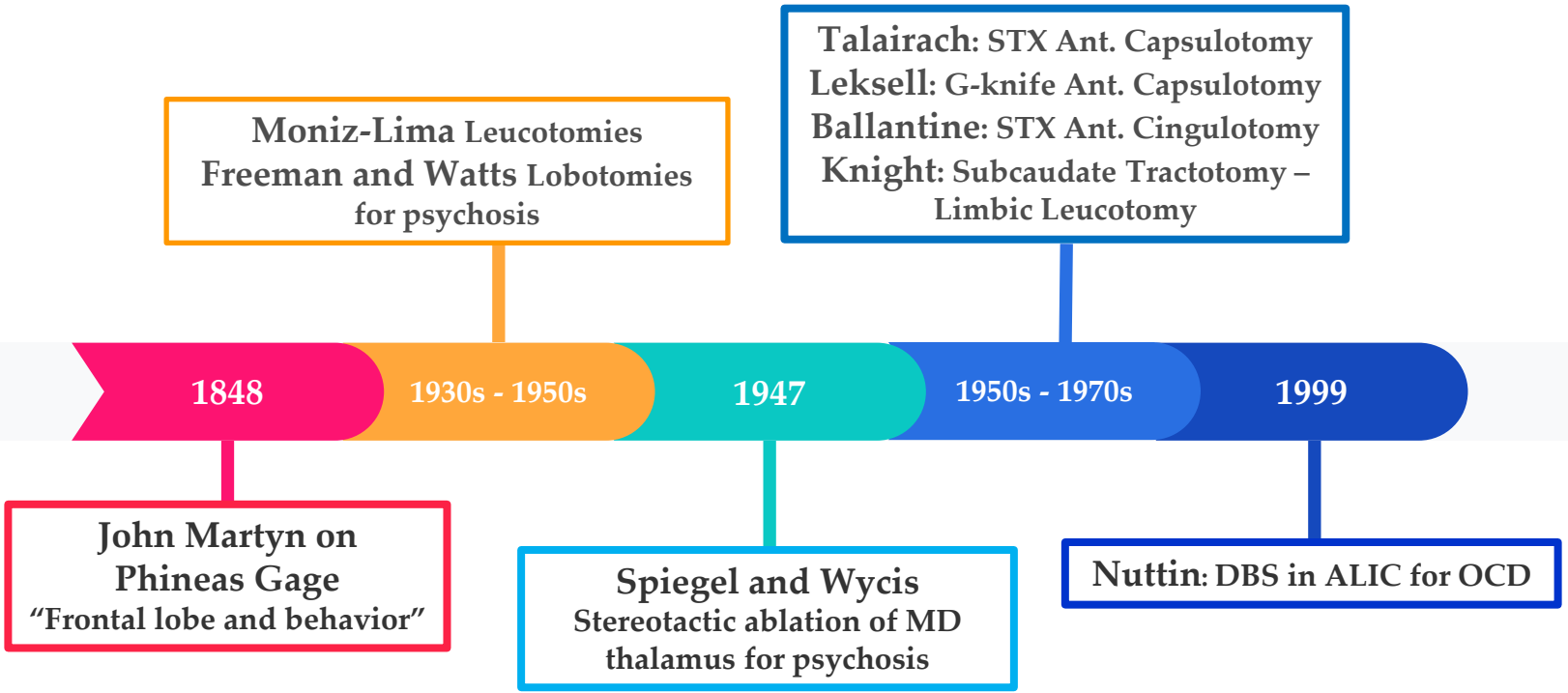
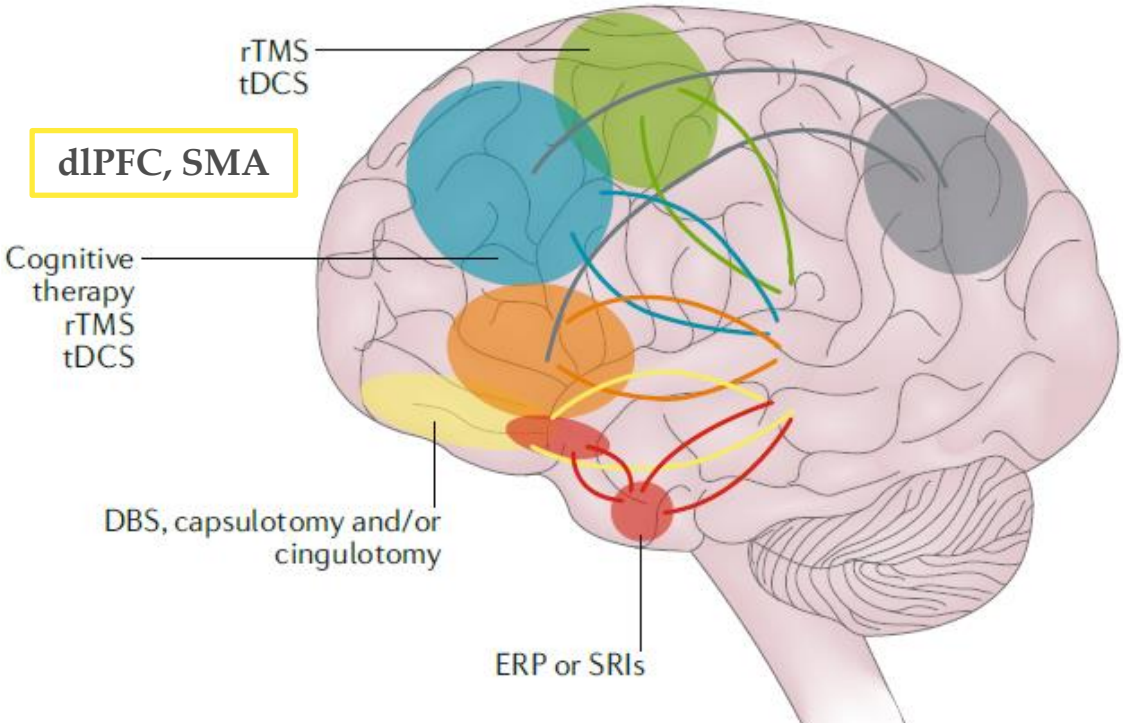
Surgical treatments

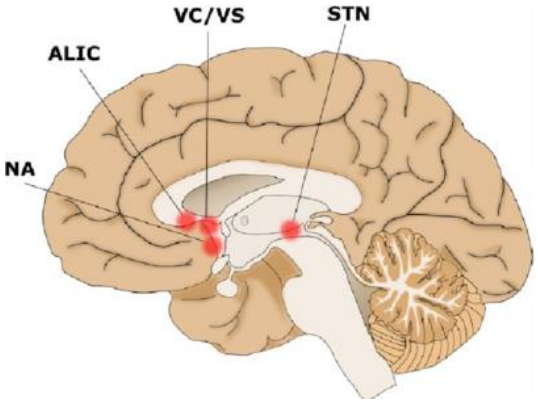
- **Inclusion criteria**
  - Obsessive–compulsive disorder (**OCD**) must be the **main diagnosis**
  - **Yale- Brown Obsessive–Compulsive Scale score ≥28** (or ≥14 if only obsessions or only compulsions are present)
  - **5 years** of **severe OCD** symptoms despite adequate treatment trials
  - Independent confirmation of **refractoriness to treatment**
    - **3** adequate **trials** with a **SRI** (at least one with clomipramine)
    - **2** adequate **augmentation** strategies (such as antipsychotics or clomipramine)
    - **20 hours** of OCD-specific **CBT** (such as exposure and response prevention)
  - Age **18–75 years**
  - Ability to provide informed consent
  - Appropriate expectations of the outcomes of surgery

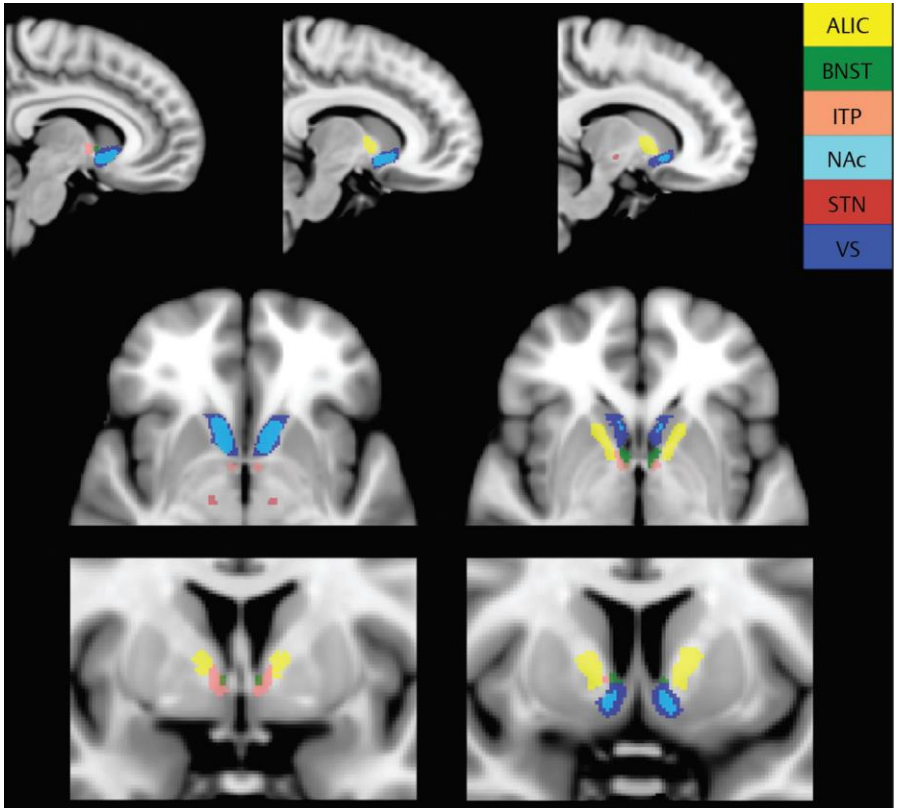

Talairach: STX Ant. Capsulotomy
Leksell: G-knife Ant. Capsulotomy
Ballantine: STX Ant. Cingulotomy
Knight: Subcaudate Tractotomy – Limbic Leucotomy
Moniz-Lima Leucotomies
Freeman and Watts Lobotomies
for psychosis
1848
1930s - 1950s
1947
1950s - 1970s
1999
John Martyn on Phineas Gage
"Frontal lobe and behavior"
Spiegel and Wycis
Stereotactic ablation of MD thalamus for psychosis
Nuttin: DBS in ALIC for OCD

Neuromodulation and Neurosurgery



Deep Brain Stimulation





Deep Brain Stimulation

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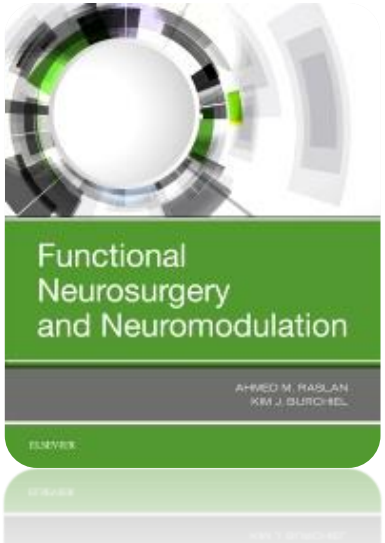
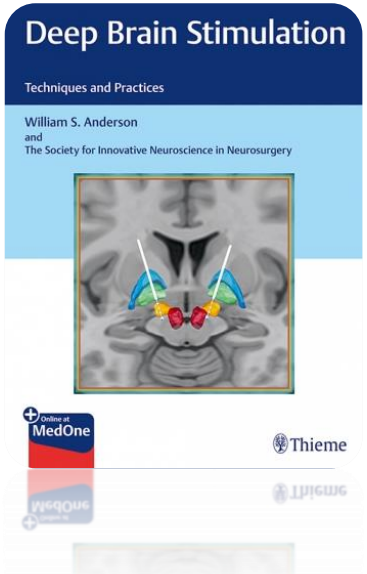
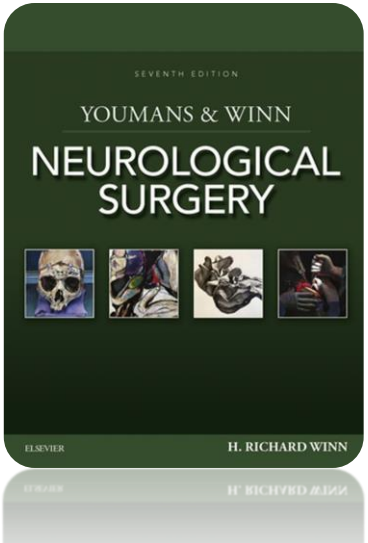
- **Current targets:**
  - The anterior limb of the internal capsule (**ALIC**)
  - Ventral capsule and ventral striatum (**VC/VS**)
  - Nucleus accumbens or the ventral caudate nucleus (**NAcc**)
  - Subthalamic nucleus (**STN**)
  - Inferior thalamic peduncle (**ITP**)

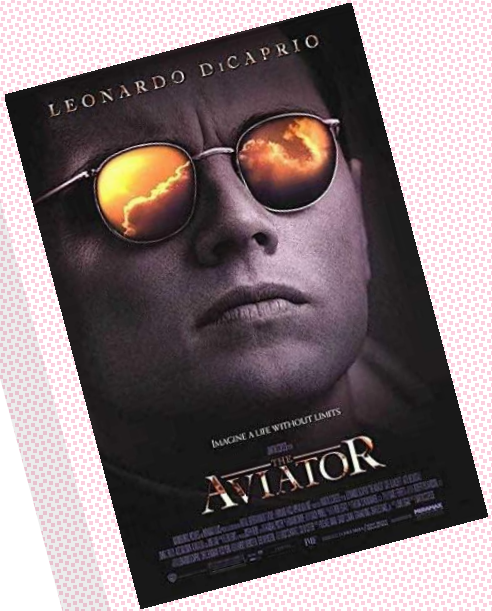
References…

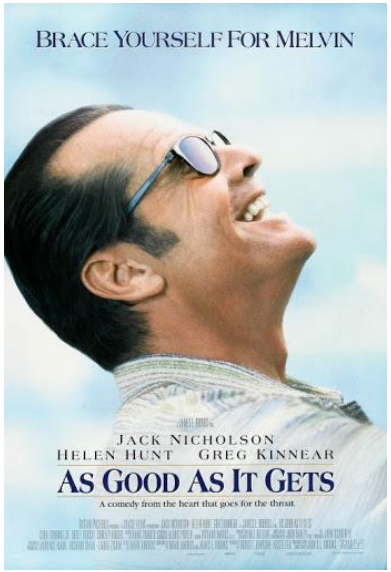
- **Stein, D.J., Costa, D.L.C., Lochner, C. et al. Obsessive–compulsive disorder. Nat Rev Dis Primers** 5, 52 (2019). https://doi.org/10.1038/s41572-019-0102-3











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Thank You…

Any Questions?

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