



Surgery for Tourette's Syndrome

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Definition

- ▶ **Gilles de la Tourette's syndrome (TS)** is an **idiopathic neuropsychiatric** disorder characterized by **chronic motor** and **vocal tics**
 - ▶ **Unknown etiology**
 - ▶ **Prevalence:**
 - ▶ **0.3-1%** of the general population
 - ▶ **Boys > Girls** (4-5 : 1)
 - ▶ **Age at onset: mean at 5-7** with **peak at 10y/o**

Definition

- ▶ **Diagnosis based on**
 - ▶ **Chronic involuntary motor and phonic tics**
 - ▶ **Not attributable to drugs or known medical causes**
 - ▶ **Persist for no less than 1 cumulative year**

- ▶ **Clinical course**
 - ▶ **Frequency and severity of tic expression: “waxing and waning pattern”**
 - ▶ **By late adolescence to early adulthood**
 - ▶ **Symptoms stabilize or remit in ~2/3 of the population**

Clinical Findings

- ▶ **Motor tics:** sudden, repetitive, and purposeless
 - ▶ **Simple:** involving **one muscle group**
 - ▶ **Tonic** (isometric contractions): tensing of the abdominal muscles
 - ▶ **Dystonic:** shoulder rotation, oculogyric deviation
 - ▶ **Clonic** (rapid movements): eye blinking, facial twitching, head, neck or limb jerking
 - ▶ **Complex tics:** involve **several muscle groups**
 - ▶ **May often appear purposeful**
 - ▶ **Gesturing, hopping, body jerking**

Clinical Findings

- ▶ **Phonic tics:** sudden, repetitive, and purposeless
 - ▶ **Simple:** involving **one muscle group**
 - ▶ **Throat clearing**
 - ▶ **Coughing**
 - ▶ **Grunting**
 - ▶ **Complex tics:** involve **several muscle groups**
 - ▶ **Humming**
 - ▶ **Making animal sounds**
 - ▶ **Coprolalia**

Clinical Findings

- ▶ **Tics:**
 - ▶ **Worsen:** under stress, fatigue or excitement
 - ▶ **Improve:** engagement in mental or physical activity, during focused attention
 - ▶ **Involuntary** or **semi-voluntary**
 - ▶ **Premonitory urge:** in up to **2/3** of cases
 - ▶ **Self-injurious tics:** **15-20%** of cases

Clinical Findings

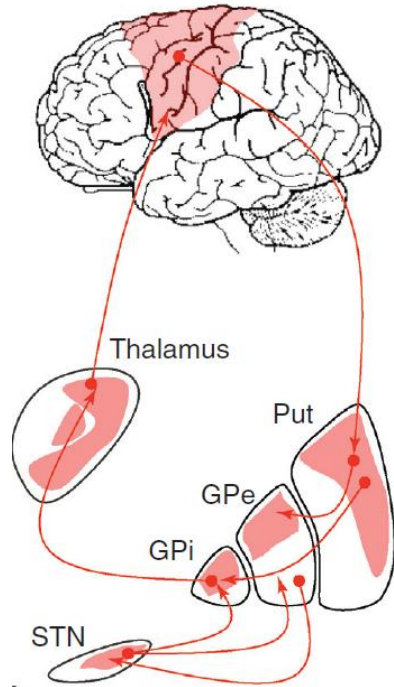
- ▷ **Some notable points**
 - i. **By age 10**
 - ▶ The **ability to suppress** tics is observed
 - ▶ Suppression typically results in stronger **rebound tic expression**
 - ▶ First report **premonitory sensations**
 - ▶ **Urges** associated with dystonic tics and signal the oncoming behavior
 - ▶ **Distinguish TS** from similar disorders
 - ii. **Highly heritable**
 - iii. Substantial rate of **comorbidities (up to 80%)**
 - ▶ Highest: **ADHD** and **OCD**

Pathophysiology

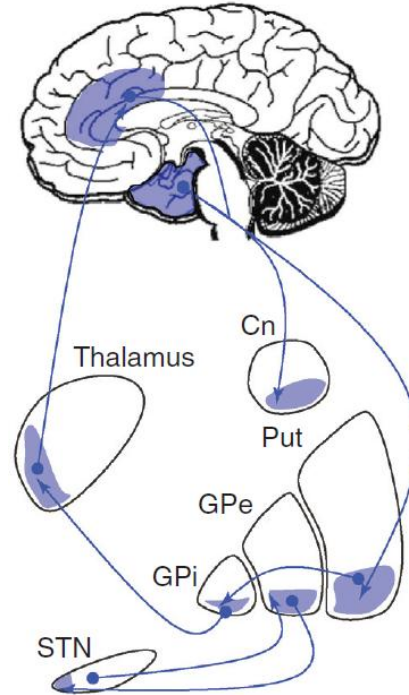
- ▶ **Dysfunction** in the “**cortico–basal ganglia–thalamocortical**” pathway especially
 - ▶ **Motor** circuits
 - ▶ **Limbic** circuits

- ▶ **Dopamine**: the most widely accepted involved neurotransmitter
 - ▶ Dopamine **D2 receptor antagonists**: effectively **reduce tic severity**
 - ▶ **Dopamimetic** drugs: **exacerbate symptoms** of TS

Sensorimotor and premotor cortex



Limbic and paralimbic cortex, hippocampus, and amygdala



Non-surgical Treatments

- ▶ Treatment is **targeted** toward relieving
 - ▶ Tic severity and frequency
 - ▶ Disruptive symptoms presented by comorbidities

Medical Treatments

▷ **Behavioural Therapies:**

- ▶ Comprehensive Behavioural Intervention for Tics (**CBIT**)
 - ▶ ▼ number and severity of tics by **26–31%**

I. Habit reversal training

II. Competing response training

III. Exposure and response prevention

- ▷ Group therapy, Videoconference, Tele-medicine approaches

Medical Treatments

- ▷ **Mild cases**
 - ▷ **α 2- adrenergic agonists** (particularly in patients with comorbid **ADHD**)
 - ▷ **Clonidine, Guanfacine**
- ▷ **Moderate to severe cases**
 - ▷ **Neuroleptics** (antidopaminergic effects)
 - ▷ **Pimozide, Haloperidol, Risperidone**
 - ▷ Side effects: extrapyramidal symptoms, sedation, weight gain
 - ▷ **Aripiprazole**
 - ▷ **Partial agonist and antagonist**
 - ▷ **Lower incidence of side effects**
- ▷ **Isolated motor tics:** Botulinum toxin injection (effective and well tolerated)

Medical Treatments

▷ **Latest AAN and ESSTS guideline:**

- ▶ **No pharmacological treatments** warranted **high confidence** in their efficacy for tic reduction
- ▶ **Aripiprazole:** the **most common choice** for **all age groups**
- ▶ **Haloperidol:** more commonly considered in **adults** than in children
- ▶ **Tiapride:** more often considered in **children** and **adolescents** than in adults

Medical Treatments

- ▶ **Latest AAN and ESSTS guideline:**
 - ▶ **Ecopipam (dopamine D1-receptor antagonist):**
 - ▶ **Significant improvement** of total tic scores with an overall safe profile
 - ▶ **Valbenazine and Deutetrabenazine**
 - ▶ **RCTs failed** to show significant response
 - ▶ **Cannabinoids: experimental**

Treatments

- ▶ **Non-invasive neuromodulation**
 - ▶ **TDCS**
 - ▶ **rTMS**
 - ▶ **Inconsistent results in clinical studies**
 - ▶ **The current AAN guidelines and the European guidelines:**
 - ▶ **Do not recommend** non-invasive brain stimulation for the treatment of tics

Surgical Treatment

▷ Deep Brain Stimulation

- ▶ **Not approved** by the US **FDA** or regulatory agencies in other countries
- ▶ Over **300 cases** worldwide
- ▶ Reported **mean improvements** in tic severity: **45.1–52.7%**

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Tic severity**
 - ▶ **Quality of life**
 - ▶ **Failure of non-invasive treatments**
 - ▶ **Behavioral comorbidities**
 - ▶ **Age**

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Tic severity**
 - ▶ **Marked severity: YGTSS score of 35 or more consistent over the past 6 months**
 - ▶ **Additional modifiers**
 - ▶ **Self injurious tics** such as **whiplash** or **head snapping** tics
 - ▶ **Malignant TS:** the symptom complex should lead to
 - ▶ 2 or more emergency department visits
 - ▶ At least 1 hospitalization associated with self-injury

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Quality of life: great impairment of function and enjoyment of life**
 - ▶ **Generic QoL measures**
 - ▶ **Disease-specific QoL tools**
 - ▶ **YGTSS impairment score**
 - ▶ **Gilles de la Tourette syndrome QoL (GTS-QOL) scale**

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Failure of non-invasive treatments: <25% decrease in YGTSS score**
 - ▶ **Resistance to at least 3 drug classes for at least 12wks trial of each**
 - ▶ **Alpha-adrenergic agonist** (clonidine, guanfacine)
 - ▶ **A typical and an atypical dopamine antagonist**
 - ▶ **1 from another class** (clonazepam, topiramate, tetrabenazine)
 - ▶ **Refractory to Comprehensive Behavioral Intervention Therapy (CBIT)**

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Behavioral comorbidities**
 - ▶ Present in **~90% of patients** and include **ADHD, OCD, anxiety** and **mood** disorders
 - ▶ **If untreated or poorly controlled** would be associated with **lower quality of life scores** regardless of DBS status
 - ▶ **Should be stabilized** for **at least 6 months** before DBS surgery

Surgical Treatment

- ▶ **5 pillars in patient selection for DBS in Tourette syndrome**
 - ▶ **Age**
 - ▶ Age is **not a strict criteria**
 - ▶ In **severe cases presenting below age 18 years**, a local ethics committee and a multidisciplinary screening team should be involved

Surgical Treatments

▷ Deep Brain Stimulation

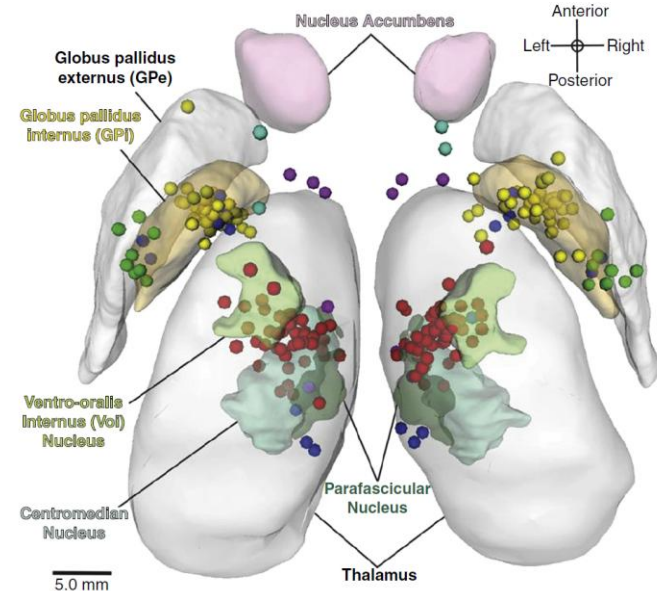
▶ Inclusion criteria

- ▶ Minimum age of **25 years** (**not absolutely**)
- ▶ **Severely disabling** condition (documented by **videotape**, **YGTSS > 35**)
- ▶ **Refractory** to pharmacologic and behavioral therapy (**at least 10 sessions**)
 - ▶ Centrally-acting alpha2-adrenergic agonists (clonidine, guanfacine)
 - ▶ At least two dopamine antagonists, one typical (haloperidol, pimozide) and one atypical (risperidone)
 - ▶ Other drugs (benzodiazepines, topiramate, sertraline)
- ▶ **Comorbid psychiatric or neurological symptoms** should be **under treatment** and considered **stable over the course of 6 months**
- ▶ **Stable social environment with adequate support**

Surgical Treatments

▷ Deep Brain Stimulation Targets

- ▶ Medial thalamus
- ▶ GPi
- ▶ **GPe**
- ▶ Internal capsule/nucleus accumbens (IC/NAcc)

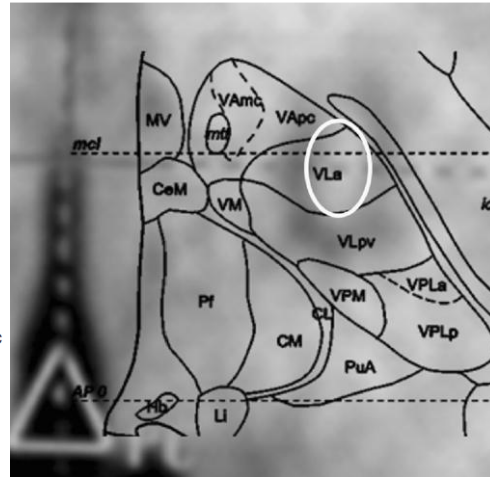
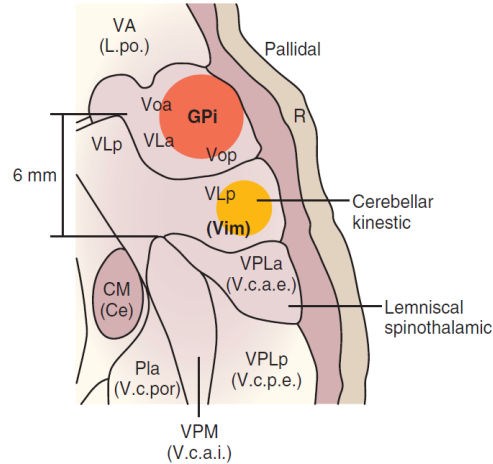


Surgical Treatments

▷ Deep Brain Stimulation Targets

▷ Medial thalamus

- ▷ Convergence of the centromedian nucleus, the substantia periventricularis, and the nucleus ventro-oralis internus



Surgical Treatments

- ▷ **Deep Brain Stimulation Targets**

- ▷ **GPI**

- ▷ **Posteroventrolateral**

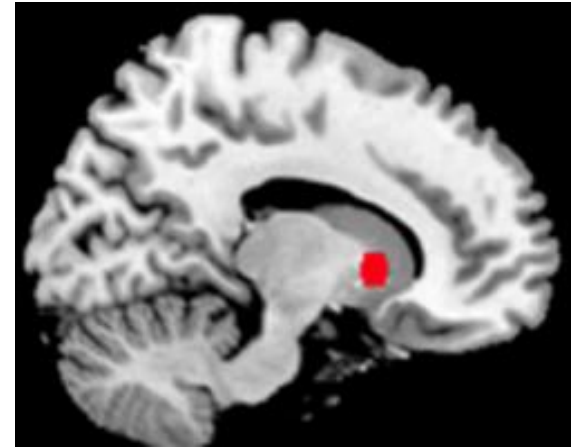
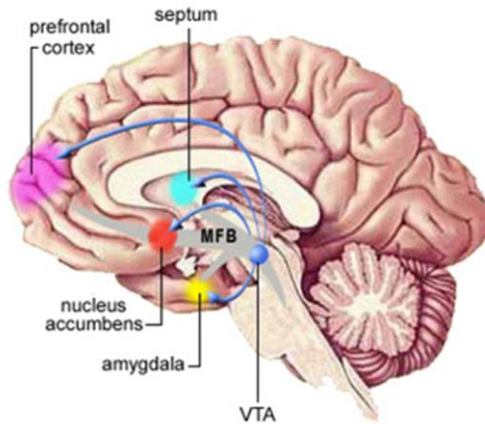
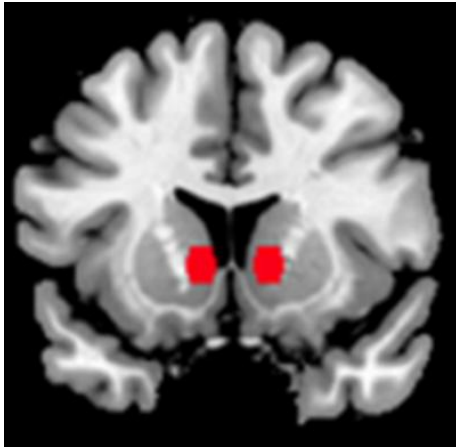
- ▷ Being **more** targeted in **primary studies**

- ▷ **Anteromedial (limbic)**

- ▷ **More recent studies with the concept that TS is more a “limbic” than a “motor” disorder**

Surgical Treatments

- ▷ Deep Brain Stimulation Targets
 - ▶ Internal capsule/nucleus accumbens (IC/NAcc)





Thank You!

