

Tourette Disorder (TD)

An Update

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Outline of Lecture

- **Briefly review Tourette Disorder (TD) criteria**
- **Learn to spot tics**
- **Review of TD through the life span**
- **Recent answers to previously perplexing questions.**
 - How good are various medications in helping tics?**
 - Do children with TD have tics worsen with psychostimulants?**

Question 1

- **A 12 year old boy has phonic tics for 8 months and no motor tics. What is the appropriate diagnosis?**
- **A-Chronic phonic tic disorder**
- **B-Transient phonic tic disorder**
- **C-Tourette Disorder**
- **D-None of these**

Question 2

- **A 10 years old boy meets criteria for Tourette Disorder. He has co-morbid ADHD. What is the drug of choice to treat the latter symptoms?**
- **A-risperidone**
- **B-guanfacine**
- **C-atomoxetine**
- **D-psychostimulants**

Question 3

- You wish to start a boy with Tourette Disorder on 0.05 mg of clonidine to improve tics. He weighs 40 kilograms. What daily dosage would you plan to treat him with?
- A- 0.1-0.15 mg/day
- B- 0.8-0.9 mg/day
- C- 0.6-0.7 mg/day
- D- 0.2-0.3 mg/day

Question 4

- All of the drugs EXCEPT the following have been shown to be effective in reducing tics.
- A-haloperidol
- B-clozapine
- C-clonidine
- D-risperidone

Question 5

- Which of the following states are true of TD?
- A-Coprolalia must be present to make a diagnosis
- B-Tics generally improve during adolescence
- C-Motor tics are generally more severe than vocal tics
- D-Vocal tics are generally more severe than motor tics

History of TD

- 1885 Georges Gilles de la Tourette, student of Charcot
- from 1885-1965 only 50 cases described and treatment was entirely psychoanalytic
- in 1965, TD diagnosis “re-medicalized” with use of haloperidol spearheaded by Shapiros and Tourette Syndrome Association (TSA)

DSM-IV Criteria for TD

- **Fluctuating course of multiple motor and one or more vocal tics**
- **Tics many times a day for more than 1 year**
- **Variable locations & frequency of tics over time**
- **Onset before 18 years (range 2- 15 years)**
- **Exclude substance abuse and CNS diseases like Huntington Chorea, postviral encephalitis**
- **Exclude common transient motor or phonic tics by duration and chronic motor or chronic phonic tics**

Secondary Causes of Tic Disorders (MTTINN) “empty tin”

- **Metabolic - Wilson Disease, hyperthyroidism**
- **Trauma - head trauma**
- **Toxic - amphetamines, cocaine and speed abuse, neuroleptic tardive Tourette, CBZ, L-DOPA (phonic), CO, manganese**
- **Infectious - viral encephalitis, Sydenham chorea**
- **Neoplasm - basal ganglia tumor**
- **Neurologic - Mitochondrial encephalomyopathy, Parkinsonism, Huntington Chorea, neurocanthocytosis, Meiges Syndrome**

Characteris-tics

- clonic or dystonic or tonic
- brief intermittent movements or sounds
- lessen with sleep, (but present through all stages) and purposeful activity
- variable degree of suppression possible: “relatively irresistible” or “temporarily suppressible”
- “premonitory sensory phenomenon (PSP)”- anticipatory urges and “just so” phenomena
- “disinhibition” or complex behaviors known to be dangerous
- “site sensitization”

Common Simple Tics

- **Phonic or Vocal: throat clearing, sniffing, coughing, screeching, yelling out, hiccoughing**
- **Motor: eye blinking, shoulder jerking, head turning, eye widening, dystonic eye movement, abdominal tensing, tongue movements**
- **Used to be believed, if tics suppressed, they would rebound, but not true (Meidinger 2005)**

Common Complex Tics

- Phonic or vocal: repeating words or phrases, echo self or others, changes of prosody or intonation: **echolalia, palilalia, coprolalia**
- Motor: facial grimacing, complex touching movements like retracing steps through a doorway, kissing, jumping, **echopraxia, copropraxia, “blocking tics”**

Prevalence of Tics and TD

- Tic prevalence-- 1 in 5 children, more motor
- TD prevalence DSM-IV = 4-5/10,000
- Most authors =1/1,000 for full blown TD in males and 1/10,000 in girls
- Milder variants occur in an unknown percentage of children: in one community study 1/95 boys and 1/759 girls (Burd et al 1986)

In a Swedish community sample 0.6% with TS, 1.3% with chronic motor/vocal tics, 4.8% with transient tics(Khalifa, von Knorring 2005)

Natural History of TD

- behavioral problems often develop first with ADHD
- first simple tics 7 years, usually motor
- phonic and complex tics emerge years
- waxing and waning course with volleys of tics replaced by new and different tics
- possible to find triggers (anxiety) for exacerbations
- children with earliest onset are most severely involved

Natural History of TD-cont

- **worst tics occur between 9-11 years (10.6 yrs, Bloch et al 2006)**
- **OC symptoms in late latency of early teens: Forty-one percent of patients with TS reported at one time experiencing at least moderate OCD symptoms. Worst-ever OCD symptoms occurred approximately 2 years later than worst-ever tic symptoms.**
- **tics tends to improve in late adolescents (Leckman et al 1998) and most adults have some tics, and usually more than they believe**

Can predict severity of adult tics and OCD with high resolution MRI

- Volumes of the caudate nucleus correlated significantly and inversely with the severity of tic and OCD symptoms in early adulthood. Caudate volumes did not correlate with the severity of symptoms at the time of the MRI scan (Bloch et al 2005)

Leckman 1998

Clinical Course of Tourette's Syndrome

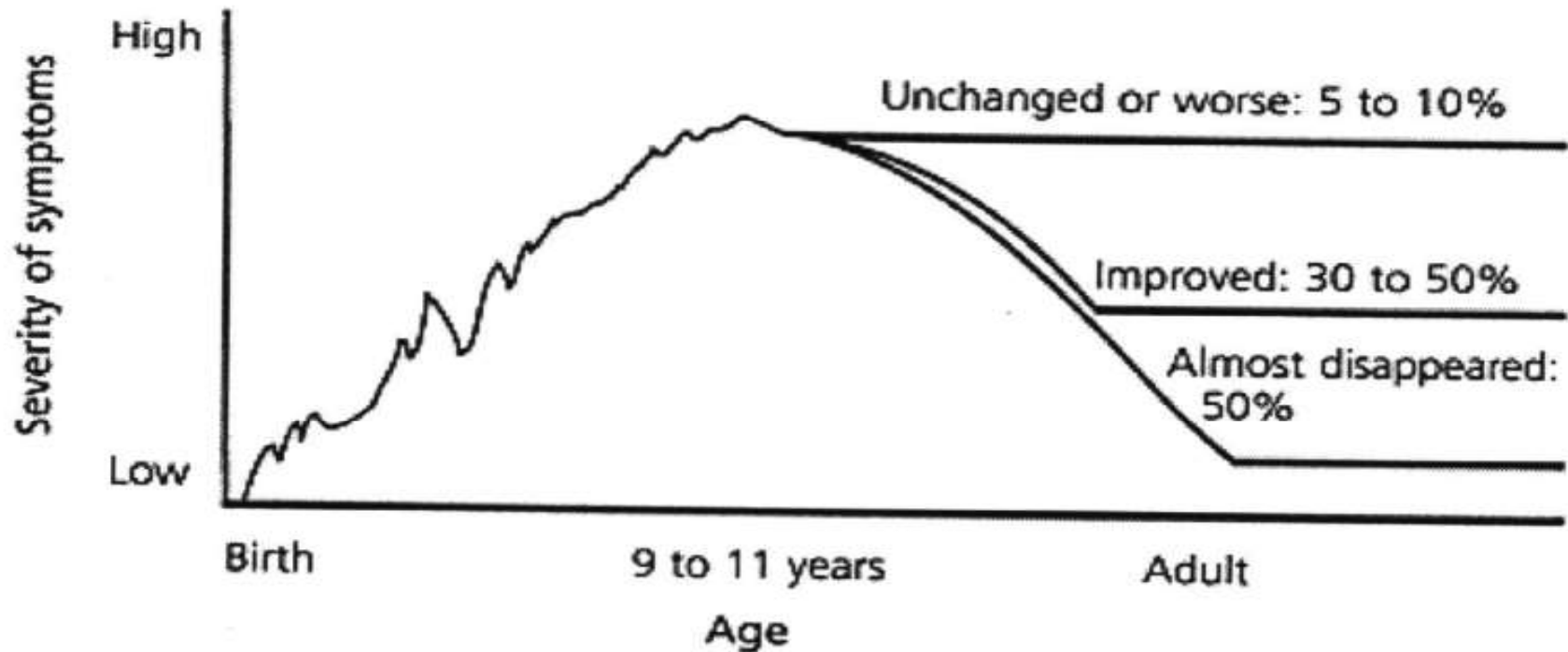


FIGURE 1. The clinical course of Tourette's syndrome. Onset typically occurs before seven years of age and the disorder is usually recognized two to three years after onset. In most children, the severity peaks at nine to 11 years of age. About 5 to 10 percent of patients have an intensifying course with little or no improvement. In about 85 percent of patients, symptoms diminish during and after adolescence.

Co-morbidity of TD

- **ADHD 50%**
- **Learning disorders 20-30%**
- **Anxiety disorders 20-30%**
- **Mood Disorder 20-30%-including Bipolar Disorder**
- **Aggression or oppositional behavior, enuresis, sleep disturbances, migraine**
- **OCD nearly 50% of patients with TD have some degree of obsessive-compulsive features. Most patients with TD have only mild OCB and would not meet the DSM-IV diagnostic criteria for OCD. (Como 2005) v 6% of kids with OCD have TD (Coffey 2005)**

Obsessions and Compulsions (OC)

- **obsessions are repeated mental violent images, or mental repetition of words or phrases, or repeated counting or preoccupation with numbers which despite efforts cannot be completely controlled**
- **compulsions are repeated actions which are experienced as necessary to do to ward off impending disaster, or, for young children, just done without a sense of why**
- **it can be difficult to distinguish tics from compulsive behaviors**

Promonitory Sensory Phenomenon in adults

(Kwak 2003)

- N=50 adults
- Premonitory sensations were reported by 46 (92%)
- Most common sensation was an urge to move and an impulse to tic ("had to do it").
- Intensification of premonitory sensations, if prevented from performing a motor tic, was reported also in 37 patients (74%), 36 patients (72%) reported relief of premonitory sensations after performing the tic, and
- 27 of 40 (68%) described a motor tic as a voluntary motor response to an involuntary sensation, rather than a completely involuntary movement.

PSP and development (Banaschewski 2003)

- **Lack of developmental information on premonitory sensory phenomena (PSP) and suppressibility of tics**
- **The 254 outpatients (212 males, 42 females) with TD had an age range of 8 to 19 years,**
- **The reported data suggest that PSP is experienced rarely in younger children with TD Increasing PSP with age merely seems to reflect cognitive development**

“We must see Tourette’s as a window, not merely on the pathophysiology of the basal ganglia and diencephalon, but on what it means to be human and to live in the world.”

— Oliver Sacks

General Principles of Evaluation/Treating TD

Assess and treat symptoms that interfere with the individual's optimum development and growth Tic treatment?

Must weigh personal embarrassment and severity of tics with possible side effects and risks of pharmacological intervention **and may decide not to treat tics**

or may decide to treat tics or OCD or ADHD or impulsivity or enuresis or insomnia or anxiety or self abusive behaviors with non-pharmacologic interventions or psychotropics,

most impaired, those who end up in hospital have TD+MDD or BD (Coffey 2005)

Medication for tics

- ❖ **Start with low doses and go slow**
- ❖ **Remember that part of the definition of TD is variable ticing over time, therefore it is very hard to gauge efficacy against fluctuating symptoms**
- ❖ **Use a pre-treatment side effect forms and scales eg: CYBOCs, ADHD scales, tic scales (Yale Global Tic Severity Scale)**
- ❖ **Use of videotaping of tics- Rush Video Rating Scale**
- ❖ **Be patient, do a thorough treatment trial**
- ❖ **May only use medication to treat tics during pre-teen years**

Psychopharmacology for TD

Tics

clonidine/guanfacine
risperidone and
other atypicals
TCAs
pimozide
clonazepam

ADHD/Impulsivity

psychostimulants
atomoxetine
clonidine/guanfacine
AAP augmentation

OCD and Anxiety

SSRIs
CMI
clonazepam haloperidol

- bupropion, imipramine, chlopromazine, thioridazine, antihistamines may worsen tics
- clozapine was found to be ineffective in TD
- SSRIs may have indirect effect in reducing inner tensions but no effects on tics directly

Combined Data for improvement in tics in kids with CMT and TD from DBPC studies (YGTSS) (*active drug-placebo)

- **Metoclopramide** **26% (Nicolson et al 2005)***
- **Desipramine** **30% (Spencer 2002)***
- **Guanfacine** **31% (Scahill 2001)***
- **Risperidone** **25% (Scahill 2003)***
- **Ondansetron** **no difference (Toren 2005)**
- **Mecamylamine** **no difference (Silver 2001)**
- **Baclofen** **no difference (Singer 2001)**
- **Fluoxetine** **no difference (Scahill 1997)**

Risperidone v. Clonidine

- 1 head-to-head with RSP v. clonidine (Gaffney 2002) for children 7-14 yrs with TD (8 wks)
- Tics--improvement 21 % RSP and 26 % clonidine
- ADHD-- responders 29% RSP and 50% clonidine
- OCD-- responders 63% RSP and 33% clonidine
- Side effects RSP had more mild symptoms , but RSP group had 2 kg weight gain

Psychostimulants In Kids with TD

**It used to be a “no-no” to use
psychostimulants in kids with tics or
even if they had first degree family
members with tic**

**Remember cant make a diagnosis of
transient, chronic tic disorder or TD if
precipitated by drugs**

2 Questions

- **Do children with no history of tics develop tics with psychostimulants at rates higher than placebo?**
- **Do the tics of children with chronic tics or TD worsened when psychostimulants added?**

Do children with no history of tics develop tics on psychostimulants more than placebo?

- **N=416, 5 studies Concerta, MPH tid in DBPC trials for up to 2 years incidence Concerta=4% MPH=2.3% and Placebo=3.7% (Palumbo 2004)**
- **N=91, Placebo and MPH in children with ADHD w/o tics: 20% on MPH developed tics and 17% of those on placebo developed tics (Law and Schachar 1999)**

Do children with tics worsen with psychostimulants?

- TD/ADHD DBPC study, n=20, Rxed with MPH and DAS, 3 withdrew---tics emerge at higher dosing (0.43mg/kg/dy), if sustained MPH, tics got better (Castellanos et al 1997)

Do children with tics worsen with psychostimulants?

- TACT study : n=136 with 4 arm study of kids with chronic tics and ADHD-----MPH, CND, CND+MPH and placebo
- Tics- the overall severity of tics decreased in all active arms
- Worsening of tics with clonidine =26%. MPH= 20% and placebo =22%
- ADHD: CND best for impulsivity /HA and MPH best for inattention with best outcome CND +MPH (TS Study Group, 2002)
- Take Home Lesson: Most kids with CMT or TD treated with MPH tics will improve, about 20% will worsen

Clonidine

- presynaptic alpha 2 agonist and postsynaptic alpha 2A,B,C agonist, also imidazoline I-1 receptor effects (DIRTY DRUG)
- contraindications: SA/AV node, Raynauds, DM
- start low-at 0.025 mg or 0.05 mg once daily and gradually increase to 5-9 micrograms/kg/day
- short acting behaviorally, need tid or qid dosing-12 week trial
- major side effect is sedation and dry mouth. withdrawal hypertension
- overdose: 1993-99:10,000 “exposures”; 57% < 6 yrs- 1 death (Klein-Schwartz 2002) fewer, more serious with patch (Roberge 2000)

But 6 months later----

- **late onset on nightmares or terrors- withdraw gradually, add a sleeper for a short while or switch to patch**

Clonidine patch

- Advantage of smoother delivery and not worry about withdrawal hypertension
- TTS 1, 2 and 3 equals 0.1, 0.2 and 0.3 mg daily dose
- Wash area, dry and patch; 5 day with 2 day overlap with onset and offset of 1-2 days
- Watch for irritation beneath the square patch
- Can use nasal cortisone spray (Flonase, Nasonex, Rhinocort, Beconase, Nasacort, and Nasrel) beneath patch
- Can cover with Opsite

GUANFACINE

- “cleaner” than clonidine--- alpha 1A agonist
- 1-3 mg q day (start low and go slow)
- Consider BID-TID
- Less sedation and rebound hypertension
- Only 1 DBPC study---kids with ADHD+tic disorder, 1.5-3 mg/day shows improvement in 37% CTRS-ADHD (Scahill et al 2001)

Phonic tics and treatment with BoTox in adults (Porta 2004)

- **Treat with BoTox to vocal cords**
- **Mean response time was 5.8 days**
- **Mean duration of response was 102 days**
- **Premonitory experiences dropped from 53% to 20%.**
- **Hypophonia was the only side effect of note (80% of patients)**

TD Summary

- **Keep diagnosis of TD in mind as you evaluate children**
- **TD best viewed across life span**
- **Multiple co-morbidities**
- **Treat only when development is affected**
- **Consider psychostimulants with ADHD and TD**
- **Current treatments for tics are only moderately helpful**

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Answers

- **Question 1-B**
- **Question 2-D**
- **Question 3- D**
- **Question 4-B**
- **Question 5-B**