**Objective**

- **Dis-inhibition**
  Discuss neurological dis-inhibition in Tourette syndrome as a basis for tics & epiphenomena

**Overview**

- Tics & associated problems
- Assessment
- Tic management (non-Rx)
  - Conventional
  - Experimental

**Take Home Points:**

- TS is not rare
- Tics are usually mild, not catastrophic
- In most people with TS, tics are one of many related complications
- Address main problems, often not tics
**Tic Disorders: Characteristics**

- **Tic Definition**
  - motor or phonic
  - involuntary (unvoluntary?)
  - sudden and rapid
  - recurrent
  - non-rhythmic and stereotyped

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**Tics: Characteristics**

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<td>• Gestures</td>
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<td>• Words, obscenities</td>
<td>• Dystonic postures</td>
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<td></td>
<td>• Imitative (“echoic”)</td>
<td>• Self-abusive or vulgar</td>
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<td>• Speech atypicalities</td>
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Anatomic evolution of tics

Anatomic evolution of tics

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Anatomic evolution of tics

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Anatomic evolution of tics

With permission – Leonardo “Leo” da Vinci

Tic Disorders: Characteristics

• Premonitory urge
• Tics can usually be suppressed

Transient Tic Disorder

• DSM-IV-TR™ Criteria
  – Multiple (and/or single) motor and/or vocal
  – Many times/day (4 weeks – 1 year)
  – Onset before 18 years
  – Not due to substance or medical condition
**Chronic Tic Disorder**
(Motor or Vocal)

- DSM-IV-TR™ Criteria
  - Multiple (or single) motor or vocal
  - Many times/day and at least 1 year
  - Onset before 18 years
  - Not due to substance or medical condition

**Tourette’s Disorder**

- DSM-IV-TR™ Criteria
  - Multiple motor plus 1 or more vocal
  - Many times/day and at least 1 year
  - Onset before 18 years
  - Not due to substance or medical condition

**Epidemiology**

- Prevalence
  - 1% males (or more)
  - Male > Female (3-to-10 times)

**Etiology**

- Neuro-anatomy and function
- Neurotransmitters

**Tics: Pathophysiology**

- Dis-inhibition
  - “sensori-motor gating”
  - “filtering”
- Fixed action patterns / Motor pgms

**URGE → TIC → RELIEF**
Genetics

- TS is genetic in origin
- TS is inherited
  - family, twin and adoption studies
- Non-genetic factors also present
  - Gestational exposure?
  - Perinatal?
  - Hormonal?

Genetics

- Major genes are involved
  - autosomal dominant w/incomplete penetrance?
  - polygenic?
  - additive?
- Genomic regions suspected
  - Seeking susceptibility genes in the regions
- Epigenetic factors

Genetics

- First identified gene mutation: SLITRK1 chromosome 13
  - Identified October 2005
  - Differs from previous findings, which are limited to likely gene regions

Abelson JF et al. Sequence Variants in SLITRK1 are Associated with Tourette's Syndrome. Science

Genetics

- Gene mutation: W317X (dominant negative) chromosome 15
- Identified May 2010 (father & all 8 kids)

Histidine HDC Histamine

Ercan-Sencicek et al. L-Histidine decarboxylase and Tourette's Syndrome. NEJM
**Genetics**
barriers to identifying genes

- Diagnosis based on behaviors
- Defining the TS phenotypic spectrum – “endophenotypes”
- Family pedigree problems
- Environmental influences
- Combinations of genes may be involved
- Symptoms decrease with age
- Transient tics

**Differential Diagnosis of tics**

- Compulsions
- Habits
- Stereotypies
- Allergies
- Sydenham chorea
- Various involuntary neuromuscular

**Diagnostic Pitfalls 101**

- Subject or clinician unaware of tics
- Waxing and waning nature of tics
- Tics are suppressible

**Diagnostic Pitfalls 102**

- T.S. is not rare
- T.S. is usually not catastrophic
- Few have coprolalia

**Assessment: co-morbid conditions**

- ADHD
- Obsessions/Compulsions
- Learning interferences
- Behavioral disorders
- Developmental disorders
- Mood disorders
- Anxiety
- Social difficulties (including PDDs)

**Clinical Course**

- < 7 ADHD
- 7 Simple motor tic (head)
- 8 Vocal tic
- 11 OCS + peak tic severity
- > 11 tics ↓ (but lifelong in 50-90%)
Management

• General Guidelines
  – Education
  – Monitoring (tics and non-tics)
  – Containment

• Is additional treatment needed:
  – for tics?
  – for co-morbid conditions?

Management: “co-morbid” conditions

  – Family dysfunction
  – OCD & other anxiety disorders
  – ADHD
  – Learning difficulties
  – Behavioral Disorders
  – Sleep disturbances
  – Other self-injurious behaviors

Management: tics

• Education & Accommodation
• Medications
• Experimental
  – Behavioral
  – Integrative
  – Surgical

Management: tics

• Education & Accommodation
  
  Tourette Syndrome Ass’n
  
  • Teacher in-service
  • Classroom education
  • Teacher as role model
  • Tic breaks/sanctuaries

Management

• Perspectives:
  – The child
  – The parent
  – The school
  – You
Management: tics

- Experimental: **Behavioral**
  - CBIT (Comprehensive Behavioral Intervention - Tics)
  - HRT (Habit Reversal Training)
    - Awareness Training
    - Competing Response
    - Relaxation & Social Support
- FA (Functional Analysis)
  - Social situations that influence behaviors

A common sense guide to complementary/alternative medicine

<table>
<thead>
<tr>
<th>Effective?</th>
<th>YES</th>
<th>NO</th>
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<tr>
<td>Safe? YES</td>
<td>Recommend</td>
<td>Tolerate</td>
</tr>
<tr>
<td>NO Monitor closely or discourage</td>
<td>Discourage</td>
<td></td>
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Pharmacotherapy

**KEY POINTS!**
- Do not assume medication is necessary
- Address comorbid condition(s)
- Complete tic remission is rare
- Stimulants are generally safe
Pharmacotherapy

Supportive evidence (short-term safety/efficacy)

- Category A: Good
- Category B: Fair
- Category C: Minimal

Pretty much everything known to humankind tried for tics

- Alkaloids: nicotine, reserpine
- Alpha adrenergic agonist: clonidine, lofepramine, guanfacine
- Anti-cholinesterase: galantam
- Anti-convulsant:LEVETIRACETAM
- Anti-depressant (tricyclic): desipramine, nortriptyline
- Anti-hypertensive: clonidine, guanfacine, methylphenidate
- Anti-Parkinson: pergolide
- Anti-psychotic (other): tetrabenazine
- Atypical neuroleptic: haloperidol, pimozide, ziprasidone, quetiapine
- Atypical neuroleptic (N/A in US & Canada): sulpiride, tiapride
- Benzodiazepine: clonazepam
- Caesarean: diazepam
- Dopamine agonist: ropinirole
- Dopamine anticonvulsant: aminopyridazino derivatives
- MAO inhibitor: selegiline
- Muscle relaxant: baclofen
- Neutrotoxin: botulinum toxin A
- Selective NE reuptake inhibitor: atomoxetine
- Typical neuroleptic: fluphenazine, haloperidol

Pharmacotherapy for tics:

European experts ratings

- 1st tier: Clonidine, Guanfacine, Baclofen, Topiramate, Levetiracetam, Clonazepam
- 2nd tier: Pimozide, Fluphenazine, Risperidone, Aripiprazole, Olanzepine, Haloperidol, Ziprasidone, Quetiapine, Sulpiride, Tiapride
- 3rd tier: BoTox

Pharmacotherapy for tics: American opinions

- 1st tier: Clonidine, Guanfacine, Baclofen, Topiramate, Levetiracetam, Clonazepam
- 2nd tier: Pimozide, Fluphenazine, Risperidone, Aripiprazole, Olanzepine, Haloperidol, Ziprasidone, Quetiapine, Sulpiride, Tiapride
- 3rd tier: Dopamine agonists, Tetrabenazine, BoTox

Pharmacotherapy for tics

- Mild tics
  - No medication treatment

Pharmacotherapy for tics

- Mild tics w/ or w/o comorbid ADHD
  - Monotherapy:
    - α-adrenergic agonists
    - Stimulants
    - Atomoxetine
Pharmacotherapy for tics

• Moderate tics
  – α-adrenergic agonists and/or:
  – Atypical neuroleptics
• Severe tics
  – Atypical neuroleptics
  – Typical neuroleptics

Pharmacotherapy for tics

• Category A
  – Typical Neuroleptics
    • Haloperidol
    • Pimozide
  – Atypical Neuroleptics
    • Risperidone

Pharmacotherapy for tics

• Category B
  – Typical Neuroleptics
    • Fluphenazine
  – Atypical Neuroleptics
    • Ziprasidone
    • Aripiprazole
  – Other
    • Clonidine
    • Guanfacine
    • Botulinum toxin

Pharmacotherapy for tics

• Category C
  – Atypical Neuroleptics
    • Olanzapine
    • Quetiapine
  – Other
    • Baclofen
    • Nicotine patch or chewing gum

Other options that may be effective
– Benzodiazepines
  • Clonazepam
– Anticonvulsants
  • Topiramate

Take Home Points: Clarifying Common Misconceptions

• TS is not rare
• Tics are usually mild, not catastrophic
• In most people with TS, tics are one of many related complications
• Address main problems, often not tics
**For further information, including Rx discussion:**

Tourette Syndrome Association, Inc.

[www.tsa-usa.org](http://www.tsa-usa.org)

NEWLY DIAGNOSED Video Webstream with Dr. John Walkup

**Extensive Resources in Medical Home partnership:**

Developmental-Behavioral Pediatrics

[Depts.washington.edu/dbpeds](http://Depts.washington.edu/dbpeds)

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