Tourette Syndrome and Infectious Neuropsychiatric disorders

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Tourette Syndrome

- Increased popular awareness of disorder
  - TV
  - Books
  - Film
Tourette Publications

1960’s

Today
Public Perception of Tourette Syndrome on YouTube

Mary Jane Lim Fat, BSc¹, Erick Sell, MD¹,², Nick Barrowman, PhD¹,³, and Asif Doja, MD¹,²

• Negative perceptions/depictions continue

Lim Fat 2012
Affected: ocd/b, tic, adhd, anxiety, depression
Jean Marc Itard

- Initial description, 26 year old woman
  - Marquise de Dampierre
    - Tics, bizarre cries, “Mais tout cela sans delire, sans aucun trouble des facultees mentales”
    - (“But all of this without folie or frenzy, without any trouble in mental abilities or aptitudes”)
    - Coprolalia → recluse

- “Case 10”, reported by Charcot and Tourette.
Historical Tourette

• Mozart
  – “scatological” writings
  – Echolalia, pallilalia, coprographia
  – Movements

• Dr. Samuel Johnson
  – “Dr. Johnson is often muttering pious ejaculations, when he appears to be talking to himself.” Vocalizations
  – “..yet his appearance was rendered strange and somewhat uncouth by convulsive cramps…Motor Tic
  – “his anxious care to go in and out at a door or passage, by a certain number of steps from a certain point” OCD

Tourette: a Creative Edge?

Simkin 1992
Ashoori 2007

Pearce 1994
“Recurrent, non-rhythmic, stereotyped movements (motor tic); or sounds produced by moving air through the nose, mouth or throat (vocal tic)”
Tic

- Simple
- Complex
  - Touching, smelling, copropraxia
  - Echolalia, pallilalia, coprolalia
- Dystonic
- “Sensory”
Tic Examples
Tourette Syndrome - Diagnostic Criteria

Table 1 Diagnostic Criteria

<table>
<thead>
<tr>
<th>Diagnostic and Statistical Manual or Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tourette syndrome (307.23)</strong></td>
</tr>
<tr>
<td>A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not</td>
</tr>
</tbody>
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  necessarily concurrently                                                                                           |
| B. The tics occur many times a day (usually in bouts) nearly every day or intermittently throughout a period of more |
  than a year; and during this period there was never a tic-free period of more than 3 consecutive months             |
| C. Onset before age 18 years                                                                                       |
| D. The disturbance is not due to the direct physiological effects of a substance (eg, stimulants) or a general |
  medical condition (eg, Huntington’s chorea or postviral encephalitis)                                              |

<table>
<thead>
<tr>
<th>Transient tic disorder (307.21)</th>
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<tbody>
<tr>
<td>A. Single or multiple motor or vocal tics</td>
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<tr>
<td>B. The tics occur many times a day, nearly every day for at least 4 weeks, but for no longer than 12 consecutive months</td>
</tr>
<tr>
<td>C. Onset before age 18 years</td>
</tr>
<tr>
<td>D. The disturbance is not due to the direct physiological effects of a substance (eg, stimulants) or a general medical</td>
</tr>
</tbody>
</table>
  condition (eg, Huntington’s chorea or postviral encephalitis)                                                       |
| E. Criteria have never been met for Tourette disorder or chronic motor or vocal tic disorder                          |
Tourette Syndrome

- broadened criteria?
  - OCD
  - ADHD
- Spectrum Disorder

Transient Tic Disorder  Chronic Tic Disorder  Tourette
Epidemiology

- **Bruun 1984**
  - US prevalence 0.05%

- **Comings, 1990**
  - Definite TS, males, 0.6%
  - Time factor removed: 1/95 male (1%) 1/759 female

- **Mason, 1998**
  - Observational study
  - 3%
    - Referrals, 0.05%

- **Jankovic 2001**
  - 4%

- **Lanzi 2004**
  - ~3%

- **Montgomery County, MD**
  - ~15-20 patients/day
  - 2-5 Tourette, tic/week
Clinical Features

- Onset 2-15 years
- Commonly misdiagnosed initially
- Tic: simple, complex, dystonic
- Echolalia, pallilalia, coprolalia
- Comorbid features paramount

Jankovic 2001
Clinical Features

• Tic
  – Worsened symptoms with fatigue, stress
  – Decreased with relaxation, ETOH, orgasm
    • Video games
  – Typically disappear during sleep
    • arousals
  – Continuous Tic
    • Emergency Room admissions
  – Tics of note

Pollakiuria in Children with Tic Disorders

Huei-Shyong Wang, MD; Hsieh-Lin Chang¹, MD; Siao-Wen Chang², MD, PhD
Clinical Features

- Tics are suppressible
- Tics suggestible
- Inner “tension” prior to tic, requiring behavior to relieve—premonitory urge
  - Often misidentified
    - Allergy, muscle pain, ophthalmologic abnormalities
- Increased Limb movements during sleep, sleep abnormalities
Clinical Features

- Sensory Tic/Premonitory Urge: 93% responders
- Males greater than female
- Generally children > 10 years
Diagnostic Challenge

• Misidentification of tic
  – Allergy
    • Kim 1997
  – Muscle pain/”pull”
  – Asthma
    • Hogan 1999
  – Psychogenic cough
  – “perioral dermatitis”
  – “Low-lying” tonsils
    • Birring 2004
TS - Comorbid findings

• ADHD 20-80%
• OCB/OCD ~ 50%,
  – Often difficult to distinguish from complex tic
• LD
• Aggression, self injurious behavior
• ODD
• Sleep, sexual disorders
Pathophysiology

• cortical–striatal–thalamocortical pathways
  – Dopaminergic hypersensitivity
    • decreased CSF HVA
    • Suppression of tic via antagonists
    • Occasional exacerbation of tic by dopaminergic stim

• Other considerations
  – Noradrenergic
  – Serotonergic

Cortical thickness differences

Sowell 2008
Animal Models

- Simple motor tics induced by striatal activation (injection of GABA$_A$ antagonist)
Genetics

- **SLITRK1**
  - Abelson 2005

- **Autosomal Dominant, with variable penetrance, sex dependent expression**

- **Concordance for monozygotic twins, ~ 50-90%**
  (higher if criteria broadened)

- **Adoption studies - essentially no relatives affected**
Genetics

• Bilineal inheritance may be important
  – May correspond with degree of severity in children
    • Lichter, 1999
  – One quarter TS patients with bilineal inheritance
    • Hanna 1999
Infection and movement disorders

Prototype:

– Sydenham Chorea
  » OCD, movement phenomenon
  » Neuropsychiatric complications
    often most disabling/long-lasting

• Post Rheumatic/Sydenham
  – Proportion go on to develop
    TS/PANDAS
  » Walker 2005
**PANDAS**

- **Pediatric Autoimmune Neurologic Disease** Associated with **Strep**
  - OCD
  - Tic
  - Myoclonus
  - ADHD

- Remains controversial
  - Inconsistent presence of antibodies
  - Difficult to distinguish between TS/PANDAS immunologically
  - Sera does NOT cause increased stereotypies in animals
Tourette: Treatment

- Reassurance, education, biofeedback
- Tics - Medical
  - Clonidine → Atypicals → haldol/Pimozide → Tetrabenazine
    - QT, tardive dyskinesia?
  - Localized/Vocalization → botulinum toxin
- Anxiety, OCB/D
  - CBT
  - SSRI, Abilify
- Comorbid ADHD
  - Stimulants
  - Clonidine
Tourette: Treatment

- Smaller Series
  - Dopamine Agonists
    - Selegeline, pramipexole (Kurlan 2012)
  - ω-3 fatty acids

- Anecdotal reports
  - Zofran
  - Baclofen
  - Nicotine
  - cannabinoids

- Non-medical
  - Acupuncture
  - Biofeedback
  - CBT/Habit reversal
Surgical Treatments

• DBS and Tourette
  – Shahed 2007
  • GPi
  – Veerle Visser-Vandewalle 2003
    • Medial Thalamic
  – Ackerman 2006
    • Medial Thalamic
      – centromedian nucleus, the substantia periventricularis, and the nucleus ventrooralis internus
Tourette: Treatment

• ~ 80% children do not receive treatment for Tic, appropriately

• However…
  – Significant proportion with comorbid challenges
    • Attention Deficit 50-80%
    • Obsessive Compulsive disorder/behavior 40-50%
    • Anxiety
    • Learning disorders 20-40%
    • Depression
    • Rage
    • Oppositional defiant disorder
    • Sleep impairments
  – Kostanecka-Endress 2003
Treatment of comorbidities

• Focus on success in school, employment, socially
• Attentional concerns often paramount, learning and behavioral difficulties follow
• Newer agents
  – Atomoxetine, intuniv, capvay
• Stimulant therapy safe, effective
  – TS study group, 2002, expedited publication
TS: Treatment

• Immune modulation
  – No place currently for uniform treatment with immune suppressants, IVIG, antibiotics
  – If clear association with infectious precipitants and *recurrent*, may consider prophylaxis

Swedo 2004, Walker 2005
TS: prognosis

• Quality of life
  – Corresponds with Tic severity
  – Children rate QOL lower than their parents

• Indication of some degree of improvement in Tic in adulthood

• Reported resolution of tics in adults
  – 50% still have tics during observation

• Continued symptoms of Tic for at least a third
  – Dooley 2006, Bloch 2006
Adolescent Implications

• Sydney

• “…when you tic it is a challenge to concentrate, and when you have trouble concentrating in the classroom you miss a lot of the assignment and have to ask questions. … It is hard enough to be in a very competitive high school, let alone be different. I try not to pay attention to stares, but it has affected me. “

• “On the other hand, TS has made me the caring and compassionate person that I am. I understand what people with disabilities go through and feel like and it has shaped me into a very understanding person of other people’s difficulties.”

• “I am very fortunate that I have been going to a camp with other kids and teens that have TS because I have made so many lifelong friends and I always feel comfortable around them.”
Malignant Tourette

- Jankovic, 2007
  - Injury related to repetitive tic
    - Eye, rectum, cervical spine
Tourette Syndrome and The Law

- Disinhibition
  - “Rage Attacks”
    - OCD → Rumination → inappropriate behaviors

- Impulse control
  - Increased tendency to Vandalize, Fighting, Drug abuse/ETOH, stealing
    » Comings, 1987

Tourette Syndrome and The Law 2006, Jankovic
Conclusion

• Tourette Syndrome and Tic disorders are common
• Although tic may be problematic, most common difficulties for patients are comorbid challenges
• Genetic factors large contribution, exogenous factors play a role
• Therapy multidisciplinary, and spanning the life of the patient
• Reassurance, encouragement, advocate, teach
Outcome
• Thanks for your attention!