Tourette Syndrome and Infectious Neuropsychiatric disorders

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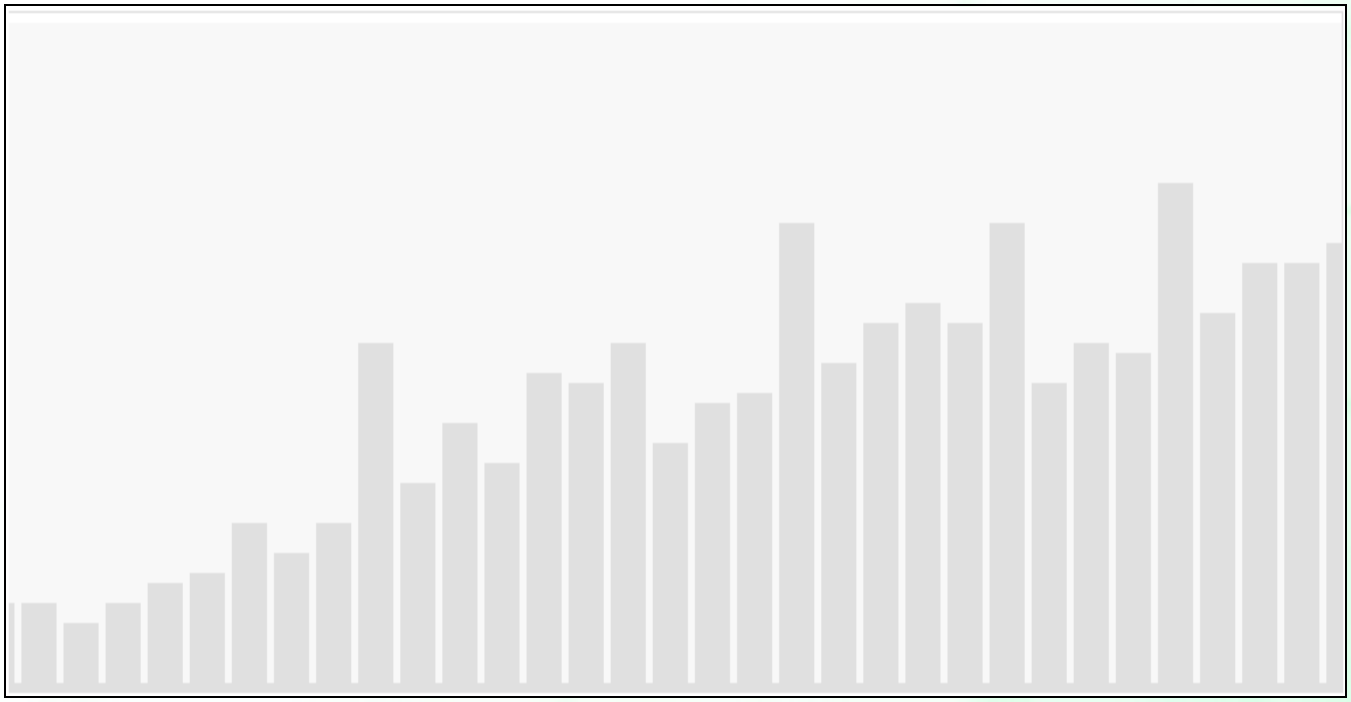
Tourette Syndrome

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

Tourette Publications



1960’s

Today

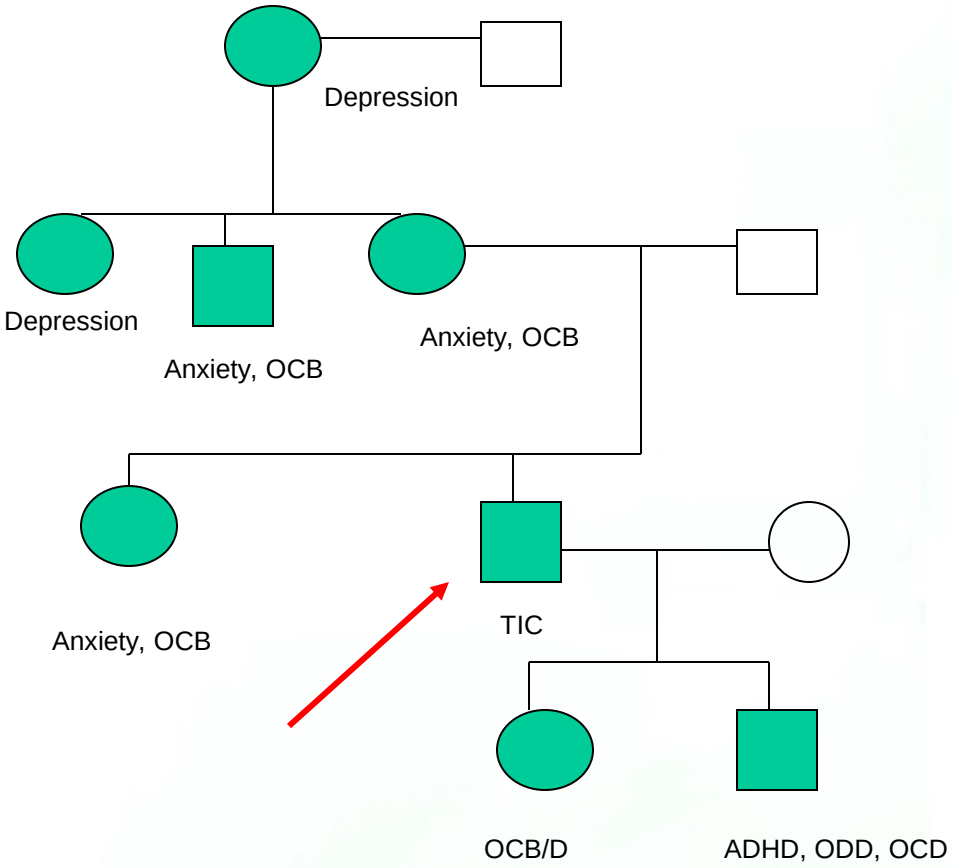
Original Article

Public Perception of Tourette Syndrome on YouTube

Mary Jane Lim Fat, BSc[1], Erick Sell, MD[1,2], Nick Barrowman, PhD[1,3], and Asif Doja, MD[1,2]

- Negative perceptions/depictions continue

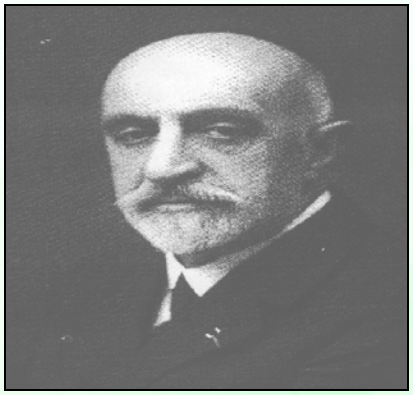
Lim Fat 2012



= 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.

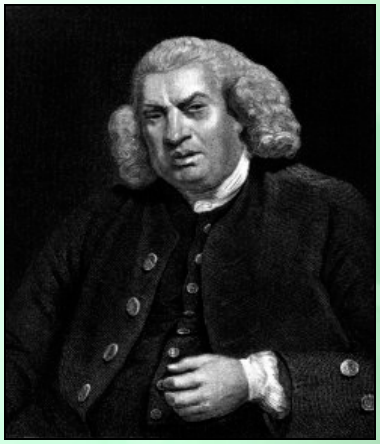


Historical Tourette

- *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

Tic Definition

"Recurrent, non-rhythmic, stereotyped movements (*motor tic*); or sounds produced by moving air through the nose, mouth or throat (*vocal tic*)"

Riley 2006

Tic

- Simple
- Complex
  - Touching, smelling, copropraxia
  - Echolalia, pallilalia, coprolalia
- Dystonic
- “Sensory”

Tic Examples

Jankovic

Tourette Syndrome - Diagnostic Criteria

Table 1 Diagnostic Criteria

Diagnostic and Statistical Manual or Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)[34]

Tourette syndrome (307.23)

A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not 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)

Transient tic disorder (307.21)

A. Single or multiple motor or vocal tics

B. The tics occur many times a day, nearly every day for at least 4 weeks, but for no longer than 12 consecutive months

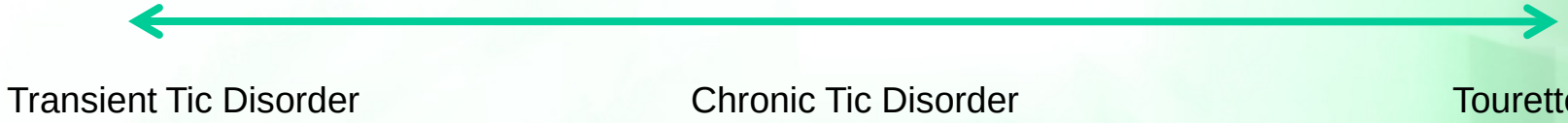
C. Onset before age 18 years

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)

E. Criteria have never been met for Tourette disorder or chronic motor or vocal tic disorder

Tourette Syndrome

- broadened criteria?
  - OCD
  - ADHD
- Spectrum Disorder



Epidemiology

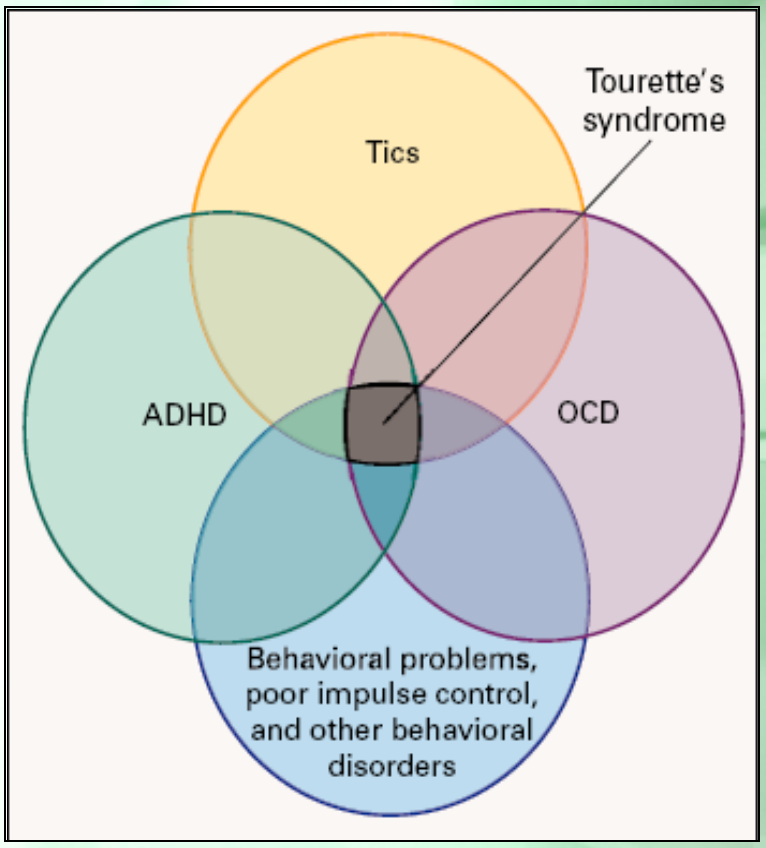
- **Bruun 1984**
  - US prevalence 0.05%
- **Comings, 1990**

  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

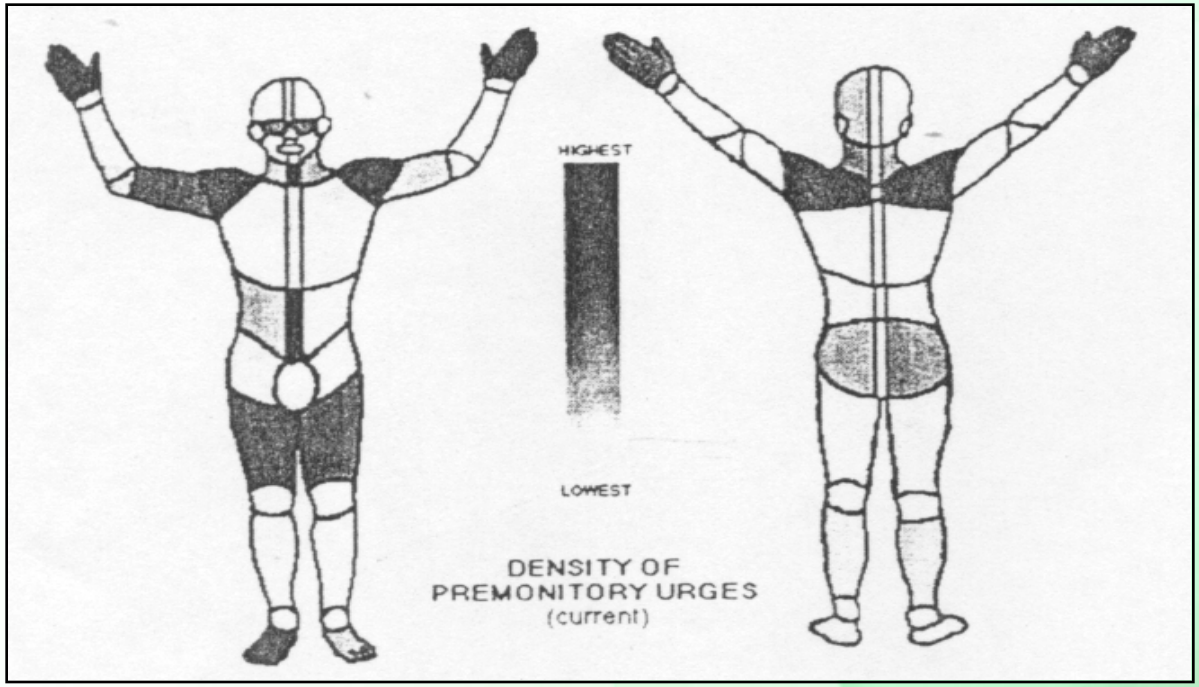
Huei-Shyong Wang, MD; Hsieh-Lin Chang[1], MD; Siao-Wen Chang[2], MD, PhD

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

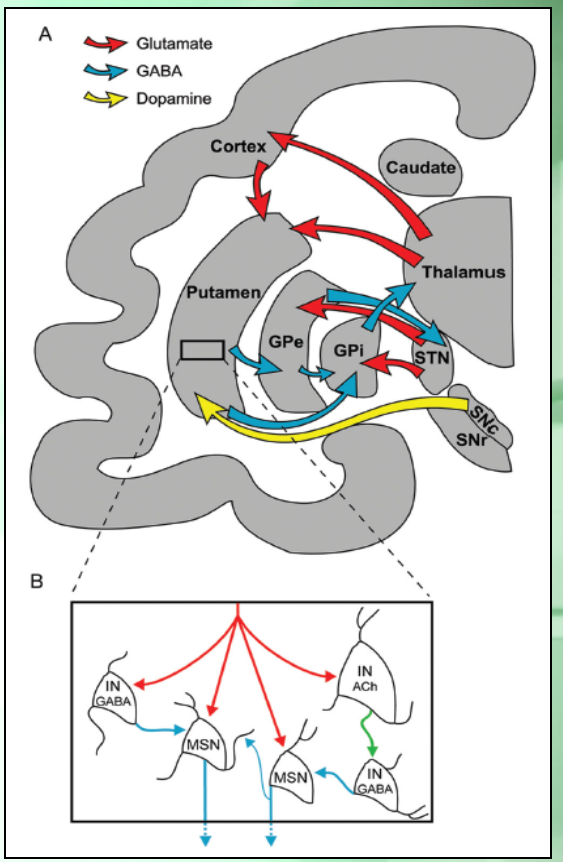
- Misidentification of tic
  - Allergy
    - Kim 1997
  - Muscle pain/”pull”
  - Asthma
    - Hogan 1999
  - Psychogenic cough
  - “perioral dermatitis”
  - “Low-lying” tonsils
    - Birring 2004

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

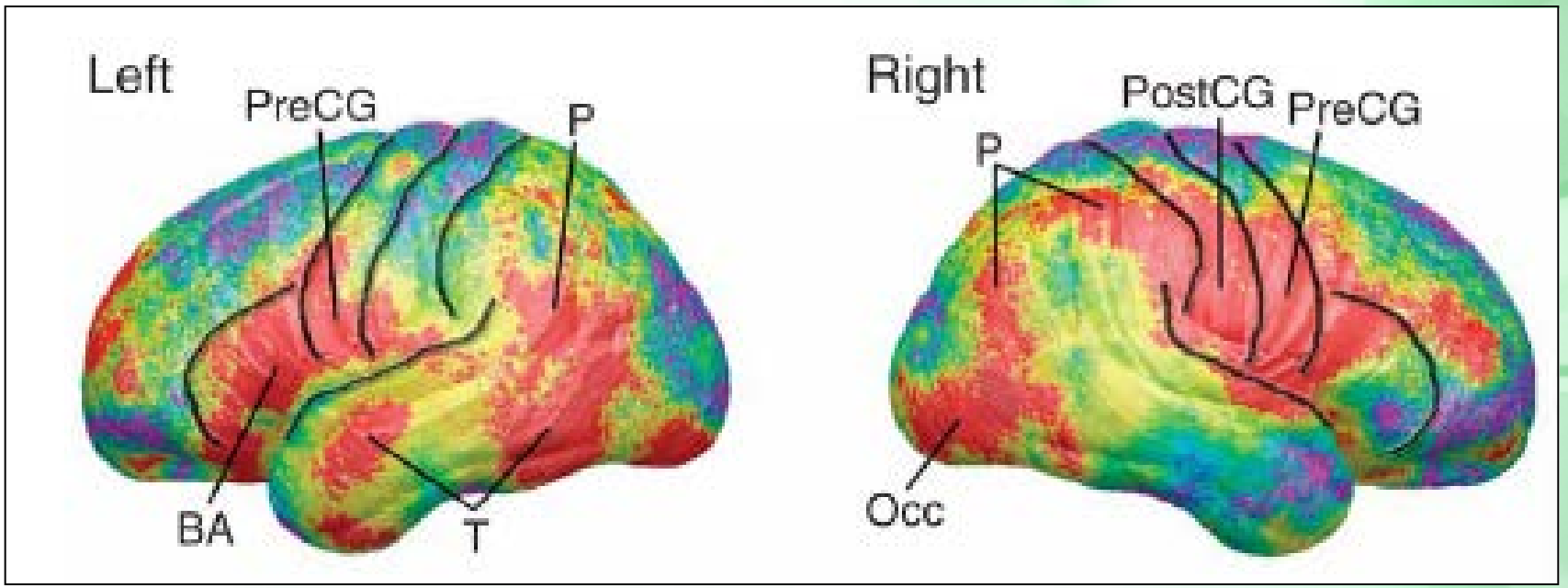
Pathophysiology

- **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



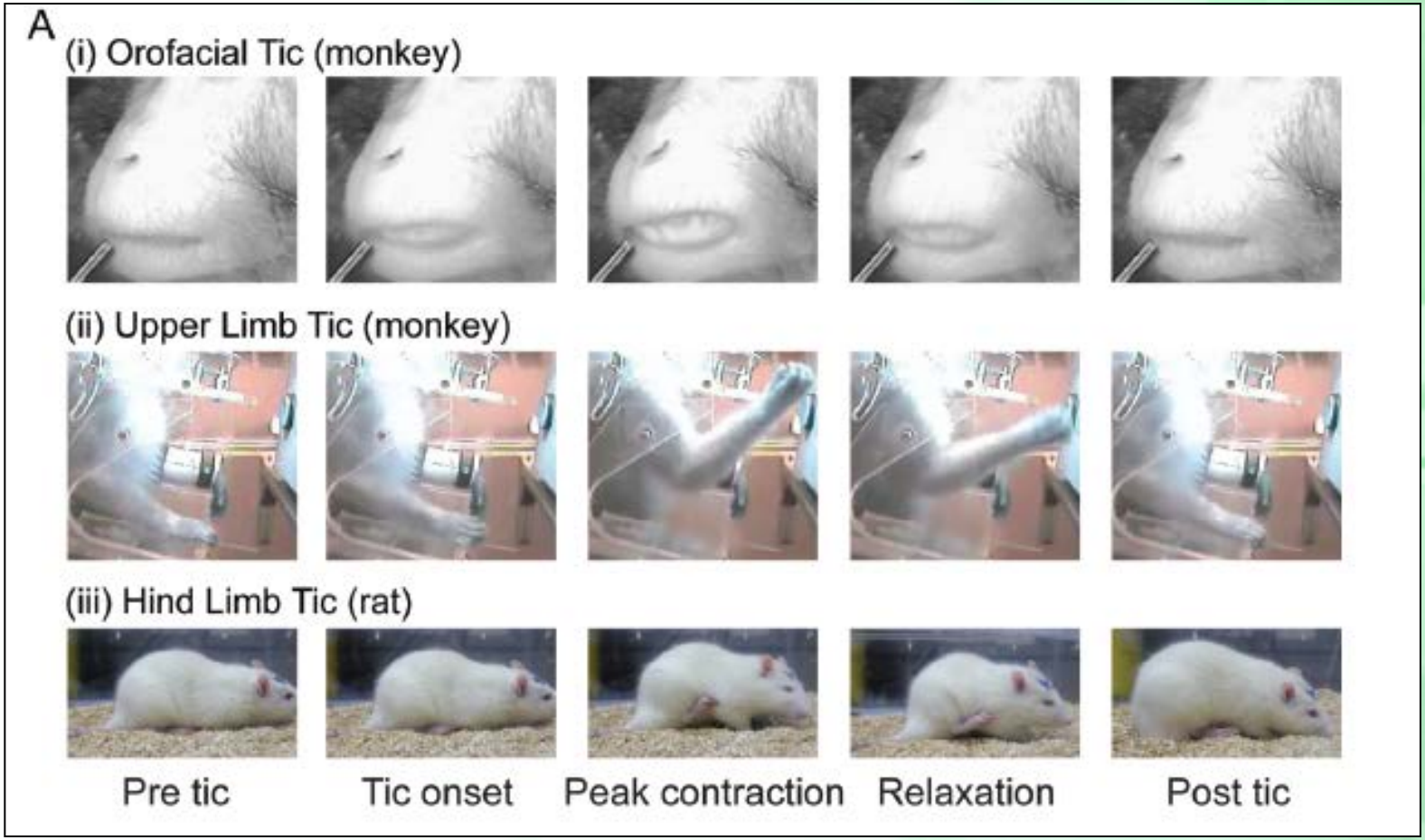
Brito 1997, Saka 2003, Singer 2005, Segawa 2005, Bronfeld 2012

Cortical thickness differences



Sowell 2008

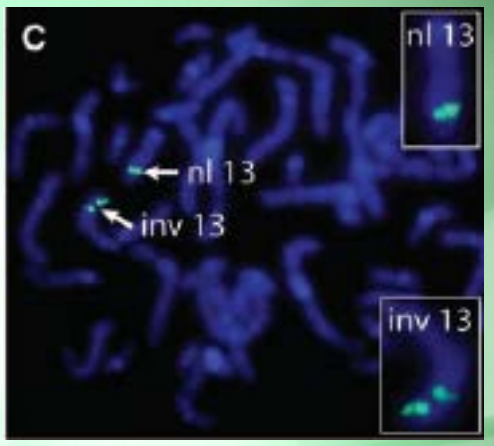
Animal Models



- Simple motor tics induced by striatal activation (injection of $GABA_A$ antagonist)

Bronfeld 2012

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

- ***P***ediatric ***A***utoimmune ***N***eurologic ***D***isease ***A***ssociated with ***S***trep
  - 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

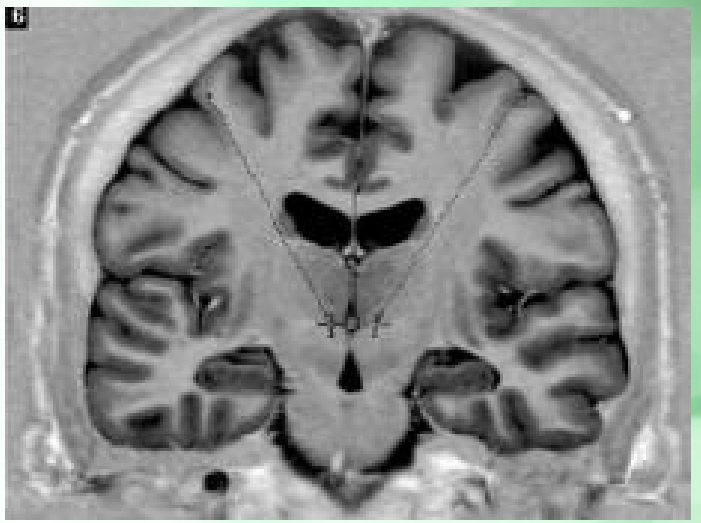
- Reassurance, education, biofeedback
- Tics - Medical
  - Clonidine→Atypicals→haldol/Pimozide →Tetrabenazine
    - QT, tardive dyskinesia?
  - Localized/Vocalization → botulinum toxin
- Anxiety, OCB/D
  - CBT
  - SSRI, Abilify
- Comorbid ADHD
  - Stimulants
  - Clonidine

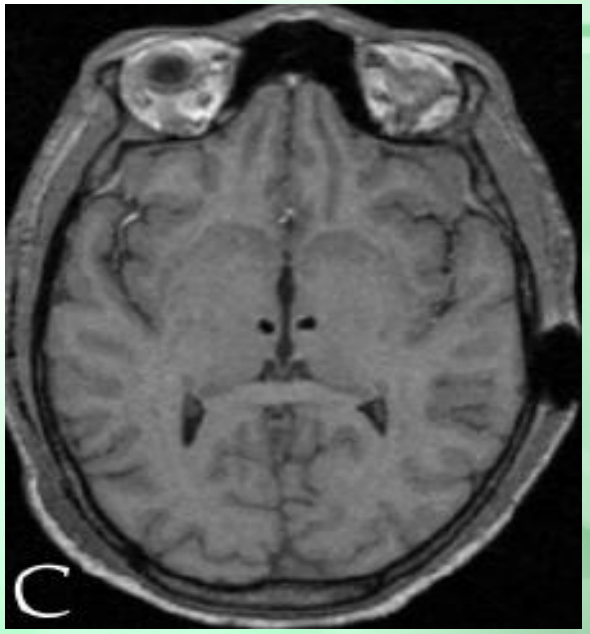
Tourette: Treatment

- Smaller Series
  - Dopamine Agonists
    - Selegeline, pramiprexole (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





Maciunas 2007

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!