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<th>Advisory Board</th>
<th>Speaker's Bureau</th>
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Discussion of Off Label Use of Medication

- Discussion of all medications should be considered “off label” unless explicitly noted otherwise
Historical Context

- Childhood chorea (Sydenham’s chorea)
- Charcot and Freud, and Tourette
- Psychology
- Neurology
- Neuropsychiatric
  - Neurological
  - Genetics and environment
  - Behavioral and functional
Sorting Out Clinically Complex Cases

- What do complex cases look like?

- **TS Plus** = TS + ADHD + OCD + Condition X
Complex Clinical Presentations

- Tics Plus and separation anxiety disorder
- Tics Plus and other anxiety disorders
- Tics Plus and pervasive developmental disorders
- Tics Plus and disruptive behavioral disorders
- Tics Plus and major depression
- Tics Plus and bipolar disorder
- Tics Plus and substance abuse
- Tics Plus and personality disorders
Tic Disorder Treatment

- Antipsychotic efficacy studies
  - Haloperidol, pimozide, ziprasidone, risperidone
- Alpha agonists – clonidine and guanfacine
- Other somatic treatments
  - ECT
  - Repetitive transcranial magnetic stimulation
  - Deep brain stimulation
- Behavioral treatment
  - Numerous very small studies focusing on habit reversal training
  - Large scale trials in children and adults
Tic Suppression Interventions
Small, Medium and Large

- Small – Commonly used
  - Clonidine
  - Guanfacine

- Medium – Not commonly used
  - TCAs
  - Benzodiazepines
Tic Suppression - Large

- **Old antipsychotics**
  - Fluphenazine (Prolixin®)
  - Pimozide (Orap®)
  - Haloperidol (Haldol®)

- **New Antipsychotics**
  - Risperidone (Risperdal®)
  - Ziprasidone (Geodon®)
  - Aripiprazole (Abilify®)
  - Tetrabenazine
  - Quetiapine (Seroquel®)
  - Olanzapine (Zyprexa®)
  - Clozapine (Clozaril®)
  - Others
Antipsychotics - European Style

- Sulpiride
- Tiapride
Tic Suppression - Larger Botulinum Toxin

- Single muscle
- Long acting
- Reversible
Tic Suppression - Larger

- Electroconvulsive treatment
  - Self-injurious behavior
- Repetitive Transcranial Magnetic Stimulation (rTMS)
Tic Suppression - Largest Behavioral Neurosurgery

- Ablative surgery
  - Complex cases
  - Results for tics are mixed
- Deep brain simulation
  - News worthy cases
  - One small open trial
First Large Prospective Study

- Servello et al., JNNP, 2007
- 18 patients
- Vo-CM-PF thalamus
- Blinded on-off eval (but not reported in detail)
- F/U 3 – 17 months
- 2 complications: 1 from picking at incision, 1 abdominal hematoma
Summary

- Many treatment options for people with Tourette syndrome
- Many somatic treatments
  - Tics
  - Co-occurring conditions
Non Pharmacological Strategies for Tics
Tics and the Environment

- Tic worsening
  - Excitement and stress
  - Fatigue
  - Attending to tics
  - Free to tic

- Tic improvement
  - Calm focused activities
  - Deep relaxation
  - Inhibiting environments

- Adults’ experience with behavioral strategies
Comprehensive Behavioral Intervention for Tics

- Theoretical Model
- Habit Reversal Training
  - Awareness training
  - Competing response training
  - Sustaining adherence
- Function-based Intervention
  - Contextual factors that support or maintain expression
Theoretical Model

- Tics only early
- Increased self consciousness
- Increased attention by others
- Self-identification of tic patterns and ad hoc management strategies
- Onset of premonitory sensation ~age 10
- Ticcing to relieve premonitory sensation
Habit Reversal Training

- Awareness training

- Purpose of CR
  - A voluntary behavior that is physically incompatible with the tic urge or tic itself

- Characteristics of CR
  - Incompatible with the tic
  - Less socially noticeable than the tic
  - Patient can do CR for the required duration across multiple situations
  - Can fade the CR over time
<table>
<thead>
<tr>
<th>Tic</th>
<th>Competing Response</th>
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<tr>
<td>Arm Movements</td>
<td>Push hand down on thigh or abdomen and push elbow in towards hip</td>
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<tr>
<td>Eye Blinking</td>
<td>Systematic, voluntary, soft blinking consciously main-tained at a rate of one blink per 3-5 seconds</td>
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<tr>
<td>Leg Movements</td>
<td>Place feet flat on floor and push downward. If standing, lock knees</td>
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<tr>
<td>Vocal Tics</td>
<td>Diaphragmatic breathing keeping in mind inhale/exhale pattern in context of tic</td>
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<tr>
<td>Mouth/facial Movements</td>
<td>Clench jaw while pressing lips together</td>
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Function-based Interventions

- Assess and address antecedents and consequences
  - Provoking experiences
  - Social consequences
    - Positive reinforcement – active rewards
    - Negative reinforcement – escape consequences
### Types of Reinforcement

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<tr>
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<th>Positive Reinforcement</th>
<th>Negative Reinforcement</th>
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<td>Internally Reinforcing</td>
<td>Provides gratification</td>
<td>Relieves distress</td>
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<tr>
<td>Externally Reinforcing</td>
<td>Attention and support</td>
<td>Avoidance</td>
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- **Positive Reinforcement**
  - Internally Reinforcing: Provides gratification
  - Externally Reinforcing: Attention and support

- **Negative Reinforcement**
  - Internally Reinforcing: Relieves distress
  - Externally Reinforcing: Avoidance
Behavior Therapy for Children With Tourette Disorder
A Randomized Controlled Trial

John Piacentini, PhD
Douglas W. Woods, PhD
Lawrence Sechel, PhD, MSN
Sabine Wilhelm, PhD
Alan L. Peterson, PhD
Susanna Chang, PhD
Golda S. Ginsburg, PhD
Thilo Deckersbach, PhD
James Dziura, PhD
Sue Levi-Pearl, MA
John T. Walkup, MD

Tourette disorder is a chronic neurologic disorder characterized by motor and vocal tics. Prevalence estimates in school-aged children range from 1 to 10 per 1000, with a rate of 6 per 1000 replicated in several countries. Tics are usually brief, rapid movements (eg, blinking, facial grimacing) or vocalizations (eg, throat clearing, grunting) but can include more complex movements and vocalizations. Tics begin in childhood; severity peaks in early adolescence and often declines in young adulthood. Epidemiologic and clinical data indicate that Tourette disorder can be associated with considerable impairment and social isolation in school-aged children. Tics are commonly preceded by premonitory

Context Tourette disorder is a chronic and typically impairing childhood-onset neurologic condition. Antipsychotic medications, the first-line treatments for moderate to severe tics, are often associated with adverse effects. Behavioral interventions, although promising, have not been evaluated in large-scale controlled trials.

Objective To determine the efficacy of a comprehensive behavioral intervention for reducing tic severity in children and adolescents.

Design, Setting, and Participants Randomized, observer-blind, controlled trial of 126 children recruited from December 2004 through May 2007 and aged 9 through 17 years, with impairing Tourette or chronic tic disorder as a primary diagnosis, randomly assigned to 8 sessions during 10 weeks of behavior therapy (n=61) or a control treatment consisting of supportive therapy and education (n=65). Responders received 3 monthly booster treatment sessions and were reassessed at 3 and 6 months following treatment.

Intervention Comprehensive behavioral intervention.

Main Outcome Measures Yale Global Tic Severity Scale (range 0-50, score >15 indicating clinically significant tics) and Clinical Global Impressions-Improvement Scale (range 1 [very much improved] to 8 [very much worse]).

Results Behavioral intervention led to a significantly greater decrease on the Yale Global Tic Severity Scale (24.7 [95% confidence interval (CI), 23.1-26.3] to 17.1 [95% CI, 15.1-19.1]) from baseline to end point compared with the control treatment (24.6 [95% CI, 23.2-26.0] to 21.1 [95% CI, 19.2-23.0]) (P<.001, difference between groups, 4.1; 95% CI, 2.0-6.2) (effect size=0.68). Significantly more children receiving behavioral intervention compared with those in the control group were rated as being very much improved or much improved on the Clinical Global Impressions-Improvement scale (52.5% vs 18.5%, respectively, P<.001; number needed to treat=3). Attrition was low (12/126, or 9.5%); tic worsening was reported by 4% of children (5/126). Treatment gains were durable, with 87% of available responders to behavior therapy exhibiting continued benefit 6 months following treatment.

Conclusion A comprehensive behavioral intervention, compared with supportive therapy and education, resulted in greater improvement in symptom severity among children with Tourette and chronic tic disorder.

Trial Registration clinicaltrials.gov Identifier: NCT00218777

JAMA. 2010;303(19):1929-1937
www.jama.com
Comprehensive Behavioral Intervention for Tics

- Habit Reversal Training
  - Awareness training
  - Competing response training
  - Sustaining adherence

- Function-based Intervention
  - Contextual factors that support or maintain expression
CBITS Study Design

Assessment Schedule:

Week: 0 5 10 23 36

126 Subjects with TS or CTD

CBIT

Psychoeducational Support

Responder

Non-Responder

Booster

Booster

Booster

Booster

Booster

Booster

Booster

Booster
Responder Status at Week 10

(CGI-Improvement = 1 or 2)

- CBIT: 52.5%
- PST: 18.5%

P < 0.0001
Moderators

- None
- Close
  - Med status
  - ADHD
Durability

- 87% of responders to acute phase treatment maintained response
What does this all mean?
Depends on the audience

- Psychology
- Psychiatry
- Neurology
- Primary care doctors
- Other medical professionals
- Kids
- Families
- School personnel
- Advocacy organizations
Change In Advice

- **Old - intuitive**
  - Ignore tics
  - Can’t be controlled
  - Don’t punish
  - Behavioral treatments don’t work
  - Don’t try to suppress
  - Suppression worsens tics
  - Suppression worsens premonitory urges
  - New tics develop when you suppress

- **New - counterintuitive**
  - Become more aware
  - Learn to manage
  - Reward successful management
  - Use behavioral strategies
  - Tics don’t get worse with behavioral treatment
  - Premonitory urge will fade away
  - New tics don’t develop when you use behavioral strategies
New Treatment Paradigms

- Readiness for reducing tic severity
  - Comorbidity management
  - Family and child intervention for “CBIT Lifestyle”
- CBIT
- CBIT + Meds
- Meds + CBIT
- Meds + CBIT to CBIT only
- Training nurses in Neurology clinics
- Parent training for children under 9 yrs
Not without controversy

- Neurological disorder
- What will teachers say?
- Tics get worse when you suppress
- If you suppress other tics will get worse
- How can one focus on activities if they are suppressing?
How about this??

- Tourette syndrome
- Structural-reflex disorder
- Neurocranio Vertical Distractor (NCVD)
  - Brendan Stack DDS, MS
  - Anthony Sims DDS
Pathophysiology

- Prepubertal facial growth
  - Synchronization of muscle and bones growth
  - Misalignment can happen resulting in nerve compression and irritation
  - Irritation of the facial nerve (premonitory sensation?) and close proximity to cranial and other nerves leads to reflexive contraction of musculature
The Procedure

- Moving the mandible down and forward
- Tongue depressors
- Construct an appliance
- Speech training etc
- Long term natural or surgical restructuring of the TMJ joint
Dental Websites

- Dr. Stack Tourette Syndrome
- Dr. Anthony Sims Tourette Syndrome
Summary

- New effective treatments bring excitement and hope
  - Behavioral strategies
  - Neurosurgery
- If you think about it, it makes sense
- Lots more to learn to realize the full promise of new treatments for tic severity