Tourette’s Disorder and Tics
Child and Adolescent Psychopharmacology

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Barbara J. Coffey, MD, MS

Division Chief, Child and Adolescent Psychiatry
Professor, Department of Psychiatry and Behavioral Sciences
University of Miami Miller School of Medicine
Tourette’s Disorder and Tics: Learning Objectives

- At the end of this session, the participant should be able to:
  - Describe a **systematic approach** to disentangling tics and psychiatric comorbid symptoms to prioritize targets for treatment
  - Interpret relevance of **recent research** findings for application to treatment of youth with tics and Tourette’s Disorder
  - Preview **potential new drugs** in the pipeline for treatment of tics
  - Select **approved and off label treatments** for Tourette’s and tic disorders
"Young man, go to your room and stay there until your cerebral cortex matures."

WEDNESDAY JUNE 18
Tics and Tourette’s Disorder: Epidemiology (Scahill, L. et al; Morbidity and Mortality Weekly Report CDC; 2009)

- CDC Prevalence of Diagnosed Tourette’s Disorder in Youth Age 6-17 in 2007 in US

  - National Study of Children’s Health
  - 0.3-1% US
  - 3x more common in boys than girls
  - 2x more frequently diagnosed age 12-17 vs. 6-11
Prevalence of Lifetime Diagnosis: Tourette Syndrome (parent)  
(National Survey of Children's Health, United States, 2007)

•† Selected Diagnoses, age 6-17: Among children ever diagnosed with TS, 79% also had been diagnosed with at least one other selected diagnosis.
Neurobiological Substrates of TD

(Leckman et al; JCAP, 2010; 20 (4); 237-247; McNaught, K, and Mink. J. Neurology; 2011; 7; 667-676)

• **Tics**: thought to result from dysfunction in cortical and sub-cortical regions involved in habit formation, including basal ganglia (BG), thalamus and frontal cortex

• Tics, like habits, link sensory cues with motor actions

• **Cortico-striatal-thalamic-cortical (CSTC) circuits**: are composed of multiple, overlapping but largely parallel circuits that direct information from cortex to sub-cortical structures and back

• Tics represent **failure of cortical inhibition** of unwanted motor programs generated in the BG
Gilles de la Tourette Syndrome
Robertson et al. (2017)

Figure 4 | CSTC circuit.

Figure 1. Clinical Hallmarks of Tourette’s Syndrome.
The diagnosis is based on the occurrence of tics along with behavioral disorders, including attention-deficit–hyperactivity disorder (ADHD) and obsessive–compulsive disorder (OCD). Other behavioral disorders include anxiety and mood disorders, learning disorders, sleep disorders, conduct and oppositional behavior, and self-injurious behavior.
Clinical and Demographic Characteristics of Non-specialized and Specialized Clinic Patients with TD

<table>
<thead>
<tr>
<th></th>
<th>Non-specialized Clinic patients (N=92)</th>
<th>Specialized Clinic patients (N=103)</th>
<th>Overall Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Current Age</td>
<td>10.8</td>
<td>3.23</td>
<td>10.8</td>
</tr>
<tr>
<td>SES</td>
<td>2.0</td>
<td>1.13</td>
<td>2.2</td>
</tr>
<tr>
<td>Past GAS</td>
<td>47.9</td>
<td>7.50</td>
<td>48.6</td>
</tr>
<tr>
<td>Current GAS</td>
<td>51.3</td>
<td>7.32</td>
<td>51.9</td>
</tr>
<tr>
<td>% Male</td>
<td>82</td>
<td>90</td>
<td>81</td>
</tr>
</tbody>
</table>

Informativeness of Structured Diagnostic Interviews in the Identification of Tourette’s Disorder in Referred Youth

(Coffey B, Biederman J, Spencer T et al. J Nerv Ment Dis. 2000;Sep;188 (9):583-588)
### Comorbidity of TD Subjects by Ascertained Site: Mood Disorders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-specialized Clinic Patients</th>
<th>Specialized Clinic Patients</th>
<th>Overall Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 92)</td>
<td>(N = 103)</td>
<td></td>
</tr>
<tr>
<td>Pure TD (Non-comorbid)</td>
<td>2 / 2%</td>
<td>5 / 5%</td>
<td>0.31</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td>45 / 49%</td>
<td>56 / 54%</td>
<td>0.49</td>
</tr>
<tr>
<td>Any Bipolar Disorder</td>
<td>20 / 22%</td>
<td>16 / 16%</td>
<td>0.24</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>9 / 10%</td>
<td>4 / 4%</td>
<td>0.09</td>
</tr>
<tr>
<td>Any Mood Disorder</td>
<td>55 / 60%</td>
<td>59 / 57%</td>
<td>0.65</td>
</tr>
</tbody>
</table>

- **Design:** Cross-sectional structured diagnostic interviews with TS (n = 1374) and TS-unaffected family members (n = 1142).

- **Results:** Lifetime prevalence of any psychiatric comorbidity among individuals with TS was **85.7%**; 57.7% had 2 or more psychiatric disorders. 72.1% met criteria for OCD or ADHD. Other disorders, including mood, anxiety, and disruptive behavior, each occurred in approximately 30%.

- **The age of greatest risk for the onset of most comorbid psychiatric disorders was between 4 and 10 years.**

- TS was associated with increased risk of anxiety (odds ratio [OR], 1.4; 95%CI, 1.0-1.9; P = .04) independent from comorbid OCD and ADHD; however, high rates of mood disorders (29.8%) may be accounted for by comorbid OCD (OR, 3.7; 95%CI, 2.9-4.8; P < .001).

- **Conclusion:** Psychiatric comorbidities are common among individuals with TS, and most comorbidities begin early in life.
Diagnostic Evaluation: Tourette’s Disorder and Tics

- **Semi-structured diagnostic interviews:** Children's Schedule for Affective Disorders and Schizophrenia (K-SADS) can improve classification and assessment of comorbidity. Reduces errors of omission.

- **Standardized rating scales:** improve diagnostic reliability in research studies; helpful in clinical care.


- **YGTSS domains:** number, frequency, intensity, complexity and interference (0-50), and tic related impairment (0-50).

- **SNAP (Parent, Teacher):** quantitative evaluation of ADHD symptoms.

- **C-YBOCS:** semi-structured evaluation of OCD symptoms.
"These medicines all taste pretty good—let’s approve them."

Easter Saturday (Australia—except TAS, WA)/
/Easter (Western, Orthodox)
“Ask your mother if this medicine is right for you.”
The Challenges of Treating Tics!

TD and Tics: Treatment Overview

- **Tics**: Most patients with mild tic symptoms need only monitoring, education, and guidance. Tics causing distress or impairment should be treated.

- **ADHD and OCD**: Since comorbid symptoms are more likely to persist and cause significant functional impairment, treatment is usually necessary.

- **Behavioral treatment of tics (habit reversal therapy)** is now established. *This is recommended first line treatment.*

- There are no published studies of combination pharmacotherapy and behavioral treatment of tic disorders/Tourette’s Disorder.
Professor Gallagher and his controversial technique of simultaneously confronting the fear of heights, snakes, and the dark
Comprehensive Behavioral Intervention for Tics Study (CBIT) (Piacentini, J. Woods, D. Scahill et al. JAMA; 2010;303 (19):1929-1937)

Three phases:

1) Awareness training: premonitory urge/sensation
2) Competing response training
3) Social support

Two parallel studies compared behavior therapy to supportive therapy (PST)
Child study: 126 children (ages 9-17) with TD/CTD; JAMA; 2010
Adult study: 120 children and adults (ages 16+) with TD/CTD: completed; Arch Gen Psych 2012

CBIT is only useful for patients with mild tics. Mean baseline tic severity was comparable in medication trials.

**CBIT requires considerable effort for patients.** Attrition was comparable in CBIT and psychopharmacology trials.

**Gains in tic severity are likely to be modest and may not endure over time.** Effect sizes were similar to medication trials. Most medication trials are short term (6-8 weeks). CBIT results were durable in 85% at 6 month follow up.

**CBIT may result in tic substitution or tic worsening.** Tics increased in 4% of CBIT subjects and 6% of control patients.

Trained CBIT practitioners and insurance coverage for CBIT are lacking. Pilot studies of home based CBIT and CBIT for primary care practitioners are underway.

**Effective behavior therapy could lead to recasting TS as a psychological disorder rather than a neurological condition.** There is only one brain and it has psychological and neurological functions!!!
Only formally approved (labeled) treatments for TD:
- **D2 dopamine antagonists: conventional neuroleptics**
  - *Haloperidol (Haldol) and pimozide (Orap)*
  - *Aripiprazole (Abilify)* (Physicians Desk Reference, 2016)

*Haloperidol*: effective for tics, superior to placebo (Shapiro et al. 1968, 1978)


**Aripiprazole**: effective for tics, superior to placebo (Yoo et al; 2013)

Other interventions
- Psychoeducation; referral to the Tourette Association
- *Habit reversal therapy (Comprehensive Behavioral Intervention for Tics)*
- Individual/ family therapy; educational consultation
Daily Doses of Frequently Prescribed Tic Medications


<table>
<thead>
<tr>
<th>Medication</th>
<th>Range of daily dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>0.25-4.0mg</td>
</tr>
<tr>
<td>Pimozide</td>
<td>0.5-8.0mg</td>
</tr>
<tr>
<td>*Risperidone</td>
<td>0.125-3.0mg</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>1.0-15.0mg</td>
</tr>
<tr>
<td>*Clonidine</td>
<td>0.025-0.4mg</td>
</tr>
<tr>
<td>*Guanfacine</td>
<td>0.25-4.0mg</td>
</tr>
</tbody>
</table>
Current treatments are ineffective and/or intolerable in many patients

Off label treatments are more frequently prescribed than approved, dopamine D2 receptor antagonists in the US

**Potential New Treatments:**

- Novel formulation of existing agents
- Glutamatergic/GABAergic agents
- Presynaptic dopamine depleting agents
Guanfacine in Children with Tic Disorders: A Multi-Site Pilot Study

- Guanfacine is commonly used to treat tics in children with Tourette’s Disorder, but the extended release formulation has not been evaluated.

- **Overall Goal:** to determine whether extended release guanfacine (GXR) warrants further study in a large scale trial.

- *Immediate-release guanfacine is frequently used in children with TD, but dosing, time to effect and adverse effects with GXR are unknown.*

- **Design:** Multi-site, randomized, double-blind, placebo-controlled, parallel-group design, followed by an 8-week extension for subjects who show positive response to guanfacine in the double-blind phase.

- Subjects who were randomly assigned to placebo and did not show improvement were offered 8-week, open-label treatment with GXR.

- **Primary Aim:** To evaluate benefit of flexibly dosed GXR on tic severity in 42 children with Tourette’s Disorder as measured by the Total Tic score of the YGTSS.

- **Results:** study is completed; results are pending
Extended-Release Guanfacine (GXR) Does Not Show a Large Effect on Tic Severity in Children with Chronic Tic Disorders (CTD)  

- **METHOD:** 8-week RCT in N=34 youth ages 6 to 17 years (mean = 11.1) with CTD.

- **RESULTS:** At baseline, mean YGTSS total score was 26.3 for GXR group vs. 27.7 for placebo.
  - GXR group: (mean final daily dose 2.6 mg.); mean YGTSS total score declined to 23;  
  - \( p = 0.08; \) **effect size = 0.35.**
  - PBO group: declined to 24.7; \( p = 0.08; \) **effect size = 0.38.**

- There was **no significant difference** in the rate of positive response on CGI-I between GXR and PBO (19% vs. 22%; \( p = 1.0).\)

- **Adverse Effects (AE):** Most common: fatigue, drowsiness, dry mouth, headache, and irritability. Two subjects on GXR discontinued due to AE (depressed mood) and one for of lack of efficacy; two subjects on PBO discontinued for lack of efficacy.

- **CONCLUSION:** This pilot study did not confirm a clinically meaningful effect size within GXR group. These results do not support the launch of a larger efficacy trial for tics in youth with CTD.
Appendix A
Figure 1. Design showing subject disposition

R = Randomization

Guanfacine

Responder
8-week open extension

Non-responder
Exit

8 weeks
double-blind

Responder

Non-Responder
8-week open-label

**Table 1. Characteristics of Study Participants at Baseline (N=34)**

<table>
<thead>
<tr>
<th></th>
<th>Guanfacine, n = 16</th>
<th>Placebo, n = 18</th>
<th>Test statistic, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, M (SD)</td>
<td>11.5 (3.03)</td>
<td>10.8 (3.2)</td>
<td>t(32) = 0.62, p = 0.5</td>
</tr>
<tr>
<td>Gender, males, n (%)</td>
<td>11 (69)</td>
<td>12 (67)</td>
<td></td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>16 (100)</td>
<td>17 (94)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>—</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity, Hispanic</td>
<td>3 (19)</td>
<td>4 (22)</td>
<td></td>
</tr>
<tr>
<td>Tic disorder, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TD</td>
<td>14 (87.5)</td>
<td>15 (83)</td>
<td></td>
</tr>
<tr>
<td>Chronic motor TD</td>
<td>2 (12.5)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td>Chronic vocal TD</td>
<td>—</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>ADHD, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized anxiety disorder, n (%)</td>
<td>8 (50)</td>
<td>4 (22)</td>
<td></td>
</tr>
<tr>
<td>OCD, n (%)</td>
<td>3 (19)</td>
<td>3 (17)</td>
<td></td>
</tr>
<tr>
<td>ODD, n (%)</td>
<td>3 (19)</td>
<td>4 (22)</td>
<td></td>
</tr>
<tr>
<td>Separation anxiety disorder, n (%)</td>
<td>3 (19)</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>Tanner stage, N stage 1 or 2, n (%)</td>
<td>10 (63)</td>
<td>11 (61)</td>
<td></td>
</tr>
<tr>
<td>YGTSS total score, M (SD)</td>
<td>26.3 (6.61)</td>
<td>27.7 (8.7)</td>
<td></td>
</tr>
<tr>
<td>YGTSS motor score, M (SD)</td>
<td>15.2 (2.61)</td>
<td>17.2 (3.44)</td>
<td></td>
</tr>
<tr>
<td>YGTSS phonic score, M (SD)</td>
<td>11.1 (6.13)</td>
<td>10.4 (6.73)</td>
<td></td>
</tr>
<tr>
<td>YGTSS impairment, M (SD)</td>
<td>29.8 (8.18)</td>
<td>28.6 (8.01)</td>
<td></td>
</tr>
<tr>
<td>CGI severity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately ill</td>
<td>12 (75)</td>
<td>9 (50)</td>
<td></td>
</tr>
<tr>
<td>Markedly ill</td>
<td>4 (25)</td>
<td>6 (33)</td>
<td></td>
</tr>
<tr>
<td>Severely ill</td>
<td>—</td>
<td>3 (17)</td>
<td></td>
</tr>
<tr>
<td>TSSR (parent), M (SD)</td>
<td>26.9 (22.83)</td>
<td>24.6 (16.94)</td>
<td></td>
</tr>
<tr>
<td>PUTS, M (SD)</td>
<td>19.8 (5.39)</td>
<td>20.9 (8.18)</td>
<td></td>
</tr>
<tr>
<td>ADHD RS (parent), M (SD)</td>
<td>19.7 (12.29)</td>
<td>17.5 (13.65)</td>
<td></td>
</tr>
<tr>
<td>DBRS, M (SD)</td>
<td>8.8 (6.59)</td>
<td>5.6 (7.37)</td>
<td></td>
</tr>
<tr>
<td>CY-BOCS, M (SD)</td>
<td>9.6 (10.41)</td>
<td>10.5 (11.43)</td>
<td></td>
</tr>
<tr>
<td>ROARS, M (SD)</td>
<td>3.1 (2.87)</td>
<td>2.2 (2.87)</td>
<td></td>
</tr>
</tbody>
</table>

*p* < 0.05.

*ADHD RS, attention-deficit/hyperactivity disorder rating scale; CGI, clinical global impressions; CY-BOCS, Children’s Yale-Brown Obsessive Compulsive Scale; DBRS, Disruptive Behavior Rating Scale; M, mean; OCD, obsessive compulsive disorder; ODD, oppositional defiant disorder; PUTS, Premoritory Urge for Tics Scale; ROARS, Rage Outbursts and Anger Rating Scale; SD, standard deviation; TD, tic disorder; TSSR, Tic Symptom Self-Report; YGTSS, Yale Global Tic Severity Scale.
Extended-Release Guanfacine (GXR) Does Not Show a Large Effect on Tic Severity in Children with Chronic Tic Disorders (CTD)
(Murphy T, Fernandez T, Coffey B, et al. JCAP. 2017;27(9):762–770.)

![Graph showing YGTSS total score, motor, and phonic; guanfacine versus placebo. YGTSS, Yale Global Tic Severity Scale.](image-url)
How do we know what’s inside?

I see glutamate!
N-Acetylcysteine in the Treatment of Pediatric Tourette Syndrome: Randomized, Double Blind, Placebo Controlled Trial (Bloch, M. Panza, K. et al. JCAP 2016; 26 (4) 327-334)

- **Background:** NAC modulates glutamatergic systems and functions as an antioxidant with minimal adverse effects.
- **Methods:** N=31 children and adolescents age 8-17 with TS randomly assigned to NAC or PBO for 12 weeks.
- **Primary outcome:** change in TTS of YGTSS
- **Results:** There was no significant difference between NAC and PBO was found in tic reduction or any secondary outcomes.
- **Conclusion:** No evidence for efficacy of NAC in treatment of tics. This stands in contrast to studies of OCD spectrum in adults (TTM, OCD) but similar to pediatric TTM.
### Table 1. Baseline Characteristics of Subjects

<table>
<thead>
<tr>
<th>Demographic characteristic</th>
<th>NAC</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male</td>
<td>5/12</td>
<td>2/12</td>
</tr>
<tr>
<td>Age (mean [SD])</td>
<td>12.4 (1.4)</td>
<td>11.5 (2.8)</td>
</tr>
<tr>
<td>Age of onset (mean [SD])</td>
<td>6.8 (1.4)</td>
<td>6.1 (2.4)</td>
</tr>
<tr>
<td>Duration of illness (mean [SD])</td>
<td>5.6 (3.4)</td>
<td>5.4 (2.8)</td>
</tr>
<tr>
<td>Comorbid OCD (n [%])</td>
<td>2 (12%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Comorbid ADHD (n [%])</td>
<td>6 (35%)</td>
<td>9 (64%)</td>
</tr>
<tr>
<td>Pharmacological treatment for tics (current/ever)</td>
<td>7 (41%)/</td>
<td>6 (43%)/</td>
</tr>
<tr>
<td>Current antidepressant use (n [%])</td>
<td>11 (65%)</td>
<td>11 (79%)</td>
</tr>
<tr>
<td>Current antipsychotic use (n [%])</td>
<td>5 (29%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Current α-2 agonist use (n [%])</td>
<td>7 (41%)</td>
<td>0</td>
</tr>
<tr>
<td>Current psychostimulant use (n [%])</td>
<td>2 (12%)</td>
<td>5 (36%)</td>
</tr>
<tr>
<td>Behavioral treatment for tics (current/ever)</td>
<td>2 (14%)/</td>
<td>5 (36%)/</td>
</tr>
<tr>
<td>YGTSS (mean [SD])</td>
<td>27.1 (7.2)</td>
<td>26.3 (7.7)</td>
</tr>
<tr>
<td>PUTS (mean [SD])</td>
<td>24.4 (4.6)</td>
<td>23.8 (4.1)</td>
</tr>
<tr>
<td>CGI – Severity (mean [SD])</td>
<td>3.7 (1.1)</td>
<td>3.9 (0.6)</td>
</tr>
<tr>
<td>ADHD-RS (mean [SD])</td>
<td>17.6 (9.2)</td>
<td>23.7 (11.8)</td>
</tr>
<tr>
<td>CYBOCS (mean [SD])</td>
<td>6.9 (8.3)</td>
<td>10.7 (9.0)</td>
</tr>
<tr>
<td>CDI (mean [SD])</td>
<td>25.1 (2.5)</td>
<td>24.9 (2.7)</td>
</tr>
<tr>
<td>MASC (mean [SD])</td>
<td>41.6 (15.4)</td>
<td>23.8 (4.1)</td>
</tr>
</tbody>
</table>

NAC, active N-acetylcysteine treatment; OCD, obsessive-compulsive disorder; ADHD: attention-deficit/hyperactivity disorder; YGTSS, Yale Global Tic Severity Scale; PUTS, Premontory Urge Tic Scale; CGI, Clinical Global Impressions; ADHD-RS, ADHD Rating Scale; CYBOCS: Children Yale-Brown Obsessive-Compulsive Scale; CDI, Children’s Depressive Inventory; MASC, Multidimensional Anxiety Scale for Children.
FIG. 2. Effects of N-acetylcysteine (NAC) and placebo on tic severity (Yale Global Tic Severity Scale [YGTSS]). There was no significant effect of NAC on tic severity over time in comparison with placebo.
• **Background:** SD-809 (deutetrabenazine), an inhibitor of vesicular monoamine transporter type 2 (VMAT2), depletes presynaptic DA and may have utility in treatment of various hyperkinetic movement disorders, including tics.

• **Aims:** Explore safety, tolerability and preliminary efficacy of SD-809 in adolescents with tics associated with Tourette Syndrome (TS).

• **Methods:** In an open-label design, TS patients (age 12-17 years) were titrated over 6 weeks to a dose up to 36 mg/day. Titration phase was followed by a maintenance phase at this dose for 2 weeks.

• An independent, blinded rater assessed tic severity with the Yale Global Tic Severity Scale (YGTSS) and tic impact with the TS-Clinical Global Impression (TS-CGI).

• Safety was assessed by monitoring adverse events (AEs), vital signs, physical examination, 12-lead ECGs, clinical laboratory tests and safety scales.

- **Methods:** Adolescent patients* (mean age 16 years; range: 12-18) with moderate-to-severe tics associated with TS
- Open-label treatment x 8 weeks (dosage: 6-36 mg/day)

![Graph showing 6 weeks titration and 2 weeks maintenance]

- Mean dose at Week 8 = 32.0 mg (Range: 18-36 mg)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=23)</th>
<th>Week 8 (N=20)</th>
<th>Change</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TTS Score</td>
<td>31.6</td>
<td>20.8</td>
<td>-11.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean TS CGI</td>
<td>4.7</td>
<td>3.6</td>
<td>-1.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
• **Results**: N= 23 patients received SD-809 and had at least 1 post-baseline YGTSS assessment.

• Mean (SD) YGTSS Total Tic score at baseline was 31.6 (7.9) which decreased by 11.6 (8.2) at endpoint, a **37.6% reduction in tic severity (p<0.0001)**.

• PGIC results at week 8 indicated that more than 75% of subjects described themselves as much or very much improved, compared to before treatment.

• Mean dose at endpoint was 32.1 mg/day.
**Results**: One week after withdrawal of SD-809, statistically significant increases were observed in a number of YGTSS component scores.

- No serious or severe AEs were reported.
- One subject withdrew from the study for an AE of irritability that was unrelated to study drug.

**Conclusion**: SD-809 was well tolerated and associated with clinically meaningful improvement in tic severity.

- Results support further development of SD-809 for treatment of TS. A large Phase II/III global trial will take place soon. Investigator meeting for flexible dose randomized controlled trial took place January 25-27 in Houston, so this trial is good to go!!!
Deutetrabenazine in Tics associated with Tourette syndrome.
Jankovic J, Jimenez-Shahed J, Budman C, Coffey B. et al.
Tremor Other Hyperkine Mov. 2016; 6.
doi: 10.7916/D8M32W3H

• Most common AEs were headache, fatigue, irritability and somnolence
• None serious or severe
"If you have any mental-health issues you'd like to discuss, now would be a good time."
"If you're happy and you know it, stick with your dosage."

THURSDAY

SEPTEMBER 25
Psychiatric comorbid disorders (ADHD, OCD, mood and anxiety) are highly prevalent in children and adolescents with Tourette’s Disorder and often start early in life. They should be comprehensively evaluated and usually need treatment.

CBIT (Habit reversal therapy) has an established evidence base and is suggested as first line treatment for mild-moderate tics. Currently there are only 3 medications labeled with indication for treatment of Tourette’s Disorder and they are all neuroleptics. Effective but tolerable pharmacotherapy is much needed.

Novel treatments, including VMAT2 inhibitors, are under investigation and are promising... but more studies are needed..... Stay tuned!!
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Wayne Goodman, M.D.
Professor, Department of Psychiatry, Icahn School of Medicine at Mount Sinai

Vilma Gabbay, M.D. M.S
Associate Professor, Department of Psychiatry, Director, Pediatric Mood and Anxiety and Disorders

Dorothy Grice, M.D.
Professor, Department of Psychiatry, Director, Pediatric OCD

Ariz Rojas, Ph.D.
Assistant Professor, Department of Psychiatry

Blanca Garcia-Delgar, M.D. Visiting Research Fellow

Maxwell Luber, B.A. Research Assistant

Melissa Fluehr, B.A Clinical Coordinator