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PSYCHIATRY ACADEMY

ADHD, Tics and Tourette Syndrome

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Disclosures

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Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose

Brief ADHD Background

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- Co-occurring conditions: 50-80%
  - Anxiety, ODD, conduct, ASD, mood disorders, tic disorders
  - Learning disorders and language problems

- Clinical course:
  - Hyperactivity/impulsivity reduce
  - Inattention persists

American Academy of Pediatrics Clinical Practice Guideline

ADHD and Self-Regulation

- Emotional lability in 40-75%
  - Low frustration intolerance, impatience, quickness to anger, labile, easily excitable
- Executive Dysfunction:
  - 90% in those with ADHD
  - Disinhibition, working memory, organization / planning

Kofler et al (2019) *J Abnorm Child Psychol*
Surman et al, AJP 2011

ADHD Treatment Summary

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- **FDA-approved medications:**
  - Stimulants (Effect size: ~1.0)
  - Non-stimulants: Atomoxetine, Guanfacine ER, Clonidine ER, Viloxzine (ES ~0.7)
- **Pre-school age (4-6):**
  - Parent Training in Behavioral Management (PTBM)
    - Methylphenidate-based agents safe and effective for severe, impairing sx
- **Latency age (6-12):**
  - FDA-approved medication and PTBM
  - Pharmacology:
    - Strong evidence for stimulants
    - Sufficient for atomoxetine, guanfacine ER, clonidine ER, viloxazine (ES: 0.7)
- **Adolescent age (12-18):**
  - Strong evidence for pharmacology
    - Behavioral treatment if available (school functioning skills) as add-on

American Academy of Pediatrics Clinical Practice Guideline

The MTA Cooperative Group (1999). Arch Gen Psychiatry

Faraone et al (2021) ECAP

ADHD Functional Impact

- Family:
  - Increased conflicts and stress at home
- Friends:
  - Worse social / communication skills
  - Less friendships
- Quality of life:
  - Worse physical, social, psychological experience
  - Worsened self-perception / self-esteem

- Increased risk for
  - Psychiatry comorbidity
    - E.g. substance use disorders
  - Lower educational achievement
  - Increased rates of incarceration
  - Premature death

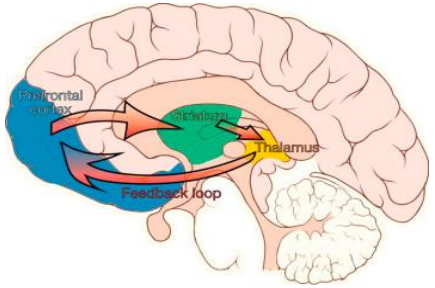
Wehmeier et al (2010). J of Adolescent Health
El Malhany et al. and McGuire et al., 2015

Background on ADHD and Tic Overlap

- ADHD is most common co-occurring condition in TS/Tic disorders (60+%)
  - 20% of children with ADHD have co-occurring tic disorder
- When ADHD and tics are co-occurring
  - ADHD (*vs tics*) is associated with impairment on neuropsychological performance / executive functioning
  - Tic disorders have limited functional impact on ADHD symptoms

Rizzo et al (2013) *Euro Journal of Paed Neurology*

- Shared neurocircuitry disruption:
  - Frontocortico-striatal-thalamo-cortical (CSTC) circuitry
  - Associated with impulsivity and compulsivity
  - Responsible for regulation
    - Cognitive (ADHD / executive function), Motor (tic), and Affective processes (OCD)



Beddows 2015 - http://scitechconnect.elsevier.com/neurobiology-basis-of-ocd/. Modified from original image, credits: Patrick J. Lynch and C. Carl Jaffe.

Functional Impact of Tic/ADHD Overlap

- Worse ADHD symptoms associated with greater tic severity
  - Also inversely associated with ability to suppress tics
- Suppression of tics may exacerbate inattention in ADHD
- Tic/ADHD combo associated with
  - Worse social and academic impairment, greater psychopathological burden, worse quality of life
  - Additional co-occurring disorders:
    - Oppositional defiant disorder, intermittent explosive disorder
  - Worse social deficits

Rizzo et al (2013) *Euro Journal of Paed Neurology*

AAN Tourette Syndrome Practice Recommendation Summary

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- Ensure assessment for co-occurring ADHD is performed
- Evaluate the burden of ADHD in those with tics
- Ensure appropriate ADHD treatment is provided in those with functionally impairing ADHD

AAN Practice Guidelines Summary Recommendation

Treatment of ADHD and Tics (TACT): Targeted Combined Pharmacotherapy Study

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- Treatment study in children with ADHD + chronic tic disorders
  - 4 groups, 35 youth per group, 16 weeks study
  - Clonidine, methylphenidate (MPH), Combined, placebo
  - First 8 weeks started clonidine or placebo; Second 8 weeks added MPH or placebo
- ADHD symptoms: improved in all three active groups
  - COMB group > Clon / MPH > placebo
- Tic symptoms: improved in all three active groups
  - Combined treatment > Clonidine alone > Methylphenidate alone > placebo
- Clonidine helpful for impulsivity/hyperactivity; MPH for inattention
- Equal worsening of tics in clonidine (26%), MPH (20%), placebo (22%)

Tourette Syndrome Study Group (2002). Neurology.

Cohen et al … Bloch (2015); JAACAP

- Meta-analysis 22 studies (Cohen et al … Bloch 2015; JAACAP)
  - Evaluated for new-onset tics or tic worsening
    - Stimulant and placebo groups not different!
    - Stimulant ~5.7%; Placebo ~6.5%
    - Risk ratio: 0.99, p=0.96
- That said:
  - Each child is unique…
  - Wait 1-2 weeks
  - Amphetamines may be less well tolerated…
    - Supratherapeutic doses may associate with worsened tics (Castellanos et al (1997) JAACAP)

Recent Cochrane Update

- RCTs in youth with tic disorders and co-occurring ADHD
  - 8 studies, 510 participants, 3-22 weeks duration
    - Methylphenidate, clonidine, desipramine, dextroamphetamine, guanfacine, atomoxetine, selegiline
    - Measured: ADHD home, ADHD school, tic symptom severity
- In youth with tics and ADHD:
  - Methylphenidate, clonidine, guanfacine, desipramine, atomoxetine **reduce ADHD** symptoms
  - Guanfacine, clonidine, methylphenidate, methylphenidate + clonidine, and desipramine **reduce tic** symptoms
    - Desipramine was beneficial, but worse risk/benefit ratio so not generally recommended
    - High-dose dextroamphetamine exacerbated tics (1 study)
- Given methodological difficulties, **no evidence-based** recommendations when selecting initial treatment

Osland, Steeves, Pringsheim. 2018. Cochrane Review
Malmivaara. 2020. Dev Med and Child Neur

TS and ADHD Pharm Summary

- Stimulants in patients with tics previously were avoided, but they shouldn't be!
  - No difference in tic onset or worsening in stimulant vs. placebo group (Cohen et al 2015)
  - Stimulant / alpha agonist combo led to tic and ADHD symptom reduction and least amount of side effects (Treatment of ADHD and Tics Study 2022)

- Though stimulants are **not** shown to worsen tics, one may see exacerbation in individual cases
  - Can try another stimulant
  - Can try augmenting with alpha agonist, or switching to alpha agonist / atomoxetine
  - Can consider alpha-agonist first for tic/ADHD combination
    - Alpha-agonists more effective for tics when there is co-occurring ADHD

Cohen et al. (2015) J Am Acad Child Adolesc Psychiatry
Tourette Syndrome Study Group (2002). Neurology.
Osland, Steeves, Pringsheim. 2018. Cochrane Review

Other Considerations…

- Amantadine?
- Namenda?
- Bupropion?
- Viloxazine?

Borison et al 1983
Morrow et al 2021
Findling et al 2007
Surman et al 2013

Non-Pharmacology Treatment

- Tics:
  - Comprehensive behavioral intervention for tics (CBIT)
    - Gold standard behavioral therapy for those children and adolescents with tics
- ADHD:
  - Parent Behavioral Management Training (PBMT)
  - Sprich et al (2016) J of Child Psychology and Psychiatry
    - Manualized CBT approach for reducing residual ADHD symptoms
    - Demonstrated efficacy of CBT for adolescents with ADHD with persisting symptoms despite medications

Challenges in CBIT delivery

- Co-occurring ADHD may moderate effect of behavioral tic treatment (McGuire et al., 2014)
- Treatment is “tic-specific” (Woods et al., 2011), may not target quality of life/psychosocial functioning

Modified CBIT study (MCBIT)

- Developed behavioral approach called MCBIT
  - Modified Comprehensive Behavioral Intervention for Tics (Greenberg et al., 2023)

- Modified Comprehensive Behavioral Intervention for Tics: Treating Children with Tic Disorders, Co-occurring ADHD and Psychosocial Impairment
  - Develop protocol that modifies current treatment by combining CBIT with CBT for ADHD and other CBT techniques
  - Conduct small pilot study randomizing youth with tic disorders and ADHD to standard CBIT group or modified CBIT group

Aims:

- Determine the treatment feasibility and acceptability of the developed protocol
  - Retention rates, randomization process, satisfaction
- Pilot test treatment's effectiveness
  - Tics (Yale Global Tic Severity Scale- YGTSS)
  - ADHD (Vanderbilt Assessment Scale)
  - Quality of Life (PedsQL)
  - Clinical Global Impression Scales (CGI-I)

Format of Sessions

- Structure
  - Ten 55min weekly sessions
    - Two additional relapse prevention sessions every other week
  - Four assessment periods
    - Baseline, mid-point, final session, 3 months post
- All subjects:
  - Binder, CBIT hand-outs
- MCBIT subjects:
  - Additional hand-outs, including session outlines, summaries, visual aids, homework reminders
  - Fidget toys, “brain breaks”
- Each session:
  - Fill out Likert forms, patient CGI-I forms

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Take Away MCBIT Points

- MCBIT was feasible and acceptable for youth with co-occurring tics and ADHD
  - Similarly well-tolerated to traditional CBIT
- MCBIT and CBIT groups both demonstrated improvements:
  - Tic severity, tic-related impairment and ADHD symptoms
  - Changes were maintained through follow-up
- Results not sufficiently superior to recommend MCBIT over CBIT for this population
- Benefit of behavioral treatments that target co-occurring conditions concurrently
  - Modular, multi-symptom-targeting approach may be helpful to some youth with tics and ADHD

Greenberg et al 2023