ADHD in Special Populations:
Preschool, Autism, Epilepsy, Prenatal Exposure

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Disclosures

• Research funding: NIMH, Seattle Children’s Child Health, Behavior, and Development Center, UW Garvey Institute for Brain Health Solutions

• No personal conflicts of interest

• I will be discussing off-label indications for certain medications
Objectives

1. Review standard ADHD stimulant titration strategies

2. Appreciate how age and comorbidities complicate diagnosis and treatment

3. Learn how to adjust treatment strategies in special populations.
ADHD Statistics

• Prevalence: 7.8%-11.0%
• Boys>Girls
• Median age at diagnosis: 6

ADHD Statistics

Currently take medication 69.3%

Do not currently take medication 30.7%

MPH or AMP

Stimulant not used in step 1

Atomoxetine

Alpha Agonist

(Bupropion or TCA)

Adapted from Pliszka et al JAACAP 2006
ADHD: Standard Methylphenidate Titration

Ritalin
- 5 mg TID = 15 mg/day
- 10 mg TID = 30 mg/day
- 15 mg TID = 45 mg/day

Concerta
- 18 mg daily x 5d
- 36 mg daily x 5d
- 54 mg daily x 5d

Booster
## ADHD: Stimulant Titrations

<table>
<thead>
<tr>
<th>Methylphenidate</th>
<th>Amphetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerta:</td>
<td>Adderall XR:</td>
</tr>
<tr>
<td>18mg→36mg→54mg</td>
<td>10mg→20mg→30mg</td>
</tr>
<tr>
<td>Focalin XR:</td>
<td>Vyvanse:</td>
</tr>
<tr>
<td>10mg→15mg→20mg</td>
<td>30mg→50mg→70mg</td>
</tr>
</tbody>
</table>
ADHD in Preschool
Social-emotional Milestones

• Seeks to please friends
• Engages in fantasy play
• More likely to agree to rules
• Enjoys singing/dancing/acting
• More independent
Emotional and Behavioral Impairments

- Attention-deficit/Hyperactivity Disorder
- Autism Spectrum Disorder
- Oppositional Defiant Disorder
- Posttraumatic Stress Disorder
- Major Depressive Disorder
- Anxiety Disorders
- Sleep Disorders

ADHD in Preschool: Assessment

• Clinical suspicion
• Detailed history of symptoms
• Collateral from 2+ contexts
  • Strengths and Difficulties Questionnaire (SDQ)
• IMPAIRMENT
ADHD in Preschool: Behavioral Treatments

- Dyadic and behavioral treatments are first line
  - Behavioral Parent Training
  - Parent-child Interaction Therapy (PCIT)
Positive Parenting

- Positive reinforcement for positive behaviors
- Active ignoring of negative behaviors
- Appropriate consequences for behaviors that cannot be ignored
More Non-medication Treatment Options

- Regular physical exercise
- Time in nature
- Diet
- Sleep hygiene
- School supports
More Non-medication Treatment Options
ADHD in Preschool: PATS

• NIMH multi-center randomized crossover efficacy trial
• 3-5.5 y/o with severe ADHD unresponsive to 10 week psychosocial intervention
• 37/279 patient parents said behavioral treatment resulted in satisfactory improvement

Greenhill et al. JAACAP 2006.
ADHD in Preschool: PATS

- Stimulants are generally effective
  - ES = 0.4-0.7
  - Lower doses provided better balance of benefits and side effects

- Lower response rates compared to older children
  - ES in MTA Study (7-9 y/o) = 0.5-1.3

- Higher rate of side effects
  - 11% attrition vs <1% in MTA

Greenhill et al. JAACAP 2006.
PATS at 6 years

- ADHD diagnosis is stable over time – 89% still meeting diagnostic criteria
- Children with comorbid ODD or Conduct Disorder had higher rates of ADHD.
- Girls experienced a steeper symptoms decline (but girls’ baseline symptoms more severe).
- Some indication of long-term benefit based on parent ratings.

## Preschool vs School Age

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Agent</th>
<th>Effect Size</th>
<th>Attrition due to SEs</th>
<th>Avg optimum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATS (3-5 y/o)</td>
<td>MPH IR</td>
<td>0.35-0.66</td>
<td>11%</td>
<td>0.7 +/- 0.4 mg/kg/day</td>
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<tr>
<td>MTA (7-9 y/o)</td>
<td>MPH IR</td>
<td>0.52-1.31</td>
<td>&lt;1%</td>
<td>1.0 +/- 0.5 mg/kg/day</td>
</tr>
</tbody>
</table>

Greenhill et al. JAACAP 2006.
Wigal et al. JAACAP 2006.
ADHD in Preschool: MPH titration

MPH IR
2.5 mg PO BID x7d

MPH IR
5 mg PO BID x7d

If effective AND well-tolerated, consider switch to once daily formulation, NTE 10mg/day
ADHD in Preschool: Guanfacine titration

Guanfacine IR 0.25mg PO BID x2 weeks

Guanfacine IR 0.5mg PO BID
ADHD and Autism
## ADHD and Autism

<table>
<thead>
<tr>
<th>Prevalence of Autism Spectrum Disorder in 8-year-olds (2016)</th>
<th>Data Courtesy of CDC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td><strong>Prevalence</strong></td>
</tr>
<tr>
<td>---------</td>
<td>----------------</td>
</tr>
<tr>
<td>Overall</td>
<td>18.5 per 1,000</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>29.7 per 1,000</td>
</tr>
<tr>
<td>Girls</td>
<td>6.9 per 1,000</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18.5 per 1,000</td>
</tr>
<tr>
<td>Black</td>
<td>18.3 per 1,000</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>17.9 per 1,000</td>
</tr>
<tr>
<td>Hispanic***</td>
<td>15.4 per 1,000</td>
</tr>
</tbody>
</table>
ADHD and Autism

ADHD
- Inattention
- Hyperactivity

ASD
- Communication
- RRBI

Social
ADHD and Autism

• In prior version of DSM, ASD was an exclusion criterion for ADHD. Not so in DSM-5

• 22-83% of children with ASD meet criteria for ADHD

• Shared heritability:
  ▪ 50-72% of contributing genetic factors overlap

Sokolova E. J Autism Dev Disord. 2017
ADHD and Autism: RUPP

- Double-blind, placebo controlled, crossover trial with open label continuation using MPH in children with moderate to severe hyperactivity
- N=72, ages 5 to 14
- 49% responded with ES = 0.2-0.54
- SEs led to 18% attrition

RUPP Autism Network. JAMA 2005
<table>
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<tr>
<td>RUPP (5-14 y/o)</td>
<td>MPH IR</td>
<td>0.20-0.54</td>
<td>18%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

RUPP Autism Network. JAMA 2005
ADHD in Autism: MPH titration

MPH IR 2.5 mg PO BID x7d

MPH IR 5 mg PO BID x7d

Consider switch to long acting, proceed with caution
ADHD and Epilepsy
ADHD and Epilepsy

- ADHD in epilepsy: ~30%
  - Boys = Girls
  - Inattentive > Hyperactive
- Epilepsy in ADHD: 2.3% (0.5% gen pop)

Besag et al. Epileptic Disord 2016
Socanski et al. 2013. Epilepsy Behav 2010
ADHD in Epilepsy: Assessment

• Clinical suspicion
• Detailed history of symptoms
• Collateral from 2+ contexts
  ▪ Vanderbilt
• Neuropsychological testing

• IMPAIRMENT
ADHD in Epilepsy: Safety of standard treatments

- Methylphenidate:
  - Multiple studies since 1997 show neutral effect on seizure exacerbation.
  - One showed EEG improvements.

- Atomoxetine:
  - 4 studies since 2007 imply no effect on seizures

- (Risperidone)
  - Small study 2004 implied no effect on seizures

Besag et al. Epileptic Disord 2016
ADHD in Epilepsy: Stimulant Titration

Concerta 18mg x7d → Concerta 36mg x7d
ADHD and Prenatal Drug Exposure
ADHD and prenatal drug exposure

- Substances typically used in combination

- Direct effects of drug exposure AND environmental factors both impact fetus
ADHD and prenatal alcohol exposure

- FAS: 0.3 to 9 per 1000 children with FAS
- FASD: 1-5% in US

ADHD and prenatal alcohol exposure
ADHD and prenatal alcohol exposure
ADHD and prenatal alcohol exposure

Williams et al. Pediatrics 2015
ADHD and prenatal alcohol exposure
FASD: Neurodevelopmental

- Cognitive/Learning
- Visual/Spatial
- Memory
- Executive functioning
- Attention
FASD: Neurodevelopmental

FASD more impaired than ADHD
- Verbal Fluency
- IQ
- Shifting Attention
- Verbal Encoding
- Daily Living Skills
- Face and Emotion Processing

FASD not significantly different from ADHD
- Problem Solving
- Set Shifting
- Complex Motor Skills
- Static Balance
- Social Skills
- Communication Skills
- Parent Reports of Behavior

FASD less impaired than ADHD
- Basic Motor Control
- Focused Attention
- Sustained Attention
- Retrieval

Mattson et al. Neuropsychol Rev. 2011
ADHD and prenatal exposure: Optimal arousal theory

![Graph showing optimal arousal levels for ADHD and ASD](image-url)
## ADHD and Prenatal exposure

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Dysfunction</th>
<th>Differences</th>
<th>Stimulus changes needed</th>
</tr>
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<tbody>
<tr>
<td>Autism</td>
<td>Easily over aroused</td>
<td>Downward shift in need for central stimulation or reduced ability to modulate or habituate stimulus input</td>
<td>Reduce sensory input</td>
</tr>
<tr>
<td>ADHD</td>
<td>Under aroused</td>
<td>Shift in level of central stimulation found to be optimal from inadequate neurotransmission of incoming stimulation</td>
<td>Respond to stimulant medications and increases in arousal</td>
</tr>
<tr>
<td>FAS</td>
<td>Arousal dysfunction</td>
<td>Slower gating of incoming stimulation and reduced capacity to inhibit attending to distracting stimuli</td>
<td>Respond to simplification of sensory input (fewer distracters and slower presentation)</td>
</tr>
<tr>
<td>Cocaine Exposure</td>
<td>Heightened arousal responses</td>
<td>Over aroused by stimulation and difficulties returning to baseline levels. Also has difficulties with maintaining inhibitory control</td>
<td>Monitoring of arousal level so stimulus input can be modified when too high. Longer periods allowed for recovery of functioning</td>
</tr>
</tbody>
</table>
ADHD and prenatal exposure: Titration

- Modify expectations based on type of PE
- Monitor closely for SEs, esp irritability/activation
- Lower threshold to transition to non-stimulants
Questions?

The Presidential Press and Information Offices of Azerbaijan.
Accessed via Wikicommons 5-10-22
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