PSYCHIATRIC COMORBIDITY IN AUTISM SPECTRUM DISORDER
PART II: ADHD & IRRITABILITY/AGGRESSION

Pediatrics TeleECHO
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OBJECTIVES

• Brief summary of last week
• Questions from the end of last session
• Assessment & Treatment for ADHD
• Assessment & Treatment for Disordered Mood & Irritability/Aggression
• Case discussions
Main Points from Last Week

- High burden for individuals with ASD and their caretakers
- Determining psychiatric co-morbidity in ASD is difficult
- Anxiety in 50% of children with ASD
- Depression in 10-20% of children with ASD & is more likely the higher the functioning & awareness of social deficits
- Treatment is multi-disciplinary

Review Principles of Psychopharmacology in ASD

- Start with drugs that have less risk adverse effects before moving to atypical antipsychotics.
- "START LOW[ER] AND GO SLOW[ER]"
- Medications generally less tolerated
  - SSRIs; pre-pubertal children more likely to become activated.
  - Start on weekend (especially stimulants)
  - Warn of potential side effects
- Often maximum benefit achieved at lower doses
- Frequent follow-up, especially after initiation
- Consider a treatment hierarchy
- Most trials off label
QUESTIONS FROM LAST SESSION

- What to do about caregiver resistance to psychotropic medication:
  - Seek to understand their beliefs first
    - Cultural, religious reasons?
  - There may be unspoken fears of certain side effects
    - Risperidone & gynecomastia
    - “I don’t want [a medication] to change who my child is.”
  - Medications are one tool to help their child benefit from other important services
  - Emphasize shared decision making
    - Though in some cases caregivers need you to be direct with recommendations
  - “Join” with them. Appreciate their thoughtfulness. If you still sense defensiveness: “What do I [providers] most misunderstand about what it’s like for you to parent your child?”
  - Attempt to “de-normalize” serious symptoms/behaviors and the risk to patient & family safety (especially other children in the home).
  - If they still say no, let parents know your door is always open
QUESTIONS FROM LAST SESSION

- Ideas to decrease anxiety for ASD patients while in clinic
  - Immediately room patient upon arrival
  - Ask caregivers what will help their child be most comfortable
  - Ask if there are specific sensory impairments
  - Minimize the number of transitions
    - Doing everything in same room versus separate room for potential pain.
  - Consider purchasing sensory items
  - Utilize the same staff if possible
  - Close approximations/slow shaping/desensitization
  - Decrease stimulation
    - Lights off in rooms with windows
  - Consider seeing patients elsewhere (Tele med, in the hall*, stairs*, their car*)
QUESTIONS FROM LAST SESSION

What to do is a patient has been on an SSRI for months (years) with ongoing symptoms and considering augmentation:

- Titrate the dose further
- Trial off medication
  - Especially if efficacy in question
- Target different (or residual) symptom cluster like sleep or ADHD
- Cross taper to a different SSRI
  - No standard approach
  - Consider half-life of medication
    - Reduces likelihood of discontinuation
  - Cross to equivalent versus lower dose of new agent
  - Stop one & start other right away
- Two trials in same class
  - Unless significant adverse reaction from one
ADHD

- Inattention, hyperactivity, impulsivity, distractibility across settings
- Impulsivity: **behavior without adequate thought**; tendency to act on a whim, may have high potential for harm
  - Wandering/elopement, attempting to get out of cars [or drive them], swimming without ability
- In DSM-IV could not have ASD & co-morbid ADHD
  - But a number of studies led to change in DSM-5
- Prevalence of ADHD in children with ASD
  - 30-80%


### ADHD ASSESSMENT

#### Vanderbilt Rating Scale

**Vanderbilt ADHD Diagnostic Parent Rating Scale**

<table>
<thead>
<tr>
<th>Parent's Name</th>
<th>Today's Date</th>
<th>Child's Name</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Instructions:** Each rating should be based on the extent to which you think your child and child's behavior are described over the past six weeks. Use the chart below to rate your child's behavior. Circle the number that best describes your child's behavior. **Does not apply:** Does not apply when the child is not at home or at school. **Comments:**

<table>
<thead>
<tr>
<th>Behavior</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

**Sample Questions:**

1. Does your child have trouble stopping talk when others talk, or do they talk too much when others talk?
2. Does your child have trouble paying attention to things that are important to everyone?
3. Does your child have trouble finishing things that need to be finished?
4. Does your child have trouble holding their attention during school or while playing?
5. Does your child have trouble completing their homework or schoolwork?
6. Does your child have trouble keeping up with their homework or schoolwork?

**My Indirect Impulsivity Tests**

- Kids don't always do what they're asked to do.
- Kids have trouble paying attention to things that are important to everyone.
- Kids have trouble finishing things that need to be finished.
- Kids have trouble holding their attention during school or while playing.
- Kids have trouble completing their homework or schoolwork.
- Kids have trouble keeping up with their homework or schoolwork.

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**Note:** The Vanderbilt Rating Scale is a tool used to assess ADHD symptoms in children. It helps in identifying areas where a child may struggle with attention, impulsivity, and organization. This information is crucial for developing effective strategies and interventions to support the child's success in various settings.
PHARMACOTHERAPY FOR ADHD

- Alpha agonists
  - Guanfacine (Tenex)
  - Clonidine (Catapres)

- Stimulants
  - Methylphenidate IR (Ritalin) first
  - Long acting less tolerated
  - Amphetamine/Dextroamphetamine (Adderall)

- NE reuptake inhibitor
  - Atomoxetine (Strattera)

- Refractory to above:
  - Consider atypical anti-psychotics or Depakote

Hyperactivity & Impulsivity > Inattention
Caution with low weight or selective diet
Adderall - mood side effects
Theoretical anxiety benefit
Comorbid irritability & aggression
Need for lab monitoring
Metabolic side effects

Hyperactivity & Impulsivity > Inattention
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OTHER TREATMENTS FOR ADHD

- Environmental modifications
  - 1:1 supervision
  - Locks & alarms on doors, iD tags, visual prompts
- OT “sensory diet”:
  - Hyporesponsive: jump on mini-trampoline, swinging, and resistive physical work, such as swimming and use of playground equipment
  - Hyperresponsive: weight vests, bean bag chair, body sock, The Big Hug, joint compressions
- Regular breaks (recess!)
- Limit recreational electronic screen time:
  - Greater cumulative hours of use predicts poor executive functioning
  - No screen time for <2 years old, 1 hour for kids 2-5 yrs, kids 6 & older need limits (no more than 2 hours), family contract
- Cognitive training programs:
  - Neurofeedback programs for ADHD applied to ASD?
DISORDERED MOOD IN ASD

• Emotions can fluctuate minute to minute, depending on environment.
• Moods can be reactive & poorly modulated.
• Neurobiological basis for this?
• Consider Developmental Level

Versus Bipolar Disorder, DMDD, PMDD, Substance Induced Mood Disorder, MDD, Dysthymia, or Cyclothymia
BIPOLAR DISORDER

- Occurrence of manic and depressive episodes
- Rates in ASD vary from 2% to 27%
- Symptoms may be masked by core features of ASD
- Baseline behaviors may become more intense or exaggerated during manic or depressive episodes
- Maintain a low suspicion unless
  - Family psychiatric history clearly positive for BD
  - Clear disruptive episodes
  - Distinct change from baseline


DSM 5 CRITERIA FOR MANIA

- Distinct period of abnormally & persistently elevated, expansive, or irritable mood lasting at least 1 wk & present most of the day
- With 3 of the following (4 if mood is only irritable)
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - Increased talkativeness
  - Flight of ideas/racing thoughts
  - Distractibility
  - Increased goal directed activity/psychomotor agitation
  - Engagement in high risk activities

Adaptation: for limited verbal ability during the mood disturbance requires 2 of the following (3 if mood is only irritable).

In ASD you may also see:
- Increased aggression
- Changes in appetite
- Psychosis
- Increased hyperactivity/psychomotor agitation

TREATMENT FOR BIPOLAR DISORDER IN ASD

• Leave it for the psychiatrists!
  • Lithium, Depakote, Lamotrigine, Tegretol, Atypical Antipsychotics

But…
### TREATMENT FOR INSOMNIA

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melatonin</td>
<td>1 to 6 mg PO qHS</td>
<td>Well studied &amp; tolerated</td>
</tr>
<tr>
<td></td>
<td>sleep initiation</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.025 to 0.2 mg</td>
<td>Tolerance</td>
</tr>
<tr>
<td>Trazodone</td>
<td>25 to 200 mg</td>
<td>Priapism risk</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>3.75 to 15 mg</td>
<td>Increased appetite</td>
</tr>
<tr>
<td>Don’t forget</td>
<td>sleep hygiene first!</td>
<td>Limit screen time</td>
</tr>
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<td></td>
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</tbody>
</table>
IRRITABILITY

- Depression
- Mania
- DMDD
- PMDD
- Generalized Anxiety Disorder
- PTSD
- Traumatic Brain Injury
Irritability

• Describes proneness to anger
• Research Domain Criteria framework: the reaction to blocked goal attainment

Irritability in ASD

• Studies leading to FDA approval of Risperidone & Aripiprazole defined irritability as: self-injurious behavior, aggression to others, tantrums, and mood lability.
PREVALENCE OF AGGRESSION IN CHILDREN WITH ASD

Fig. 1. Percentage demonstrating aggression across age groups.
Only 2 FDA approved medications:

1. Risperidone – multiple RCTs (ages 5-17)
   • Start at 0.25 mg PO daily or BID. Titrate in 0.25 to 0.5 mg increments. Effective doses up to 2 mg daily

2. Abilify – 2 large RCTs (ages 6-17)
   • Start 1 to 2 mg PO daily. Effective doses 1 to 10 mg daily

Both come in liquid concentrations of 1mg/1mL

Make sure irritability is severe & occurs across environments

Some caregivers will describe this as “life-altering”
RISKS OF ANTIPSYCHOTICS

Extrapyramidal Side Effects

• **Dystonia**: abnormal contraction muscles of eyes (oculogyric crisis), head, neck, limbs, or trunk developing within a few days of starting or raising dose

• **Parkinsonism**: bradykinesia, resting tremor, rigidity - usually appears days to weeks after starting, but in rare cases the onset delay may be several months or more

• **Akathisia**: subjective restlessness, accompanied by excessive movements (fidgety legs, rocking from foot to foot, pacing, inability to sit still), developing within a few weeks of starting or raising dose

• **Tardive dyskinesia**: involuntary movements of tongue, lower face & jaw, & extremities (sometimes pharyngeal, diaphragmatic, or trunk muscles) developing with use of a neuroleptic for at least a few months.

• **Withdrawal dyskinesias**: usually lasts less than 8 weeks

Neuroleptic Malignant Syndrome: combination of autonomic instability, elevated temperature, rigidity and elevated levels of creatine phosphokinase (CPK), can be fatal

Metabolic Side Effects

• **Weight gain**

• **Hyperglycemia**

• **Hyperlipidemia**
MONITORING FOR SIDE EFFECTS OF ANTIPSYCHOTICS

- Baseline measures of vital signs, weight/BMI, and blood glucose and monitored at regular intervals.

- Abnormal Involuntary Movement Scale at baseline and regular intervals (every 6 to 12 months)

- Consider EKG if history of cardiac disease

- In our practice at least yearly A1c & Lipid panel

- Abrupt discontinuation (unless NMS suspected) not recommended due to risk of withdrawal dyskinesia
Consider Metformin

- One double blind, randomized, placebo controlled in kids with ASD ages 6-17 yrs
  - Decreased BMI z-scores at 16 weeks
- 250 mg PO BID up to 1000 mg PO BID
- Diarrhea, metabolic acidosis

Or Topamax

- 25 mg PO qHS up to 100 mg PO qHS
- Cognitive slowing

Depakote

• I typically use
  • DR Sprinkles (can open capsules and sprinkle on soft food; shouldn’t be chewed)
  • ER formulation (must be at least 10 years old)
• Start at 125 mg PO BID for Sprinkles. Or 250 mg PO qHS for ER.
• Also has been studied for impulsive aggression
• Requires more regular lab monitoring (trough, CMP, CBC)
• Risk of hyperammonemia, thrombocytopenia, pancytopenia, liver toxicity, pancreatitis, weight gain

• Treat active medical problems
• Functional Behavioral Analysis
• Occupational Therapy
• Speech Therapy
• Parent training
  • Block aggressive behaviors, non-reactive, neutral tone
• Treat insomnia
• Inpatient psych hospitalization
• Out of home placements
- QUESTIONS?
- COMMENTS?
- CASES?