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

Pediatrics TeleECHO

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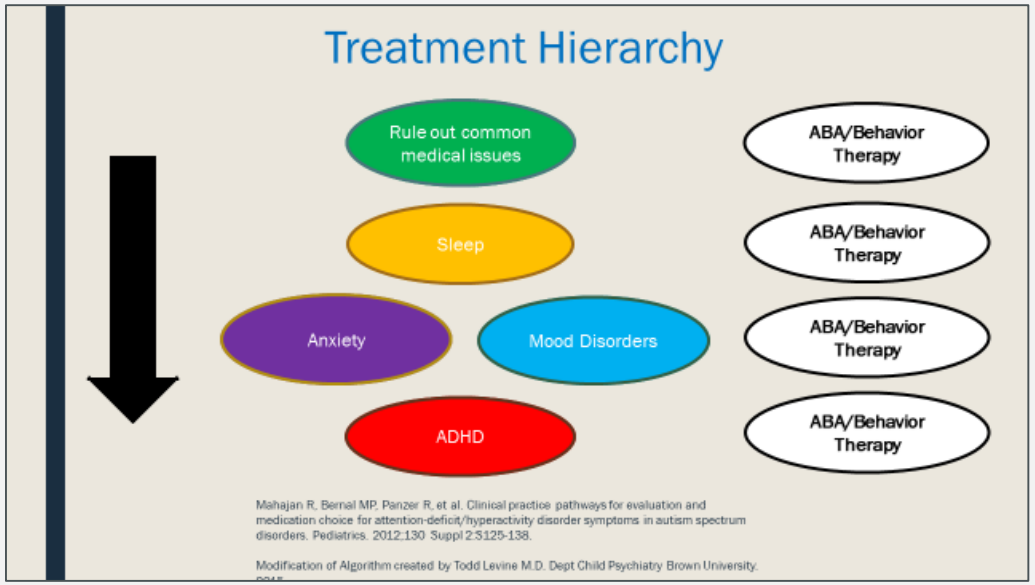
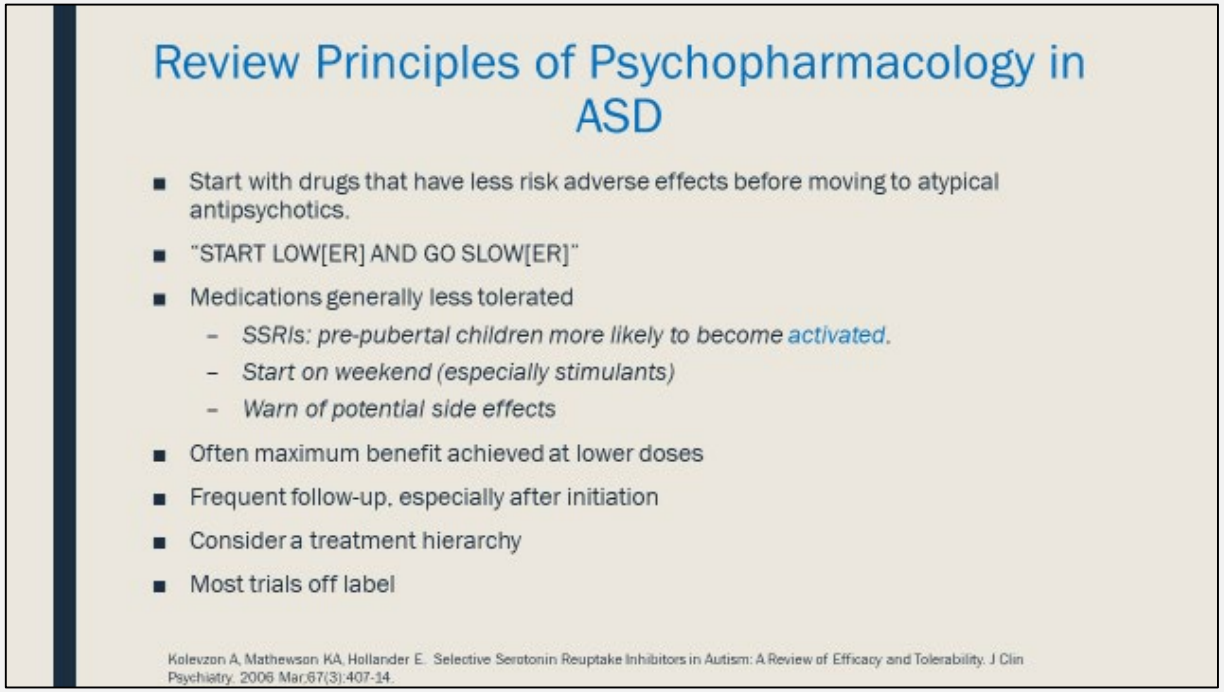
OBJECTIVES

- 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





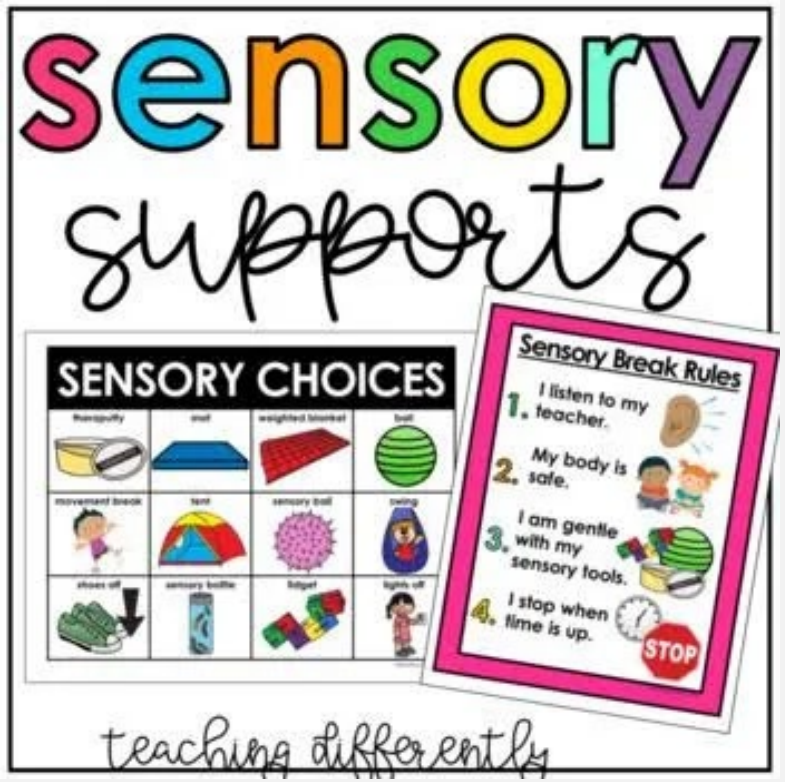
QUESTIONS FROM LAST SESSION

- 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*)


HAND HELD
MASSAGE
ROLLER


sensory
supports
SENSORY CHOICES
Sensory Break Rules
1. I listen to my teacher.
2. My body is safe.
3. I am gentle with my sensory tools.
4. I stop when time is up.
STOP
teaching differently


SCHOOL HEALTH


bluedaisy
SENSORY
THERAPY TOOL

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%

Van der Meer JM, et al. Are Autism Spectrum Disorder and ADHD different manifestations of one overarching disorder? J Am Acad Child Adolesc Psychiatry. 2012;51:1160-1172.

Mahajan R, Bernal MP, Panzer R, et al. Clinical practice pathways for evaluation and medication choice for attention-deficit/hyperactivity disorder symptoms in autism spectrum disorders. Pediatrics. 2012;130 Suppl 2:S125-138.

ADHD ASSESSMENT

Vanderbilt Rating Scale

CHILD STUDY CENTER
Department of Pediatrics
University of Oklahoma Health Sciences Center

Vanderbilt ADHD Diagnostic Parent Rating Scale

Parent's Name: _____ **Today's Date:** _____ **Child's Name:** _____ **Age:** ____

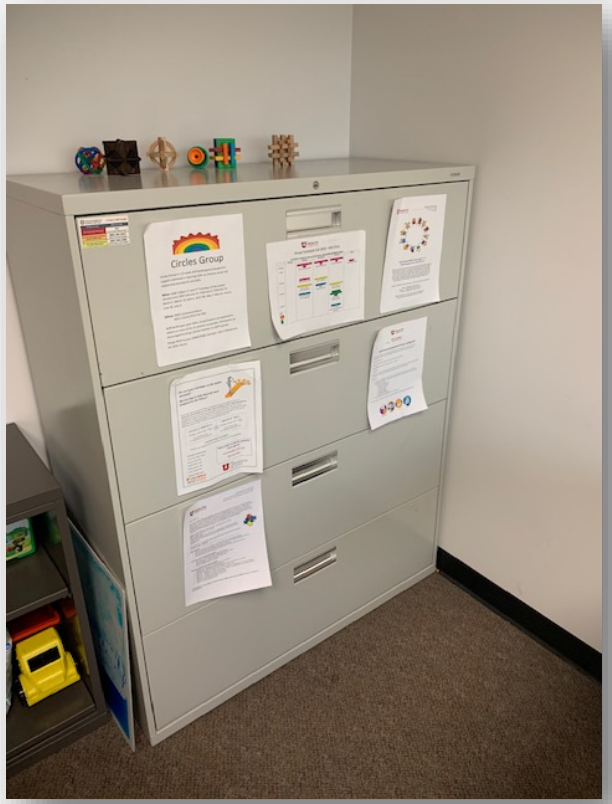
Directions: Each rating should be considered in the context of what is appropriate for the age of your child and should reflect that child's behavior in the last 6 months.
Is this evaluation based on a time when the child ☐ was on medication ☐ was not on medication ☐ not sure?

BEHAVIOR:	never	occasionally	often	very often
1. Does not pay attention to details or makes careless mistakes; for example, homework.	0	1	2	3
2. Has difficulty attending to what needs to be done.	0	1	2	3
3. Does not seem to listen when spoken to directly.	0	1	2	3
4. Does not follow through when given directions and fails to finish things.	0	1	2	3
5. Has difficulty organizing tasks and activities.	0	1	2	3
6. Avoids, dislikes, or does not want to start tasks that require ongoing mental effort.	0	1	2	3
7. Loses things needed for tasks or activities (assignments, pencils, or books).	0	1	2	3
8. Is easily distracted by noises or other things.	0	1	2	3
9. Is forgetful in daily activities.	0	1	2	3
10. Fidgets with hands or feet or squirms in seat.	0	1	2	3
11. Leaves seat when he/she is supposed to stay in his/her seat.	0	1	2	3
12. Runs about or climbs too much when he/she is supposed to stay seated.	0	1	2	3
13. Has difficulty playing or starting quiet games.	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor".	0	1	2	3
15. Talks too much.	0	1	2	3
16. Blurts out answers before questions have been completed.	0	1	2	3
17. Has difficulty waiting for his/her turn.	0	1	2	3
18. Interrupts or bothers others when they are talking or playing games.	0	1	2	3
19. Argues with adults.	0	1	2	3
20. Loses temper.	0	1	2	3
21. Actively disobeys or refuses to follow an adult's requests or rules.	0	1	2	3
22. Bothers people on purpose.	0	1	2	3
23. Blames others for his/her mistakes or misbehaviors.	0	1	2	3
24. Is touchy or easily annoyed by others.	0	1	2	3
25. Is angry or bitter.	0	1	2	3
26. Is hateful and wants to get even.	0	1	2	3
27. Bullies, threatens, or scares others.	0	1	2	3
28. Starts physical fights.	0	1	2	3
29. Lies to get out of trouble or to avoid jobs (i.e., "cons" others).	0	1	2	3
30. Skips school without permission.	0	1	2	3
31. Is physically unkind to people.	0	1	2	3
32. Has stolen things that have value.	0	1	2	3
33. Destroys others' property on purpose.	0	1	2	3
34. Is physically mean to animals.	0	1	2	3
35. Has set fires on purpose to cause damage.	0	1	2	3
36. Has broken into someone else's home, business or car.	0	1	2	3
37. Has stayed out at night without permission.	0	1	2	3
38. Has run away from home overnight.	0	1	2	3
39. Is fearful, anxious, or worried.	0	1	2	3
40. Is afraid to try new things for fear of making mistakes.	0	1	2	3
41. Feels useless or inferior.	0	1	2	3
42. Blames self for problems, feels at fault.	0	1	2	3
43. Feels lonely, unwanted, or unloved; complains that "no one loves him/her".	0	1	2	3
44. Is sad, unhappy, or depressed.	0	1	2	3
45. Feels different and easily embarrassed.	0	1	2	3

PERFORMANCE: How is your child doing?	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
1. Rate how your child is doing in school overall.	1	2	3	4	5
2. How is your child doing in reading?	1	2	3	4	5
3. How is your child doing in writing?	1	2	3	4	5
4. How is your child doing in math?	1	2	3	4	5
5. How does your child get along with you?	1	2	3	4	5
6. How does your child get along with brothers and sisters?	1	2	3	4	5
7. How does your child get along with others his/her own age?	1	2	3	4	5
8. How does your child do in activities such as games or team play?	1	2	3	4	5

If more than six items from questions 1 - 9 or 10 -18 are rated 2 or 3, how old was your child when you first noticed these behaviors? _____

My Indirect Impulsivity Tests



PHARMACOTHERAPY FOR ADHD

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

→ Hyperactivity & Impulsivity > Inattention

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

→ Caution with low weight or selective diet

Adderall - mood side effects

- NE reuptake inhibitor
  - Atomoxetine (Strattera)

→ Theoretical anxiety benefit

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

→ Comorbid irritability & aggression

Need for lab monitoring

Metabolic side effects

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

Wozniak,J Mania in Children With Pervasive Developmental Disorder Revisited. J Am Acad Child Adolesc Psychiatry, Vol 36(11):1552–1559.

Leyfer, O.T. et al. (2006). Cormorbid Psychiatric Disorders in Children with Autism: Interview Development and Rates of Disorders. J Autism Dev Disord, 36:849-861

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

Fletcher et al 2007. Diagnostic Manual-Intellectual Disability: A Textbook of Diagnosis of Mental Disorders in Person with Intellectual Disability. Chapter 18, pages 297-299

TREATMENT FOR BIPOLAR DISORDER IN ASD

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

But…

TREATMENT FOR INSOMNIA

Melatonin
- 1 to 6 mg PO qHS
- sleep initiation

→ Well studied & tolerated

Clonidine
- 0.025 to 0.2 mg

→ Tolerance

Trazodone
- 25 to 200 mg

→ Priapism risk

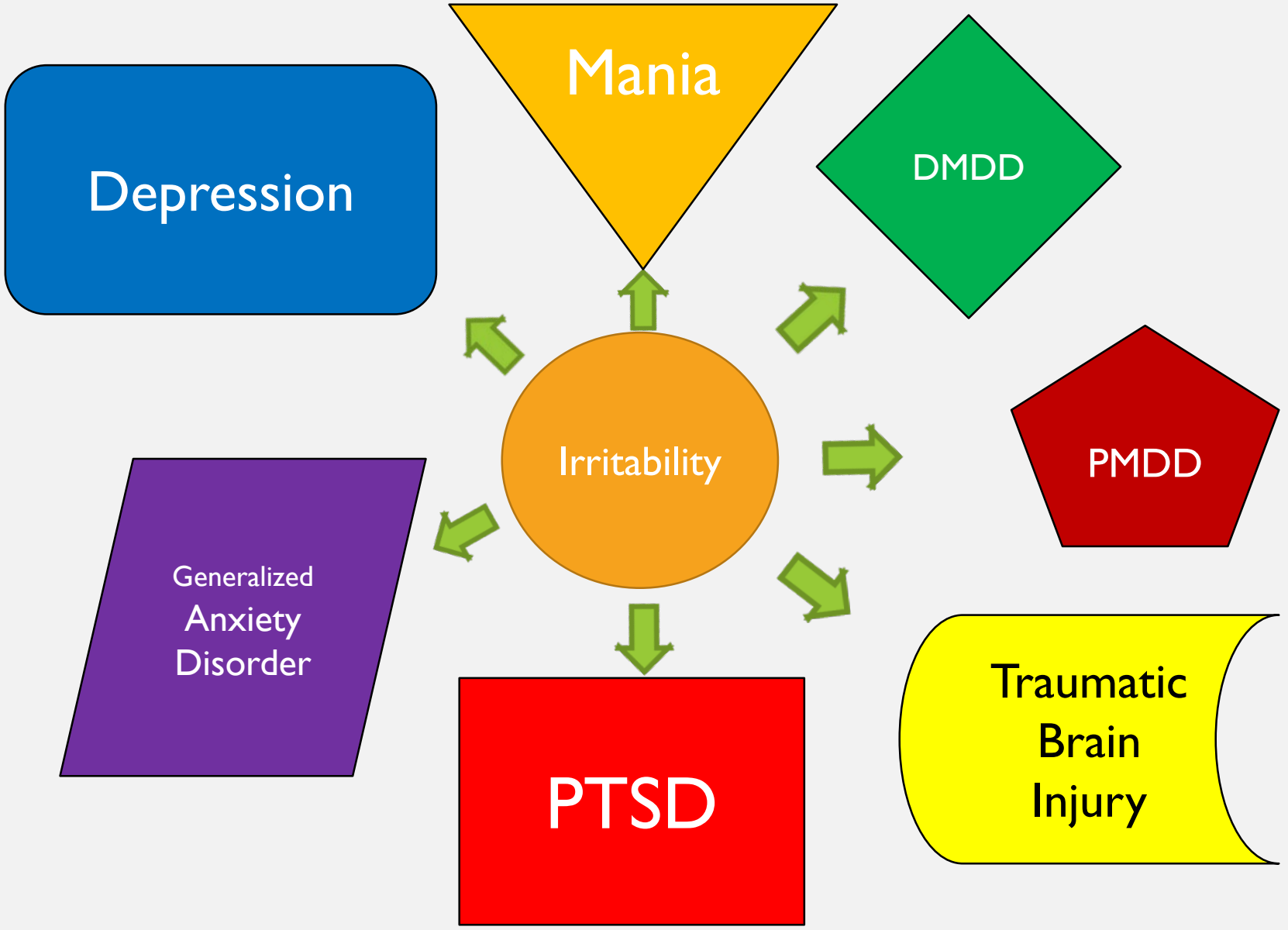
Mirtazapine
- 3.75 to 15 mg

→ Increased appetite

Don't forget sleep hygiene first!

→ Limit screen time

IRRITABILITY



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.

Stringaris A., Taylor E. Oxford University Press; New York: 2015. Disruptive Mood. Irritability in Children and Adolescents.

Insel T., Cuthbert B., Garvey M. Research Domain Criteria (RDoC): toward a new classification framework for research on mental disorders. Am J Psychiatry. 2010;167:748–751.

PREVALENCE OF AGGRESSION IN CHILDREN WITH ASD

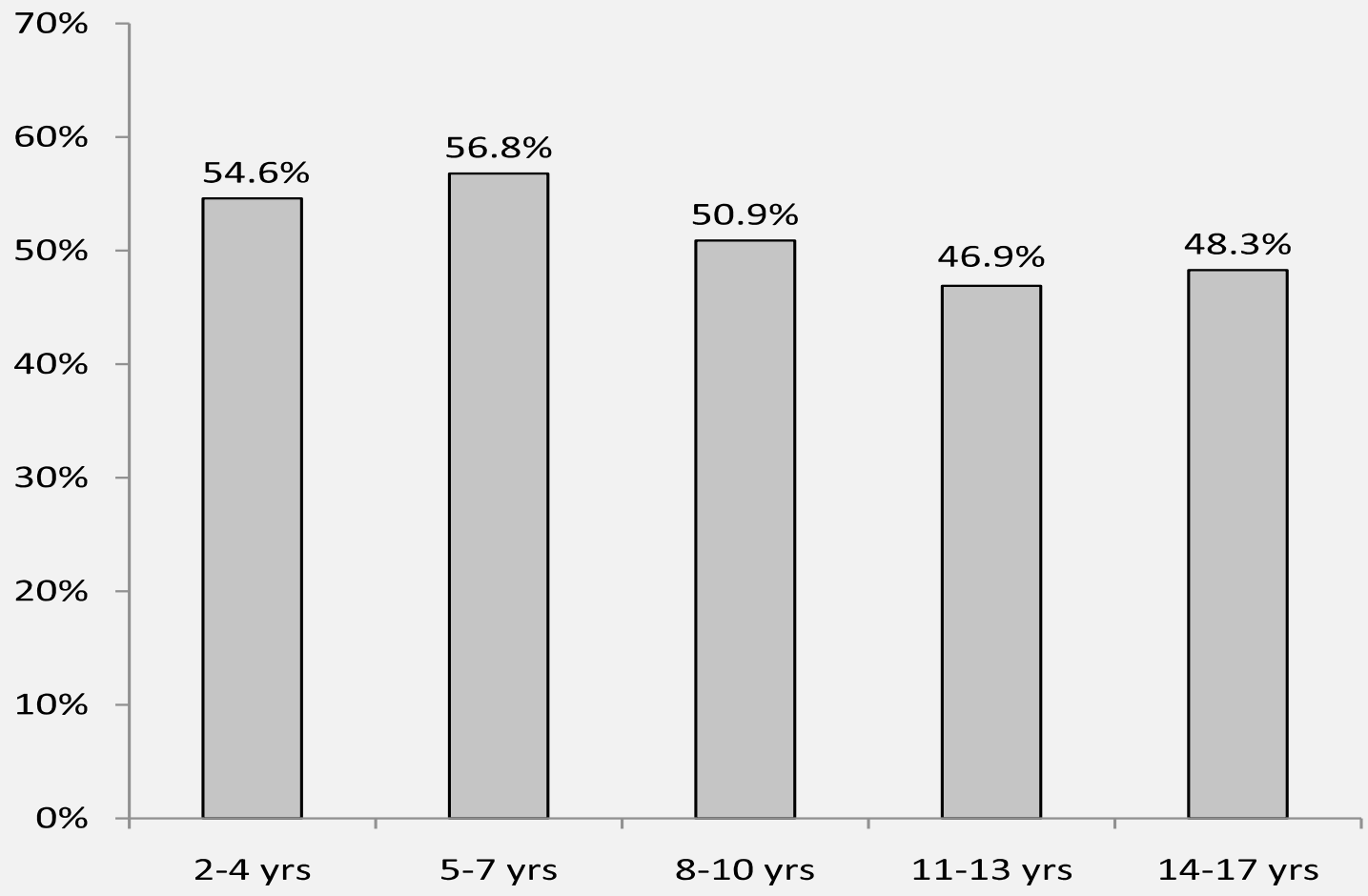


Fig. 1. Percentage demonstrating aggression across age groups.

EVIDENCE BASED MEDICATION FOR IRRITABILITY & AGGRESSION

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 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"

McCracken JT, McGough J, Shah B, et al. Risperidone in children with autism and serious behavioral problems. N Engl J Med

Ching H, Pringsheim T. Aripiprazole for autism spectrum disorders (ASD). Cochrane Database Syst Rev 2012 May 16;5:CD009043. doi: 10.1002/14651858.CD009043.pub2.

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 a 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)
  - https://www.psychcongress.com/videos/aims-exam-instructional-video
- 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

American Academy of Child and Adolescent Psychiatry. PRACTICE PARAMETER FOR THE USE OF ATYPICAL ANTIPSYCHOTIC IN CHILDREN & ADOLESCENTS. 2016.

IF SIGNIFICANT CLINICAL BENEFIT FROM ANTIPSYCHOTICS FOR IRRITABILITY/AGGRESION BUT HIGH WEIGHT GAIN…

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

Anagnostou E, Aman MG, Handen BL, et al. Metformin for Treatment of Overweight Induced by Atypical Antipsychotic Medication in Young People With Autism Spectrum Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2016;73(9):928–937. doi:10.1001/jamapsychiatry.2016.1232

EVIDENCE BASED MEDICATION FOR IRRITABILITY & AGGRESSION

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

Hollander et al. Divalproex Sodium vs Placebo for the Treatment of Irritability in Children and Adolescents with Autism Spectrum Disorders. Neuropsychopharmacology. 2010 Mar; 35(4): 990–998.

OTHER TREATMENTS FOR IRRITABILITY & AGGRESSION

- 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?