Psychopharmacology Review: Management of Maladaptive Behaviors, Irritability and aggression in Youth with ASD

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Baylor College of Medicine

Agenda

1. **Review of ASD Diagnostic Criteria**
2. **Clinical Pearls for treating ASD + comorbid conditions**
   - Review of Psychopharmacology treatment for management of irritability and impulsive aggression with ASD
   - Review of medications used to treat youth with ASD and Bipolar Disorder
3. **Psychopharm Review of treatment of youth with ASD and ADHD**
4. **Summary and Conclusions**

Learning Objectives

Review evidence for medications treating irritability/aggression/self-injury in ASD

Summarize efficacy and adverse effects of key agents (risperidone, aripiprazole) and other classes of medications.

Discuss guideline recommendations and monitoring

ASD Clinical Features and Associated Conditions

ASD is characterized by a constellation of core clinical features and associated conditions

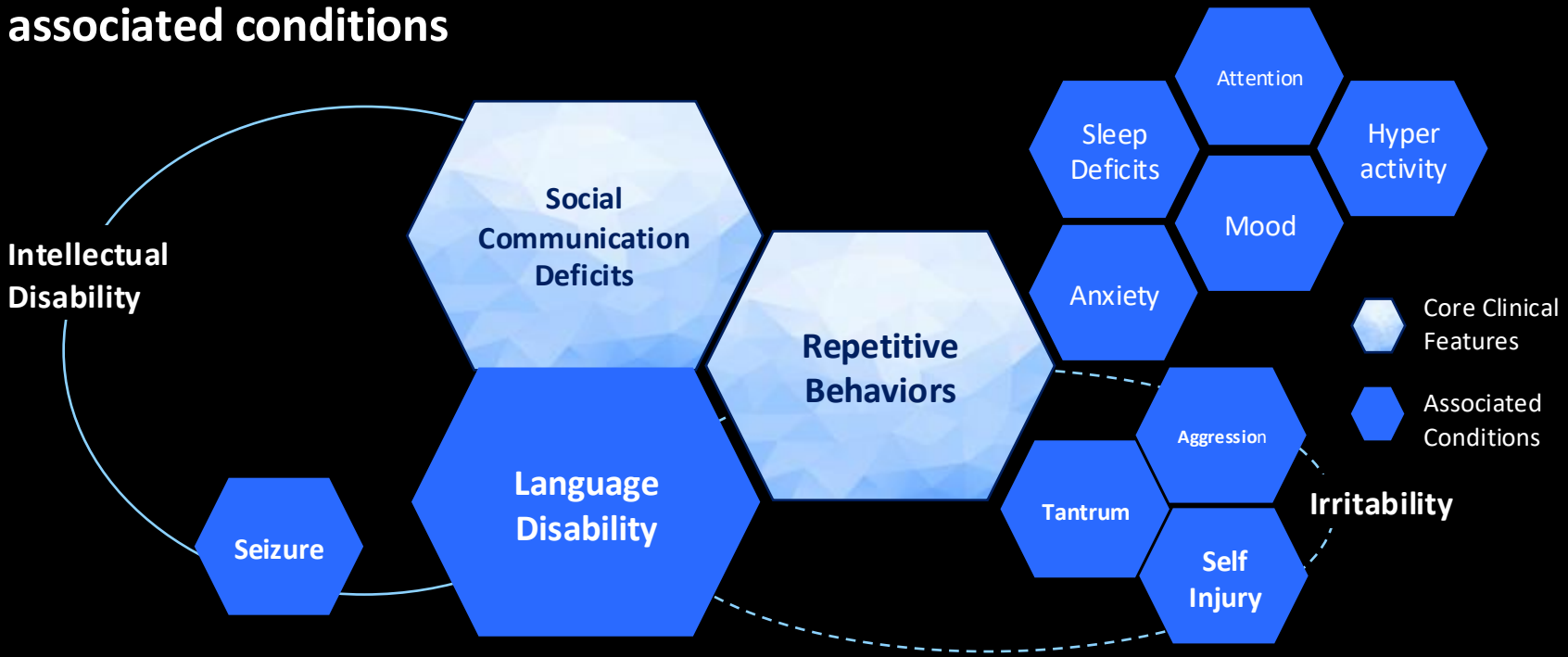


Image Based on: Klinger, L., Dawson, G., Burner, K. &Crisler, M. Autism Spectrum Disorder.In E.J. Mash & R.A. Barkley (Eds.), (2014). *Child Psychopathology, 3rd* Guildford Press.

DSM-5 Autism Criteria

The child must have:

- Persistent deficits in each of 3 areas of social communication and interaction

- Plus at least 2 of 4 types of restricted/repetitive behaviors

Social Communication and Interaction	Restrictive and Repetitive Behavior
Difficulty with social/emotional reciprocity (give and take)	Repetitive speech / use of objects
Difficulty with non-verbal communication	Routines, rituals, distressed by change
Difficulty establishing or maintaining relationships	Narrow, fixated interests
	Heightened sensory sensitivity

Overview of the Problem

Irritability, aggression, and self-injury occur in a subset of youth with ASD and cause functional impairment

Non-pharmacologic interventions (behavioral, environmental) are first-line where feasible

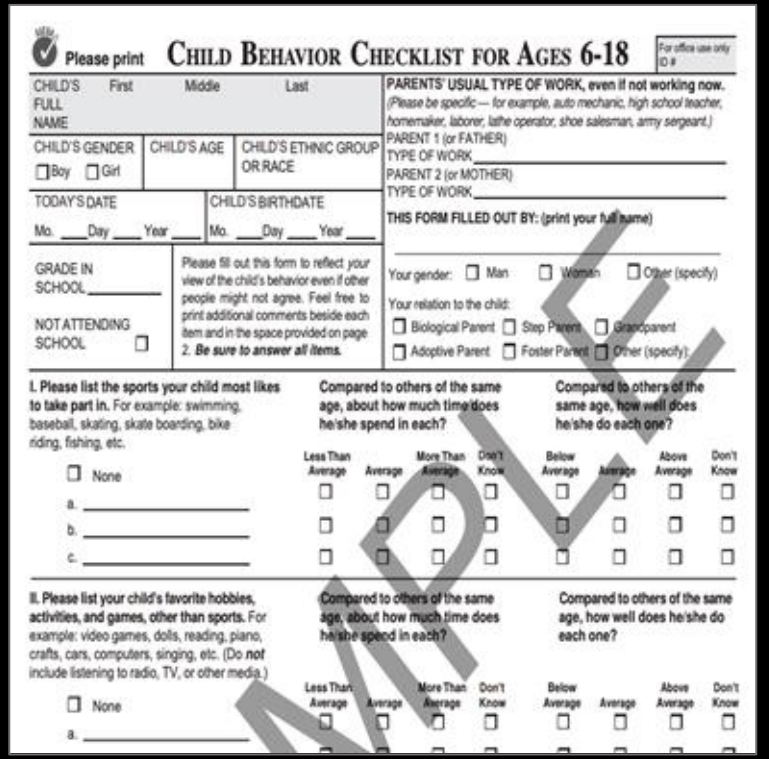
Medications considered when behaviors are severe, dangerous, or refractory to behavioral interventions

Aggressive Behavior in ASD

Approximately 25% of children with ASD have aggressive behaviors including:

- Irritability and agitation
- Self-injurious behaviors
- Property destruction
- Outbursts of frustration and distress
- "Tantrums/meltdowns"

Aggression can be quantified with the Child Behavior Checklist which assesses a child's propensity to "get in many fights," "hit others," "physically attack people," and to have "temper tantrums or hot temper" on a 3-point scale.



Please print **CHILD BEHAVIOR CHECKLIST FOR AGES 6-18**

For office use only ID #

CHILD'S FULL NAME First Middle Last

CHILD'S GENDER ☐Boy ☐Girl | CHILD'S AGE | CHILD'S ETHNIC GROUP OR RACE

TODAY'S DATE Mo. ___ Day ___ Year ___ | CHILD'S BIRTHDATE Mo. ___ Day ___ Year ___

GRADE IN SCHOOL _____

NOT ATTENDING SCHOOL ☐

Please fill out this form to reflect your view of the child's behavior even if other people might not agree. Feel free to print additional comments beside each item and in the space provided on page 2. ***Be sure to answer all items.***

PARENTS' USUAL TYPE OF WORK, even if not working now. *(Please be specific — for example, auto mechanic, high school teacher, homemaker, laborer, lathe operator, shoe salesman, army sergeant.)*

PARENT 1 (or FATHER) TYPE OF WORK _____

PARENT 2 (or MOTHER) TYPE OF WORK _____

THIS FORM FILLED OUT BY: (print your full name) _____

Your gender: ☐ Man ☐ Woman ☐ Other (specify)

Your relation to the child: ☐ Biological Parent ☐ Step Parent ☐ Grandparent ☐ Adoptive Parent ☐ Foster Parent ☐ Other (specify)

I. Please list the sports your child most likes to take part in. For example: swimming, baseball, skating, skate boarding, bike riding, fishing, etc.

Compared to others of the same age, about how much time does he/she spend in each? Less Than Average | Average | More Than Average | Don't Know

Compared to others of the same age, how well does he/she do each one? Below Average | Average | Above Average | Don't Know

☐ None

a. _____

b. _____

c. _____

II. Please list your child's favorite hobbies, activities, and games, other than sports. For example: video games, dolls, reading, piano, crafts, cars, computers, singing, etc. (Do *not* include listening to radio, TV, or other media.)

Compared to others of the same age, about how much time does he/she spend in each? Less Than Average | Average | More Than Average | Don't Know

Compared to others of the same age, how well does he/she do each one? Below Average | Average | Above Average | Don't Know

☐ None

a. _____

SAMPLE

1. Hill, et al, Res Autism Spectr Disord, 2014; CBCL, Achenbach & Rescorla, 2000; 2001

General Guidelines for management of Aggression in ASD

Overall:

Children with ASD and comorbid conditions require **intense educational, behavioral, parental, and psychopharmacological intervention**

Evidence Supports:

- **Strong evidence for Risperidone and Aripiprazole, but evidence is limited for many agents utilized to manage aggression and irritability in ASD**

More Evidence Needed:

- **More evidence needed for naltrexone, N-acetylcysteine however has been helpful in reducing aggression.**
- **CBD oil should be used with caution because of concerns with drug interaction and lack of standards in quality control**

Risperidone Review

RUPP Autism Network (JAMA, 2002): n=101 children (5–17y) randomized to risperidone vs placebo for 8 weeks.

Mean improvement in ABC-I subscale: −14.9 (risperidone) vs −3.6 (placebo); $p<0.001$.

Response rate (≥25% reduction in irritability): 69% vs 12% (NNT≈2).

Adverse effects: weight gain (mean +2.7 kg), somnolence, increased appetite, drooling.

Aripiprazole: Review

Owen et al., JAACAP 2009; Marcus et al., Pediatrics 2009 — n≈300 combined participants, ages 6–17.

8-week RCTs showed significant reduction in ABC-I scores vs placebo (effect size ≈ 0.8–1.0).

Adverse effects: sedation (20%), weight gain (mean +1.3–1.5 kg), drooling, extrapyramidal symptoms (6–10%).

Discontinuation for adverse events in 10–15% of cases.

Management of Aggression in ASD

Medication Class	Medication Studied	Evidence for treating aggression
Antipsychotics	Risperidone*, Aripiprazole*, Olanzapine, Lurasidone	Strong *FDA approved for agitation and irritability
Alpha-2 Agonists	Guanfacine, Clonidine	Strong for hyperactivity
Mood stabilizers	Lithium	Limited
Serotonin reuptake inhibitors	Sertraline, Fluvoxamine, Citalopram	Insufficient
Anti-Epileptic Drugs (AEDs)	Valproate, Oxcarbazepine, Topiramate, Levetiracetam, Lamotrigine	Insufficient
Opiate antagonists	Naltrexone	Limited

Management of Aggression in ASD

Medication Class	Medication Studied	Evidence for treating aggression
Mucolytic agents	N-Acetylcysteine (NAC)	Limited
Cannabinoid	Cannabidiol (CBD oil)	Weak/Insufficient
GABA agonist	Arbaclofen	Limited
Loop diuretic	Bumetanide	Limited
Xanthine analog	Pentoxifylline	Insufficient
NMDA antagonist	Amantadine	Strong (as adjuvant therapy) Limited (as monotherapy)

A significant proportion of these children will have drug-refractory aggression

Adler et al., 2015

Systematic chart review of 250 individuals referred to an autism and treatment clinic for initial ASD evaluation:

135 patients met DSM-IV-TR criteria for ASD

Drug-refractory was defined as persistence of symptoms despite:

- Previous trials of **risperidone (at least 2 mg/day)** and **aripiprazole (at least 5 mg/day)** OR
- Three or more psychotropic drugs that target aggressive behaviors (may include risperidone or aripiprazole)

→ **Of these, 40% had drug-refractory aggression**

1. Adlr et al., *Autism*, 2015; Matson et al., *Research in developmental disabilities,* 2014.

Clinical management of drug-refractory aggression in ASD varies widely

Of the patients with drug-refractory aggression…

Many patients had a trial of

- Risperidone 86%
- Aripiprazole 83%
- Quetiapine 43.4%
- Sertraline 41.5%
- Clonidine 32.1%
- Other SSRIs 24%

Few patients (<5%) had a trial of

- Alpha 2 agonists
- Benzodiazepines
- Typical antipsychotics
- Mood stabilizers
- Anticonvulsants

Additional research is needed to understand optimal treatment algorithms for drug-refractory aggression in ASD

Adler et al 2015

Atypical Antipsychotics: Targeting Irritability in ASD

Drug	Dosage	Sample Size	Type of Study	Results
Lurasidone	Once-daily, fixed doses of 20 and 60 mg/day	149 children	Randomized, double-blind, fixed-dose, placebo-controlled study	No significant improvement of the ABC-I
Olanzapine	10.7 mg/day (on average)	23 children	Open-label study involving two periods: a screening/washout period of about 2 weeks (period I) and a 12-week open-label therapy period (period II).	Showed significant improvement on three subscales of the ABC-I

1.Loebel, Antony, et al. "Lurasidone for the Treatment of Irritability Associated with Autistic Disorder." *Journal of Autism and Developmental Disorders*, vol. 46, no. 4, 11 Dec. 2015, pp. 1153–1163.
2. Loebel, A., Brams, M., Goldman, R. S., Silva, R., Hernandez, D., Deng, L., Mankoski, R., & Findling, R. L. (2016). Lurasidone for the Treatment of Irritability Associated with Autistic Disorder. Journal of autism and developmental disorders, 46(4), 1153–1163. https://doi.org/10.1007/s10803-015-2628-x

Atypical Antipsychotics: Targeting Irritability in ASD

Drug	Dosage	Sample Size	Type of Study	Results
Paliperidone	7.1 mg/day (on average)	25 adolescents and young adults	Prospective, 8-week open-label study	CGI-I Scale score of 1 or 2 (very much or much improved) and ≥25 % improvement on the ABC-I
Ziprasidone	98.7 mg/day or 1.7 mg/kg/day	42 children and adolescents	Retrospective open-label study, 10.8 month average	40% responders for improved CGI-I

1. Stigler, K. A., Mullett, J. E., Erickson, C. A., Posey, D. J., & McDougle, C. J. (2012). Paliperidone for irritability in adolescents and young adults with autistic disorder. Psychopharmacology, 223(2), 237–245. https://doi.org/10.1007/s00213-012-2711-3
2. Dominick, K., Wink, L. K., McDougle, C. J., & Erickson, C. A. (2015). A Retrospective Naturalistic Study of Ziprasidone for Irritability in Youth with Autism Spectrum Disorder. Journal of child and adolescent psychopharmacology, 25(5), 397–401. https://doi.org/10.1089/cap.2014.0111

Atypical Antipsychotics: Targeting Irritability in ASD

Drug	Dosage	Sample Size	Type of Study	Results
Quetiapine	294 +/- 78 mg/day (range 200-600 mg/day	19 youths	7-week, randomized, double-blind, placebo-controlled pilot study	Significant improvements in clinician-assessed CGI-S and CGI-I scales.

1. Connor, D. F., McLaughlin, T. J., & Jeffers-Terry, M. (2008). Randomized controlled pilot study of quetiapine in the treatment of adolescent conduct disorder. Journal of child and adolescent psychopharmacology, 18(2), 140–156. https://doi.org/10.1089/cap.2006.0007

Atypical Antipsychotics: Targeting Irritability in ASD

Aripiprazole, risperidone: Strong evidence for reducing irritability, self-injury, and hyperactivity. First line treatment, FDA-approved to target irritability in ASD.

Lurasidone: Limited evidence for reducing irritability. Randomized double-blind study found no difference in primary endpoint at 6-weeks.

Olanzapine: Evidence for reducing irritability in both double-blind and open label studies, but significant weight gain and sedation.

Atypical Antipsychotics: Targeting Irritability in ASD

Paliperidone and Ziprasidone: May be beneficial but larger trials are needed to establish efficacy and safety

Quetiapine: Mixed results so not recommended to target irritability

1. Deb, S., Roy, M., Limbu, B., Akrout Brizard, B., Murugan, M., Roy, A., & Santambrogio, J. (2023). Randomised controlled trials of antipsychotics for people with autism spectrum disorder: A systematic review and a meta-analysis. *Psychological Medicine,* 1-9. doi:10.1017/S003329172300212X

Walter – Case History

- **Walter is a 12-year-old male with Down Syndrome and Autism Spectrum Disorder, Level 3.**
- **He was recently taken to the ER for aggressive behaviors towards family, throwing feces, and destroying objects at home. He bites, hits, and throws things when upset.**
- **He was discharged from the ER on Aripiprazole 2.5 mg daily & 5 mg nightly and Depakote 250 mg twice daily.**
- **Mom and teachers continue to report daily aggressive behaviors when Walter gets upset, and teachers are having difficulty managing him.**
- **Mom discontinued Aripiprazole out of frustration, stating she felt like neither the ER nor outpatient physicians were helping her.**
- ***At this time, what would you have done?***

Walter – Treatment

- **Started Olanzapine ODT (Zyprexa Zydis) 5 mg twice daily + a 10 mg as needed dose for emergencies.**
- **Continued Depakote 250 mg twice daily.**
- **Agreed to not re-trial Aripiprazole due to mother's strong opposition.**
- **Psychoeducation and setting reasonable expectations discussed with mother.**

Walter – 4 Week F/U

- **Walter returned in 4 weeks, and Mom stated "it's like night and day."**
- **Aggressive outbursts have reduced from daily to less than 1 time per week.**
- **Intensity of outbursts has significantly decreased. She is able to better predict when an outburst will occur and has only needed to give the Olanzapine 10 mg as needed dose 3 times in 4 weeks.**
- **School has been very impressed with change in behavior, and teachers reported 0 incidents since changing regimen.**
- **While Walter stills throws his feces, Mom has come to understand that this behavior is more related to him being uncomfortable at having a dirty diaper than it is due to him being malicious.**

Maria – Case History

- **Maria is a 16-year-old female with Autism Spectrum Disorder, Level 3.**
- **Mom reported Maria has been physically aggressive and showed bruising all over Mom's body from being hit, grabbed, pinched, and shoved into walls at home.**
- **She is on a regimen of Risperidone 2 mg twice daily and Clonidine 0.1 mg twice daily.**
- **Despite this regimen, Maria's aggression has persisted multiple times every day both at home and at school. Mom has had to pick up Maria almost daily from school.**
- **Due to her distress and frustration, Mom has obtained and started filling out paperwork for admission to a residential treatment center.**
- ***Mother wants to know what options for treatment to manage maladaptive behaviors…***

Maria – Treatment

- **Started Chlorpromazine (Thorazine) 25 mg three times every day.**
- **Risperidone was decreased to 1 mg three times daily to decrease risk of eps.**
- **Clonidine 0.1 mg twice daily was continued.**

Maria – 6 Week F/U

- Maria returned for follow up after six weeks. When asked how she had been behaving, her mother said "I feel like I have my baby back!”
- Frequency of aggression had decreased to “0” episodes, and the intensity of anger has reduced.
- Now when Maria gets frustrated, it is expressed through crying instead of yelling and hurting people.
- She has not had any major incidents at school, and she is able to follow instructions at school without being dysregulated.
- Mom is no longer considering placement at a residential treatment center and feels that she is more confident as a parent and capable of providing care.

Case history presentation acknowledgement

Andrew Wang, MD, PGY-5, Child and Adolescent Psychiatry Fellow at Baylor College of Medicine.

Selective Serotonin Reuptake Inhibitors (SSRIs)

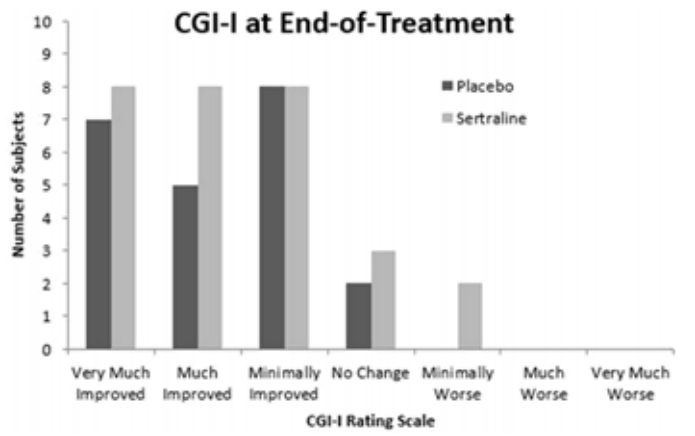
Drug	Dosage	Sample Size	Type of Study	Results
Citalopram[1]	10-20 mg/day (mean 16.5mg/day)	N = 149	Double-blind placebo RCT	Minor improvement in irritability subsection of ABC-C, but not clinically significant
Sertraline[2]	2.5 mg/day if under 4 years old, 5 mg/day if over 4 years old	N = 58	Double-blind placebo RCT	No significant behavioral change detected by ABC-C or VABS-II rating scales

1. King, B. H., Hollander, E., Sikich, L., McCracken, J. T., Scahill, L., Bregman, J. D., Donnelly, C. L., Anagnostou, E., Dukes, K., Sullivan, L., Hirtz, D., Wagner, A., Ritz, L., & STAART Psychopharmacology Network (2009). Lack of efficacy of citalopram in children with autism spectrum disorders and high levels of repetitive behavior: citalopram ineffective in children with autism. Archives of general psychiatry, 66(6), 583–590.
2. Potter, L. A., Scholze, D. A., Biag, H. M. B., Schneider, A., Chen, Y., Nguyen, D. V., Rajaratnam, A., Rivera, S. M., Dwyer, P. S., Tassone, F., Al Olaby, R. R., Choudhary, N. S., Salcedo-Arellano, M. J., & Hagerman, R. J. (2019). A Randomized Controlled Trial of Sertraline in Young Children With Autism Spectrum Disorder. *Frontiers in psychiatry*, *10*, 810. https://doi.org/10.3389/fpsyt.2019.00810

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Sertraline
- Fluvoxamine
- Citalopram
- Currently there is **insufficient evidence that SSRIs have any role** in treating aggression

A randomized control trial in children with ASD showed no benefit of sertraline compared to placebo



Source: Potter et al., *Frontiers in Psychiatry*, 2019

N-acetylcysteine (NAC)

- Proposed mechanism: N-acetylcysteine lowers glutamate levels which decreases cortical excitability
- Existing evidence suggests efficacy in improving irritability

Drug	Dosage	Sample Size	Type of Study	Results
N-Acetylcysteine [1]	900 mg weeks 1-4, 1800 mg weeks 4-8, 2700 mg weeks 8-12	N = 33	12- week double-blind placebo RCT	Significant improvement in irritability on ABC scale
N-Acetylcysteine [2]	600-900 mg/day	N= 50	10-week double-blind placebo RCT	Significant improvement in irritability on ABC scale

1. Hardan, A. Y., Fung, L. K., Libove, R. A., Obukhanych, T. V., Nair, S., Herzenberg, L. A., Frazier, T. W., & Tirouvanziam, R. (2012). A randomized controlled pilot trial of oral N-acetylcysteine in children with autism. Biological psychiatry, 71(11), 956–961.
2. Nikoo, M., Radnia, H., Farokhnia, M., Mohammadi, M. R., & Akhondzadeh, S. (2015). N-acetylcysteine as an adjunctive therapy to risperidone for treatment of irritability in autism: a randomized, double-blind, placebo-controlled clinical trial of efficacy and safety. Clinical neuropharmacology, 38(1), 11–17.

Amantadine

Proposed mechanism: NMDA receptor antagonist (non-competitive, weak) with neuroprotective and anti-inflammatory properties

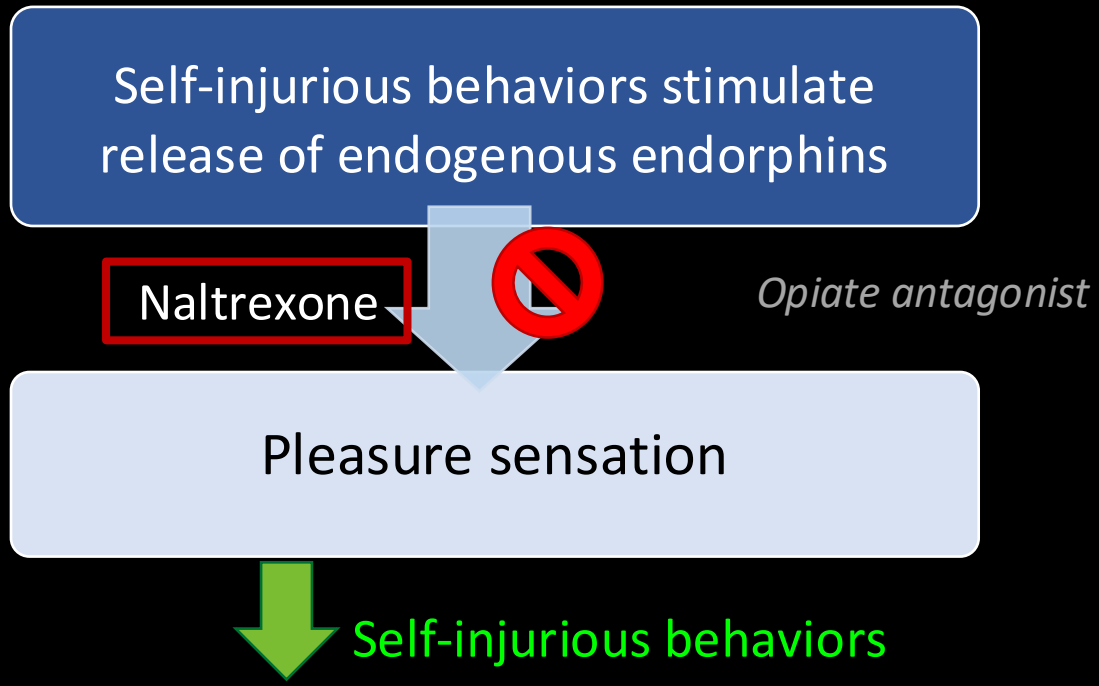
RCTs show mixed results on efficacy for decreasing aggressive behaviors

Drug	Dosage	Sample Size	Type of Study	Results
Amantadine [1]	100mg or 150mg per day depending on patient weight	N = 40	10-week double-blind placebo RCT	Significant improvement in irritability at 10 weeks, no significant improvement at 5-weeks (ABC scale)
Amantadine [2]	5.0 mg/kg per day	N = 39	4-week double-blind placebo RCT	No significant improvement in irritability on ABC scale

1: Mohammadi, Mohammad-Reza, et al. "Double-Blind, Placebo-Controlled Trial of Risperidone Plus Amantadine in Children With Autism." *Clinical Neuropharmacology*, vol. 36, no. 6, 2013, pp. 179–184, 10.1097/wnf.0b013e3182a9339d.
2: King, Bryan H., et al. "Double-Blind, Placebo-Controlled Study of Amantadine Hydrochloride in the Treatment of Children With Autistic Disorder." *Journal of the American Academy of Child & Adolescent Psychiatry*, vol. 40, no. 6, June 2001, pp. 658–665, 10.1097/00004583-200106000-00010.

Naltrexone

Mechanism:
Naltrexone is a reversible competitive antagonist at opioid receptor sites.



Sabus et al. *Pharmacotherapy*. 2019 June;39(6):645-664.

Shane – Case History

- 10 year old biracial male with history of ASD type 3 and ADHD combined type.
- He presented for evaluation because he had been treated by a prior psychiatrist with the following medications.
  - Risperidone 1 mg po BID
  - Guanfacine ER 1 mg po q am and Guanfacine IR in pm
  - Although frequency of aggressive outbursts towards mother, teachers had decreased, he was still hitting himself on the head multiple times a day when frustrated.

Shane
Case History
Slide 2

- Mother reports concerns that they will be reported to CPS because of his repeated head hitting. He is wearing arm restraints for many hours a day.
- Family history is also positive for anxiety and mood disorders.
- Discussed possibility of anxiety precipitating self injurious behaviors but mother reports that they cannot identify clear cut precipitants except for occasional removal of the IPAD.
- Decision was made to start Naltrexone 50 mg po q daily. He weighed 106 lbs so this was approximately 1 mg/kg day.

Shane-case study slide 3

- Follow up:
- Shane was seen after 4 weeks. Frequency of self hitting had decreased so he wore arm restraints far less frequently. Parents felt less concerned about potential head injury. Dose was increase to Naltrexone 50 mg po BID.
- He was seen for follow up at 6 weeks. Parents reported that ther was a dramatic reduction in self injury and they had used arm restraints only twice in the past week.

Naltrexone: Conclusions

- Evidence is limited, but RCTs (n = 4-41) found modest improvement or no improvement in irritability, aggression, and self-injurious behavior
- Given the limited neuropharmacologic options for children with ASD and SIB, reasonable to attempt therapy with naltrexone when other therapies have failed
- Dosing: recommended starting at 0.5 mg/kg daily and titrating up to 1.5-2 mg/kg based on response and/or adverse side effects. Typically well-tolerated with favorable safety profile.

1. Bolton et al. *BMC Med*. 2019;17(1):10.
2. Elchaar et al. *The Annals of Pharmacotherapy*. 2006;40(6):1086-95.
3. Roy et al. *Journal of Intellectual Disability Research*. 2015;59(4):293-306.
4. Persico et al. *Progress in Neuropsychopharmacology & Biological Psychiatry*. 2021;110:110326.

Alpha-2-agonists

- **Evidence on treating irritability and self-injury is limited**
- A number of small studies have demonstrated improvement with hyperactivity
  - Guanfacine: Posey et al,. 2004, Scahill et al, 2006, Scahill et al, 2015
  - Clonidine: Jaselskis et al. 1992, Fankhauser et al. 1992, Ming et al., 2008
- Important side effects
  - Neurological: Drowsiness, irritability, headache
  - Cardiovascular: Hypotension, bradycardia
  - Gastrointestinal: Constipation

1. Posey et al., *J Child Adolesc Psychopharmacol*. 2004; Scahill et al., *J Child Adolesc Psychopharmacol*. 2006; Scahill et al., *Am J Psychiatry*, 2015
2. Jaselskis et al., *J Clin Psychopharmacol,* 1992; Fankhauser et al., *J Clin Psychiatry*, 1992; Ming et al., *Brain Dev,* 2008

Lithium

The evidence for using lithium in treating aggression is limited

- Case series found improvement with mood disorders and manic symptoms in children with ASD, but not aggression or irritability

- Retrospective chart review (n=14) found that 73.7% of patients with ASD and maladaptive behaviors improved on lithium based on CGI-I rating

1. Cantiano et al., *Clinical Neuropharmacology*, 2015; Mintz M & Hollenberg E. *Psychopharmacology Bulletin*. 2019; Tatavarty et al. *Neuron*. 2020
2. Siegel M et al. J Child and Adolescent Psychopharmacology 2014;24 (7): 399-402

Anti-Epileptic Drugs (AEDs)

A few antiepileptics meds have shown potential to decrease irritability:

- Valproate
- Oxcarbazepine
- Topiramate

The current data is conflicting

- Small studies suggestive of improvement in irritability (e.g. Hollander et al. 2010, Belsito et al. 2001, Wasserman et al. 2006)
- Limited number of placebo-controlled studies either do not support or are inconclusive regarding anticonvulsant medicine for irritability in ASD

1. Canitano R. Clinical Neuropharmacology. 2015; Hollander et al., *Neuropsychopharmacology*, 2010
2. Belsito et al., *J Autism Dev Disord*, 2001
3. Wasserman et al., *Int Clin Psychopharmacol,* 2006

Clinical Recommendations & Monitoring when using atypicals

- **Begin with lowest effective dose; titrate slowly and reassess frequently.**
- **Baseline and periodic monitoring: weight, BMI, fasting glucose, lipids, blood pressure, prolactin as indicated.**
- **Use shared decision-making; combine medication with behavioral supports; plan for medication taper trials when stable.**

Practical Tips for Clinicians

Document target behaviors and baseline severity to measure response.

Frequency of angry outbursts, aggression, self injury
Frequency of use of prn medications

Set realistic goals (reduction in frequency/intensity, harm minimization).

Ask parents/caretakers to identify precipitants and work with behavioral therapists to work on ways to divert and find other safer ways to express frustration

Discuss side effects, long-term risks, and monitoring plan with families.

Summary

- Management of irritability, impulsive aggression and self injury can pose unique challenges to clinicians due to communication limitations, management of side effects and lack of FDA approved treatments.
- Pharmacological interventions can successfully reduce frequency of aggression, irritibility and self injury; however, benefits and risks need to be carefully discussed with the family and caregivers
- Therapies need to be tailored for each patient and may include multiple medications to address comorbid conditions.

The bottom line….

- **Atypical antipsychotics (risperidone, aripiprazole) have the strongest empirical evidence for short-term reduction of irritability in youth with ASD.**
- **Benefits must be balanced against metabolic and other adverse effects — monitor closely.**
- **Integrate medications into a multimodal plan emphasizing behavioral interventions and careful measurement.**

- *"Treating a child with autism can be challenging and humbling but is ultimately rewarding because managing maladaptive behaviors enables the child to improve learning and gain acceptance in the family and their community."*
- *Thank you for the work that you do for children with ASD*

Alice R. Mao, M.D.