

Managing Irritability/Aggression In The Context of IDD in Primary Care

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Objectives

- What is Irritability?
- Assessment Approaches
- Intervention
 - Safety
 - Crisis Services
 - Emergency Room Usage
 - Medication

Irritability/ Aggression: Case Illustration

- 14yo boy with ASD, non-verbal, with multiple, daily episodes of self-injury and aggression that include banging his head against hard surfaces, biting his wrist and shoulder, head butting, and “chinning.” Behaviors have been present since early childhood but more intense with onset of puberty 1 year ago. Worse at home and when constipated.



What do we mean by *Irritability*?

- Abnormal sensitivity
- Tendency to exhibit uncontrolled anger or aggression
- Up to 30% of children with autism have symptoms of irritability, including
 - 24.5% aggression
 - 30.2% severe tantrums
 - 16% deliberate self-injurious behavior (SIB)
 - Particularly problematic in young children
 - May be particularly challenging or dangerous in adolescence, especially among boys
- (Lecavalier JADD 2006)

What are the reasons people with ASD present?

- Easily frustrated (60%)
- Inattention (50%)
- Hyperactivity (40%)
- Temper tantrums (30%)
- Irritability (20%)
- Fearful/Anxious (13%)
- Harming self (11%)
- Destroying property (11%)
- Physical fighting (5%)

Most of That List Can Be Collapsed Into.....

“Irritability”



“Irritability”

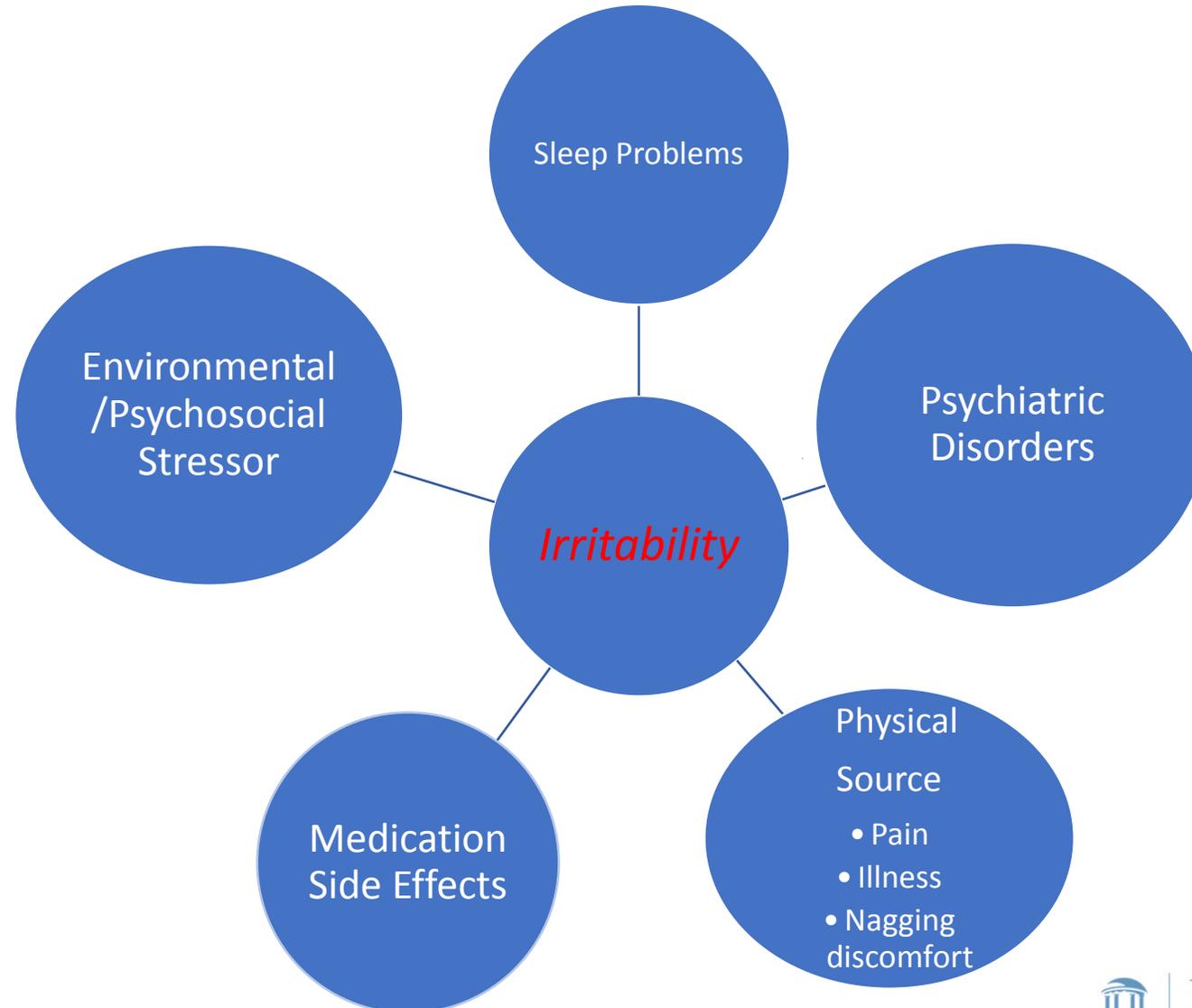
- Irritability in IDD/ASDs



- *This is a convenient way of lumping many problem behaviors into one category but it does not do justice to the complexity of any one of these challenges or their causes*
- *Two medications are FDA indicated for the treatment of “Irritability associated with Autism”*
 - Aberrant Behavior Checklist- ***Irritability Subscale***
- ***Associated? Yes***
 - *Dismissible? NEVER*



Irritability for Anyone



Irritability in I/DD or ASD



Guiding Principle:

Irritability

- Its NOT okay to try to treat “Irritability” in ASD/ IDD directly with medication *until*:
 - A systematic evaluation has been completed and alternative approaches trialed

OR

- Acute/sub-acute safety risks lead potential benefits to outweigh risks.
 - Meanwhile: ongoing assessment/consideration to other irritability drivers

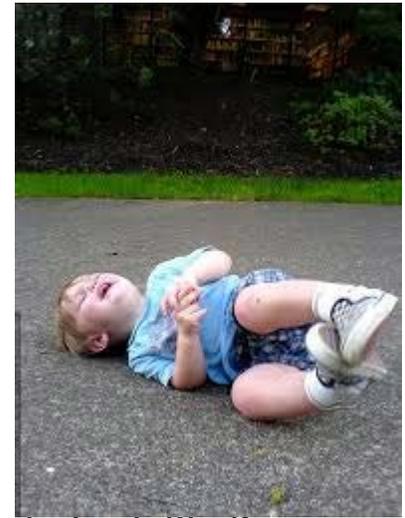
Assessment of Aggressive Outbursts/Agitation Episodes

- The first part of assessment is understanding the level of danger/risk to the patient and to others



Assessment of Severity/Safety

- Severity/Safety in Aggressive Outbursts
 - Understand the topography of the tantrum/outburst:
 - How often? How long? What happens?
 - What does the worst episode look like? What does the most minor episode look like?
 - Hitting of others? Who are the targets?
 - Parents, Siblings, Infants?
 - Property destruction?
 - Self-Injury via biting of self, hitting of self, head banging?
 - Extent of injuries to date?
 - Are eyes/orbits being hit, windows/glass broken?
 - Ears being hit? How hard? Bruising?
 - Is elopement/running part of the episode?
 - How far from home has the individual gone? Any close calls to date? Do they respond to verbal directions to stop? How often is this a component?
 - Is there any elopement/running not associated with an anger episode?
 - Are there any pools or bodies of water in the immediate area?



Assessment of Severity/Safety

- Severity/Safety in Aggressive Outbursts
 - What is the worst injury anyone has sustained?
 - How are extreme moments being handled by caregivers?
 - Is redirection to a safe place being used?
 - Is restraint being employed and by whom?
 - Is restraint placing patient or caregiver at risk for injury?
 - What if anything has been done to safety proof the environment/home:
 - Door alarms, adequate door locks?
 - Removal of projectiles from key areas?
 - Is there a fence in the yard?
 - Bodies of water in the immediate area?



Assessment of Severity/Safety



- Caregiver Health and Safety
 - Screen caregiver depression and anxiety
 - Any active treatment?
 - Screen caregiver suicidality
 - Passive suicidal ideation among highly stressed caregivers is common
 - Active suicidality is rare, but should be asked/inquired about
 - Screen for caregiver substance abuse/dependence
 - Do not rule out this possibility
 - There is emerging evidence that caregivers are increased risk for substance abuse especially in the context of high externalizing behaviors

Red Flags for Immediate Intervention via Emergency Services and/or Social Services

- Self-injury is getting worse and worse AND:
 - Mental status changes secondary to severe head banging
 - Ocular injury, auricular injury, dental injury
- Child is at imminent risk for accidental injury or death
 - Elopement, drowning
- Others in the environment are at high risk for significant injury by the patient
 - Example: an infant sibling in high chair has been knocked over during explosive outburst by the patient of interest
- Caregiver is at significant risk for self harm, suicide, harm to the patient or impaired and unable to provide care

Things to Keep in Mind

- The vast majority of these presentations are “*acute on chronic*” meaning a recent worsening of a longstanding explosive behavior challenge.
- Families may have a raised threshold for what constitutes an emergency because of their chronic exposure to very challenging behaviors.
- Families may be fearful of calling 911 for help or fearful about a potential negative experience in the emergency room.
- Many/most explosive episodes will remit in minutes to hours and having extra people in the immediate area maintains safety in the meantime.
 - The need for transportation from the office to the ED is rare.

Developing an Emergency Plan



- Does family work with some type of behavioral health agency already?
 - Do they know the emergency plan with that agency?
- Do they know how to contact mobile crisis support for their area in NC?
 - <http://crisissolutionsnc.org/>
 - 2 hour response time on average
- Calling 911
 - Be sure to request state special needs loved one and request a Crisis Intervention Trained (CIT) officer
 - <http://crisissolutionsnc.org/cit/>



Developing an Emergency Plan



- Going to the Emergency Room
 - Families should be guided to the closest ER
 - Some ERs have more comfort than others serving the IDD population
 - Families should understand that most ER visits for explosive behavior will NOT result in psychiatric or other admission
 - Families should understand that in the current resource climate, there will be significant time (days) spent in the emergency room prior to a disposition if it is determined admission is necessary.
 - Families should understand that in some situations, a psychiatric unit may be identified some distance from the patient's home.
 - Families should understand that the ER is a good place to rule out medical factors for the crisis, maintain safety, and determine need for admission.

Developing an Emergency Plan

- Talking with Social Services
 - Neglect, Abuse is unfortunately common in this realm.
 - Consider the possibility of abuse/neglect by caregivers, service providers, school staff, and/or group home providers.
 - Child Protective Services
 - By North Carolina County:
 - <https://www2.ncdhhs.gov/dss/local/index.htm>
 - Adult Protective Services via County Social Services
 - <https://www.ncdhhs.gov/documents/dss-county-directory>

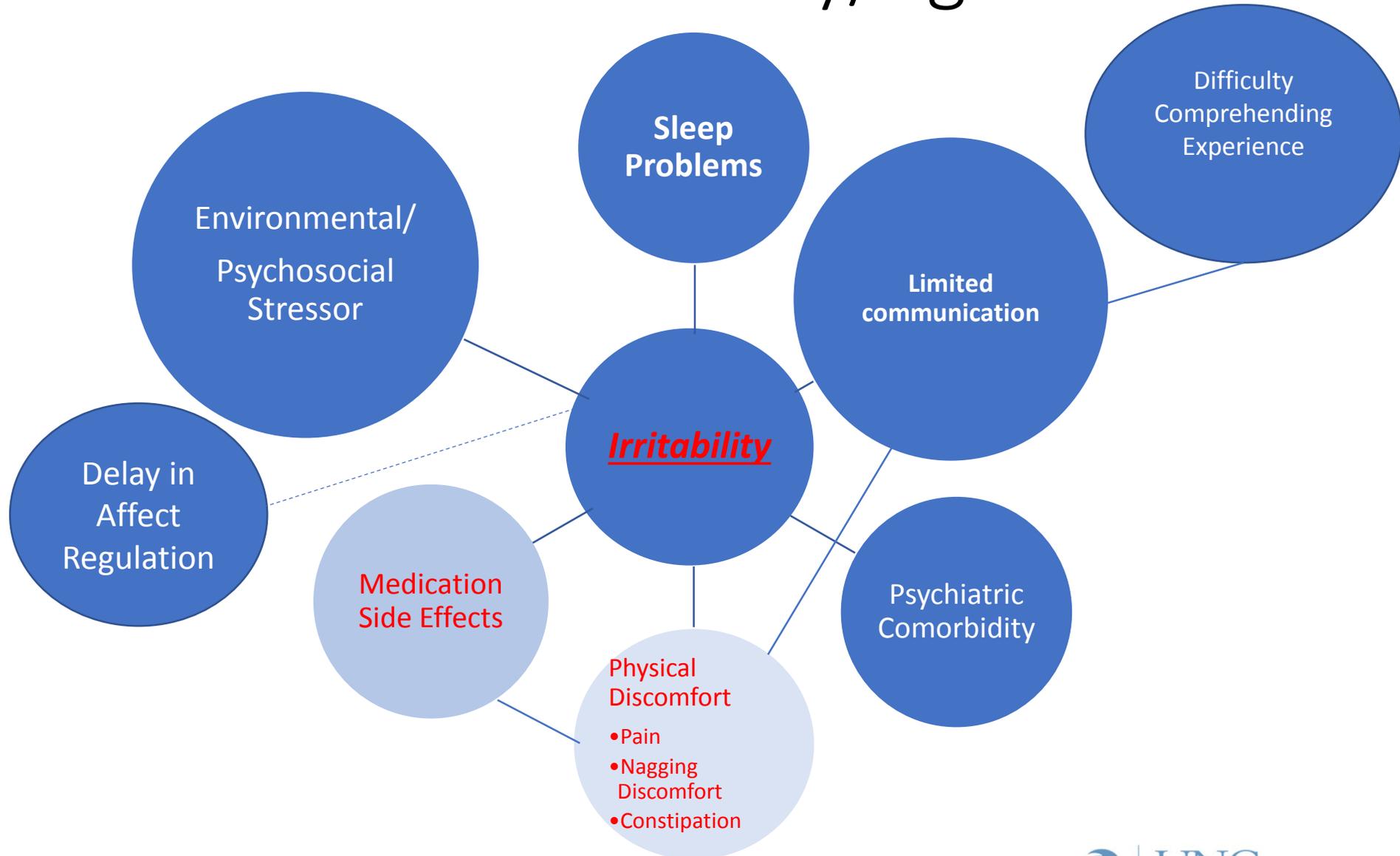


Further Assessment

- Consider this model of

“Irritability”

Potential Drivers of Irritability/Agitation



Further Assessment

- Explosive behavior/agitation crises are complex to sort out
- Often multi-factorial
- May be difficult to assess completely in a primary care setting.
- **Priorities for the Primary Care Provider :**
 - **1) Evaluate severity/safety**
 - **2) Rule out medical drivers**
 - **3) Develop an emergency plan and a next steps plan**

Further Assessment

- Top Medical Drivers of :

- Constipation/Encopresis
 - Often underestimated
- Pain
 - ENT
 - Dental
- Infection
 - Urinary
 - Pulmonary
- Insomnia
- Medication Side Effects
 - Psychostimulants (common culprit)
 - Selective Serotonin Reuptake Inhibitors (common culprit)

“Irritability”



Next Steps in Assessment:

The Ongoing Evaluation That Usually Must Happen Outside of Primary Care

- Environmental/Psycho-social stressors
 - Who? What? When? How Often?
 - Functional Behavioral Analysis
 - Avoidance, Attention Seeking, Sensory, Communication
 - *Inadvertent reinforcement by caregivers and teachers*
 - Demand expectations
 - Trauma
- Communication Function
 - Level
 - System being used-augmentative/alternative communication evaluation?
 - Extent of visual supports
- Psychiatric Co-Morbidity
 - Psychiatric Review of Systems
 - listening for “change”
 - Beware of diagnostic overshadowing

Intervention Plan:

“Irritability”

- Treat possible medical sources of **irritability**
- Consider the appropriateness ***of removal of*** or initiation of pharmacologic treatment with close follow up based on PCP comfort level/experience and/or DBP or psychiatric colleague input:
 - Call NC-Pediatric Access Line (NC-PAL) if you practice in Person, Granville, Vance, Warren, Franklin, and Halifax counties for assistance. (919)681-2909
 - <https://ipmh.duke.edu/content/ncpal>
 - If you are a physician in North Carolina who needs to speak with a UNC physician regarding your patient’s care you can call the Carolina Consultation Center’s toll free number at [1-800-862-6264](tel:1-800-862-6264) and be connected.

Guiding Principles:

“Irritability”

- Its NOT okay to try to treat **Irritability** in ASD/ IDD directly with psychiatric medication *until*:
 - A systematic evaluation has been completed and alternative approaches trialed

OR

- Acute/sub-acute safety risks lead potential benefits to outweigh risks.
 - Meanwhile:
 - Ongoing assessment/consideration to other irritability drivers
 - Resource optimization and treatment consideration



Guiding Principles:

“Irritability”

- There are no medications currently available with indication to treat core symptoms of autism.
- Only 2 medications have FDA approval to treat associated symptoms in ASD: Risperidone (ages 5-16) and Aripiprazole (ages 6-17), for severe *irritability*



Table 6 Level of evidence for primary target symptom(s)

Class	Agent	Primary target symptom(s)	Level of evidence
Alpha 2 Agonist	Clonidine	Hyperactivity	Insufficient evidence
	Guanfacine	Hyperactivity	Insufficient evidence
Antipsychotics	Aripiprazole	Irritability, hyperactivity, stereotypy	Established evidence
	Haloperidol	Behavioral symptoms	Established evidence
	Risperidone	Irritability, hyperactivity	Established evidence
	Risperidone	Repetitive behavior, stereotypy	Preliminary evidence
	Olanzapine	Global functioning	Insufficient evidence
Mood Stabilizers	Divalproex sodium/ valproic acid	Irritability	Insufficient evidence (conflicting results)
	Divalproex sodium/ valproic acid	Repetitive behavior	Insufficient evidence
	Lamotrigine	Irritability, social behavior	Insufficient evidence
	Levetiracetam	Irritability	Insufficient evidence
Norepinephrine reuptake inhibitor	Atomoxetine HCl	Hyperactivity	Preliminary evidence
Serotonin reuptake inhibitor	Citalopram	Repetitive behavior	Insufficient evidence
	Fluoxetine	Repetitive behavior	Insufficient evidence
	Clomipramine	Repetitive behavior, stereotypy, irritability, hyperactivity	Insufficient evidence
Stimulants	Methylphenidate	Hyperactivity	Promising evidence
Miscellaneous	Amantadine	Hyperactivity, irritability	Insufficient evidence
	Naltrexone	Social behavior, communication, indiscriminant learning, SIB	Insufficient evidence
	Naltrexone	Hyperactivity	Preliminary evidence
	Pentoxifylline	Irritability, social withdrawal	Preliminary evidence

Time to Update!!

Siegel M, Beaulieu AA. Psychotropic medications in children with autism spectrum disorders: a systematic review and synthesis for evidence-based practice. J Autism Dev Disord. 2012 Aug;42(8):1592-605. PubMed PMID: 22068820.

Treatment of Irritability/ Aggression: Risperidone

Risperidone:

- RUPP Autism Network study led to FDA approval in 2006 for treatment of severe irritability in ASD, ages 5-16.*
 - Multi-site RCT, N=101, children with ASD + irritability, ages 5-17
 - 8 week double-blind phase + 4-month open label phase, 21-month naturalistic follow-up
 - **69% response rate** (ABC-Irritability declined $\geq 25\%$, CGI=1 or 2) vs. 12% placebo response
 - **2/3 maintained benefit at 6 months; ongoing benefit at 21 months in most**
 - Common side effects: sedation, **weight gain**, elevated prolactin
 - **Average weight gain 5.6 kg (10.6% BMI increase) at 6 months**
 - No significant differences in EPS
 - **Long-term increased risk of excessive appetite, weight gain, enuresis (Aman et al 2015)**

Treatment of Irritability/ Aggression: Risperidone

Risperidone supportive trials:

- 8 wk RCT in Canadian ASD sample (Shea 2004): **54% response rate** (vs. 18% placebo), similar ABC-I reductions to RUPP trial (-56.9%, -64%).
- Several smaller RCTs and open-label trials support short-term **response rates of 57-72%**.
- **Addition of manualized parent training improves outcome scores, lowers optimal dose (Aman et al 2009).**
- Improvement in secondary measures of RRB, adaptive functioning, hyperactivity, social withdrawal, communication
- **Weight gain a prominent side effect in all studies**
- Long-term effects of elevated prolactin unclear



Treatment of Irritability/ Aggression: Aripiprazole

Owen et al (2009):

- 8 wk RCT, N=98, ages 6-17, with ASD + irritability, flexible dosing up to 15 mg/d
- Most (74%) taking 5-10 mg/d at study endpoint
- Significant but modest improvement on ABC-Irritability (ES=0.87)
 - Mean 8-wk ABC-I score only slightly lower than entry threshold score
- **Overall response rate 52.2%** (vs. 14.3% placebo response)

Owen R, et al. Pediatrics. 2009 Dec;124(6):1533-40.

IRRITABILITY:

Evidence Based Expectations for Antipsychotics

- Aripiprazole^{*,**}
 - Mean Improvement on ABC-Irritability among responders ≈ 12-14 pts.
 - Mean difference relative to placebo ≈ 6 pts*
 - Mean Weight Gain ≈ 4.4 lbs over 8 weeks
- Risperidone^{**}
 - Mean Improvement on ABC-Irritability among responders ≈ 15 pts.
 - Mean Weight Gain ≈ 5.7 lbs over 8 weeks (12.3 lbs @ 6 months)
- 25-30% “responder rate” (at least 25% improved)

*Ching H, Pringsheim T. Aripiprazole for autism spectrum disorders (ASD). Cochrane Database Syst Rev. 2012 May 16

**Politte LC, McDougle CJ. Atypical antipsychotics in the treatment of children and adolescents with pervasive developmental disorders. Psychopharmacology (Berl). 2014 Mar;231(6):1023-36.

Treatment of Irritability/ Aggression: Summary

- Always evaluate systematically
- Always engage behavioral therapy/environment modification/communication first or concurrently
- Consider alpha-2 agonists for meltdowns/ outbursts and low level aggression
- Risperidone or aripiprazole for severe aggression or SIB
- Consider ziprasidone as “third line”: if excessive weight gain with risperidone or aripiprazole
- Very limited evidence for anti-epileptics
- Standard metabolic monitoring with atypicals
 - Lipids, fasting glucose or HgbA1c every 6-12 months
 - Weight, BMI at every visit
- Assess for symptoms of increased prolactin (risperidone only)
 - Baseline and annually; consider blood levels annually
- Be mindful of particular challenges in weight management in ASD
- MOVEMENT OBSERVATION/EXAM



Treatment of Irritability/ Aggression: Aripiprazole

Aripiprazole side effects (across trials):

- Sedation and somnolence most commonly reported
- **Weight gain prominent (1.3-2 kg at 8 weeks)**, but magnitude not as great as in risperidone trials
- **Treatment-emergent movement concerns in 15-23%**
 - **Comparted to 8-12% for placebo**
- Vomiting, drooling also common
- **Decline in mean serum prolactin** from baseline
- **HDL declined in 30%**, elevation in other lipids and glucose less common
- No significant heart rhythm changes

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Beware!

- START LOW, GO SLOW
- CHANGE ONE MEDICATION AT A TIME
- BE PATIENT – THINK LONG TERM
- PRNS are to be avoided!!!
- DISCONTINUE/WEAN AT REGULAR INTERVALS TO ESTABLISH CONTINUING NEED
- BE PREPARED TO TRY AN INEFFECTIVE MEDICATION AGAIN AT A LATER DATE

Intervention Planning



- Begin process of resource attainment:
 - Assure relationship with appropriate Managed Care Organization (MCO) if he/she has Medicaid.
 - <https://www.ncdhhs.gov/landing-page/clone-lmemco-directory>
 - This is important because the MCO is the gateway for several services:
 - North Carolina (START) Systemic, Therapeutic, Assessment, Resources, and Treatment
 - Region Map: <https://files.nc.gov/ncdhhs/NC%20START%20Regional%20Map.pdf>
 - Adult: Direct referrals possible to the appropriate START center
 - Pediatric: Referrals for children should be made to the LME-MCO by calling them directly
 - Consider also leaving child's name with START Center directly as a back up
 - More information on the START program here: <https://www.centerforstartservices.org/locations/north-Carolina>
 - Access to NC Developmental Centers if needed is a long process but must start with the MCO
 - <https://www.ncdhhs.gov/divisions/dsohf/murdoch-developmental-center-0>

Murdoch Developmental Center



Wrapping Up

- The majority of crisis presentations in IDD relate to explosivity or irritability and are acute on chronic presentations
- Assess the medical/physical drivers of irritability and treat when possible
 - Don't forget about psychiatric medications could be part of the problem
- Connect to appropriate resources:
 - Managed Care Organization
 - Mobile Crisis
 - NC START
 - Psychiatry
 - TEACCH
 - ABA
- Use the ER sparingly, but when safety is clearly compromised
- Consider starting psychiatric medication treatment based on comfort level if appropriate

Other Helpful Resources

- **SAFETY**

- <http://nationalautismassociation.org/big-red-safety-box/>

- **Challenging Behaviors**

- <https://www.autismspeaks.org/tool-kit/challenging-behaviors-tool-kit>

- **How to access Behavior Therapy/ ABA via Medicaid/EPSDT:**

- <https://www.autismsociety-nc.org/guidance-on-medicaid-and-epsdt-regarding-autism-treatment/>

