Management of Aggression and Irritability in Autism: Family and Clinical Perspectives

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Outline and Objectives

- Present a family experience (15 minutes)
- Provide a clinical perspective on that encounter (5 minutes)
- Background on Irritability and Aggression in ASD (10 minutes)
- Assessment (10 minutes)
- Treatment (10 minutes)
  - Recommendations
  - Algorithms
- Resources
- Questions and Discussion — Family, Drs. Pierri and Winkeller (10 minutes)

Family Experience

- One family's encounter with a change in behavior
  - Family member and family background
  - What were things like before?
  - What happened?
  - How was it addressed?
- How is day to day life going now?

Clinical Perspective

- Clinical comment:
  - MW is a person with non-verbal, level 3 autism spectrum disorder
  - Prominent neurological challenges — treatment resistant epilepsy
  - Gastrointestinal challenges
  - Insomnia — sleep continuity disturbance
  - Communication difficulties
  - Need for assistance across multiple domains of self-care — feeding, toileting, dressing, mobility, self-engagement in recreational activities, daily routine, medication, 24 hour assistance required
  - Probable psychiatric comorbidity of bipolar disorder.
- The context of the challenge of irritability and aggression in autism.

Background

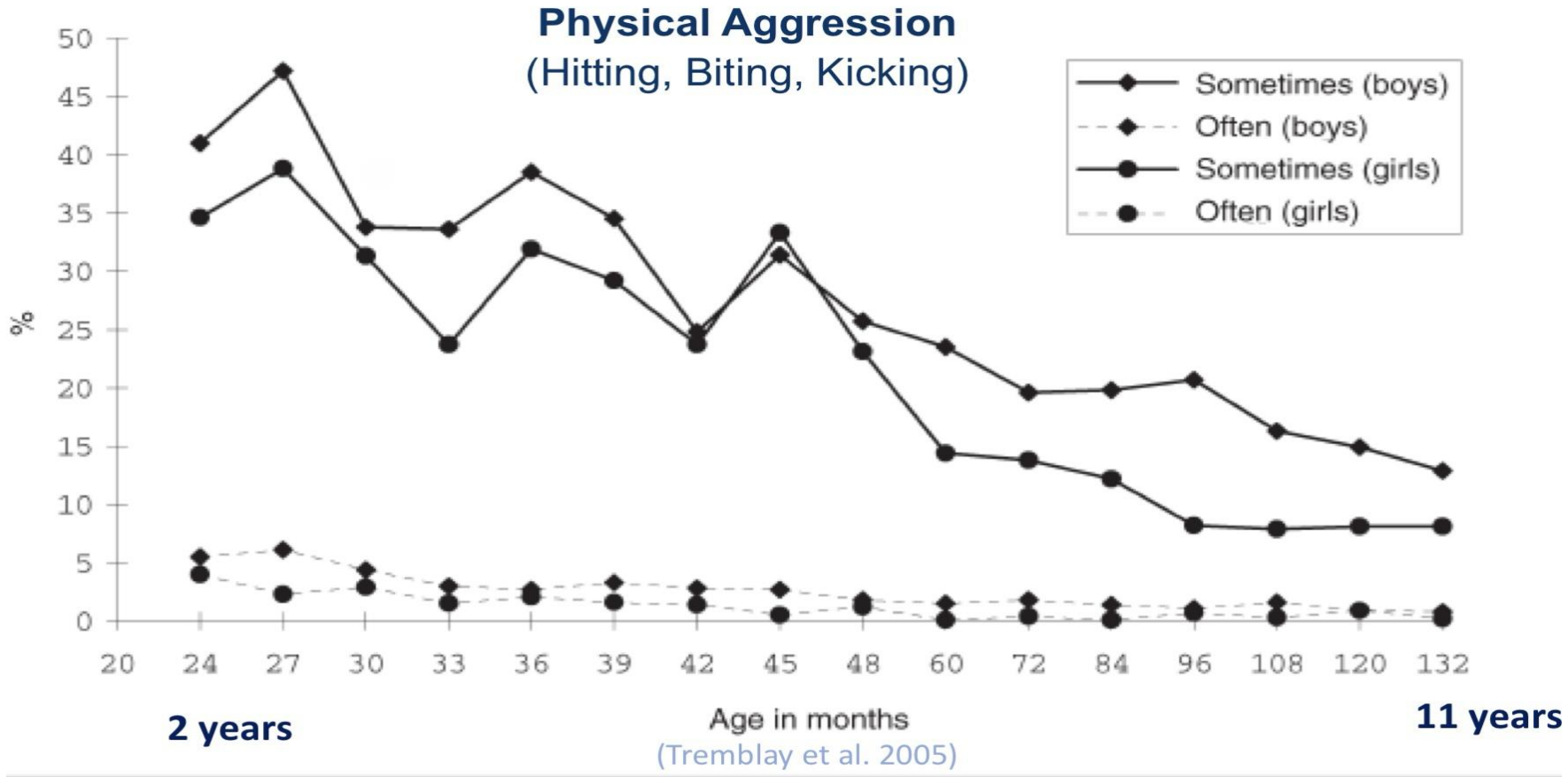
- Children and adults with ASD often present with irritability and/or emotion dysregulation
  - Difficulties regulating emotions appropriately and effectively
  - Limited control over temper
  - Excessive response to stimuli
- What does this look like? (Aberrant Behavior Checklist – Irritability items)
  - Tantrums
  - Temper problems
  - Aggression
  - Mood lability
  - Self injury
  - Screaming
  - Crying
  - Irritability — negative reactivity to the internal and external world

Aggression in Typical Development

- Often observed in young children — "terrible twos"
  - Most toddlers engage in occasional physical aggression
- Aggression occurs throughout childhood
  - Highest in toddlerhood
  - Declines from preschool through adolescence
    - Declines from 50% to 15%, boys maybe greater than girls
  - By age 5, most children develop skills that enable them to inhibit aggression
    - Sharing, turn taking, communicating wants and needs
  - 5% percent of toddlers engage in frequent aggression and 2% of 11 year-olds do

(Broidy et al., 2003; Côté et al., 2006; Nagin & Tremblay, 1999; NICHD, 2004; Tremblay 2005)

Aggression in Typical Development



(Tremblay et al. 2005)

Emotion Dysregulation in Autism Spectrum Disorder

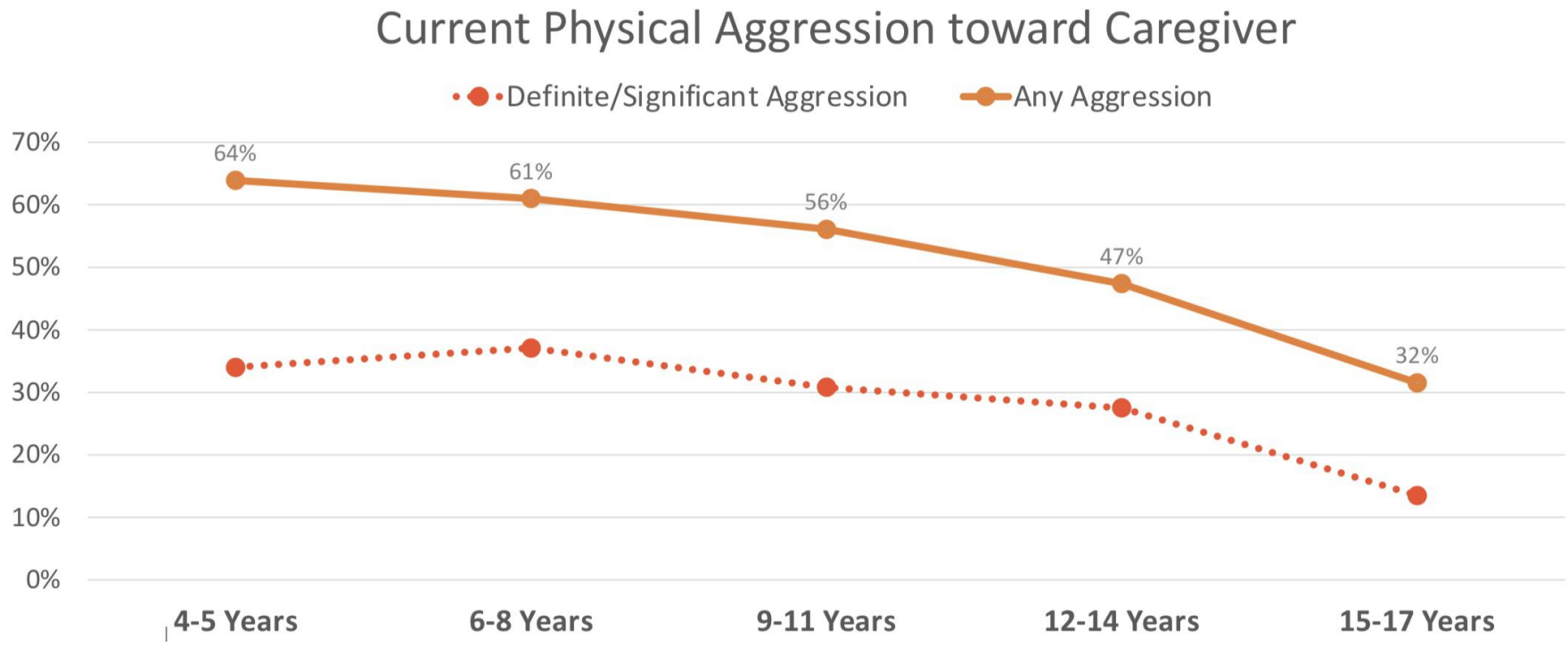
- Impaired social functioning
  - Limited verbal and social communication and problem solving
- Repetitive behaviors — limited behavioral repertoire and behavioral flexibility
  - Stereotypies
  - Ritualized behaviors
  - Insistence on sameness
- Sensory problems — vulnerability to discomfort, external, internal
  - Hypo or hyper-sensitive
  - Any sensory modality
- Intellectual disability — increase challenges in living
- Challenges in executive function

Theories of Aggression

- Physiological arousal — sensitive flight or fight response
  - Heart rate and blood pressure
  - Autonomic dysregulation
- Sensory and emotional discomfort
  - Sensory
  - Anxiety
  - Sadness
  - Pain
  - Anger
  - Shame
- Social – social demands, crowds, etc.
- Non-preferred activities

Aggression in Autism Spectrum Disorder

Kanne and Mazurek 2011
("Definite" — physical aggression intended to harm)



Incidence in Autism Spectrum Disorder

- >50% with significant emotion dysregulation
- 20% with moderate to severe levels of irritability and/or aggression *(Fung et al 2016)*
- Aggression toward caregivers – *(Kanne and Mazurek 2013)*
  - **65% to 32%, ages 4 to 17**
  - Girls as much or more than boys

Reasons for Aggression in Autism

- Reinforced — operant learning
  - Behaviors maintained by consequences
- Learned from others — social learning and learning history
  - Observing and imitating others
- Limited coping skills
  - Impairments in social cognition and information processing
  - Projected and acted on scripts and attributions

Effects of Aggression on Caregivers

- Families
  - Physical harm and injury
  - Stress, anxiety, and depression
    - Trauma syndromes
  - Social isolation, reduced social support
  - Financial costs — persons, property
- Teachers and direct care staff
  - Physical harm and injury
  - Stress and burnout
    - Trauma syndromes
  - High turnover

(Estes et al. 2009; Hastings & Brown, 2002; Jenkins et al. 1997; Lecavalier et al. 2006; Tomanik et al. 2004)

Effects of Aggression on Individuals with Autism

- Consequences — risk for progressive impairment
  - Decreased opportunity to participate in learning, recreational, and vocational opportunities
  - Frequent adverse and negative social experiences
    - Physical restraint and negative feedback from the environment
  - Trauma syndromes
  - Less participation in community activities
  - High risk for:
    - Physical injury
    - Psychotropic medication and polypharmacy
    - Psychiatric hospitalization
    - Institutional placement — forms of incarceration
    - Poor long-term outcomes

(Jacobson & Ackerman, 1993; Logan et al. 2015; Mandell, 2008; Tsakanikos et al. 2007)

Types of Aggression in Autism

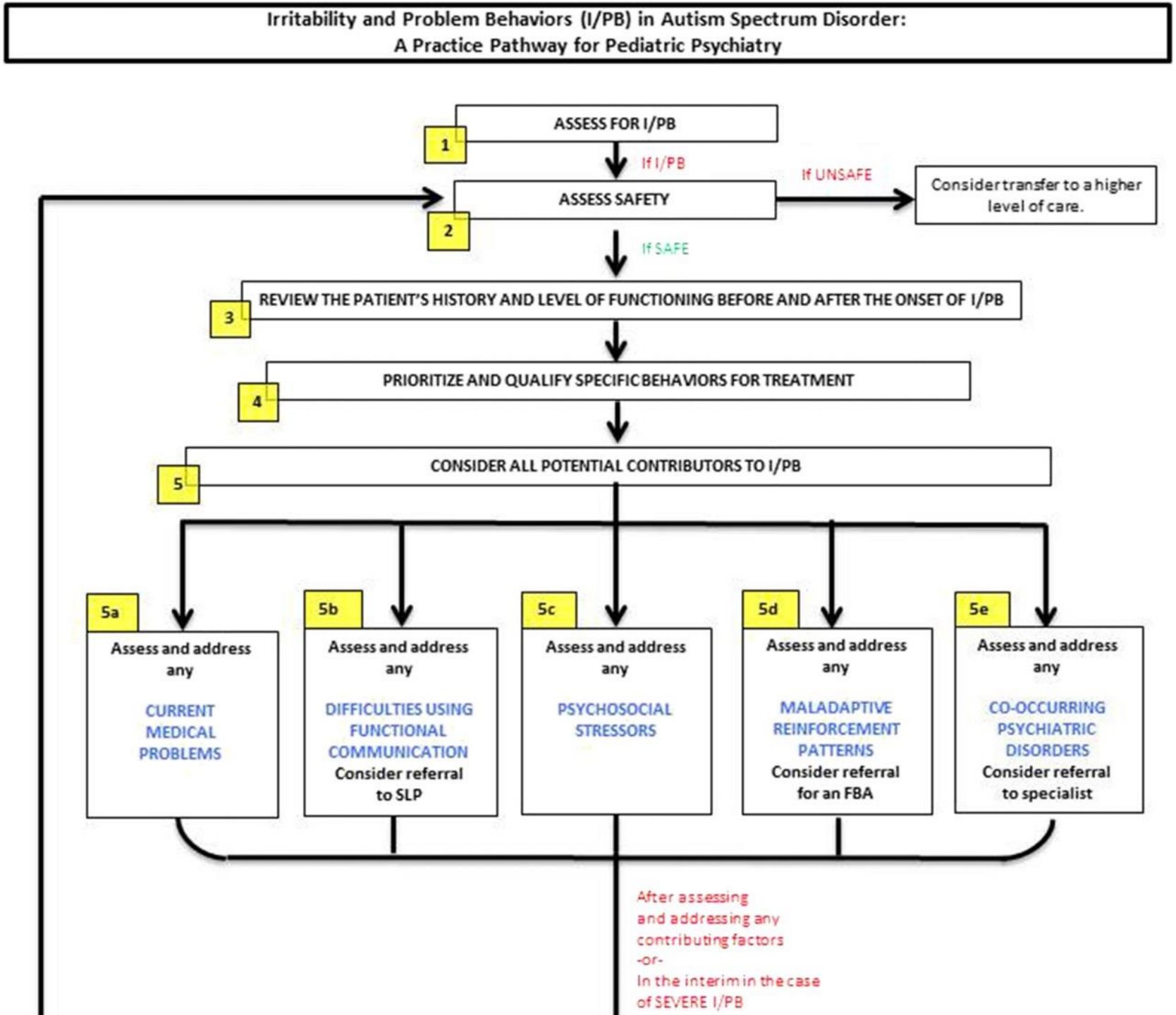
- Impulsive aggression
  - Impaired impulse control
  - Difficulties with regulating
    - Emotion
    - Arousal
    - Behavior
- Planned aggression
  - Impairments in social problem solving
    - Threats
    - Revenge

Co-occurring Conditions in Autism Associated with Aggression

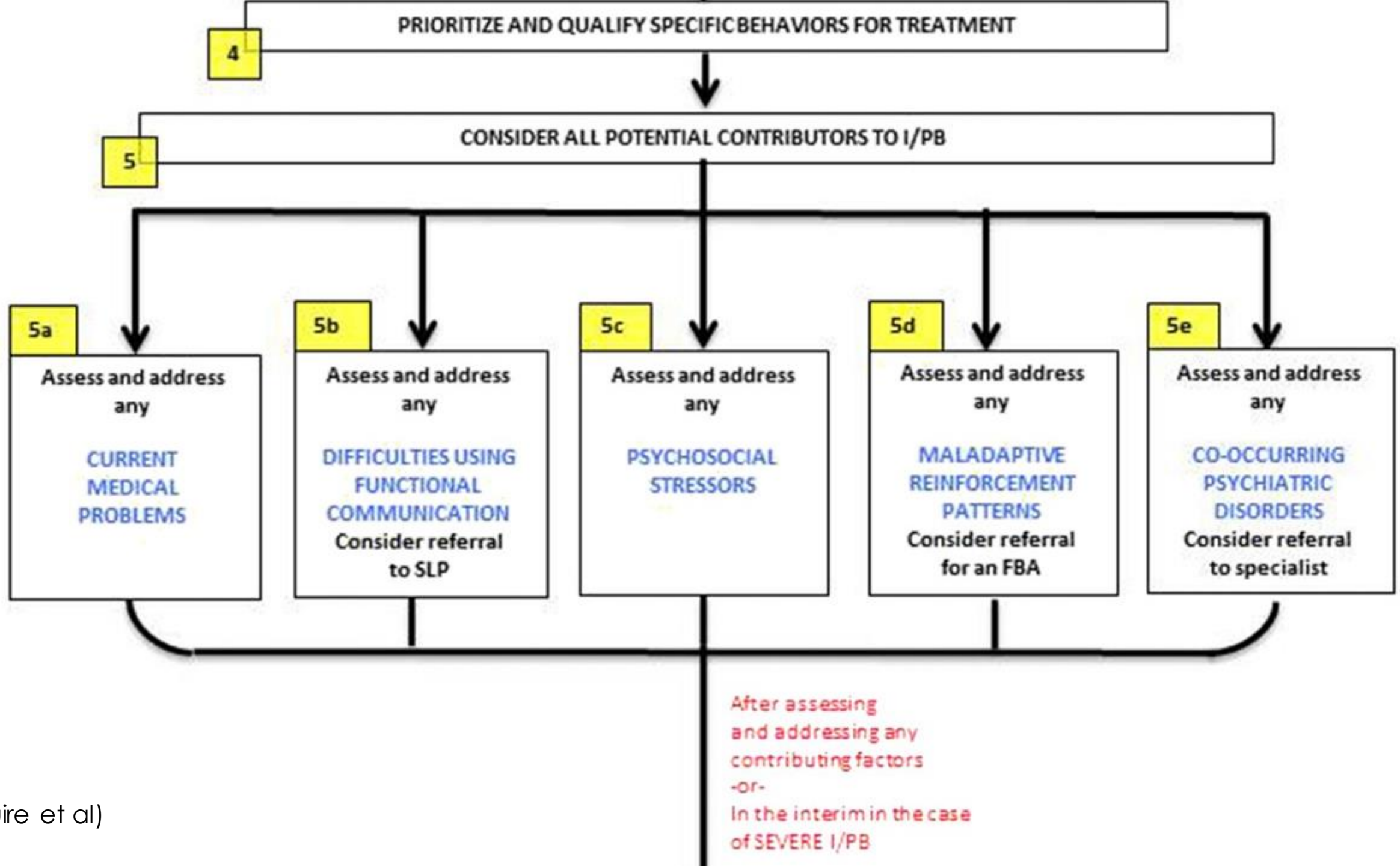
- Sleep problems
- Non-psychiatric medical
  - Constipation
  - Dental
  - Seizures
  - Infection
- Psychiatric co-morbidity
  - ADHD
  - Mood disorders
  - Anxiety disorders
  - Psychotic illness
  - Catatonia

Assessment and Treatment Planning

- Careful assessment and formulation
- Consider
  - Safety — level of care and support needed
  - Assess type, severity, frequency, and duration of aggression
  - Contributing factors
    - Health conditions –neurological, GI, ROS, etc..
    - Stressors – bereavement, social losses, environmental changes
    - Communication challenges
- Treatment approach
  - Comprehensive and family centered — caregiver support
  - Behavioral and psychosocial options
  - Pharmacotherapy



(McGuire et al)



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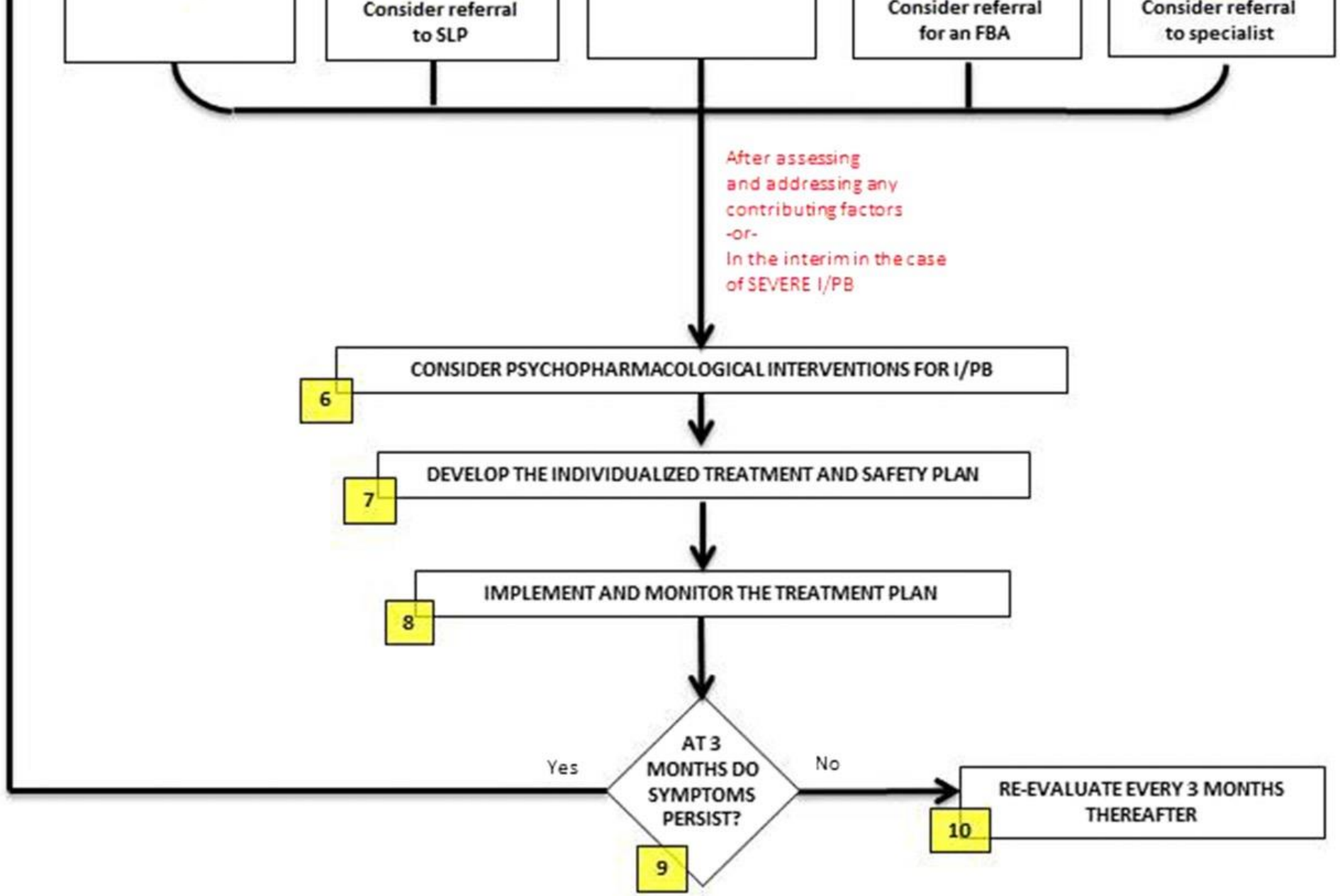


(McGuire et al)

Treatment Overview

- Behavioral interventions
  - Prevention strategies
  - Skill instruction
  - Reinforcement of appropriate behavior
- Pharmacotherapy
  - A primary or secondary option depending on acuity and co-morbidity
  - Best used in combination with behavioral intervention as part of a comprehensive family centered plan

Behavior Assessment
Functional Behavior Analysis (FBA)

- Determine factors that contribute to behavior
  - Interview parents, caregivers, and teachers
  - Direct observation across settings
  - Test conditions
- Setting, A, B, Cs
  - Antecedent
    - Event(s) before a behavior
  - Behavior
    - What happens?
  - Consequence
    - What happens after a behavior?

Purpose and Function of Behavior

- Get something
  - Desired object or activity
  - Attention
  - Food
- Avoid something
  - Non-preferred activity
  - Pain or discomfort
  - Demand
  - Situation

Interventions – Antecedent Management

- Changing antecedents
  - Prevention – trigger management
  - Prompt desired behavior
  - Examples
    - Choices
    - Organizing the environment
    - Visual supports
    - Predictable routines

Interventions - Reinforcement

- Reinforce different behaviors
  - Reinforce desired behavior
    - Alternative "replacement" behavior
      - Remove reinforcement of problem behavior
    - Incompatible behavior
    - Other behavior
- Functional communication training
  - Teach and reinforce appropriate communication skills
  - PECS
  - Communication devices — iPads, dedicated communication devices

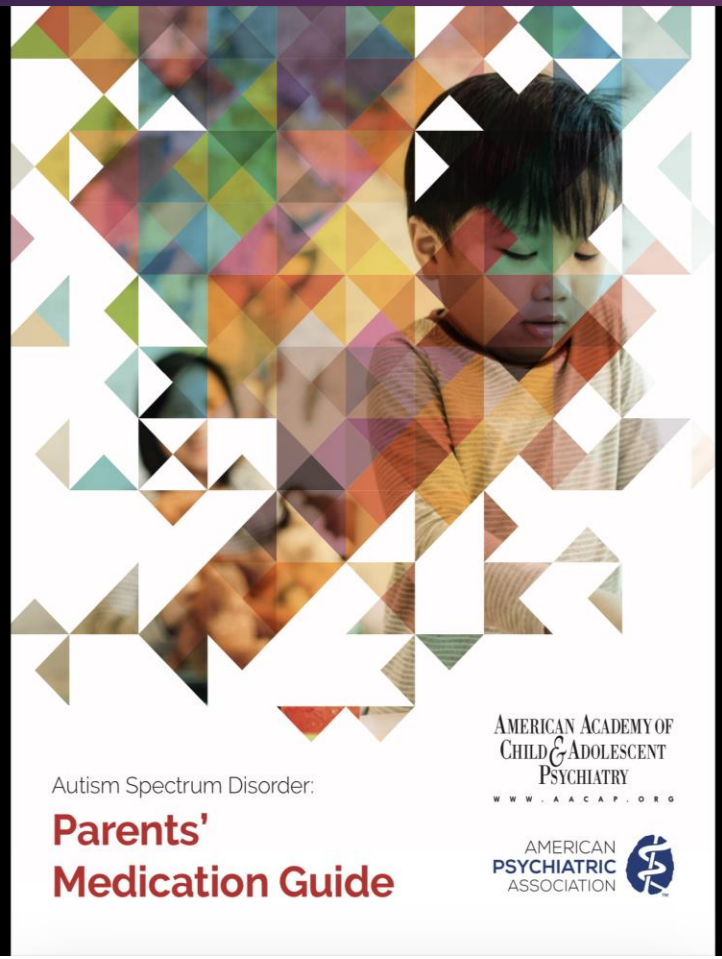
Other Interventions

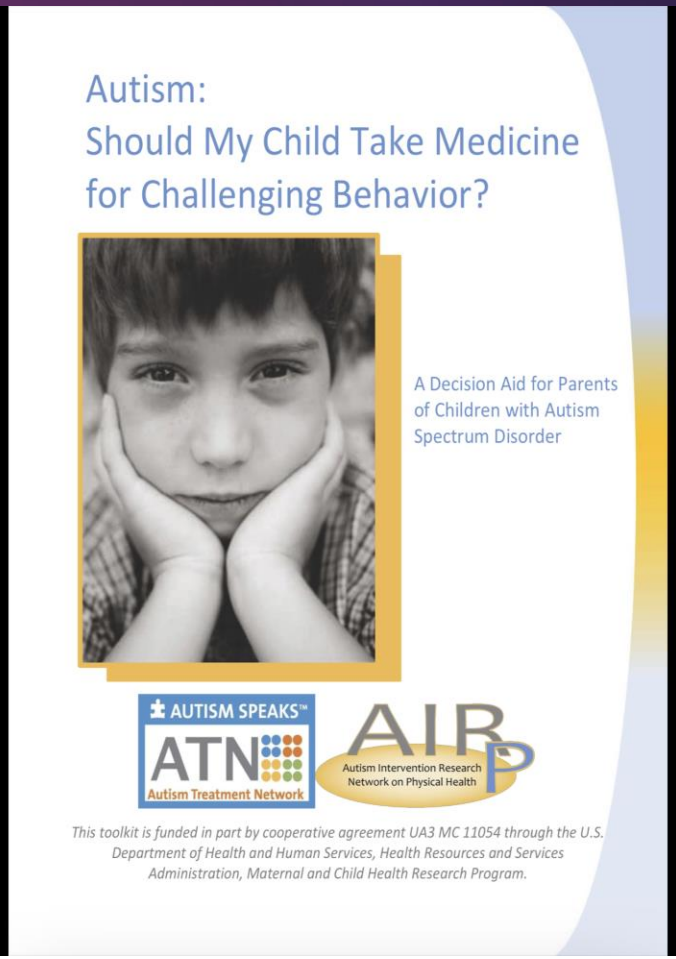
- Parent management training
  - CST — Caregiver Skills Training
  - PCIT — Parent Child Interactive Training
- Psychosocial therapies
  - CBT – Cognitive Behavioral Therapy
  - Mindfulness based approaches
- Group therapies
  - Social skills training — Peers, Wonderkids
  - "Regulating Together"
    - Caregiver and child group training

Irritability and Aggression Treatment Algorithm

- Primarily ASD related irritability
  - Mild — verbal and physical threats without intent
    - Behavioral interventions
  - Moderate — non-injurious physical aggression — persons and property
    - Alpha agonist, stimulant, atomoxetine, SSRI
  - Severe — aggression that causes physical injury
    - Risperidone or aripiprazole

Parent Guides





Autism_Spectrum_Disorder_Parents_Medication_Guide.pdf (aacap.org)

ATN/AIR-P Medication Decision Aid | Autism Speaks

Pharmacologic Pearls

- Antipsychotics (risperidone and aripiprazole) and medications used for ADHD (stimulants plus nonstimulants) were significantly more efficacious than placebo for emotional dysregulation and irritability
- Severity associated with greater improvements and a better benefit to risk ratio
- The evidence on the efficacy of opioid antagonists, diuretics, fatty acids, neuropeptides, and mood stabilizers for emotional dysregulation and irritability in ASD is currently insufficient *(Salazar de Pablo et al)*
- Irritability may be a primary presenting symptom of….
  - ADHD, anxiety disorders, obsessive compulsive disorder/behavior, depression, mania

Pharm Treatment Considerations

- Review current vitamins and meds, including complementary and alternative treatments especially if considering a psychotropic medication
- Go particularly low and slow
- More likely to be sensitive to side effects and have lower response rates (especially true for stimulants, SSRIs)
- *Goal is to improve quality of life and functioning with minimal risk and realistic expectations*

Alpha Agonists

- Indications:
  - ADHD, aggression, impulsivity, oppositionality, hyperactivity, sleep disturbance, repetitive and restrictive behaviors
  - Evidence for treating hyperactivity, impulsivity, emotional dysregulation
- Consider as first line especially for young patients, If growth concerns and/or with comorbid sleep issues
- Side effects include fatigue, irritability, hypotension, constipation, headaches, rebound cardiac issues
- Monitor BP and HR after initiation and before dose changes

Alpha Agonists

- Evidence:
  - Clonidine – small RCT
  - Guanfacine ER – RCT
  - 8 week trial, N=62, multisite, CGI response 50% vs. 9%; CYBOCS 24% vs. 1%
- Starting doses:
  - Guanfacine IR (Tenex): 0.5mg QHS for 1 week, then 0.5mg BID
  - Guanfacine ER (Intuniv): 1mg
  - Clonidine: 0.05mg qHS for at least 1 week
  - Clonidine ER (Kapvay): 0.1mg qHS

Stimulants

- At short-term follow-up, ADHD-related medications may reduce irritability slightly (SMD −0.20, 95% CI −0.40 to −0.01; 10 studies, 400 participants; low-certainty evidence), which may indicate a small effect. No effect on self-injury. No data reported on aggression (*Iffland et al)*
- Evidence for improving hyperactivity and inattention in individuals with ASD (which may improve irritability but evidence on this is limited)
  - Strong evidence for the use of methylphenidate (Ritalin)
  - No studies involving other stimulants, such as Adderall, though likely have a similar response rate
- Side effects include appetite suppression, insomnia, irritability, sadness, social withdrawal
- Monitor heart rate, blood pressure, weight, growth
- Consider using IR formulations first to assess tolerability and response

SSRIs

- Limited evidence but that doesn't mean no role
- Considerations for use
  - Variable response for treating repetitive behaviors or obsessive compulsive phenomena that is primarily a symptom of ASD
  - Per 2016 *Pediatrics* article SSRIs can be tried for anxiety in ASD
  - Depression when persists despite behavioral interventions and/or severe enough and/or when utility of/access to therapy is limited
- Side effects beyond what is standard for this medication class include increased rates of activation, irritability, impulsivity, hyperactivity, insomnia, disinhibition in those with ASD

Risperidone and Aripiprazole

- FDA approved for irritability and aggression in ASD
- Cochrane Reviews
  - Jesner OS, Aref-Adib M, Coren E. Risperidone for ASD. 2007
  - Hirsch LE, Pringsheim T. Aripiprazole for ASD. 2016.
- Meta-Analysis
  - Fung LK, Mahajan R, Nozzolillo A, et al. Pharmacologic Treatment of Severe Irritability and Problem Behaviors in Autism: A Systematic Review and Meta-analysis. Pediatrics. 2016;137(s2)
- Used with caution for severe symptoms given significant side effect profiles
  - Metabolic, restlessness, movement disorders, sedation

Risperidone

- Most studied – 3 RCTs; over 350 subjects
- Irritability, aggression, hyperactivity, and other
- Longer term follow up study
- Combined parent training and risperidone
- Dosing 0.25 to 4 mg, possibly higher
  - Half-life – 24 hours, steady state 4 – 5 days
- Hyperprolactinemia – peaks and levels off with time, remains high
- Weight gain
- EPS, sedation
- Metabolic labs baseline and 3 – 6 months thereafter
- AIMS

Aripiprazole

- 2 RCTs and long-term data < 300 subjects
- Effect comparable to risperidone
- Improves irritability, aggression, and hyperactivity
- Dosing 2 – 15 mg, possibly higher
  - 75 hour half-life, steady state 12-15 days
- Lowers prolactin
- Weight gain
- EPS and sedation
- Monitor metabolic labs
- AIMs

Clinical Case

Resources

- Autism Speaks Tool Kits
- Challenging Behaviors
  - https://www.autismspeaks.org/toolkit/challenging-behaviors-tool-kit
- Medication Decision Aids
  - https://www.autismspeaks.org/tool-kit/atnair-p-medication-decision-aid
  - https://www.aacap.org/App_Themes/AACAP/Docs/resource_centers/autism/Autism_Spectrum_Disorder_Parents_Medication_Guide.pd

Citations

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