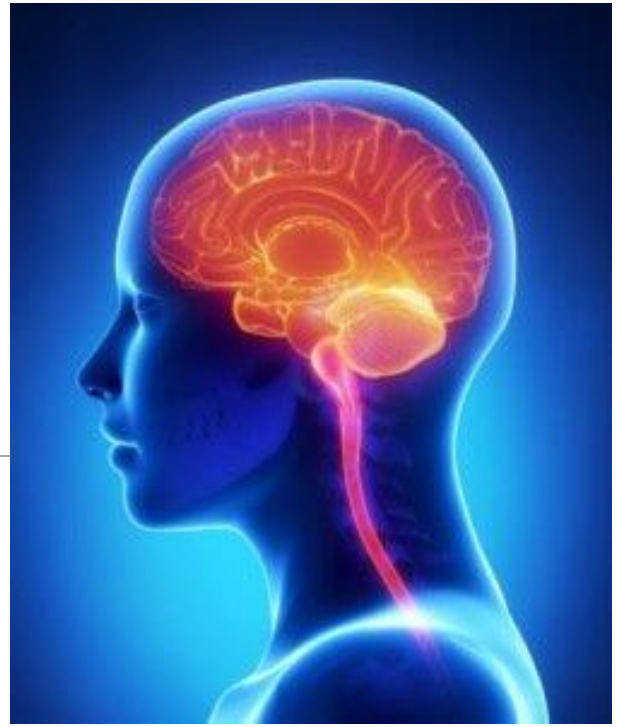
Psychiatric Disorders and Pharmacotherapy in Autism Spectrum Disorders

CHILD & ADOLESCENT MENTAL HEALTH

ECHO PROGRAM

JUNE 11, 2020



CASSIE KARLSSON MD

ASSISTANT PROFESSOR OF CLINICAL PSYCHIATRY

INDIANA UNIVERSITY SCHOOL OF MEDICINE

Overview

- Diagnosis of Comorbid Psychiatric Disorders
- Recognizing Side Effects
- The art of titrating and tapering
- Practice Questions

Common Comorbid Conditions in ASDs

- Intellectual Disability
- Seizure disorders
- **Mood Disorders**
- **Anxiety disorders**
- **ADHD**

ASD & Psychiatric Comorbidity

- Comorbid psychiatric illness is common
  - One study showed 72% of children with ASDs across intellectual abilities were found to have 2 or more comorbid psychiatric diagnoses (Leyfer et al, 2006)

  - Psychiatric comorbidity increases the level of impairment
    - Increased behavioral problems
    - Social relationship impairment
    - Decline in general functioning

Mood Disorders (Depression & Bipolar Disorder)

- Prevalence in ASDs unclear, may be increased risk
  - Higher rates of mood disorders in parents of children with ASDs (Mazefsky et al, 2008)
  - Significant psychosocial stressors (especially in higher functioning individuals aware of their social deficits)

  - Avoiding Overdiagnosis:
    - Emotion regulation is highly variable in this population: mood swings does not necessarily equal mood disorder or bipolar disorder
    - Consider baseline functioning – does this represent a qualitative/quantitative change vs. temperamental in nature?
    - Rule out underlying medical issues

Anxiety Disorders

- Often considered the most common comorbid diagnosis - 40% comorbidity rate, has been cited up to 80% (Simonoff et. al, 2008)
- Important to gather history from multiple sources, as anxiety can manifest differently in different environments, particularly in younger children
- Children often do not indicate internal distress and anxiety building up until reaching the “peak

Anxiety Disorders

- Increases in these symptoms in ASDs may be evidence of anxiety:
  - Repetitive questions or statements
  - Activity, hyperactivity, or restlessness
  - Temper tantrums
  - Crying
  - Withdrawal from or avoidance of situations
  - Aggression
  - Self-injurious behaviors
  - Stereotypies, repetitive movements or behaviors

(Autism Comorbidity Interview, ACI, Lainhart)

Attention-Deficit/Hyperactivity Disorder

- Considered common in ASDs (often diagnosed prior to ASD diagnosis)
- Important to consider the individual's mental age – how developmentally inappropriate are the ADHD symptoms?
- Differentiate from other potential etiologies that might affect attention – intellectual disability, learning disorder, hearing impairment, anxiety, mood disorder, etc.

Oppositional Defiant Disorder

- Should be diagnosed conservatively in ASDs
- Misdiagnosis of ODD leads to a misunderstanding of what is causing behaviors (ie purposeful, manipulative), and potentially ineffective treatment interventions
- Difficulty with change and insistence on routine are not generally considered “defiant” behaviors in ASD
- Annoying others is “purposeful” in ODD, and those with ASDs may not be aware their habits/behaviors annoy or impact others

Factors Complicating Psychiatric Diagnosis in ASDs

- Assessing individuals across all levels of intellectual and language abilities
- Psychiatric comorbidity in ASD poorly understood, may present/manifest differently – limited evidence
- Time-intensive assessment (parent, teacher, and self-report; clinical interview and observation)
- Difficult to distinguish ASD-related impairment from comorbidities, especially for non-episodic disorders

Targeting Treatment

- Etiology of ASDs thought to involve complex interactions between multiple genetic and environmental factors
- Few medications and limited evidence base for treating symptoms associated or comorbid with autism, and none that effectively treat core symptoms
- Behavioral interventions are the most successful approaches for treating core symptoms and improving outcomes in people with ASDs

Pharmacotherapy in ASD: Review Articles

Pharmacotherapy to Control Behavioral Symptoms in Children With Autism
Carolyn A Doyle [1], Christopher J McDougle
2012 Aug;13(11):1615-29. doi: 10.1517/14656566.2012.674110. Epub 2012 May 3.

Psychopharmacological Interventions in Autism Spectrum Disorder
Robert E Accordino [1], Christen Kidd [2], Laura C Politte [3], Charles A Henry [4], Christopher J McDougle
2016;17(7):937-52. doi: 10.1517/14656566.2016.1154536. Epub 2016 Mar 7.

Pharmacological Management of Behavioral Disturbances in Children and Adolescents With Autism Spectrum Disorders
Martine Lamy [1], Craig A Erickson [2]
2018 Oct;48(10):250-264. doi: 10.1016/j.cppeds.2018.08.015. Epub 2018 Sep 24.

Recognizing Medication Side Effects

- **Antipsychotics**
  - Akathisia
  - Extrapyramidal symptoms (cogwheel rigidity, tardive dyskinesia
  - Metabolic syndrome (weight gain, elevated lipids, elevated glucose/A1C)
  - Decrease in White Blood Cells
  - Sedation
  - QTc prolongation
  - Constipation
- **SSRIs**
  - Agitation/Aggression
  - Insomnia or sedation
  - GI upset
  - Headaches
  - Can see EPS/akathisia with SSRIs

Stimulants

Agitation/Aggression (may see a spike when the medication is wearing off)
Insomnia
Decreased appetite
Emotional Lability
High blood pressure/cardiac arrhythmia
Hallucinations

Benzodiazepines

Paradoxical reaction – agitation/aggression/insomnia
Sedation

Alpha-2 Agonists

Sedation
Low blood pressure and heart rate
Irritability
Enuresis/constipation
Dizziness/headaches

Titrating and Tapering – Tips for Success

TITRATION

- Think about starting at LOW doses, and waiting for longer periods of time before increasing the dose
  - Medications are often discontinued due to side effects before ever having a chance to be effective, forever to be listed as a “failed trial” or “adverse reaction”
  - There is often a sense of urgency to have a medication work quickly, but no time is saved if the patient has side effects, the med has to be stopped, and a new med started
    - Examples: When I hear about increased aggression on antipsychotics, I am always suspicious about side effects, and always ask what dose was started, and how quickly titrated
    - What dose ranges would you start in a child/adolescent with a neurodevelopmental disorder?

      Risperidone (0.25 to 0.5mg once daily before increasing to BID)

      Aripiprazole (1-2 mg daily before increasing to BID)

      Sertraline (12.5 mg)

      Fluoxetine (2.5 to 5 mg)

      Methylphenidate (2.5 to 5 mg)

Tapering Antipsychotics

- Cholinergic rebound
  - Symptoms may be severe but relatively brief and predictable- nausea, vomiting, restlessness, anxiety, insomnia, fatigue, malaise, myalgia, diaphoresis, rhinitis, paraesthesia, GI distress, headaches and nightmares.

- Withdrawal dyskinesia (within 4-6 wks of discontinuation)
  - Constant general chorea (can involve face/limbs/vocalizations)
  - Will usually resolve on it's own over time
  - More severe cases may require treatment (usually restarting low dose of antipsychotic and tapering more slowly)

- How to avoid withdrawal symptoms?
  - **Reduce dose by 25% every 1-2 weeks**. May need to be smaller reductions at the end of the taper. If worsening symptoms, consider holding off for longer before further reduction.

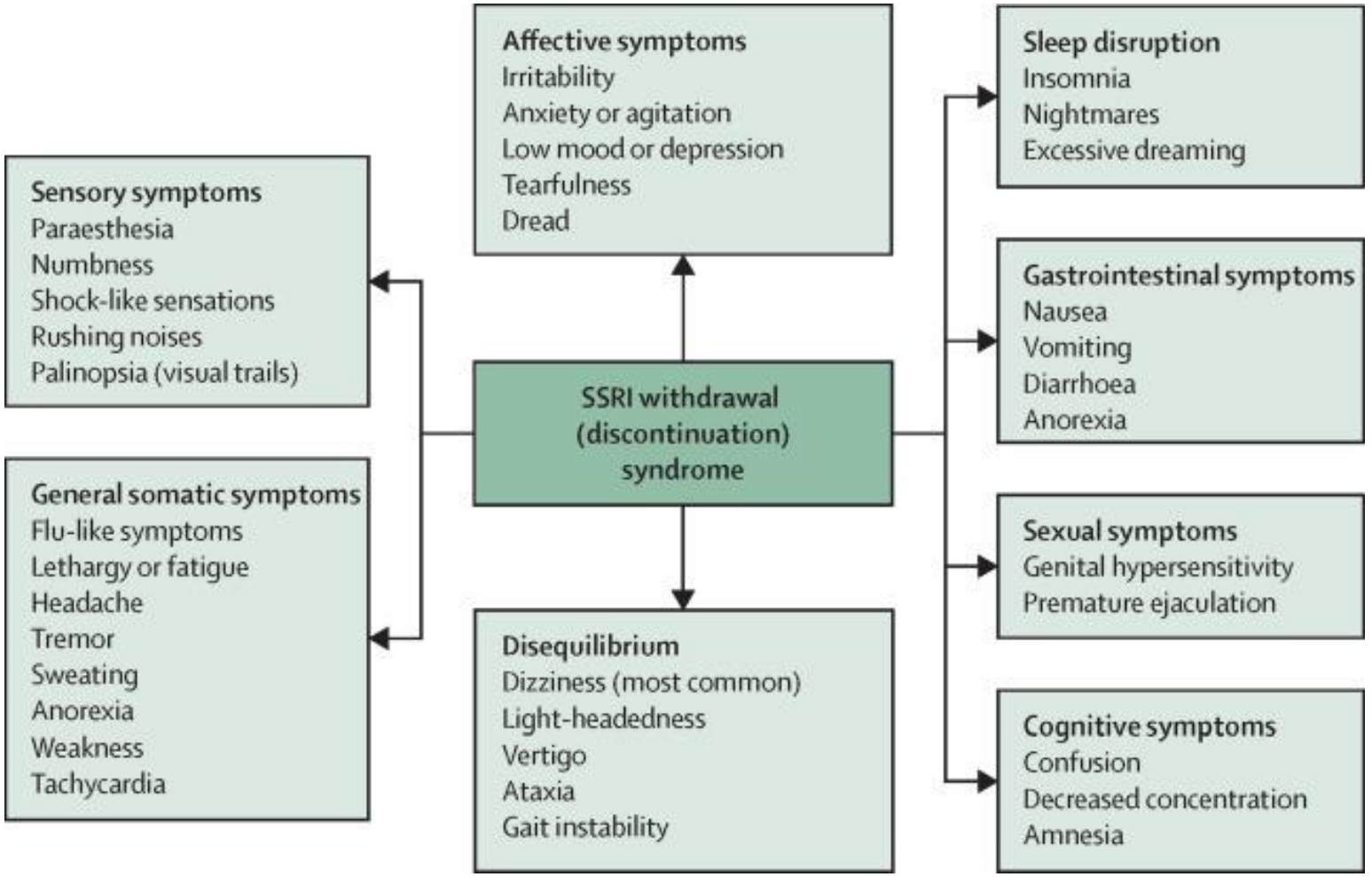
Tapering SSRIs

Withdrawal symptoms can LOOK LIKE recurrence of depression and anxiety.

Studies have shown that brief tapers over 2-4 wks minimally better than abruptly stopping SSRIs in terms of withdrawal symptoms.

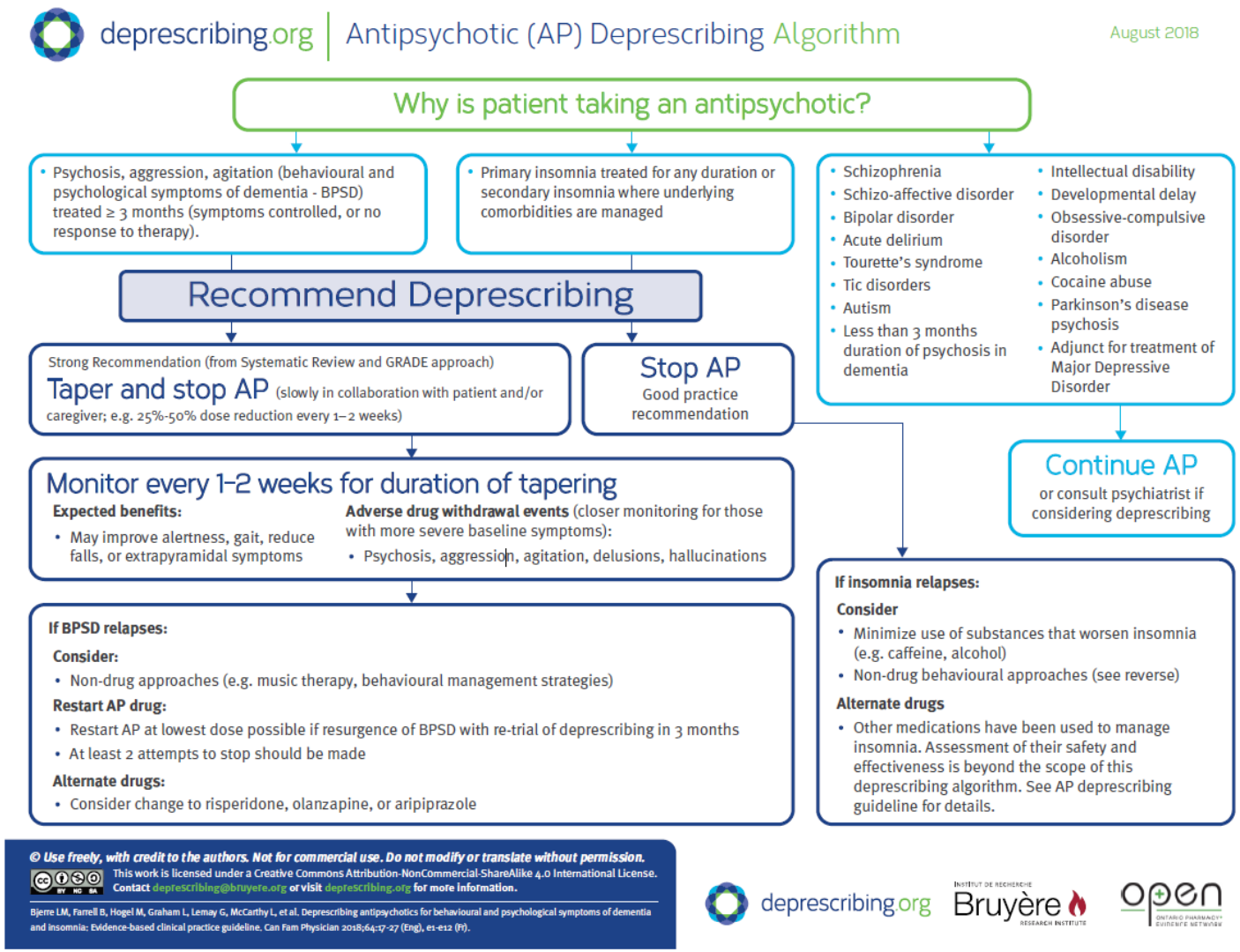
How to Avoid Withdrawal Symptoms?

Reduction by 25% every 2+ wks, likely need to reduce by smaller amounts toward the end of the taper.



Horowitz & Taylor. The Lancet. March 2019.

Deprescribing.org




PrACTiCE

Quiz

No specific medications are available or FDA approved for treating the core symptoms of Autism Spectrum Disorders

A. True
B. False

Answer: TRUE

- No medications approved or with evidence-based effectiveness in treating “core symptoms” of ASDs.

Only 2 medications are FDA-approved for behavior related problems associated with Autism in children:

- **Risperidone & Aripiprazole** – atypical antipsychotics used for the symptomatic treatment of irritability in autism, which includes aggression, deliberate self-injury and temper tantrums.

- Most medications used for symptomatic treatment of ASDs are prescribed “off-label”.

Quiz

Children with Autism Spectrum Disorders often require higher doses of medications to achieve similar results seen in typically developing children

A. True
B. False

Answer: False

- Children with ASDs are more likely to respond to lower doses of medications, and have a higher risk of side effects to common medications used in pediatric psychiatric populations.

Medications to use cautiously in children with ASDs:

- **Benzodiazepines** – increased risk of disinhibition, confusion
- **Stimulants** – increased risk of agitation/side effects, and less efficacious at treating ADHD symptoms than in typically developing children
- **SSRIs** – less efficacy in decreasing repetitive-type behaviors (ie OCD symptoms) than in the general population, and are more poorly tolerated in children with autism (ie activation)

CASE VIGNETTE

You are seeing a 7 yr-old child diagnosed with an ASD in your clinic. His parents are concerned that he has seemed more anxious and angry over the last few months and "cannot sit still". His teachers are beginning to wonder if he has ADHD in addition to Autism, and his parents think they might be right. He is even having trouble adhering to his visual schedules, which have been so helpful in the past. His parents feel distraught – things seemed to be so much better after Aripiprazole was added to treat his severe aggression several months ago, and now things are going down hill again.

Which of the following is the <u>most</u> important to recognize when treating or referring this child?

A. He has developed ADHD and needs appropriate treatment immediately to preserve recent progress at home and school.

B. He has become accustomed to his low dose of Aripiprazole, and needs an increase in dose in order to preserve his recent progress at home and school.

C. He may be having a medication side effect.

Answer: C

Recognizing Akathisia:

- Characterized by agitation, increased restlessness, driven behavior, insomnia, dysphoria, impulsivity – can include aggressive behaviors, self-injurious behaviors, even suicidality

- Prevalence ~30% in people prescribed antipsychotics in the general population, estimated much higher in children and in individuals with developmental delays

- Often misdiagnosed as ADHD, mania, psychotic agitation, or anxiety

- Children - especially those with developmental delays - have difficulty articulating this feeling of internal distress

Answer: C

What to do?

- Consider akathisia anytime your patient is experiencing these symptoms on an antipsychotic
- Be cautious when increasing antipsychotic dose - worsening “target” symptoms may be evidence of akathisia
- Consider lowering antipsychotic dose – stopping abruptly increases risk of emergent withdrawal syndrome/abnormal movements

- **Even if you are not the person prescribing these medications, recognizing these symptoms can have a significant impact on your patient’s quality of life, functioning and outcome.**

Thank you!