

Autism Spectrum Disorder and Medication Management

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Disclosures

- None financial
- Will discuss off-label use of medications

Objectives

- Review different classes of commonly used medications that target impairment impacting autistic children
- Explain current literature on leucovorin
- Share further learning opportunities

Neurodiversity Approach to Autism

- *Neurodiversity-Oriented Approach to Address Autism Wandering as a "Problem Behavior" in Pediatrics*
 - Use inclusive language that is non-stigmatizing and does not cause additional stress
 - Engage individuals as well as families as experts in their health during routine visits

➤ **Table of standard medication choices & potential side effects**

Background

Medicine Type	Target Behaviors	Possible Side Effects	
Stimulant Medicines			
<ul style="list-style-type: none"> • methylphenidate (Ritalin, Metadate, Concerta, Methylin, Focalin, Daytrana) • mixed amphetamine salts (Adderall) • dextroamphetamine (Dexedrine) • lisdexamfetamine (Vyvanse) 	Hyperactivity Short attention span Impulsive behaviors	Common: Problems falling asleep Less appetite Irritability/emotional outbursts	Less common: Anxiety Depression Repeating behaviors/ thoughts Headaches Diarrhea Social withdrawal Changes in heart rate Tics
Alpha Agonist Medicines			
<ul style="list-style-type: none"> • guanfacine (Tenex, Intuniv) • clonidine (Catapres, Catapres TTS, Kapvay) 	Hyperactivity Short attention span Impulsive behaviors Sleep problems Tics	Common: Sleepiness Irritability	Less Common: Aggression Less appetite Low blood pressure Constipation
Anti-Anxiety Medicines			
<ul style="list-style-type: none"> • fluoxetine (Prozac) • fluvoxamine (Luvox) • sertraline (Zoloft) • paroxetine (Paxil) • citalopram (Celexa) • escitalopram (Lexapro) 	Depression Anxiety Repeating thoughts Repeating behaviors	Common: GI problems (nausea, vomiting, constipation, low appetite) Headaches Problems falling asleep Sleepiness Agitation Weight gain	Less common: Seizure Thoughts of harming self Suicide Serotonin syndrome
Second Generation/ Atypical Antipsychotics			
<ul style="list-style-type: none"> • risperdone (Risperdal) • olanzapine (Zyprexa) • quetiapine (Seroquel) • aripiprazole (Abilify) • ziprasidone (Geodon) 	Irritability Aggression Self-injury Tantrums Sleep problems High activity level Repeating behaviors Tics	Common: Sleepiness Drooling Increased appetite/ weight gain	Less common: High blood sugar, diabetes High cholesterol Tardive dyskinesia (abnormal movements) Quetiapine – eye side effects Ziprasidone- heart side effects

Background



- This is a VERY QUICK discussion about the numerous medication used to address impairment
- Due to time constraints, will not discuss these VERY IMPORTANT aspects of autism and common co-existing conditions
 - Biological basis
 - Diagnostic process
 - Evidence-based therapies
 - Psychosocial support needed
 - How to address med SE

FDA approved specifically re: Autism

- 2nd generation Antipsychotics

Medication (Brand name examples)	Autism Irritability	Bipolar	Schizophrenia	Tourette
Aripiprazole (Abilify)	X	Mania/mixed: X / X*	X	X
Asenapine (Saphris)		Mania/mixed: X		
Brexpiprazole (Rexulti)			X	
Cariprazine (Vraylar)				
Clozapine (Clozaril)				
Iloperidone (Fanapt)				
Lumateperone (Caplyta)				
Lurasidone (Latuda)		Depression: X	X	
Olanzapine (Zyprexa)		Mania/mixed: X	X	
Olanzapine/Fluoxetine combination (Symbyax)		Depression: X		
Paliperidone (Invega)			X	
Quetiapine/Quetiapine XR (Seroquel / Seroquel XR)		X	X	
Risperidone / Consta (Risperdal / Risperdal Consta)	X	X	X	
Ziprasidone (Geodon)				

2nd-Gen Antipsychotics

- Serotonin-dopamine antagonists
- Intended effects
 - Reduce aggression and irritability
- Possible side effects
 - CNS: somnolence, sedation
 - Metabolic: weight gain, lipids, glucose
 - Movement: EPS, Akathisia
- Monitoring
 - VS, esp weight (baseline, 4wk, 8wk, 12wk, 6m, annually)
 - Labs (baseline, 3m, 6m, annually): A1C, lipids, cholesterol
 - EPS measure (eg DISCUS, AIMS)
- Must be given daily

2nd-Gen Antipsychotics

- Risperidone (Risperdal[®])
 - Age
 - 5+y
 - Dosing
 - Initial: 0.25mg qD (15-20kg); 0.5mg qD (50kg+)
 - Recommended: 0.5-1mg qD (15-20kg); 1-2.5mg qD (50kg+)
 - Max: 3mg qD
- Aripiprazole (Abilify[®])
 - Dosing
 - Initial: 2mg qD
 - Recommended: 5-10mg qD
 - Max: 15mg qD

Alpha agonists

- Reduces sympathetics
- Intended effects
 - Reduce purposeless motor activity
 - Improve impulsivity
- Possible side effects
 - Sedation (can also be an intended effect, ie sleep onset)
 - Hypotension
 - Headaches
- Monitoring
 - BP
- Must be given daily

Alpha agonists

- Guanfacine
 - 2 options
 - Short-acting (aka Tenex[®]) can be split or crushed; 3-4hr duration
 - Long-acting (aka Intuniv[®]) must be swallowed whole; 24hr duration
 - Dosing
 - 0.5mg to 2mg per dose for IR; BID to TID
 - 1mg to 4mg for XR; qD
 - Max: 4mg/day regardless of formulation

Alpha agonists

- Clonidine
 - 3 options
 - Short-acting (aka Catapres[®]) can be split or crushed; 3-4hr duration
 - Long-acting (aka Kapvya[®]) must be swallowed whole; 12hr duration
 - Longer-acting (aka Onyda[®]) is liquid; 24hr duration
 - Dosing
 - 0.05mg to 0.2mg per dose for Catapres; BID to TID
 - 0.1mg to 0.2mg for Kapvay; BID
 - 0.1 to 0.4mg for Onyda; qHS
 - Max: 0.4mg/day regardless of formulation

Stimulants

- MPH blocks transporter for dopamine and NE; AMPH also blocks serotonin
- Intended effects
 - Target inattention, hyperactivity, and impulsivity
- Possible side effects
 - Decreased appetite
 - Stomachache
 - Rebound phenomena
 - Difficulty falling asleep
 - Irritability
 - Overfocusing, compulsive behaviors
 - Headache
- Monitoring
 - VS
- Can allow “med holidays”

Stimulants

- Methylphenidate, immediate release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Methylphenidate (Ritalin [®] , Methylin [™] , Methylphenidate chewable)	5 mg BID – TID	3 – 4	60 mg	6 – 17	Can split or crush tablet
Dexmethylphenidate (Focalin [®])	2.5 mg BID	3 – 6	20 mg	6 – 17	Can split or crush

Stimulants

- Methylphenidate, extended release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Methylphenidate (Ritalin LA [®])	10 – 20 mg AM	7 – 9	60 mg	6 – 12	Can open and sprinkle on applesauce
Dexmethylphenidate (Focalin [®])	5 mg AM	9 – 12	30 mg	6 – 17	Can open and sprinkle on applesauce
Methylphenidate (Metadate CD [®])	10 – 20 mg AM	7 – 9	60 mg	6 – 15	Can open and sprinkle on applesauce
Methylphenidate (Concerta [®])	18 mg AM	10 – 12	6-12y: 54 mg; ≥ 13y: 72 mg	6 – 17	No

Stimulants

- Methylphenidate, extended release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Methylphenidate (Quillivant XR®)	10 – 20 mg AM	12	60 mg	6+	Oral suspension
Methylphenidate (QuilliChew ER®)	10 - 20 mg AM	8	60 mg	6+	Chewable tablet
Methylphenidate (Aptensio XR®)	10 mg AM	12	60 mg	6+	Can sprinkle on applesauce
Methylphenidate (Cotempla XR-ODT®)	17.3 mg AM	12	51.8 mg	51.8 mg	Allow to dissolve, do not crush or chew

Stimulants

- Methylphenidate, extended release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Methylphenidate HCl (Jornay PM [®])	20mg PM	24	100mg	6+	Can sprinkle on applesauce
Methylphenidate HCl ER (Relexxii [®])	18 mg AM	13	6-12y: 54 mg; ≥ 13y: 72 mg	6+	No
SDX/Serdexmethyl- phenidate and IR d-MPH/ dexmethyl-phenidate (Azstarys [®])	26.1mg (S) / 5.2mg (D)	13	52.3 mg (S) / 10.4mg (D)	6+	Can swallow or sprinkle into water, applesauce
Methylphenidate transdermal (Daytrana [®])	10 mg AM	10 – 12	30 mg	6 – 17	Transdermal

Stimulants

- Amphetamine, instant release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Mixed amphetamine salts (Adderall®)	3 -5y: 2.5mg AM 6y+: 5 mg AM or BID	5 - 8	40 mg	3+	Can split or crush
Dextroamphetamine (generic, ProCentra®, Zenzedi®)	3 -5y: 2.5mg AM 6y+: 5 mg AM or BID	4 - 6	40 mg	3 - 16	Can split or crush tablet;
Amphetamine (Evekeo®)	5 mg AM – BID	4 - 6	60 mg	3+	Can split or crush

Stimulants

- Amphetamine, extended release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Mixed amphetamine salts (Adderall XR®)	10 mg AM,	10 – 12	50 – 60 mg	6 – 17	Can sprinkle on applesauce
Mixed amphetamine salts (Mydayis®)	12.5 mg AM	12 - 16	25 mg	13 – 17	Can sprinkle on applesauce
Lisdexamfetamine (Vyvanse®) (capsules)	30 mg AM	10 – 12	70 mg	6 – 17	Can dissolve in water, yogurt or orange juice
Lisdexamfetamine (Vyvanse®) (chewable tabs)	30 mg AM	10 – 12?	70 mg	6 – 17	Chewable tablet

Stimulants

- Amphetamine, extended release

Medication (Brand Name)	Initial Dose	Duration (hour)	Peds FDA Max Daily Dose	FDA- Approved Ages	Split/Crush/ Sprinkle
Dextroamphetamine (Dexedrine Spansules [®])	5 mg AM or BID	6 – 10	50 – 60 mg	6-16	Can sprinkle
Amphetamine (Dyanavel XR [®])	2.5 – 5 mg AM	10 – 13	20 mg	6+	Oral suspension
Amphetamine (Adzenys XR-ODT [®])	6.3 mg AM	10 – 12?	18.8 mg (6-12); 12.5 mg (≥ 13)	6 – 17	Allow to dissolve, do not crush or chew
Amphetamine (Adzenys ER [®])	6.3 mg AM	10 – 12?	18.8 mg (6-12); 12.5 mg (≥ 13)	6 – 17	Suspension

SNRI

- Inhibit reabsorption of serotonin and NE
- Second-line treatment for ADHD and anxiety
- Possible side effects
 - Sleep (somnolence or insomnia), fatigue
 - GI: N/V, decreased appetite
- Monitoring
 - VS
- Must be given daily

SNRI

- Atomoxetine (Strattera[®])
 - Dosing
 - <70kg: 0.5mg/kg/day (target 1.2mg/kg/day)
 - 70+kg: 25-40mg qD (target 80mg qD)
 - Max: <70kg = 1.4/kg/day; 70+kg = 100mg qD)
- Viloxazine (Qelbree[®])
 - Dosing
 - 6-11y: start 100mg qD, titrate by 100mg weekly
 - 12-17y: start 200mg qD, can increase to 40mg after 1wk
 - Max: 400mg qD

SSRI

- Inhibit reabsorption of serotonin
- Possible side effects
 - Transient: GI upset, restlessness, nightmares
 - Common: sleep changes (eg somnolence or insomnia, vivid dreams, nightmares), sweating, weight gain
 - Less common: activation/agitation, irritability
 - Rare: QTc prolongation (citalopram), serotonin syndrome, suicidality
- Monitoring
 - VS, EKG if rx'ing citalopram + cardiac hx or on other QTc prolonging meds
- Must be given daily

SSRI

Antidepressants	MDD	Anxiety Disorders	GAD	SAD	OCD
SSRIs					
Citalopram	+ 7-17 yo	+ 7-17 yo			+ 7-17 yo
Escitalopram	<u>12-17 yo</u>	+ 7-17 yo	<u>7-17 yo</u>		
Fluoxetine	<u>8-17 yo</u>	+ 6-17 yo			<u>7-17 yo</u>
Fluvoxamine	+ 12-17 yo	+ 6-17 yo			<u>8-17 yo</u>
Paroxetine	- (harm)			+ 8-17 yo	+ 7-17 yo
Sertraline	+ 6-17 yo	+ 7-17 yo	+ 5-17 yo		<u>6-17 yo</u>
SNRIs					
Desvenlafaxine	- 7-17 yo				
Duloxetine	- 7-17 yo		<u>7-17 yo</u>		
Venlafaxine	+ 12-17 yo	+ 6-17 yo			

FDA APPROVAL

+ POSITIVE EFFICACY DATA

- NEGATIVE EFFICACY DATA

SSRI

Medication (Brand)	Initial Daily Dose (mg)	Dose Titration (Every 1- 4 Weeks)	Usual Effective Doses for MDD/Anxiety	Literature Based Max Daily Dose (mg)	FDA Max Daily Dose (mg)	Recommended Administration
SSRIs						
Citalopram (Celexa®)	Children: 2.5-10 Adolescents: 10-20	10-20	Children: 10-20 Adolescents: 20-40	Ages ≥ 6 years: 40	Not approved for pediatrics	AM (can consider divided dosing); solution available
Escitalopram (Lexapro®)	Children: 2.5-5 Adolescents: 5-10	5-10	10-20	Children: 20 Adolescents: 30	MDD 12-17 years: 20	AM (can consider divided dosing); solution available
Fluoxetine (Prozac®)	Children: 5-10 Adolescents: 10	10-20	Children: 10-20 Adolescents: 20-40	Ages ≥ 6 years: 60	MDD 8-18 years: 20 OCD 7-17 years: 60	AM; solution available
Fluvoxamine (Luvox®, Luvox CR®)	Children ≥ 8 years: 25	50	50-150	Children 8-11 years: 200 Adolescents: 300	OCD 8-11 years: 200 OCD 12-17 years: 300	BID if IR > 50 mg or HS if CR
Paroxetine (Paxil®, Paxil CR®)	Adolescents: IR 10; CR 25	10-20	20	Adolescents: IR 40; CR 50	Not approved for pediatrics	AM or HS
Sertraline (Zoloft®)	Children: 12.5-25 Adolescents: 25-50	25-50	50	Ages ≥ 6 years: 200	OCD 6-17 years: 200	AM (can consider divided dosing if ≤ 50 mg); oral concentrate available

Leucovorin

Prescription form of reduced folic acid that does not require enzymatic activation by dihydrofolate reductase (DHFR)

Maintains active intracellular folate pools even when folate metabolism or transport is impaired

Impaired folate metabolism can occur with certain genetic disorders or medication-induced impairment (eg methotrexate)



FDA APPROVED FOR MITIGATION OF METHOTREXATE & 5-FLUOROURACIL TOXICITY IN CANCER TREATMENT



FDA APPROVED FOR CEREBRAL FOLATE DEFICIENCY (CFD)



in affiliation with  BullterHealthCare

AAP Daily Briefing

Good morning Silvia Pereira-Smith

Wednesday, March 11, 2026

LEADING THE NEWS

FDA Approves Leucovorin As Treatment For Cerebral Folate Deficiency



Leucovorin

CFD is a neurological condition characterized by abnormal CSF folate with normal serum folate

Typically presents in infancy and early childhood

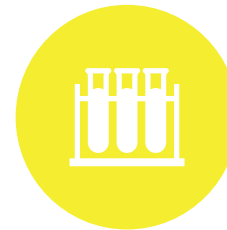
Associated with regression, seizures, tone abnormalities, microcephaly, MRI myelination changes, autism



CSF
MEASUREMENT -
LUMBAR
PUNCTURE

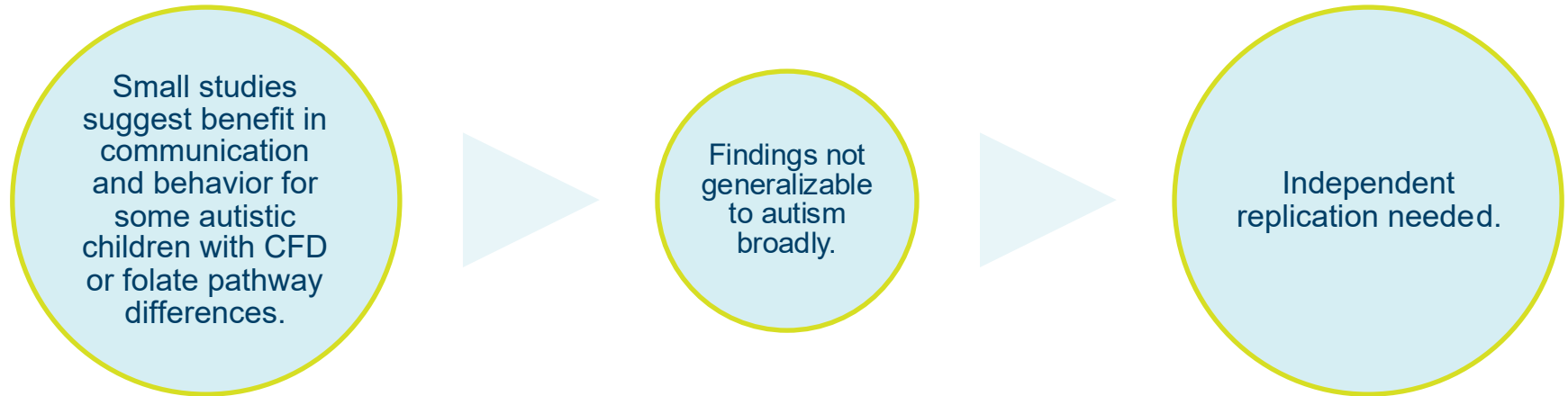


GENETIC
TESTING -
SALIVA



BLOOD FRAA
TESTING IS NOT
STANDARDIZED

Leucovorin



Most studies <100 subjects and derive from a narrow research group

No large multicenter Phase 3 RCT completed

Uncertain efficacy and safety across broader autism populations

Leucovorin

Side effects / cautions

Possible irritability or
behavioral activation

GI upset may occur

Rare severe hypersensitivity

Can mask B12 deficiency

Contraindicated in MTHFS
deficiency

Shared decision- making guidance

Genetic testing on
all patients
diagnosed with
ASD

Review limited
evidence and
discuss
uncertainty
transparently

Clarify family
goals and
outcomes of
interest

Optimize other
supports and
services

Leucovorin

AAP
Clinician
Guidance re:
Leucovorin
& Autism



SDBP Statements
On Tylenol, Leucovorin, &
Autism
<https://sdbp.org/sdbp-statements>

SDBP's Statement on Tylenol, Leucovorin and Autism

In response to the White House press conference about Tylenol, leucovorin and autism, the SDBP developed and approved two statements, a professional statement and parent/family informational sheet. These resources are available to all to help disseminate accurate information on the topic. The Parent/ Family Info Sheet is now available in multiple languages!

- [Statements for Health Care Professionals](#)
- [Statements for Patients and Families - English](#)
- [Statements for Patients and Families - Spanish](#)
- [Statements for Patients and Families - Haitian Creole](#)
- [Statements for Patients and Families - Burmese](#)
- [Statements for Patients and Families - Kiswahili](#)

Med Resources

- Autism Speaks Medication Decision Aid for Parents
- AACAP Parents' Medication Guide
 - https://www.aacap.org/App_Themes/AACAP/Docs/resource_centers/autism/Autism_Spectrum_Disorder_Parents_Medication_Guide.pdf
- SDBP
 - Educational Hub including psychopharm
- MUSC DBP CASE
 - 2nd Tuesdays from 12-1pm; free CME and CEU

Other Resource

MUSC Developmental-Behavioral Pediatrics

Mini Fellowship

Enhance your skills | Expand your impact | Improve patient care



musC
Children's
Health
Medical University of South Carolina

Who Can Apply:

- General Pediatricians
- Pediatric Healthcare Providers

Benefits:

- 300 Hour Comprehensive Curriculum
- Hands on Training
- Expert Faculty
- Networking Opportunities
- Stipend offered



Can email Dr. Michelle Macias at maciasm@musc.edu

Questions

Thank You

