

Treatment of Autism in Adults

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- Dr. Hendren does intend to discuss the use of off-label/unapproved use of drugs

Learning Objectives



- Identify successes and challenges in the developmental progression during adulthood for people with autism and their families
- Identify and effectively treat emotional and behavioral symptoms associated with autism in adults.
- Describe beneficial treatment settings for autistic adults and their families.

Autism Diagnosis Among US Children and Adults, 2011-2022

- ASD diagnosis rates **increased** substantially between **2011 and 2022**, particularly among **young adults**
- A total of **12,264,003 members** were enrolled with data extracted for individuals seeking care from one of 12 sites of the **Mental Health Research Network (MHRN)**.
- The greatest relative increase in diagnosis rate from 2011 to 2022 occurred among **26-to-34-year-olds (450%)**



Autism Assessment and Outcome

Addressing the “Cliff” for Adults With Autism Spectrum Disorder

- **Parents of young children** diagnosed with autism spectrum disorder (ASD) **desperately search for a cure** for their child’s disorder.
- Depending on their child’s severity or lack of progress, **parents shift from looking for a cure to finding arrangements** where their child can live a **fulfilling life** as an adult when they are less involved and less able to help.
- Sadly, they too often find that the **resources** they have fought for their children to receive **disappear** when their youngsters leave school.

Diagnosing ASD in Adults

- Benefit from **someone** to provide a **developmental history**
- Developmental challenges (eg, the acquisition of learnt or **camouflaging strategies**)
- High frequency of **co-occurring disorders**.
- The diagnostic process includes **referral, screening, interviews** with informants and patients, and **functional assessments**
- Possible **misdiagnosis**, especially in **women**.

Primary Care for Adults with ASD

- Children with ASD **outgrow** the services of pediatric programs and enter a **fragmented health care system** that is **unfamiliar, insufficiently knowledgeable, and underfunded** for their needs.
- **Time** constraints, the **complexity** of family involvement, the physical **environment** not being appropriately designed, and **barriers** to communicating with patients during visit

Adult Outcomes in ASD

- Young adults with ASD have the **lowest employment rate** across disabilities;
- Odds of ever having had a paid job were higher for those who were **older, white, from higher-income households**, and with better **conversational abilities, functional skills, and work experience.**

Better Doctors Visits: Advice from Autistic Adults

- Bring a **support person** to appointments
- Ensure **routine** monitoring and screening
- **Memory issues** and difficulty putting **thoughts into words**
- Support the Autistic individual in achieving their **priorities**
- Significantly more autistic adults in the **younger** versus older group scored above the clinical threshold for **anxiety, somatoform disorders and eating disorders** (Zivralı Yarar, 2022)
- Even after taking into account background, depression, and anxiety, **social support** was important for individuals' **QoL** (Charlton, 2023)
- 643 respondents said **access**, anxiety/depression, GI, sleep most important. (2024-5 survey)

Joanne Gauthier, T.K., Sylvère Moulancier, Terri Robson, Maxine Share, Fakhri Shafai, David Nicholas; An international *Think Tank* entitled “*Advancing Care Priorities for Health and Quality of Life among Older Autistic Adults and/or Adults with Intellectual Disability*” November 2023 in Vancouver, BC.

Measuring Outcomes

- **Meaningful outcomes** for the person with ASD and his or her family varies depending upon the complex definition of “meaningful”
- Although **education and employment** are often chosen as “good outcomes,” they **may not be the most meaningful** for families or individuals with ASD who identify such outcomes as **friendships, having a place to live, and health** of family members as the most meaningful.
- Differences between **male and female** individuals, **diversity**, developmental level, socialization and **loneliness**, and the success of **community partnerships** to bridge research to clinical practice can all affect what is considered meaningful.

Autism Comorbidity

ASD Medical Co-Occurring Disorders

- Sleep Disorders (50% - 80%)
- GI abnormalities (30%–70%)
- Epilepsy (30%)
- Immune Disorders
 - Food allergies, allergic rhinitis, atopic dermatitis, autoimmune disorders, asthma
 - Increased proinflammatory cytokines
- Mitochondrial Dysfunction

ASD Medical Co-Occurring Disorders

- Higher than expected rates of other medical conditions – eczema, asthma, ear and respiratory infections, headache
- Chronic fatigue risk higher in young adults with ASD (immune; Quadt, BMJ Open, 2024)
- Risk of Parkinson's like symptoms higher (6-7%) in those with ASD - genetic, motoric or degenerative?

Tye et al, *Frontiers in Psychiatry*, 2019; 23:9:751; Werner E, et al. *Arch Gen Psychiatry*. 2005;62(8):889-895. Buie T, et al. *Pediatrics*. 2010;125 Suppl 1:S1-S18. Tharp B. In: Ozonoff S, et al (Eds). *Autism Spectrum Disorders: A Research Review for Practitioners*. Arlington, VA: American Psychiatric Publishing, Inc; 2003. Task Force on DSM-IV. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Textbook Revision)*. Arlington, VA: American Psychiatric Association; 2000. Frye RE, et al. *Pediatr Res*. 2011;69(5 Pt 2):41R-47R. Kohane IS, et al. *PLoS One*. 2012;7(4):e 33224. Quadt et al, *BMJ Open*, July 22, 2024; Nadaf, *Nature*, 2024; Wallace G, 2024

ASD Differential Diagnosis or Co-Occurring

- ADHD
- OCD
- Tics and Tourette's
- Overanxious Disorder
- Depressive Disorder
- Learning Disorder
- Psychotic Disorder
- Disruptive Mood Dysregulation Disorder
- Aggression – 53% – younger; associated with medical comorbidities

Early-onset dementia among adults with autism spectrum disorder

- Case–control study, the prevalence and incidence of **early-onset dementia in individuals with ASD** was examined during 2021 using Medicaid and Medicare files.
- Compared to the general population, dementia was found to occur **more frequently** in individuals with **ASD only** (adjusted hazard ratio, 1.96; 95% CI, 1.69–2.28), as well as individuals with **ASD and co-occurring ID** (adjusted hazard ratio, 2.89; 95% CI, 2.62–3.17).
- Adults with ASD **under** the age of **65** were approximately **2.6 times** more likely to be diagnosed with **dementia** compared to the general population.

A yellow banner with a blue border, featuring a wavy top and bottom edge. The banner is centered on a white background.

**Psychopharm & CIM
Treatments for Autism
Spectrum Disorder**

Psychopharmacology Algorithm Project at the Harvard South Shore Program

- **Medication** management of **core ASD symptoms in adults**, suggest starting with **fluvoxamine** as first-line, with possible consideration of a **second SSRI trial** if there is an inadequate or no response to fluvoxamine.
- Next step, if there is **comorbid irritability**, consider a **second-generation antipsychotic**.
- If **no comorbid irritability**, possible augmenting agents: **propranolol, memantine, d-cycloserine, and oxytocin**.

Psychotropic Medication use in Adults with Autism in Italy

- **Prevalence and predictors** of psychotropic medication use in **195** autistic subjects, aged between **14 and 58**, treated in two Italian tertiary care centers.
- **58.5%** of the sample were **taking at least one medication**; **one third** were on **polypharmacotherapy**.
- **Antipsychotics** were prescribed to **40%** of the sample. Nearly **30%** of the sample were on **anticonvulsants/mood stabilizers**.
- Medications prescribed to adolescents and adults with ASD are **heterogeneous** and often rely only on **clinicians' experience**.

ADHD and ASD

- Clinically significant symptoms of **ADHD** have been reported in **16% to 66%** of youth with ASD. Rates similar for children and adults.
- Greater **impairment in adaptive functioning** and **poorer health-related quality of life** in youth with ASD and ADHD
- **Response** to ADHD medications in ASD were adversely moderated by the presence of **intellectual disability and mood lability**.
- **MPH-ER** is effective and well-tolerated in the treatment of ADHD in **HF-ASD adults**.

Alpha-2 Adrenergic Agonists & Beta Blockers

- **Clonidine** – 2 DBPC trials
 - Modest benefit for overactivity, sensory responses, decreased irritability, stereotypy, and oppositional behavior
- **Guanfacine**
 - Multisite RCT (N=62) ER for 8 weeks; modal dose 3mg
 - CGI-I 50% vs 9.4%; decreased hyperactivity
- **Propranolol**
 - Propranolol did not impact social interaction measures or language, but there were indications of a beneficial effect for anxiety (Beverdors, *Psychopharmacology (Berl)* 2024)
 - RCT up to 200mg tid for severe aggression reduced severe aggression London EB, *J Clin Psychopharmacol.* 2024;44(5):462-467.

Jaselskis CA, et al. *J Clin Psychopharmacol.* 1992;12(5):322-327. Fankhauser MP, et al. *J Clin Psychiatry.* 1992;53(3):77-82. Posey DJ, et al. *J Child Adolesc Psychopharmacol.* 2004;14(2):233-241. Handen BL, et al. *J Dev Behav Pediatr.* 2008;29(4):303-308; Scahill et al, *AM J Psychiatry* 2015

Depressive and Anxiety Symptom Trajectories in ASD and DD

- Prevalence of **comorbid depression** correlates with **higher functioning forms of ASD** and **increasing age**.
- Internalizing symptoms were associated with **lower life satisfaction** and greater social difficulties in early adulthood
- Although symptom levels in **females increase** at a **faster rate** throughout adolescence, **males** with ASD appear to have **elevated** levels of **depressive symptoms** in school age that are **maintained** into young adulthood
- **Sertraline** trial for anxiety in adults with a diagnosis of autism (STRATA) started. Rai. *Trials*, 2024 Jan 11;25(1):37.

Restricted Repetitive Behaviors and Inhibitory Control in ASD across the Lifespan

- **Adults** displayed **fewer repetitive behaviors** than children
- Having a **comorbid diagnosis of ID** was also associated with **repetitive behaviors**
- **Age-related pattern** of symptom abatement not dependent upon gender, a comorbid diagnosis of ID, or taking psychotropic medication
- However, **brain processes** underlying inhibitory control appear to be underdeveloped in ASD and **develop differently from adolescence to adulthood in ASD**

Psychotic Disorder and Bipolar Disorder in ASD

- 9062 people with ASD in Sweden followed from age 17 to 27 years
- Nonaffective **psychotic disorder** and bipolar disorder in people with non-ID ASD were 12.3 (95% CI, 9.5-15.9) and 8.5 (95% CI, 6.5-11.2), respectively, which was greater than ID ASD
- This **rate is higher** than in **age and sex** matched individuals without ASD in the general population
- May have to do with common underlying **genetic risk** factors or to **exposure sensitivity**

AOR = adjusted odds ratio.

Selten JP, et al. *JAMA Psychiatry*. 2015;72(5):483-489.

Suicide and ASD

- National survey of **185 people** with ASD aged **14 to 80** found **49%** in the clinical range for **depression** and **36%** reporting **recent suicidal ideation**. **Females** reported **higher** depression rates than males. **Loneliness and social support** operate respectively as protective and risk factors for depression and suicidal ideation.
- Nationwide survey in **Taiwan** found patients with **ASD** had **increased risk of suicide attempts** compared to those without ASD especially in **adolescents** and **young adults**.

Disruptive Mood Dysregulation Syndrome (DMDD)

- Reaction is bigger than expected
- Severe temper outbursts at least three times a week
- Sad, irritable or angry mood almost every day
- Child must be at least six years old
- Symptoms begin before age ten
- Symptoms are present for at least a year
- Child has trouble functioning in more than one place (e.g., home, school and/or with friends)
- Stimulants, antipsychotics, mood stabilizers

Catatonia and ASD

- Reports of catatonic autism are consistently associated with symptoms of **agitation, stereotypy, posturing, negativism, mutism, stupor, grimacing, and occasionally, repetitive self-injurious behaviors (SIBs)**
- Symptoms of catatonia usually **appear during adolescence and early adulthood** but may emerge at different times across the life span of a person with autism.
- Initial success with **lorazepam and with ECT** suggests that there is an **excitatory- inhibitory** mechanism involved but the effects of GABA or glutamatergic interventions may be initially effective but **do not endure**

Antipsychotics and ASD

- Aripiprazole in the treatment of challenging behavior in adults with autism spectrum disorder (Jordan et al. Pharmacology (Berl) 2012 Oct;223(3):357-60)
- Treatment of Aggression in Adults with Autism Spectrum Disorder: A Review. Im DS (Harv Rev Psychiatry. 2021 Jan-Feb 01;29(1):35-80)

Summary of Conventional Medications for Autism (Level 2)

- **Stimulants:** works for some; start low and go slow
- **Antidepressants:** maybe for anxiety; OCD and ASD negative in children but 1 positive study in adults
- **Alpha-adrenergic agonists & Beta blockers:** worth a try for anxiety but limited studies
- **Anticonvulsants:** ? mood dysregulation + neurologic abnormalities; DMDD; limited studies
- **Antipsychotics:** indication for risperidone and aripiprazole (Level 1), but adverse effects. ? asenapine, negative lurasidone study in children (Harv Rev Psychiatry. 2021 Jan-Feb 01;29(1):35-80)

Risperidone and aripiprazole (irritability) are the only FDA-approved medications or biomedical agents for treating autism.

Salazar de Pablo, G 2022; Handen BL, et al. *Int J Adolesc Med Health*. 2011;23(3):167-173. Kaplan G, et al. *Pediatr Clin North Am*. 2012;59(1):175-187.

MDMA-assisted psychotherapy with Autistic Adults

- **Improvement in anxiety scores** from baseline to the primary endpoint was significantly greater for MDMA group compared to the placebo group ($P = 0.037$).
- **Change in anxiety scores** from baseline to 6-month follow-up showed **similar positive results** ($P = 0.036$), with a Cohen's d effect size of 1.1 (CI - 0.307, 2.527).

Danforth AL, et al, Reduction in social anxiety after MDMA-assisted psychotherapy with autistic adults: a randomized, double-blind, placebo-controlled pilot study. *Psychopharmacology (Berl)*. 2018 Nov;235(11):3137-3148.

Stroud J, Rice C, Orsini A, Schlosser M, Lee J, Mandy W, Kamboj SK. Perceived changes in mental health and social engagement attributed to a single psychedelic experience in autistic adults: results from an online survey. *Psychopharmacology (Berl)*. 2024 Oct 5.

Other Agents

- **Memantine** treatment appears to be beneficial for the treatment of ASD and associated psychopathology and cognitive dysfunction in intellectually capable adults. Joshi G: Clin Psychopharmacol; 2016 Jun;36(3):262-71.
- **TMS** may offer a promising and safe treatment option for pediatric and young adult patients with IC-ASD. Smith JR, Neuropsychol Rev 2023 Dec;33(4):834-855
- **Oxytocin**-induced increases in cytokines and clinical effect on the core social features of autism Wakuda T: Brain Behav Immun. 2024 May;118:398-407.

Autism Biomedical CIM Interventions





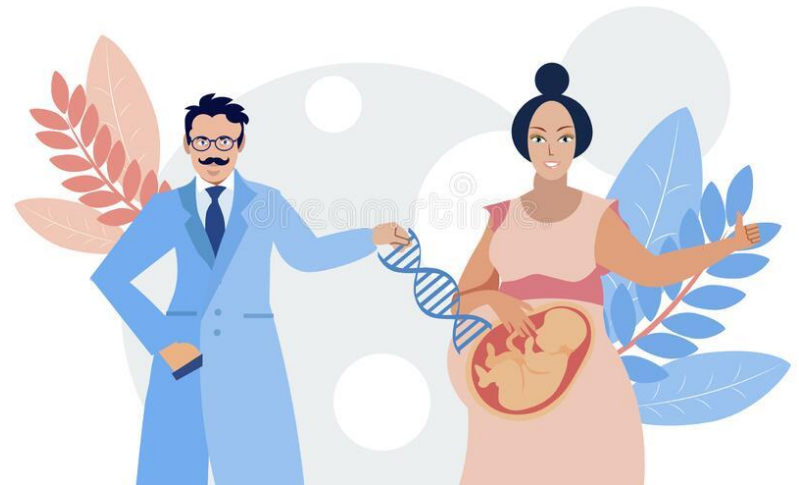
"I'm afraid you've had a paradigm shift."

A New Paradigm (Grade C Mod)

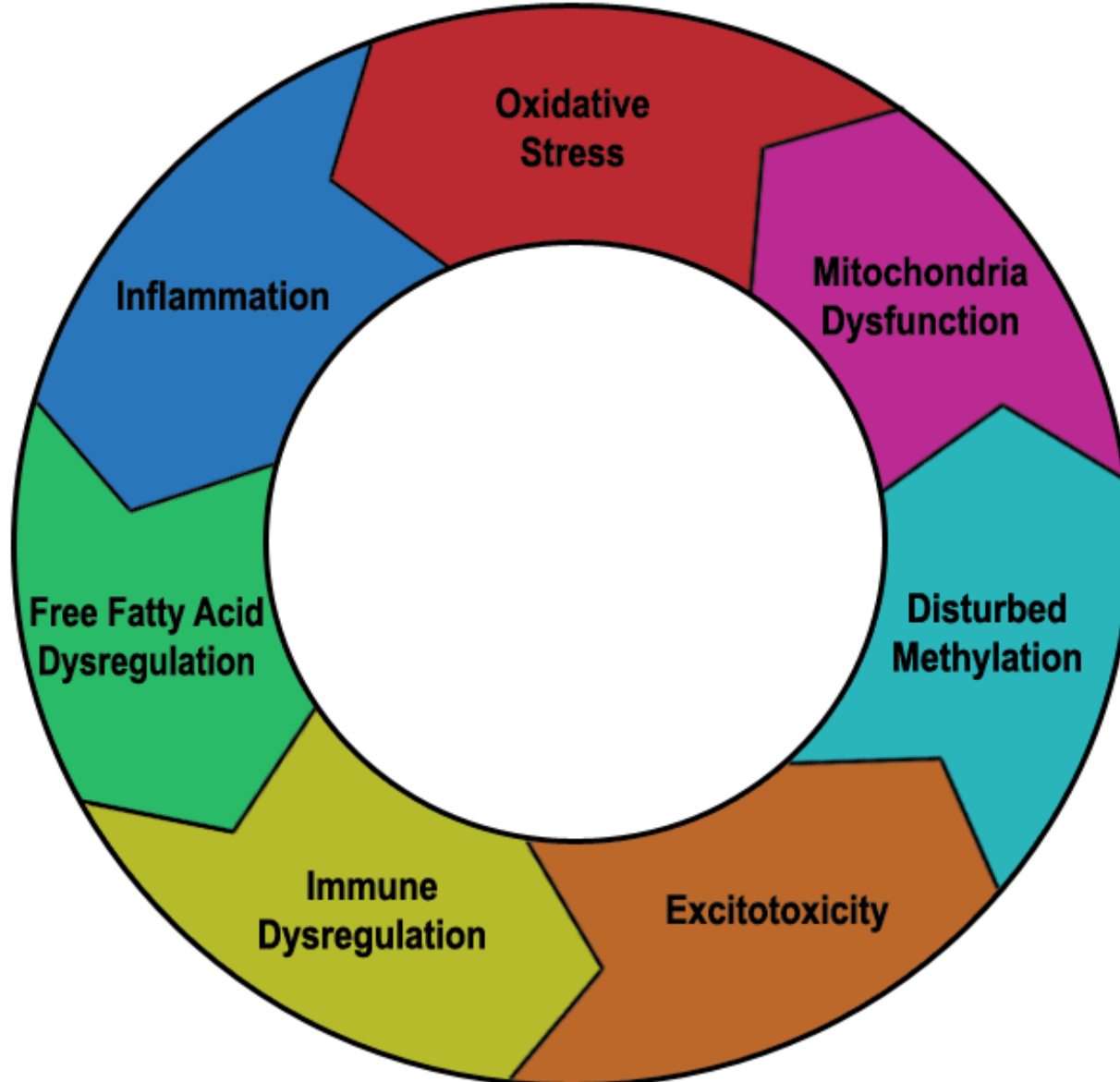
- Significant subsets of people with autism have **intestinal inflammation, digestive enzyme abnormalities, metabolic impairments, oxidative stress, mitochondrial dysfunction**, and **immune problems** that range from immune deficiency to hypersensitivity to autoimmunity
- In many cases, **improvement of autistic symptoms** is achieved by a combination of **nutritional** recommendations, prescription **medications**, and addressing the underlying **medical conditions** seen in these individuals

Gene-Environment Interactions and Endophenotype (Terroir Layer 2; Evidence Levels 2 & 3)

- Immune abnormalities/inflammation
- Oxidative stress
- Disturbed methylation
- Mitochondrial dysfunction
- Free fatty acid metabolism
- Excitatory/inhibitory imbalance
- Hormonal effects
- Microglia



Changing Processes



Excitatory/inhibitory imbalance in autism

- **Glutamate** genes are associated with **core** behavioral autism characteristics and **GABA** genes may be associated with **sensory processing**.
- Influence of **E/I imbalance** varies across autism phenotypes and brain regions, suggesting that glutamate and GABA genes play **different roles underlying different autism phenotypes** and that this may **change during development**.
- Trials underway for **memantine** and for **arbaclofen**

Targeting Shared Mechanisms

Immune/Inflammation

- Melatonin (Grade B Mod; Rec)
- IV/IG (Grade D Low; Poor)
- Corticosteroids (Grade D Low; Poor)
- Vitamin D (Grade B Mod; Rec)
- Suramin (Grade C Low; insuff)
- HBOT (Grade D Low; Poor)

Mitochondrial Function

- Carnitine (Grade C Low; Insuff)
- CoQ10 (Grade C Mod; Insuff)
- L-carnosine (Grade C Low; Insuff)

Targeting Shared Mechanisms

Oxidative Stress

- Glutathione (Grade I Low; insuff)
- Methyl B12 (Grade B Mod; neutral)
- Curcumin – anti-inflammatory and antioxidant activity (Grade I Low; insuff)
- NAC (Grade B Mod; rec)
- Sulforaphane (Grade C Mod; consider)

Neurotransmitter Production

- Tetrahydrobiopterin (Grade I Low; insuff)
- Rivastigmine & donepezil–
parasympathomimetic or cholinergic agent
(Grade I Mod; insuff)
- Galantamine – acetylcholinesterase
inhibitor (Grade I Mod; insuff)

NMDA = N-methyl-D-aspartate

Kern JK, et al. *Med Sci Monit.* 2011;17(12):CR677-CR682. Bertoglio K, et al. *J Altern Complement Med.* 2010;16(5):555-560. Darvesh AS, et al. *Expert Opin Investig Drugs.* 2012;21:1123-1140. Frye RE, et al. *Transl Psychiatry.* 2013:e237. Chez MG, et al. *J Child Neurol.* 2004;19(3):165-169. Nicolson R, et al. *J Child Adolesc Psychopharmacol.* 2006;16(5):621-629. Wang P, et al. Presented at: International Society for Autism Research; May 14, 2011; San Diego, CA. Abstract 8281. Hadjikhani N, et al. *Autism.* 2013;Epub ahead of print. Wink LK, et al. *J Child Adolesc Psychopharmacol.* 2011;21(4):375-379. Posey DJ, et al. *Am J Psychiatry.* 2004;161(11):2115-2117.

GABA

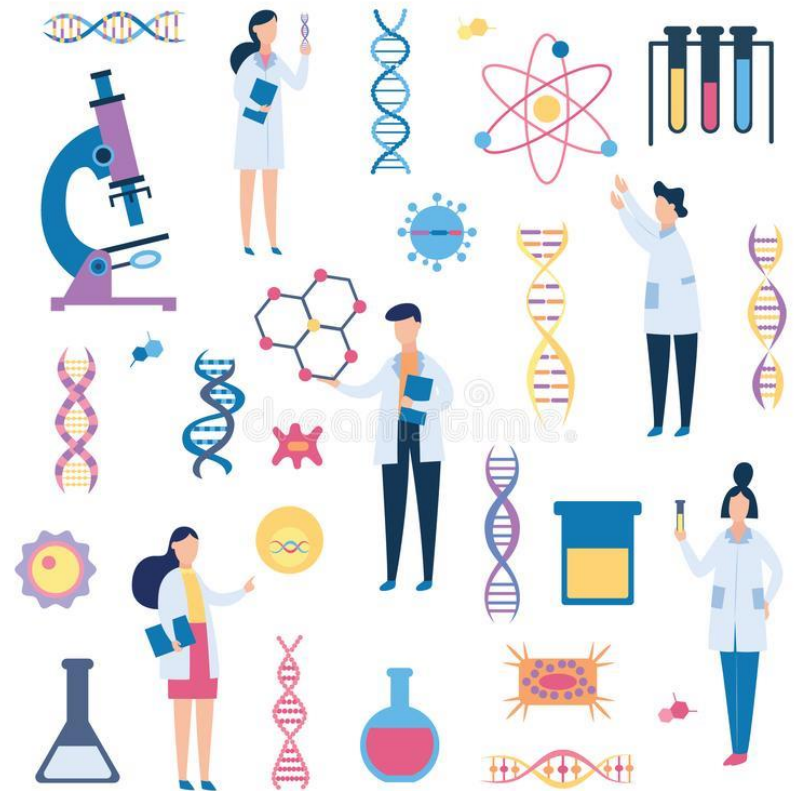
- Arbaclofen (STX209) (Grade D Mod; ineff)
- Bumetanide – diuretic (Grade I Mod; insuff)

Glutamate

- Riluzole – used to treat
amyotrophic lateral sclerosis (Grade I
Mod; insuff)
- D-cycloserine – partial agonist of
the neuronal NMDA receptor (Grade B
Mod; insuff)

BioMedical/CIM Treatments

- Melatonin
- Omega-3
- Vitamin D3
- NAC
- Methyl B12
- Vitamin/Mineral Supplements
- Diet
- Microbiome
- Pancreatic Digestive Enzymes
- CBD/THC
- Probiotics



Integrated Whole Body Approach to NDD Treatment

- Medical – genetic, neurology, GI, other medical symptoms
- Ancillary – speech, OT, OMT
- Behavioral
- Treat associated symptoms – pharmacology
- Biomedical assessment and treatments – melatonin, omega-3, vitamin D3, probiotics, digestive enzymes
- **Building personal relationships and resilience are all encompassing**



Lifting the Veil of Autism

