

# RECENT ADVANCES IN AUTISM SPECTRUM DISORDERS

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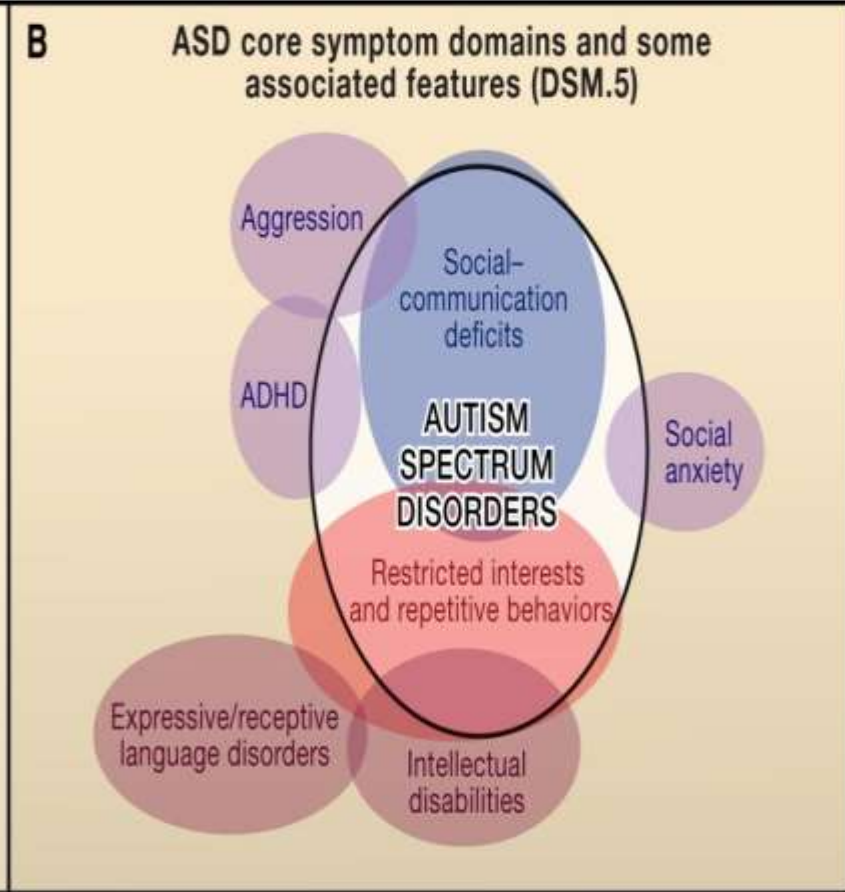
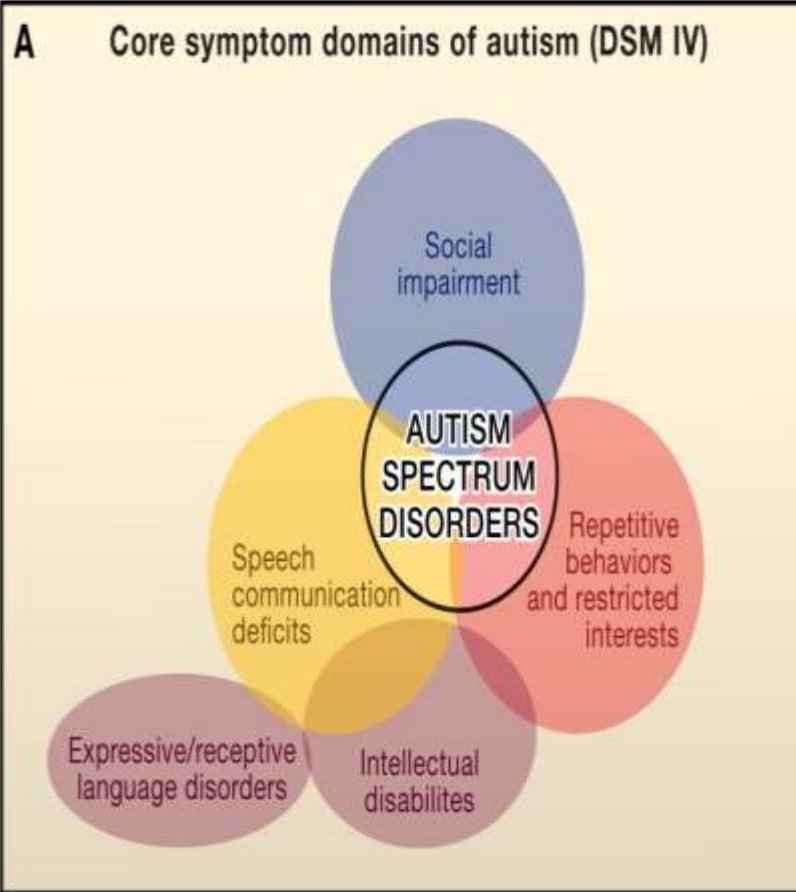




# LET'S BEGIN WITH A QUICK RECAP



# WHAT ARE THE CARDINAL FEATURES OF AUTISM ?





# SHIFT IN NOSOLOGY FROM 'AUTISM' TO 'AUTISM SPECTRUM DISORDERS'

**This also obviates the need to diagnose and classify  
Asperger's, CDD, Rett's as separate entities**





# CASE FILES

Disclaimer: None of the profiles have their real names or identities mentioned



DYPATIL PG Lecture Series 2<sup>nd</sup> November, 2023

# Case # 1



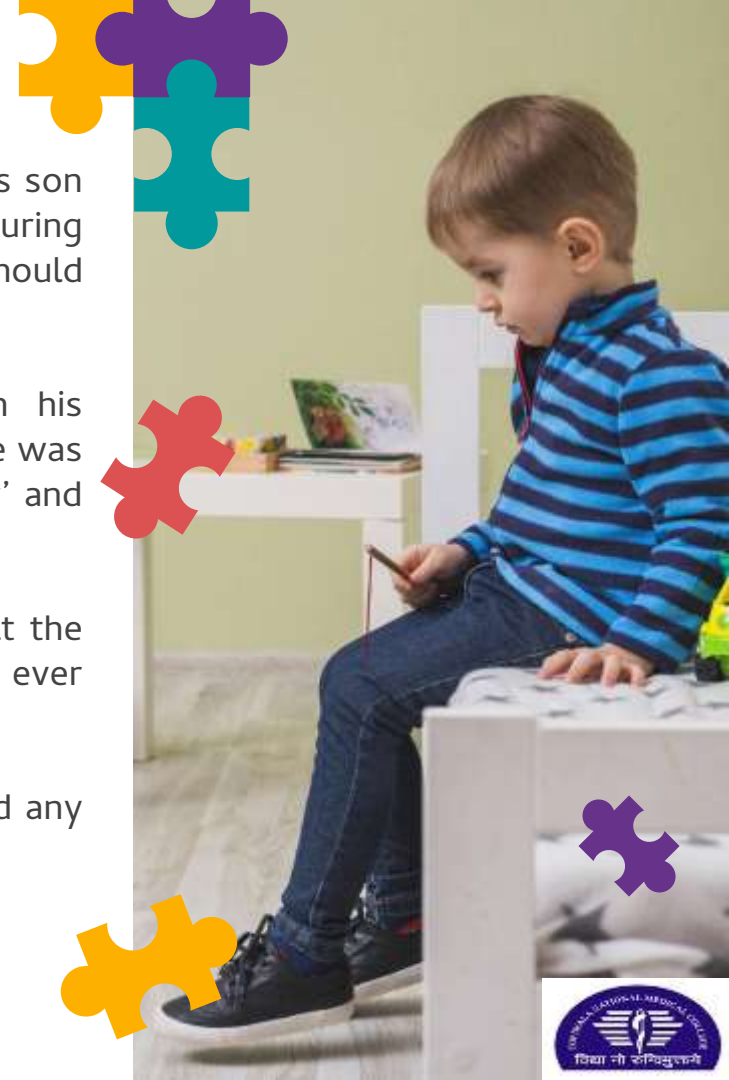


Mr. Batliboi was a 49 year old man who approached us as his son was advised to undergo autism evaluation by the school. During the process, he himself felt he had similar symptoms, and should get tested.

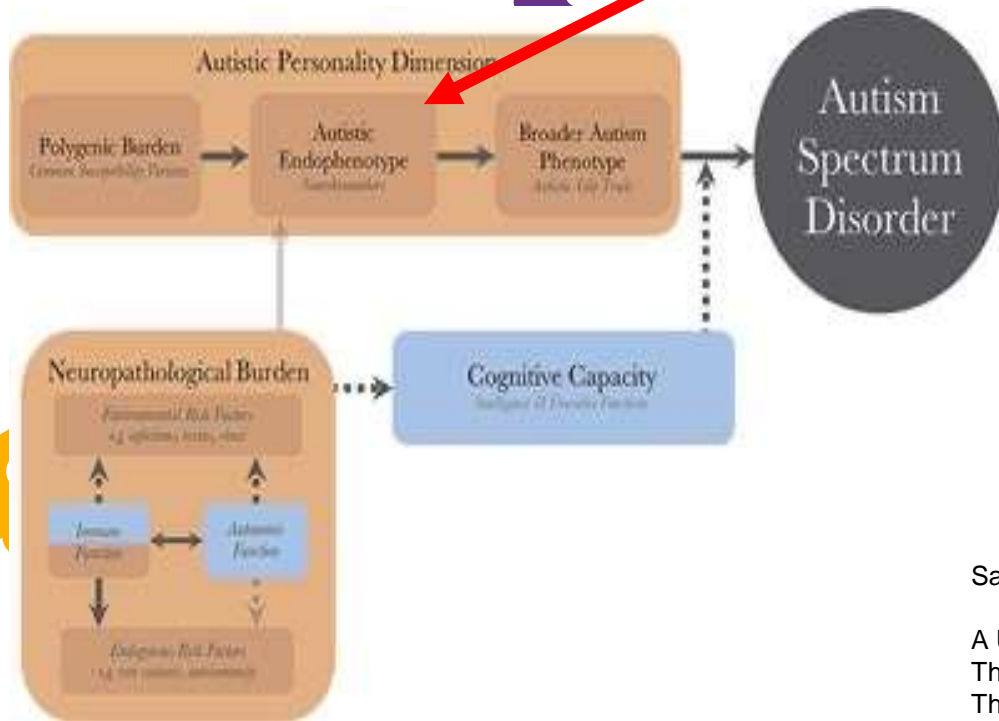
He further revealed having a strained relationship with his wife (who said he was emotionally distant). She stated that he was good at his work, but a loner. Further he was quite 'a miser' and every penny spent had to be accounted for.

He stated that he loved his wife and children, but rarely felt the need to express the same. He was a workaholic, and didn't ever feel the need to socialize or spend time in frivolous things.

What do you think is wrong with Mr. Batliboi? Does he need any intervention?



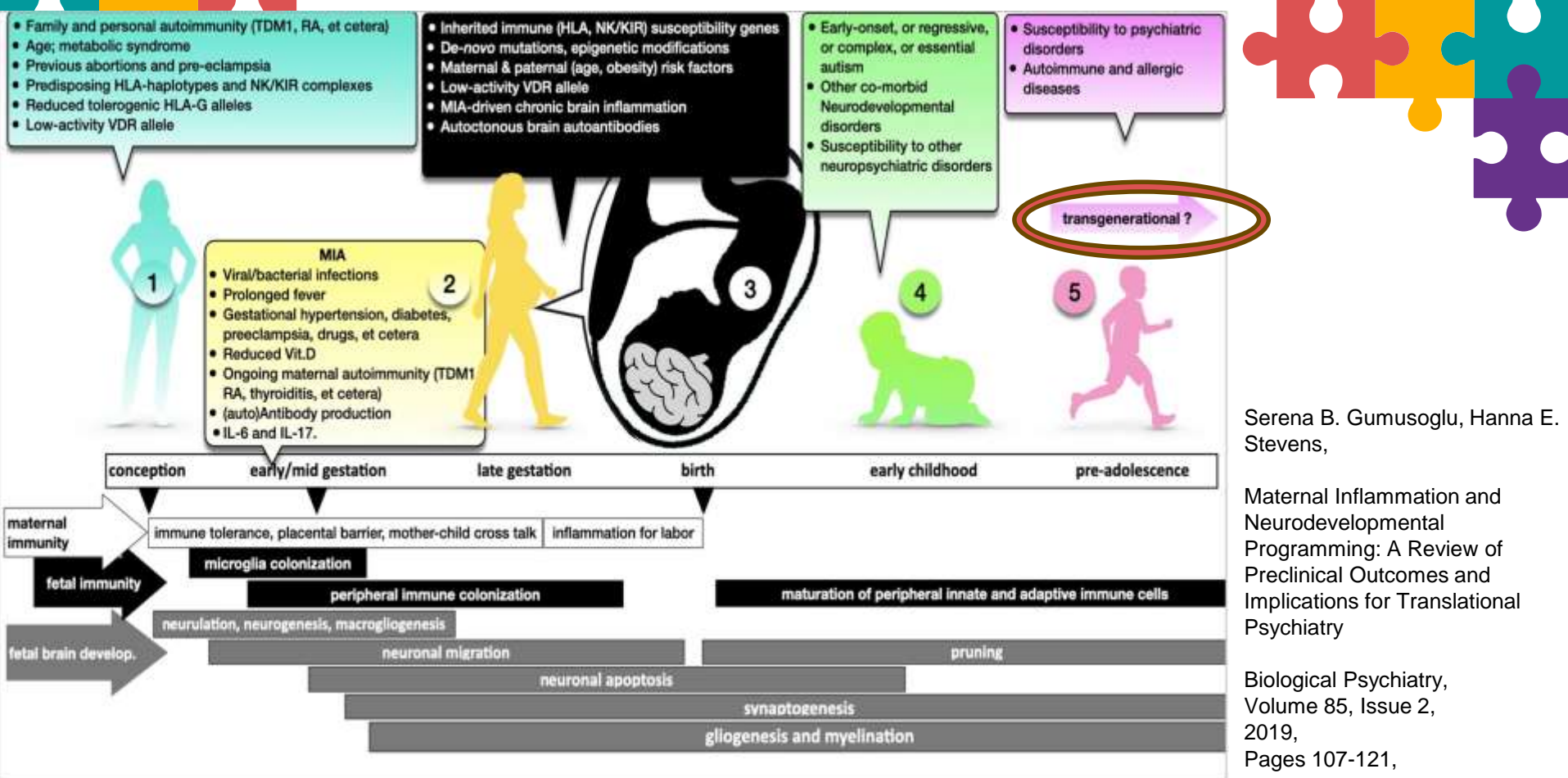




Sarovic D.

A Unifying Theory for Autism:  
The Pathogenic Triad as a  
Theoretical Framework

Front. Psy(Autism), online, 2022



Serena B. Gumusoglu, Hanna E. Stevens,


Maternal Inflammation and Neurodevelopmental Programming: A Review of Preclinical Outcomes and Implications for Translational Psychiatry

Biological Psychiatry, Volume 85, Issue 2, 2019, Pages 107-121,



# Case # 2





Anjali is Aryan's mom. Aryan was diagnosed with ASD at the age of 4 years.

She has done everything possible to help him cope with his autism.

She and her husband (both doctors) had decided not to have any more children.

She discovered last month that she conceived and it was totally unplanned. She doesn't want to undergo an MTP, thinking this is an act of God, but wants to know how early she can diagnose the younger one, if at all.

### **CAN WE HELP HER?**





In a ground-breaking report, researchers describe measurable decreases in eye contact between 2 and 6 months of age in babies who went on to develop autism spectrum disorder (ASD). The babies actually started out with typical eye-gaze patterns. But month by month, they showed steady decreases in the amount of time they looked at a caregiver's eyes in a video. Baby sibs who did not develop ASD showed the opposite pattern – with eye contact increasing month by month.

*Ami Klin and Warren Jones of Atlanta's Marcus Autism Center and Emory University, appeared online in the journal Nature*





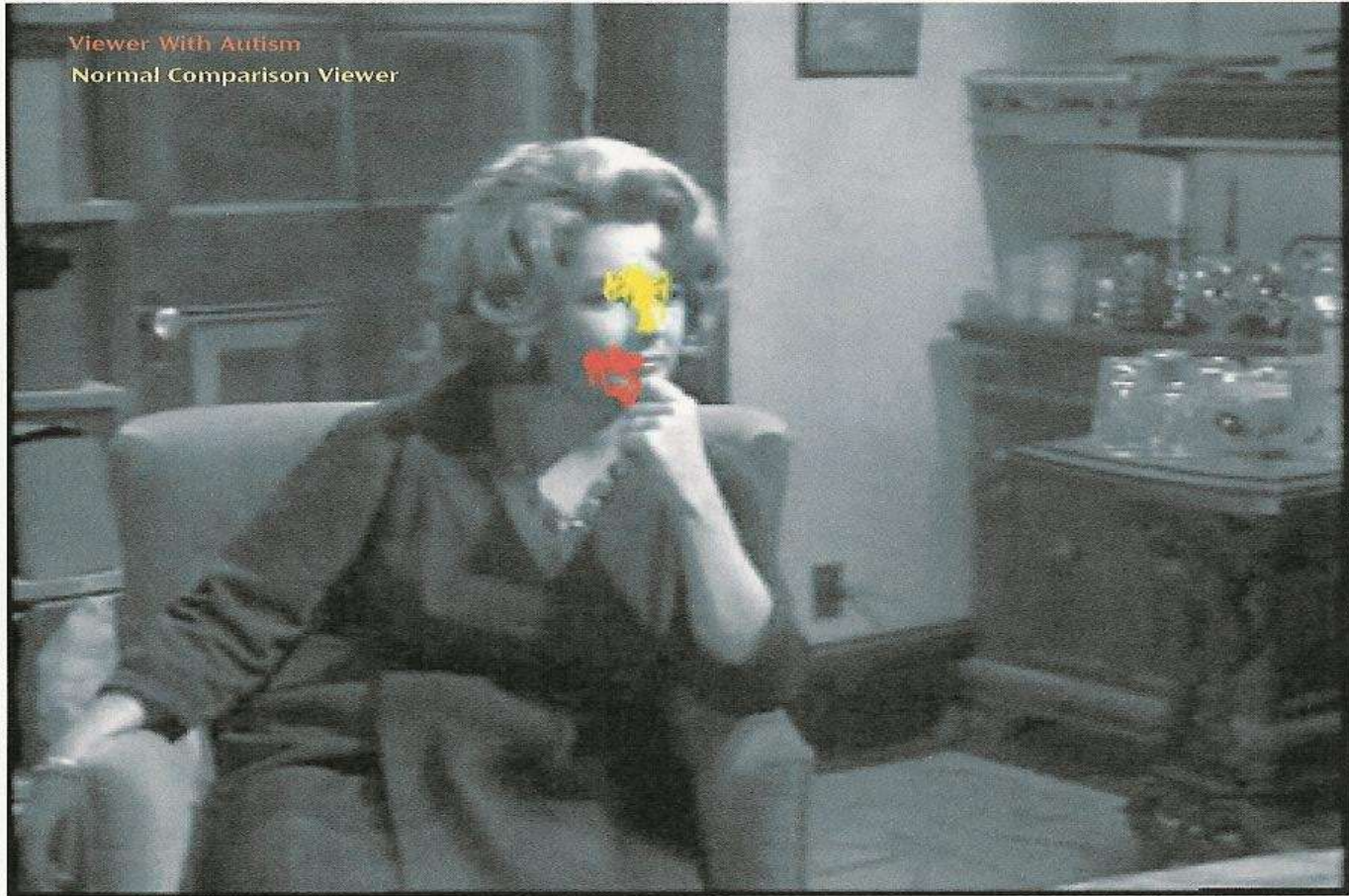


- They studied 110 infants, 59 of whom were at high risk for autism because each had an older sibling on the spectrum. The other 51 had no known relatives with autism.
- The researchers tested each infant 10 times between 2 and 24 months. Initial levels of eye contact for both groups were similar. But infants who did not develop autism increased their eye contact over time, while eye contact steadily declined among the 13 infants later diagnosed with autism. (Twelve of the 13 were from the high-risk baby siblings group.)
- In addition, those infants whose levels of eye contact diminished most rapidly were the most disabled by symptoms of autism at age 3.







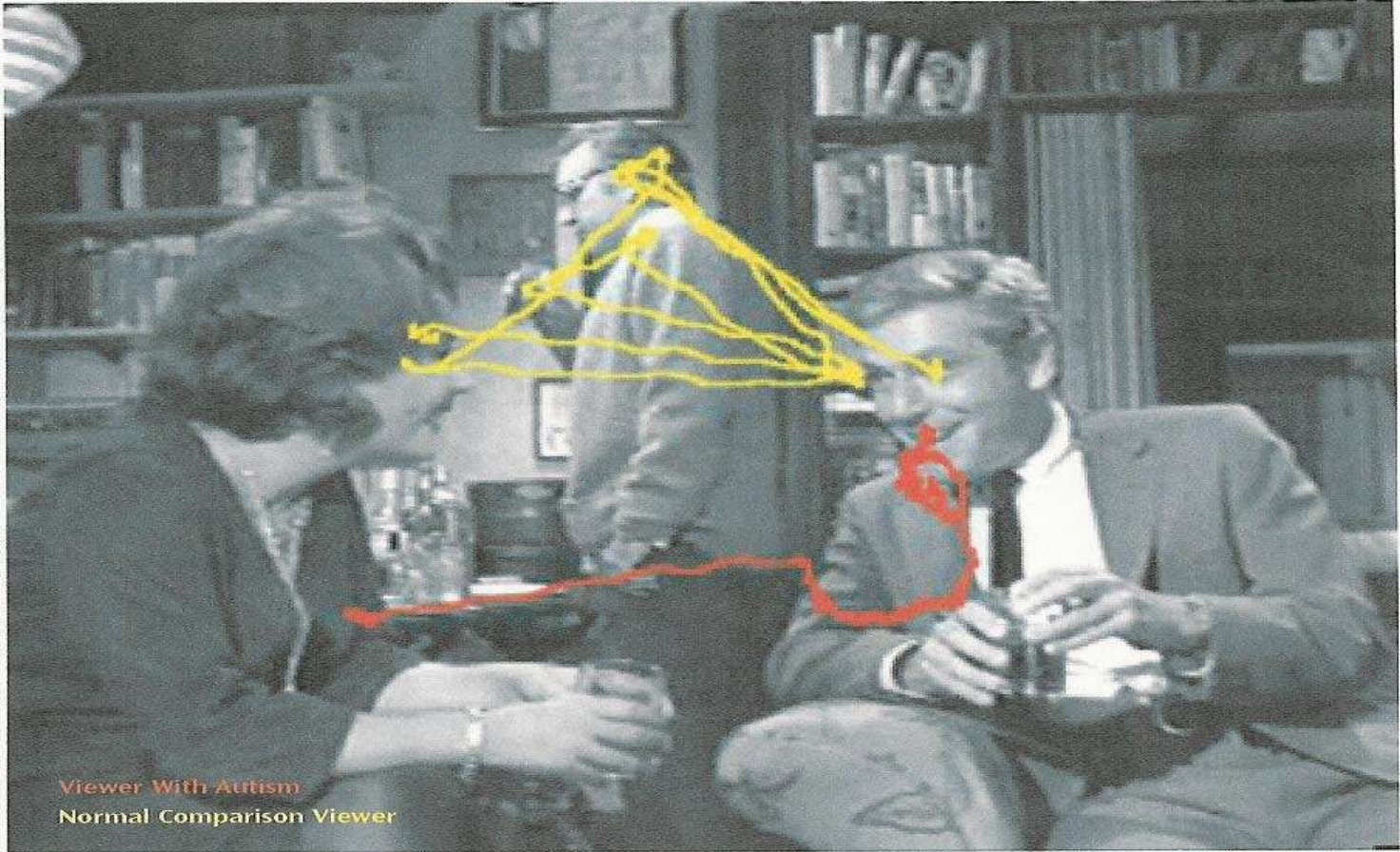




Viewer With Autism

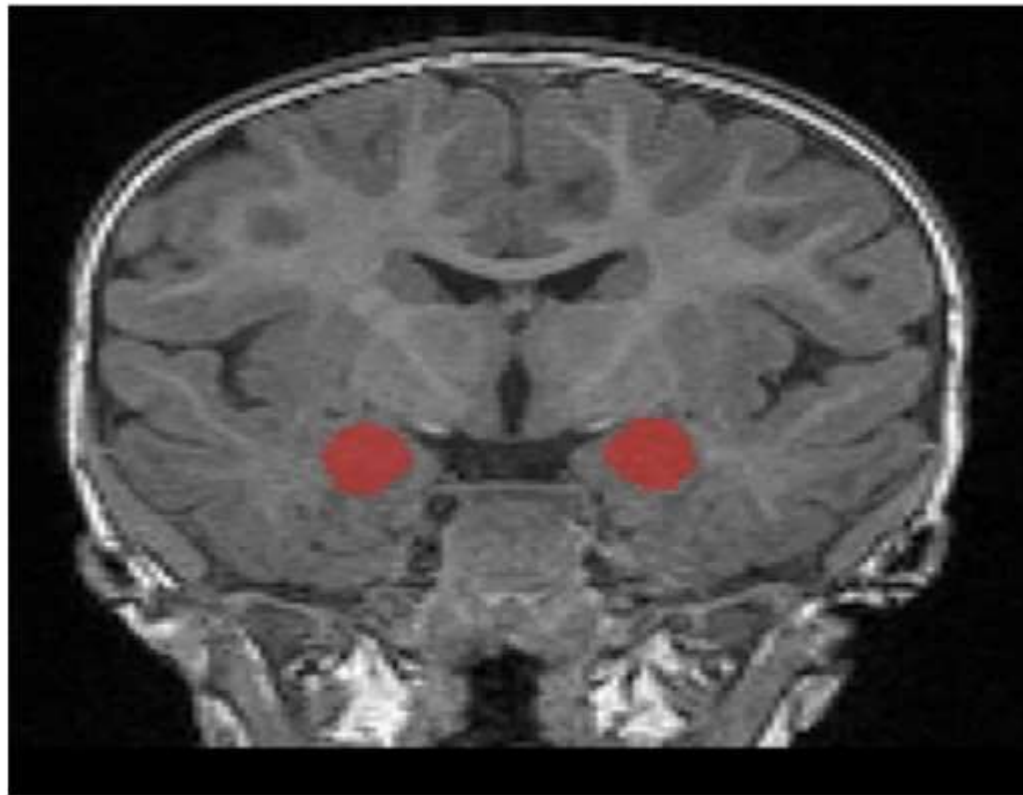
Normal Comparison Viewer





Viewer With Autism  
Normal Comparison Viewer





The amygdala (in red) grows too rapidly in babies (6-12 months) who later develop autism as toddlers.

Credit: CIDD at UNC-CH

Shen, Swanson et al

Subcortical Brain Development  
in Autism and Fragile X Syndrome:  
Evidence for Dynamic Age and Disorder  
Specific Trajectories in Infancy

AJP, 2022, online



# Case # 3





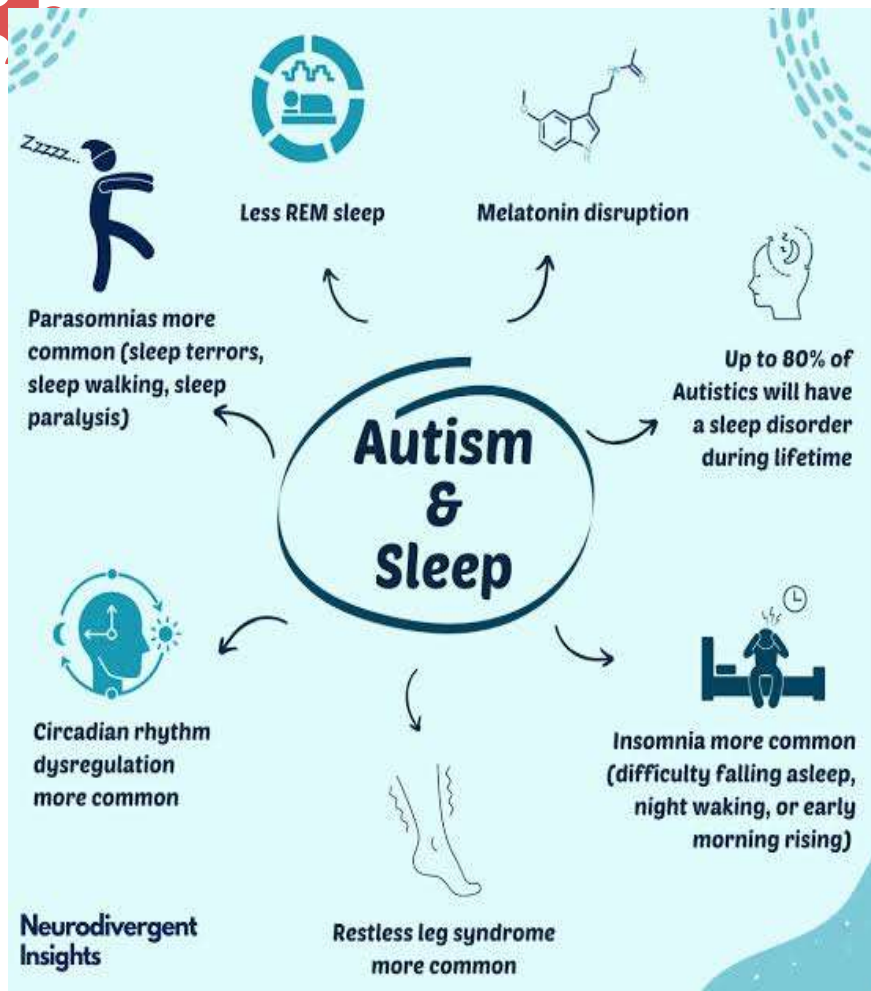
Saksham is a 12 year old brought to the child guidance clinic with primary symptoms of lack of eye contact and social interactions. He also has constant rocking movements and a fascination with chairs and stools. In the OPD too, he runs around the place and lines up all the stools like a long train. His mother claims their home also has all furniture lined up in long queues. He would get very disturbed if that sequence was not maintained.

Since he was a neonate his mother reports that he never slept through the night. He would be up every 1.5- 2 hours, play for about 1 hour, then sleep again. This pattern still existed. Only now he would get up at night and line everything in the home for about 2 hours, then sleep again. Further, this would impact his entire schedule through the day, as well as that of the parents.

Off late he had started getting a bit agitated too, but this was very occasional. The mother is at her wits end about what to do. She does report history of being a light sleeper all her life, and having insomnia through most of her pregnancy.

How do we approach this?





Autism & Sleep issues: Connections & How to Cope

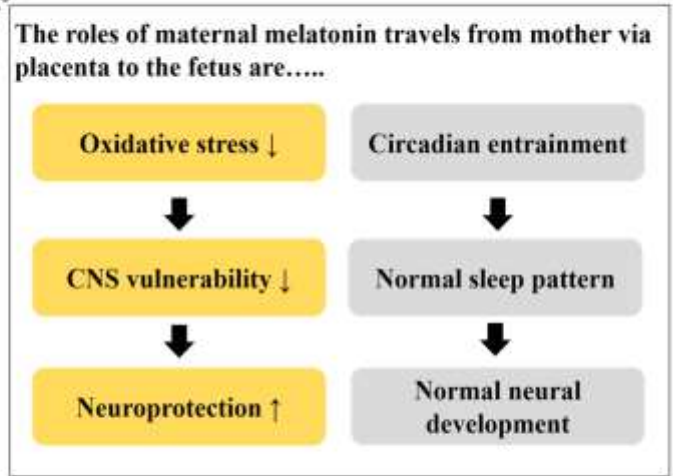
## What Causes Sleep Issues in Autism?

- Sensory issues
- Genetic factors
- Lack of melatonin
- Comorbid conditions
- Gastrointestinal issues

CHOOSING therapy



 Pineal gland  
 Placenta



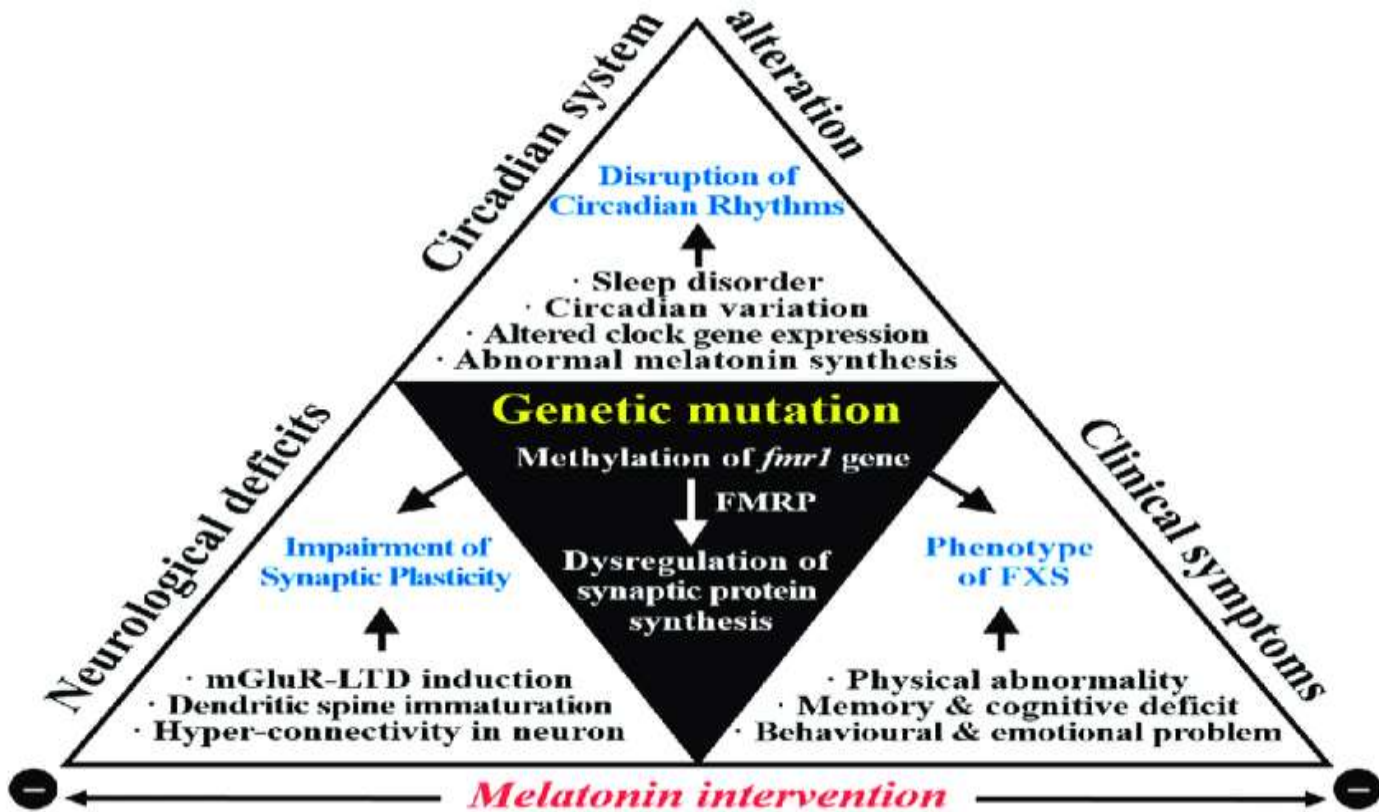
**↓ Reduce**

**Risk of ASD**

Jin, Yunho & Choi, Jeonghyun & Won, Jinyoung & Hong, Yonggeun. (2018). The Relationship between Autism Spectrum Disorder and Melatonin during Fetal Development. *Molecules*. 23. 198. 10.3390/

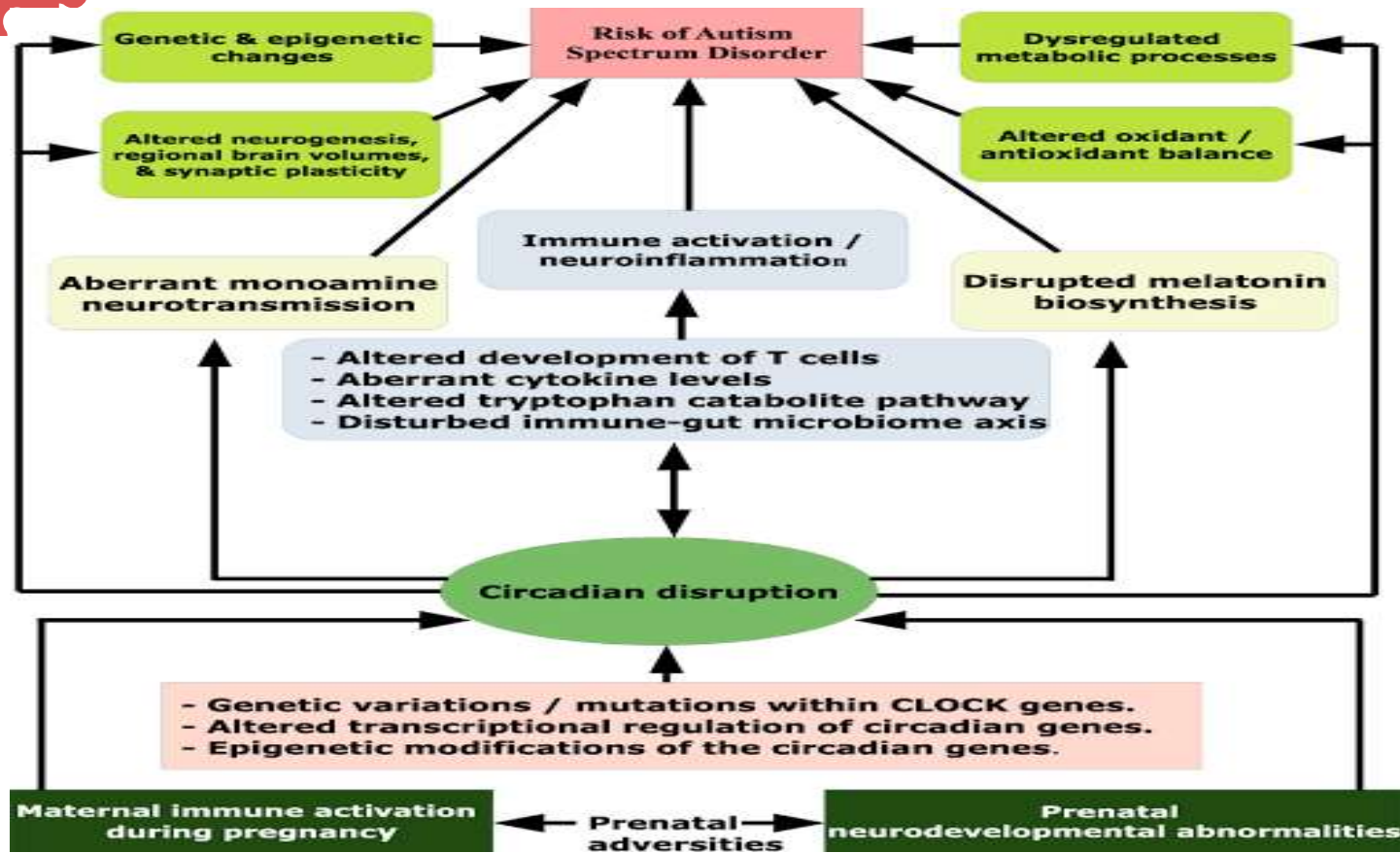


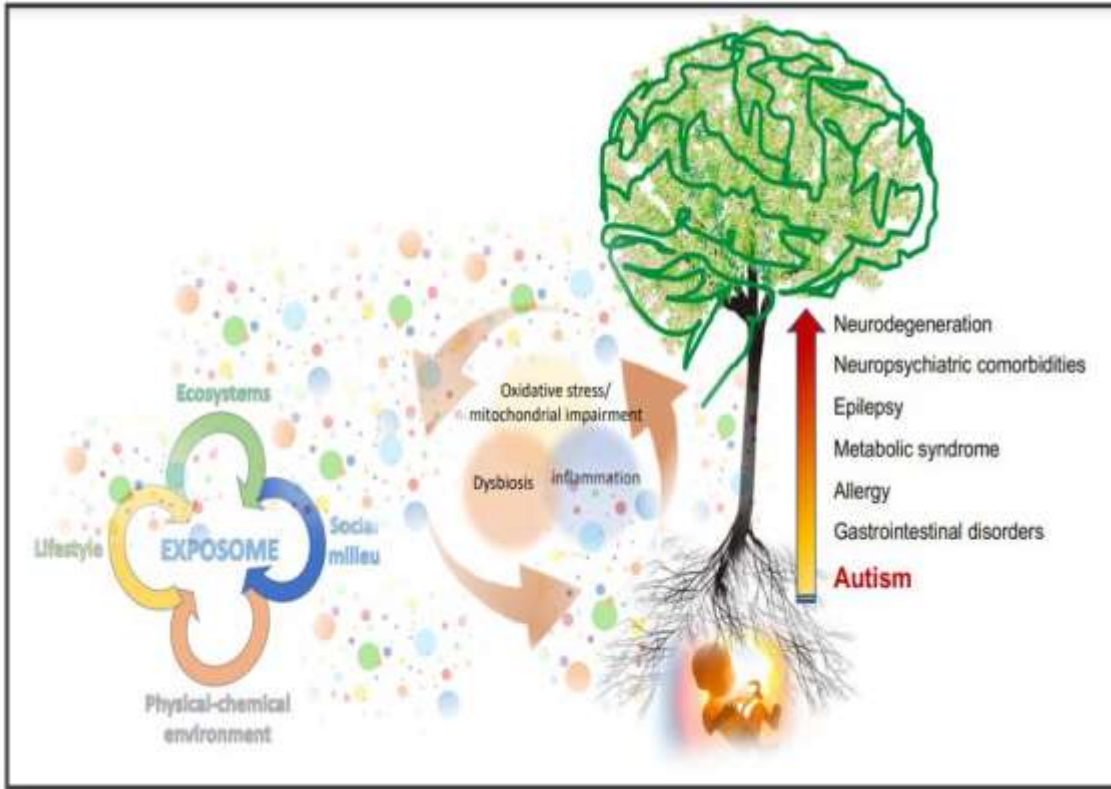




Won J, Jin Y, Choi J, Park S, Lee TH, Lee S-R, Chang K-T, Hong Y. Melatonin as a Novel Interventional Candidate for Fragile X Syndrome with Autism Spectrum Disorder in Humans. *International Journal of Molecular Sciences*. 2017; 18(6):1314.







Panisi, Cristina and Marini, Marina

Autism Spectrum Disorders: A change of Gaze in Research Opens a New Landscape to Needs and Solutions

Brain Sciences, 2022, Vol. 12, 2076-3425





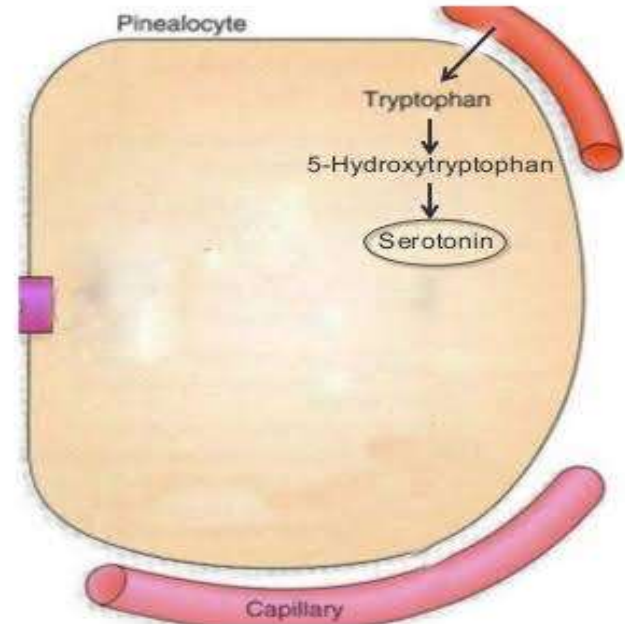
# Melatonin

## Treatment & Dosing Strategy



# Melatonin Regulation

- Melatonin is made from the amino acid tryptophan which is absorbed from blood into the pineal gland
- Tryptophan is then utilized through enzymatic reactions to yield serotonin
- During day light serotonin is stored inside the pinealocyte unavailable for further enzymatic reactions



# Melatonin for Sleep Disturbances in Children With Neurodevelopmental Disorders



Superior to placebo



Mild side effects



Recommendable  
for this population

Hotway, J. A., & Amsian, M. G. (2011). Pharmacological treatment of sleep disturbance in developmental disabilities: A review of the literature. *Research in Developmental Disabilities, 32*(3), 939–962.



Psychopharmacology  
Institute



# Clinical Approach for Sleep Disturbances in ASD: Medications



Start with melatonin



Consider the usage of  
clonidine or trazodone

Holley, J. A., & Aman, M. G. (2011). Pharmacological treatment of sleep disturbance in developmental disabilities: A review of the literature. *Research in Developmental Disabilities, 32*(3), 939-962.



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## Melatonin Dosage by Age

## Duration of Effects

5 years



1 to 2 mg

6 to 12 years



1 to 3 mg

Over 13 years



1 to 5 mg\*



Melatonin Half-life



Peak Levels



Levels Go Down

\*Consulting a doctor and starting with the lowest possible dose is recommended.

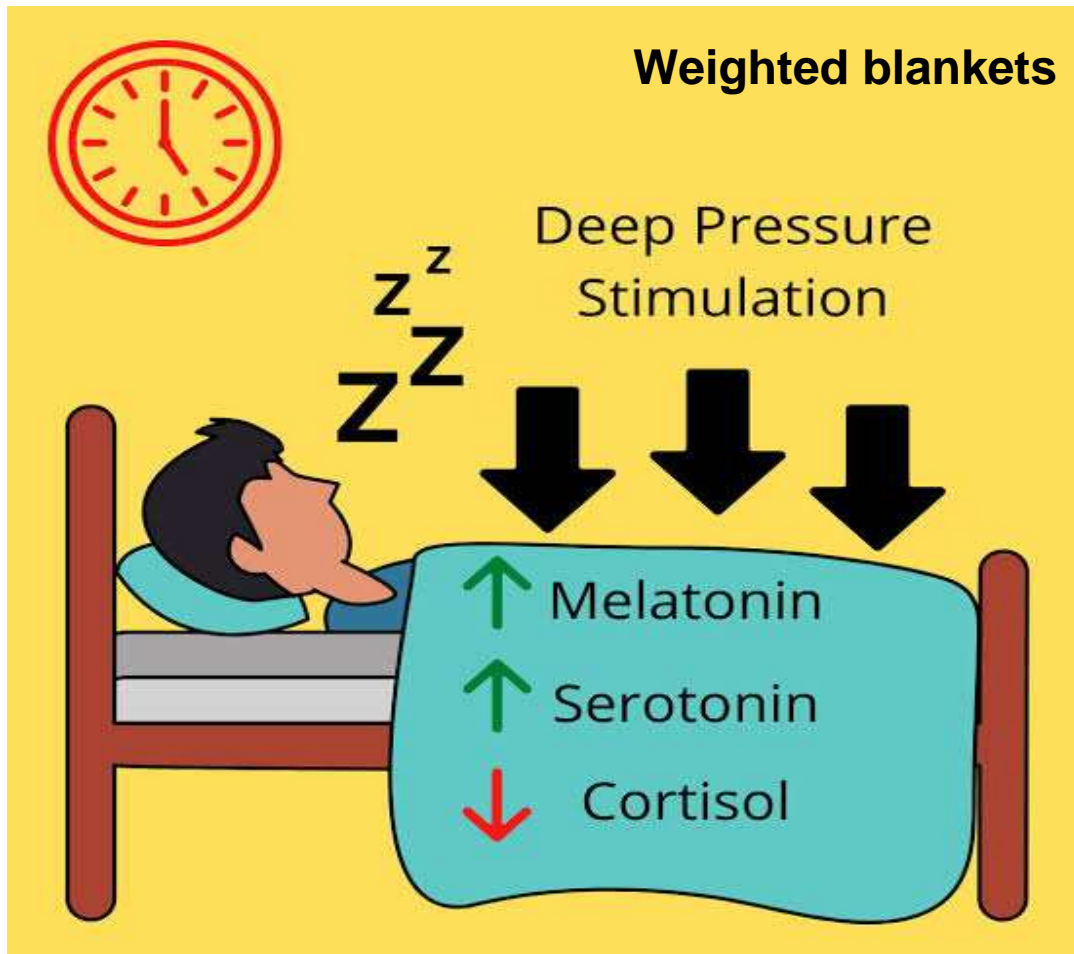


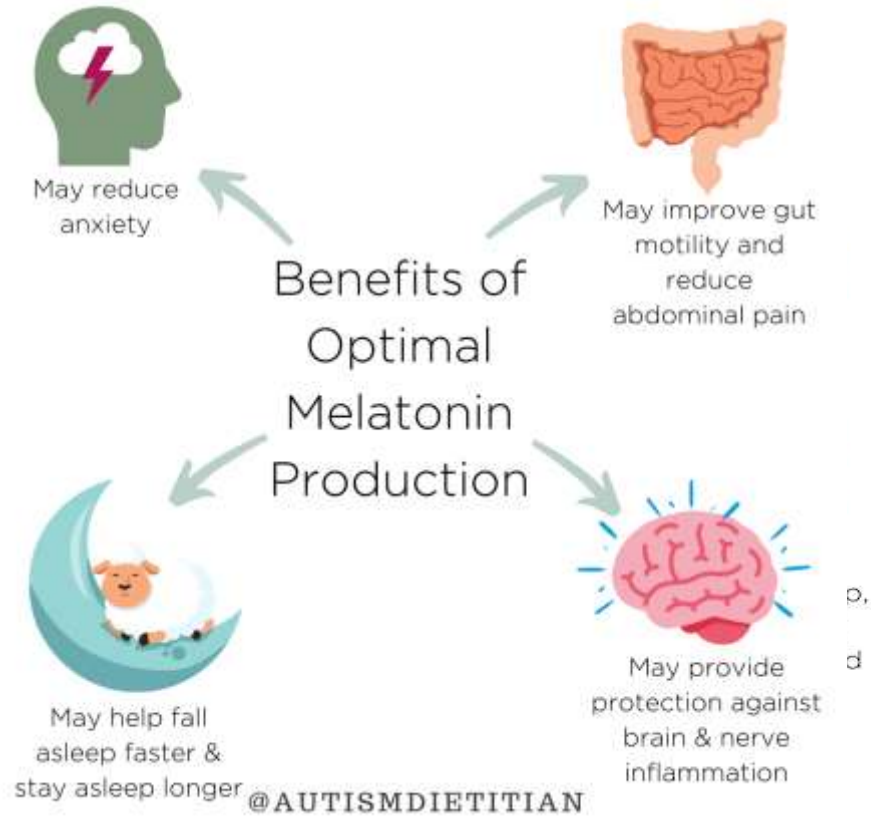




# Melatonin In therapy







# Case # 4





Mohan was a 12 year old boy, attending a special school, brought for aggressive behaviour since 1 year, multiple episodes of retching and vomiting since 5 days, repeatedly touching his genitalia and touching others inappropriately since 15 days. In the past he had been diagnosed with ?Childhood onset Psychosis v/s ASD, in a known c/o Borderline Intellectual Functioning(BIF). His developmental milestones all showed mild delay, though birth history was unremarkable.

His parents separated when he was about 6 years old. He had been diagnosed as ADHD with BIF in 2018-29 and started on Risperidone, Atomoxetine, Sertraline, Oxcarbazepine and Trihexyphenidyl. Subsequently the father took custody, and since 2020 he was treated in Mumbai. He then also had repeated handwashing and a trial of Fluvoxamine was given with Methylphenidate along with Risperidone. Subsequently, his behaviour worsened, he developed EPR with Risperidone, Olanzapine did not work, and Clozapine was thus initiated. Also his ASD work up was done, and a certificate was generated for the same. His behaviour continued to worsen and trials of naltrexone, sodium valproate etc. were all tried, with no significant change. In the 4<sup>th</sup> admission this time, he was tried on Clozapine 125 mg with minimal improvement. We could not escalate the dose further due to severe constipation.

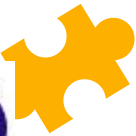
What can be the next step or course of action?





He was tried on memantine in addition to the Clozapine, and Memantine was introduced and up titrated from 5 mg to 20 mg. Within 8 weeks of the same, we saw the following changes:

1. Aggression significantly reduced
2. Rocking and disinhibited movements reduced
3. Sitting tolerance increased



# Memantine for ASD



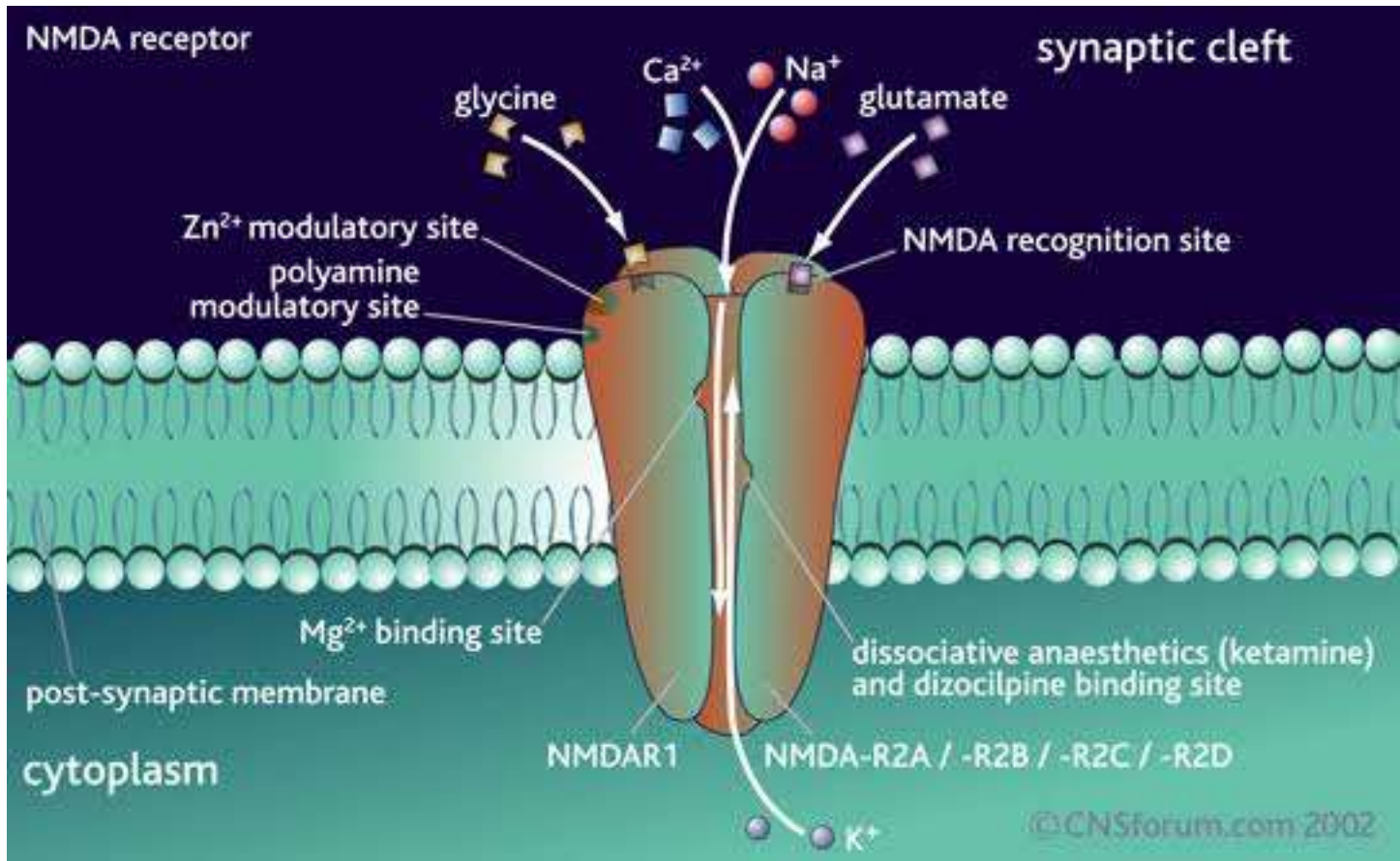
Glutamatergic dysfunction has been implicated in ASD

- Rosenberg, D., & Gershon, S. (2012). *Pharmacotherapy of child and adolescent psychiatric disorders*. John Wiley & Sons.
- Aman, M. G., Findling, R. L., Hardan, A. Y., Hendren, R. L., Melmed, R. D., Kehring-Nelson, O., Hsu, H., Trugman, J. M., Palmer, R. H., Graham, S. M., Gage, A. T., Perhach, J. L., & Katz, E. (2017). Safety and efficacy of memantine in children with autism: Randomized, placebo-controlled study and open-label extension. *Journal of Child and Adolescent Psychopharmacology*, 27(5), 403-412.



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# Evidence of Memantine Benefits in ASD



Social interaction



Language function



Memory



Behavioral symptoms



Stereotypic behaviors

- Rosenberg, D., & Gershon, S. (2012). *Pharmacotherapy of child and adolescent psychiatric disorders*. John Wiley & Sons.
- Aman, M. G., Findling, R. L., Hardan, A. Y., Hendren, R. L., Meinrad, R. D., Kefiride-Nelson, D., Hsu, H., Tiugman, J. M., Palmer, R. H., Graham, S. M., Gage, A. T., Perlich, J. L., & Katz, E. (2017). Safety and efficacy of memantine in children with autism: Randomized, placebo-controlled study and open-label extension. *Journal of Child and Adolescent Psychopharmacology*, 27(5), 403-412.



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# Memantine for Pediatric OCD

- Further RCTs are needed before it can be recommended
- It is used as an adjunctive treatment with additional improvement

Rosenberg, D., & Gershon, S. (2012). *Pharmacotherapy of child and adolescent psychiatric disorders*. John Wiley & Sons.



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# ASD

## Medication overview



# Medications used in the treatment of ASD-associated symptoms





\* FDA-approved indication.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; SGAs, second-generation antipsychotics; SSRIs, selective serotonin reuptake inhibitors.

**Formulary**

# Case # 5





Krutika, 24 yr old, came to the OPD to seek help. She always found it difficult to connect with people around her. Even in school she remembers sitting alone, as she was never taken in any group. She was good in reading and writing, and prolific at Math. She always was engrossed in studies. Now after having completed her studies in computer basics, she started working in a software firm, which does not involve too much interaction with others, and she has to create complex algorithms which she is good at. She spoke about her difficulty in social interaction, which has been since childhood. She also confided that she isn't sure of how she feels about her gender and her strong feelings for her colleague. She has never been in a relationship but experiences a strong desire to be with her female colleague. She feels its somewhat 'unconventional' , feels she is socially inept and sexually different.

What is happening to Krutika? How do we approach it?





## LGBTQ+ IDENTITY

### ARE AUTISTIC PEOPLE MORE LIKELY TO BE LGBTQ+?

**YES!**



Autistic people are twice as likely to be **LGB** than allistic people (George & Stokes, 2017), and three times as likely to be **transgender** or **gender diverse** (Warrier et al, 2020).

This might be to do with the different ways we relate to social norms in comparison to allistic people.

Regardless of why this is, **we know our own minds** and identities. **Respect and love** LGBTQ+ autistic people. We are an important part of the LGBTQ+ community, and the LGBTQ+ community is an important part of the neurodivergent community!

1/1



@neurodivergent\_insights

70%

Up to 70% identify as non-heterosexual

3-9 times more likely to identify as LGB

Sexual diversity & Autism

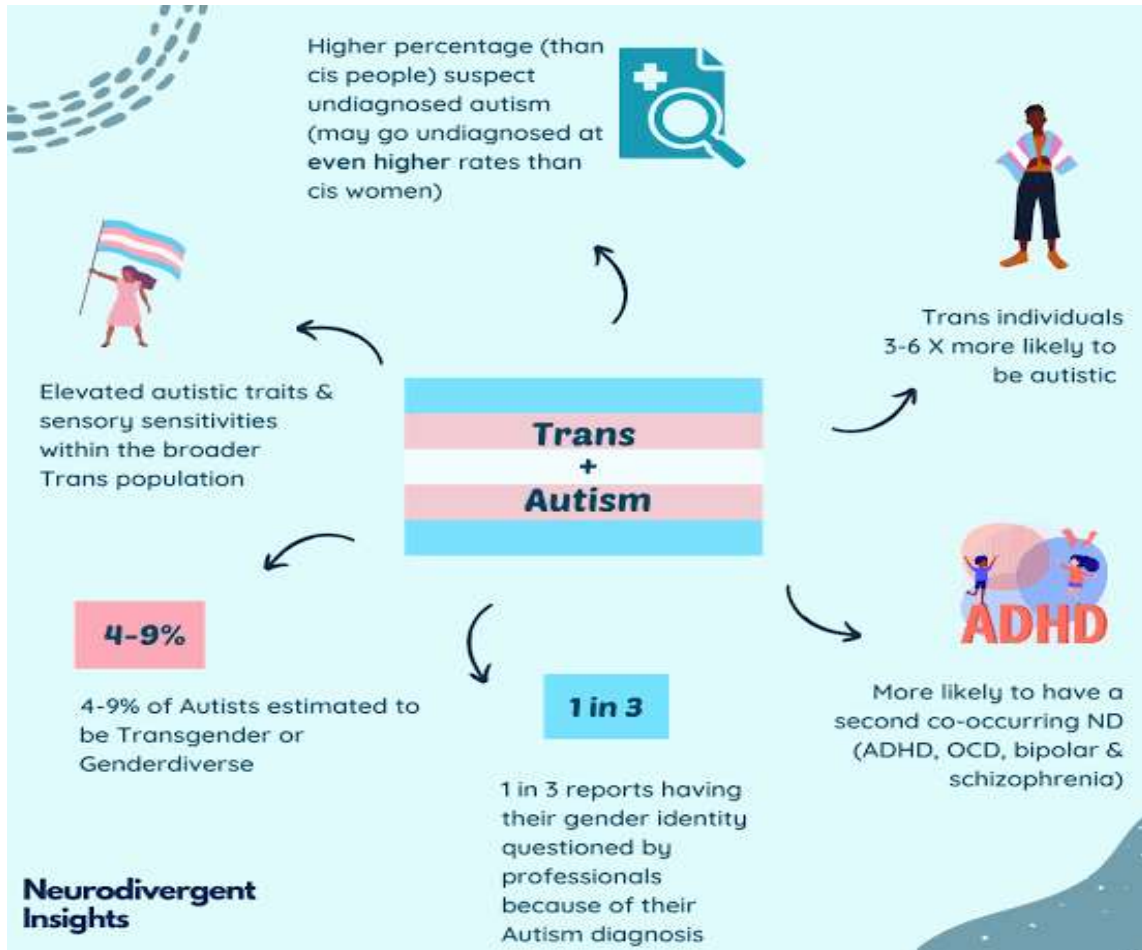
More likely to be polyamorous

More likely to identify as ACE/ARO (Asexual, Aromantic)



Less likely to adopt typical social norms around gender & sexuality. More likely to be trans, gender non-conforming & agender





# So what do we do for Krutika





Approach:

1. Take as long as needed to obtain detailed history
2. Simulate interactions with both sexes to judge pheromone reactions
3. Simulate digital/virtual interactions
4. Once ascertained, explain concept of gender identity and orientation preferably with social stories
5. Understanding boundaries in any adult relationship is a challenge for those on the spectrum, so anticipated pre-empted scenarios can be discussed





# QUICK RECAP



# Let's see what we learnt



## CASE 1

Autism  
endophenotype

## CASE 2

Eye tracking 2-6 months.  
Early clinical biomarker

## CASE 3

Melatonin is good for sleep

## CASE 4

Memantine can be tried in  
certain challenging cases

## CASE 5

LGBTQ Spectrum and ASD Spectrum overlap





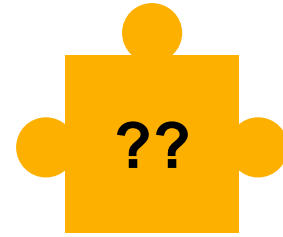
# THANK YOU

Autism needs to  
be handled with a  
heart along with a  
head



DYPATIL PG Lecture Series 2<sup>nd</sup> November, 2023





# QUESTIONS?

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# Thanks!



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