# IN THE NAME OF GOD

### COMORBIDITIES CONDITIONS IN ASD

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- Associated behavioral features include:
- Aggression
- Irritability, Temper tantrums
- Self-injurious behavior
- Hyperactivity, Impulsivity
- Attention problems
- Mood lability
- Anxiety
- Obsessions, and compulsions





## DIFFERENTIAL DIAGNOSIS OF AUTISM SPECTRUM DISORDER IN CHILDHOOD

- Neurodevelopmental
- Specific language impairment
- Intellectual disability/global developmental delay
- Mental and Behavioral
- Attention deficit hyperactivity disorder
- Oppositional defiant disorder
- Conduct disorder
- Attachment disorders
- Social anxiety disorder
- Major depressive disorder
- Obsessive-compulsive disorder
- Psychosis
- Tourette's disorder
- Selective mutism

### DIFFERENTIAL DIAGNOSIS OF AUTISM SPECTRUM DISORDER INADULTHOOD

- Anxiety and Mood Disorders
- Social anxiety disorder
- Major depressive disorder with melancholic features
- Obsessive-compulsive disorder
- Personality Disorders
- Obsessive-compulsive personality disorder
- Avoidant personality disorder
- Schizotypal personality disorder
- Schizoid personality disorder
- Psychotic Disorders
- Schizophrenia with predominant negative symptoms

# **86%**of people with autism had at least one comorbid condition.



- Comorbid conditions make it more complicated to manage and drastically influence the progress and outcomes of disorder.
- Targeted interventions based on comorbid condition.
- Treatment of comorbid symptoms improves function.
- Improved understanding of biological underpinnings.
- Change in diagnoses with aging.

### When to Consider Comorbidity

- An abrupt change from baseline.
- A severe and incapacitating problem behavior.
- Worsening of symptoms from baseline.
- When the child does not respond as expected to treatment.
- Signs of problems outside the autism spectrum are apparent.

#### ADHD

- ADHD may be the most common co-occurring psychiatric disorder among children with ASD, occurring in approximately 50% of one sample.
- ADHD in combination with ASD may confer significantly increased risk for a more complicated symptom presentation; nearly 85% of individuals with comorbid ASD/ADHD met criteria for an additional disorder.

#### **Intellectual Disability**

- In approximately 50–70 % of the individuals with ASD, an ID is present .
- $\circ$  Between 28 and 40 % of the individuals with ID have an ASD .
- $\circ$  The severity of ID is correlated with the rate of ASD.
- The social responsiveness and communication efforts of children with isolated global developmental delay/intellectual disability are usually appropriate for their developmental level, whereas those of children with ASD are aberrant for their developmental level. Clinical features that are more characteristic of ASD and coexisting global developmental delay than isolated global developmental delay/intellectual disability include impaired nonverbal behaviors and lack of social/emotional reciprocity.

#### **Communication disorders**

 In the communication disorders (apart from the new "SCD"), social skills are generally well preserved, even in the face of major language vulnerabilities.

 Language Disorder :characterized by a lack of qualitative impairment in social interaction, and the individual's range of interests and behaviors are not restricted.  Hearing impairment – In contrast to children with ASD, children with hearing impairment usually have normal reciprocal social interactions, imaginative play, normal eye-to-eye gaze, and facial expressions indicative of their intention to communicate.  Social (Pragmatic) Communication Disorder: characterized by impairment in social communication and social interactions, persistent difficulties in the social use of verbal and nonverbal communication (eg, sharing information, changing communication style to match the context or listener, following the rules of conversation and storytelling, making inferences, understanding nonliteral or ambiguous meanings of language [eg, idioms, humor]). It is distinguished from ASD by the absence of restricted, repetitive patterns of behavior, interests, or activities.

- Attachment disorder Similar to children with ASD, children with severe early deprivation or reactive attachment disorder may have abnormalities in social interaction, communication, and behavior. However, there usually is a history of severe neglect or mental health issues in the caretaker.
- In addition, the social deficits of children with attachment disorder tend to improve in response to an appropriate caregiving environment.

#### **Stereotypic Movement Disorder**

- Occurs in the absence of impairment of social interaction and language development.
- Stereotypic Movement Disorder is generally not diagnosed if the stereotypy is part of Autism Spectrum Disorder; however, when stereotypies cause self injury and become a focus of treatment, both diagnoses may be appropriate.

#### Stimulants

- Comorbid difficulties with attention are common in ASD and there is much argument about whether or not this represents a true comorbid diagnosis or an expected symptom dimension in ASD. The answer to this question is less relevant in the context of evidence that supports the use of stimulants in individuals with ASD who have significant ADHD symptom.
- A randomized controlled trial of methylphenidate in children with ASD and ADHD symptoms found a response rate of 49%
- This is lower than rates reported for children with ADHD who do not have ASD. In addition, effect sizes reported were smaller, and side effects were more frequent. Given these findings, stimulant treatment remains appropriate in some cases.

#### Anxiety disorder

 Anxiety symptoms seem to be "part and parcel" of the everyday experience of many individuals with ASD, with a large number (over40%)

• Specific Phobias or fears

- Social Anxiety
- Generalized Anxiety
- Panic Disorder

#### **Mood Disorder**

#### • **Depression**

 Depression and Mood Disorders have produced the most variable comorbidity rates of all the mental health conditions, ranging from very rare (less than 1%) to upwards of 30%.

#### • Bipolar Disorder

- Approximately 2% of adolescents in the general population meet criteria for bipolar I disorder
- A recent systematic review of the literature on adults with ASD reported similar rates, from 6 to 21%

#### **Obsessive-Compulsive and Related Disorders**

 In the largest study of co-occurring OCD and ASD to date, we found that approximately 25% of young people with OCD also had a diagnosis of ASD. To our knowledge, this is the first prevalence estimate of ASD in a clinical population of youth with OCD.

 In study by Mohammadi et al in 2019 on the prevalence of obsessive compulsive disorders among Iranian ASD was 13.5%.

## **Tic Disorders**

- In a recent large study of clinic-referred children with ASD, 23% met criteria for chronic motor or vocal tic disorder, while 18% met full criteria for Tourette's disorder.
- A study of clinic-referred adults documented that **20%** met criteria for chronic tic disorders .
- Atypical social interactions in children with tic disorder or Tourette syndrome are typically due to coexistent anxiety, impulsivity, and/or poor self-esteem related to tics.

## Psychosis

 A one study of 217 consecutive referrals to a psychopharmacology clinic found a high (20%) rate of comorbid ASD and psychosis, but caution is required in interpretation, as this sample comprised individuals referred for psychiatric care.

## Suicide

- The second leading cause of death among young people aged 10–34 in general population.
- The real prevalence is unknown and especially in ASD is underestimated.
- One third of ASD individuals reports suicidal ideation.
- Life-time suicide attempts in ASD individuals (**38%**) are also higher than in general population (8%).

## Non-suicidal self-injury

 Non-suicidal self-injury is higher in ASD individuals (63.6%) than in general population (29.8%) and significantly predicts suicidality in ASD individuals .

## Medical comorbidity

- Presence of at least one medical comorbidity was observed (59.7%).
- The number of comorbidities per subject varied from one to four.
- Overall, epilepsy is the most represented medical condition ( 15.18%), followed by allergic rhinitis (8.9%) and irritable bowel syndrome ( 6.8%).

## **Allergic condition**

- Food allergies were the most common allergic condition found in children with autism, and the association was consistent and significant in all age, sex, and racial/ethnic subgroups in the population-based.
- It has been demonstrated that a challenge with nasal allergens results in increase of autism symptoms in over half of children studied .while treatment of allergies often results in improvement in behaviours such as anxiety, hyperactivity, and irritability, commonly attributed to 'being autistic'

- Recent studies have confirmed the existence of non-celiac wheat sensitivity as a new clinical entity. Patients with a history of allergies and atopic diseases are more likely to suffer from nonceliac food sensitivity.
- Since children with autism are almost twice as likely as controls to suffer from atopy and allergies, possible wheat sensitivity in those children needs to be considered, especially when irritable bowel syndrome symptoms are present.

## **Autoimmunity in ASD**

- The connection between autism and autoimmune disorders is gaining increasing support with a number of studies demonstrating a high incidence of autoimmune conditions in autism and an association between serum levels of various autoantibodies and severity of autistic symptoms
- Family history of autoimmune diseases is significantly higher in autistic children than in general population
- Animal models show clear connections between anxiety, abnormal social behaviours and levels of proinflammatory cytokines.
- Correcting immune abnormalities in post-exposure experiment animals with immunemodulatory treatments results in normalisation of immune function, and more importantly, improvements in cognitive function and complete and lasting reversal of abnormal autism-related behaviours

## Gastrointestinal comorbidities

 Gastrointestinal problems are a commonly found in autism and may be related to problem behaviours, sensory overresponsitivity, dysregulated sleep, anxiety and irritability.



Figure I GI symptoms (left side) and GI disorders (right side) described in children with autism spectrum disorder.

Abbreviations: GI, gastrointestinal; FAP, functional abdominal pain; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; LNH, lymphonodular hyperplasia.

## Gastrointestinal symptoms

- 1.overproduction of intestinal gasses/flatulence (60%)
- 2.bloating (38%)
- 3.abdominal pain (378%)
- 4.diarrhea (28%)
- 5.burping/belching (25%)
- 6.gastroesophageal reflux symptoms (16%)
- 7.Constipation (10%)

 Analyses of the bacterial flora composition of individuals with autism have frequently revealed the presence of abnormal bacteria, as well as translocation of bacterial species to parts of gastrointestinal system that are not host to those bacteria in healthy individuals.

#### $\circ\,$ Metabolic/biochemical changes found in the urine

- Metabolic/biochemical changes found in the urine of individuals with autism further confirm the gut microbiota abnormalities revealed by stool and ileal tissue investigations.
- Endotoxemia has been observed in patients with autism, and the levels of bacterial toxins in the blood have been found to correlate to severity of autismsymptoms.

- This is believed to result from both the increased presence of pathogenic bacteria and the increased intestinal permeability seen in autism.
- A small treatment trial of oral vancomycin noted a decrease in autism-related behaviours following a course of this antibiotic.
- Possible correlation is between levels of pathogenic bacteria and severity of autistic symptoms.

## Oxidative stress, acquired mitochondrial dysfunction and metabolic abnormalities

 There is increasing evidence that mitochondrial dysfunction, perturbation in sulfur and amino acid metabolism, and high levels of oxidative stress are common in persons affected by autism.

- Elevations in metabolic markers of oxidative stress as well as reduced levels of glutathione and other cellular antioxidants have been found in many areas of the body, including the brain and primary immune cells.
- Reactive oxygen species are destructive to cells and organs, and elevated oxidative stress has been implicated in autoimmune, inflammatory, cardiovascular and neurodegenerative diseases, and cancer.

## Autonomic nervous system dysfunction

 Elevated sympathetic and lowered parasympathetic activity is frequently present in children and adults with autism whether or not they have more obvious outward symptoms or signs of autonomic abnormalities.

