

Autism Spectrum Disorders

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Disclosures

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Definition

- Autism Spectrum Disorder (ASD) in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) refers to neurodevelopmental disorders manifesting with
 - “persistent deficits in social communication and social interaction across multiple contexts,” as well as
 - Restricted, repetitive patterns of behavior, interests or activities
 - Present in early development
 - Impairment in social, occupational or other areas of current functioning.

Older (DSM-IV-TR) Diagnoses in Individuals with ASD

- Autistic Disorder: meets all DSM-IV-TR diagnostic criteria; more severe form.
- Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS): subthreshold for diagnostic criteria.
- Asperger Disorder: social impairments, restricted/repetitive interests, normal language development.

Current Prevalence

- 1 in 68 (CDC, USA)
- 25 years ago: 1 in 10,000
- Potential explanation: increased recognition, genetic predisposition, environmental toxins, better educational services

Screening

- Early detection and referral for multidisciplinary evaluation, eg at a university hospital is vital.
- Usually present by age 3 years.
- Four times more common in boys than girls.
- Modified Checklist for Autism in Toddlers (M-CHAT): should be done at 18- and 24-month doctor visits.
- Autism Diagnostic Interview – Revised (ADI-R).
- Autism Diagnostic Observation Schedule (ADOS).

Early Signs of Autism

- Not answering when name is called; deafness is often suspected
- Fails to point to things wanted
- Not communicating back-and-forth
- Distress with changes in routines or habits
- Unusual movements such as hand-flapping or toe-walking
- Regression in language; social relating and other developmental areas occurs in approximately 25% of cases around 18 months (between 15 and 24 months)

Language delays, impairments are common

- Up to 25% may not develop language
- Others may echo what is said to them
- Perseveration: repeating the same thing over and over
- Abnormal use of pronouns eg “You” in place of “I,” or “him” in place of “her,” etc.

What Causes Autism?

- Multiple genetic risk factors:
 - 2q, 7q 31-35, 11q, 15q 11-13, 16p 13.3, plus regular new identifications
 - Identical twins: 60-90% concordance
 - Fraternal twins: 0-36%
 - Siblings: increased risk 4-10%
- MET susceptibility gene for autism, brain circuit development, immune function, gastrointestinal repair

ASD and Epigenetic (Environmental) Risk Factors

- Prenatal and early postnatal infections eg. rubella, valproic acid (established)
- Genetic susceptibility to environmental factors
- Proposed: parental age, vitamin D deficiency, radiation, vaccines, environmental pollutants

ASD and Immune Dysfunction

- Hyperactivity, stereotypies in rhesus monkeys injected with IgG from mothers of offspring with autism (Martin et al. 2008)
- Neuroinflammation identified in post mortem brains, CSF (Pardo et al. 2005)

ASD and Structural Brain Abnormalities

- Excess of neurons; inadequate pruning
- Abnormal white matter before one year
- Cerebellar abnormalities

Early Intervention: may resculpt mirror neurons

- Early, intensive behavior treatment (Applied Behavior Analysis) may improve language, cognitive and adaptive skill outcomes
- Treating associated conditions (medical, psychiatric) can also improve overall outcome in terms of language and functioning
- No treatments, as of yet, to reverse core features of autism

Multidisciplinary Assessments Needed

- Audiology: rule out deafness, identifying any hearing impairment
- Physician: medical evaluation, developmental pediatrician, psychologist, neurologist if seizures suspected
- Genetic consultation: for all cases
- Psychiatrist: hyperactivity, compulsivity, aggression, self-injury
- Occupational therapy
- Speech and Language
- County Board of DD, social worker
- Local school system

Associated Conditions in ASD

- Epilepsy: Prevalence of up to 46% (Spence and Schneider, 2009), increased risk with greater degrees of intellectual disability
- Intellectual Disability (formerly Mental Retardation): prevalence of up to 66% (Wong, 2008)

Associated Conditions in ASD

- Insomnia: extremely common, try sleep hygiene, melatonin
- Gastrointestinal Symptoms, restricted food choices: extremely common; including constipation and diarrhea: avoid white flour products, give pears, plums, and prunes in place of apples and bananas for constipation
- ADHD, anxiety, depression, bipolar disorder, Tourette, other

Psychiatric Comorbidity, Aggression and Self Injury

- Clarify and rule out possible medical causes, including dental problems, otitis media, headaches, and other possible causes of distress
- Rule out possible medication causes, including older anti-seizure medications such as phenobarbital, phenytoin, ethosuximide

Psychiatric Comorbidity, Aggression and Self Injury

- While referral to a developmental pediatrician or psychiatrist may be necessary, communication and awareness of potential interactions and adverse events is vital.

Complementary and Alternative Medical (CAM) Treatments: Require Further Study

- Food Sensitivities, gluten and/or casein intolerance, celiac disease: GFCF diet, digestive enzymes, pepcid, secretin, antibiotics, probiotics
- Neurotransmitter effects: release/production: B6, Magnesium, St. John's Wort, Omega 3
- Methylation: glutathione, folinic acid, methylcobalamine

Complementary and Alternative Medical (CAM) Treatments: Require Further Study

- Possible immune improvements: Vit A, i.v.IgG, antifungals
- Hyperbaric oxygen treatment (HBOT)
- Heavy metal removal: Chelation, DMSA or DMRA

Language-Based Interventions

- Picture Exchange Communication System (PECS)
- Communication devices, books
- Computer programs
- Auditory Integration Training

Behavioral Treatments: Advise parents to “keep a positive atmosphere”

- Applied Behavior Analysis (ABA)
- TEACHH – Treatment, Education of Autistic and Communication Handicapped Children
- Parent-Child Interaction Training (PCIT)
- Floor time (Greenspan)

Psychiatric Treatment Principles Continued

- “Start low and go slow”
- Avoid benzodiazepines (disinhibition)
- SSRIs paroxetine, sertraline, inhibit cytochrome P450 2D6 in liver, and thus increase effective doses of many drugs significantly, including atypical antipsychotics (resulting often in greater weight gain), benzodiazepines, others

Psychiatric Treatment Principles Continued

- SSRIs may appear to work initially but later cause activation
- Stimulants are poorly tolerated: may worsen anxiety, sleep, appetite, mood, self-injury
- Non-stimulant ADHD medications may be tried: Atomoxetine: can use BID, watch for tachycardia, raised BP, especially with beta stimulants for asthma

Psychiatric Treatment Principles Continued

- Weight gain, metabolic syndrome, Type 2 Diabetes, with atypical antipsychotics
- Loxapine warrants further study for aggression in adolescents and adults in doses of 5-15mg per day for aggression and irritability (Hellings et al, NCDEU poster abstract, 2012)

Psychiatric Principles Continued

- Affect dysregulation of ADHD, often manifesting as rages, should not be misdiagnosed and mistreated as bipolar disorder
- Impulsive aggression may be a common presentation of comorbid ADHD after adolescence. Clarify history of hyperactivity as a child, try ADHD medications if positive (stimulant and/or nonstimulant medication)

Conclusions

- Early referral, multi-disciplinary assessment, and treatment interventions improve outcomes
- Psychotropic medication combinations in low doses may be most effective, studies are still needed
- Use an integrated approach to treatment