

# Autistic Spectrum Disorders (s. Pervasive Developmental Disorders)

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Autistic spectrum disorders – neurobiologically diverse group of conditions whose precise relationship to each other is unclear:

1. **Autistic disorder** – severe prognosis
2. **Asperger disorder** – good prognosis
3. **Rett disorder** – very severe prognosis
4. **Childhood disintegrative disorder** – very severe prognosis
5. **PDD not otherwise specified (PDD-NOS)** – moderate prognosis

- these disorders can be detected and distinguished from other forms of developmental delay before age 3 years! (parent interviews and videotapes have demonstrated manifestations as early as age 12 months)

## AUTISTIC DISORDER (s. AUTISM)

- as recently as 1970s, autistic children were commonly labeled as "psychotic".

### CLINICAL FEATURES

- diffuse pattern of abnormality across several areas of behavior.

**AUTISM** - qualitative impairments in **social interactions, communication,** and **patterns of behavior** often with mental retardation

- preoccupation with internal world - child is relatively **unresponsive to other human beings**, demonstrates **bizarre responses to his environment**, and has **unusual language development**.
- DEVELOPMENT is atypical in **social** and **language** areas (i.e. development is not merely slow or limited).

vs. **MENTAL RETARDATION** - **global** developmental delay.

**DSM-IV-TR diagnosis of AUTISM** - at least 6 of below symptoms (at least 1 item from each of 3 symptom groupings, at least 2 symptoms must come from social impairment group).

**Group 1** (qualitative impairment in **social interaction**) - at least 2 of following:

- a) marked impairment in use of multiple **nonverbal behaviors** such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction.
- b) failure to develop **peer relationships** appropriate to developmental level.
- c) lack of spontaneous **seeking to share** enjoyment, interests, or achievements with other people (e.g. by lack of showing, bringing, or pointing out objects of interests).
- d) lack of social or emotional **reciprocity**.

*Characteristic - lack of social chat (especially lack of social reciprocity), pragmatic deficits, pronoun reversal, delayed echolalia, neologisms, lack of emotion in speech, phrase repetitions, idiosyncratic use of language.*

*Autistic children treat other individuals as though they are inanimate objects.*

**Group 2** (qualitative impairments in **communication**) - at least 1 of following:

- a) delay in, or total lack of, development of **spoken language** (not accompanied by attempt to compensate through alternative modes of communication such as gestures or mime).
- b) in individuals with adequate speech, marked impairment in ability to **initiate or sustain conversation** with others.
- c) stereotyped and repetitive **use of language** or idiosyncratic language.
- d) lack of varied, spontaneous **make-believe play** or **social imitative play** appropriate to developmental level.

*Deviant communication features with limited language development (failure to learn to speak and limited language comprehension)! Echolalia, pronoun reversals (e.g. use of "you" when "I" is correct), mutism, qualitative abnormalities (e.g. sing- song or monotonous quality).*

**Group 3** (restricted repetitive and stereotyped **patterns of behavior**, interests, and activities) - at least 1 of following:

- a) encompassing preoccupation with one or more stereotyped and restricted **patterns of interest** that is abnormal either in intensity or in focus.
- b) apparently **inflexible adherence** to specific, nonfunctional routines or rituals.
- c) stereotyped and repetitive **motor mannerisms** (e.g. hand or finger flapping or twisting, or complex whole body movements).
- d) persistent preoccupation with **parts of objects**.

*Rigid, stereotyped, repetitive patterns of unusual behavior; frequently involve repetitive, self-stimulatory behavior (can be self-injurious, as arm biting, head slapping, skin picking).*

*Autistic children have great need for consistency in their environment (may decompensate if, for example, furniture is rearranged).*

*Children may look at same video or book for hours, play with string or spin wheels of car, and prefer to line up or classify toys rather than play with them.*

- delays or abnormal functioning as depicted in any one of symptom groups **must be present by age 3 years**. *Severe regression of language and sociability occurs at age 18-24 months*

- autistic children may not lack affection, but they may be selectively affectionate (may be anxious or fearful, have labile mood, and may laugh or cry without discernible cause); temper tantrums and seemingly unprovoked aggressive outbursts create social problems.
- one of earliest and most sensitive markers for autism is 1-yr-old child's **inability to point communicatively at objects** (child cannot imagine that another person would understand what was being indicated; instead, child indicates wants only by physically touching desired object or using adult's hand as tool).

**Seizures** occur in 30% autistic children! (esp. if IQ < 50).

- few **epileptic syndromes** are clearly linked to diagnosis of autism (tuberous sclerosis, Lennox-Gastaut, West syndrome, Landau-Kleffner syndrome, pyridoxine-dependent seizures).

## ETIOPATHOPHYSIOLOGY

> 60 different disease entities have been shown to be likely causes of autism (autism may be final common clinical presentation of variety neurobiological and genetic processes).

- abnormalities have been reported on every **chromosome** as associated with autism (esp. on X chromosome);
  - **fragile X** is present in 2-4% cases.
  - **tuberous sclerosis** is present in 1-4% cases.
  - **concordance** for monozygotic twins 60-90%; for dizygotic < 5%.
  - rate of autism in **siblings** is 2-6% (i.e. 6 times risk in general population).
  - many **family members** of autistic persons have broader autistic phenotype with milder features characterized by:
    - (1) less severe stereotyped repetitive behaviors
    - (2) more subtle social deficits
    - (3) normal intelligence
    - (4) lack of abnormal language features
    - (5) lack of association with epilepsy.
- > 7% children with autism have **mitochondrial** disease.
- 1/3 patients have blood [**serotonin**]↑, but 5% have ↓.
- mothers (of children with autism spectrum disorders) were twice as likely to report that they had shampooed their pets with **pyrethrin-containing antiflea / antitick shampoos** during pregnancy.
- searches for **structural abnormalities** produce similar inconsistent results (current belief is that autism reflects abnormalities within particular neural system or multiple neural systems, which are connected networks of variety brain regions).
- several **immune dysfunctions** were detected (depressed immune function, autoimmune mechanisms, or faulty immune regulation may be associated with etiology of autism).
  - major epidemiologic studies have failed to find evidence that MMR vaccine or thimerosal (mercury vaccine preservative) exposure is associated with autism.
- historical theory - **cold, distant mother figure** responsible for development of coldness and aloofness in child (i.e. growing in emotional vacuum leads to unrelatedness in child).

## EPIDEMIOLOGY

- **≥ 0.1%** of general population has classic autism by *DSM-IV* criteria.
- **males** : females = 3-4 : 1 (female prevalence increases as disease severity increases).

## DIFFERENTIAL DIAGNOSIS

- 1) mental retardation
- 2) congenital rubella syndrome, cytomegalic inclusion disease
- 3) childhood schizophrenia
- 4) hearing impairment
- 5) developmental language disorders
- 6) genetic disorders (fragile X syndrome, phenylketonuria)
- 7) profound isolation and neglect

## TESTINGS

Screen for phenylketonuria!

- **routine**:
  - 1) **chromosome analysis**; chromosomal microarray analysis is highly sensitive
  - 2) **DNA testing** for fragile X syndrome.
- relatively little is found on **physical examination** (**head circumference** is > 97<sup>th</sup> percentile in 25% patients).
- **abnormal EEG** is found in 43% patients (esp. those with lower IQs).
- **psychiatric, cognitive & linguistic assessments** are crucial so that individualized treatment can be developed, with programs aimed at appropriate level.
 

Testings can be difficult in face of severe language difficulties, but specific tests are available!
- formal “gold standard” diagnostic test - **Autism Diagnostic Observation Schedule (ADOS)** based on DSM-IV criteria - administered by psychologists.
- **IQ tests** - children with autism do better on performance items than verbal items and may show instances of age-appropriate performance despite retardation in most areas.
- **savant skills**\* (cognitive skills that are both 1 standard deviation above general population mean and 2 standard deviations above patient's own cognitive level) are present in 25% of individuals with autism whose IQ is over 35.

\*e.g. prodigious rote memory, calculation, music ability

## PROGNOSIS

**Increased mortality** is seen in autism (risk increases with age) - due to associations with severe mental retardation and epilepsy.

- **mental retardation** is present in 75% patients.
- **epilepsy** develops in 4-42% patients.
- **course of illness** is often unpredictable:
  - gradual improvement of **sociability** and **language** can occur in adulthood but with persistence of residual deficits.
  - intellectual decline can occur during adolescence (25% children experience documented loss of previously acquired skills).
  - 2-17% patients may achieve nonretarded level of cognitive and adaptive functioning.
  - mentally retarded patients who have not gained useful verbal communication by age 5 years are unlikely to live independently as adults.
- marriage is rare.

## TREATMENT

- programs are most effective when begun early (age 2-4 y) and involve intensive full spectrum interventions.
- all children aged 3-21 years who are diagnosed with autism or PDD must by law receive **appropriate education within public educational system**.
  - ensure that environment remains stable (e.g. predictable schedules, routines, personnel, and materials).
- **hospitalization** is indicated only when **self-injurious** or **aggressive** behavior can no longer be managed at home (residential treatment or long-term hospitalization is occasionally necessary).

### Behavioral interventions

N.B. difficult behaviors of individuals with autism frequently serve communicative purpose as means by which these individuals attempt to influence their environment.

*Aggressive, self-injurious, or stereotyped behaviors can indicate need for help, or they can be used to escape from stressful situations, obtain desired objects or stimulation, or protest against unwanted events.*

- traditional **applied behavior analysis (ABA)** evaluates ABC's of behavior (antecedents, behaviors, consequences) and aims to mold patient's behavior into more socially and functionally useful patterns.
- useful principles: (1) establish clear and consistent rules, (2) introduce changes one step at time, (3) explore underlying factors, (4) consider environmental modifications, (5) use obsessions as reinforcers for positive behaviors.
- autists find it difficult to attend to more than one stimulus at time, so cues must be kept simple.
- reinforcement of desired behaviors, with punishment of behavioral excesses (e.g. through time outs), can be effective.

#### **Increasing communication skills**

- children aged 6-7 years who do not develop useful speech remain highly impaired in use of verbal communication and require **alternative system**, such as signs or pictorially based systems.
- facilitated communication (therapist guides patient's hand to utilize nonverbal language systems) is not effective.

#### **Modifying social difficulties**

- highly inappropriate behaviors (screaming or masturbating in public) should be focus of treatment using behavioral techniques.
- social skills training in every situation to which person is exposed is useful.
- education of peers about effects of autism.

### **MEDICATIONS**

- only for target symptoms, symptom complexes, or comorbid disorders.

"Start low and go slow" - autistic children are more sensitive to psychoactive medications!

1. **Second-generation antipsychotics** (FDA approved - **RISPERIDONE**) - positive effects on **irritability** (aggression, deliberate self-injury, temper tantrums) → overall improvement of behavioral symptoms of autism!
  2. **Antidepressants** (SSRI, **CLOMIPRAMINE**) - decrease **obsessive stereotyped (ritualistic)** behaviors and enhance overall communication and improve social reciprocity, to minor degrees.
  3. **Stimulants** - for **attention deficit / hyperactivity** symptoms, but side effects are particularly frequent!
  4. **Beta-blockers** (**PROPRANOLOL**) - for **aggression** and **self-injurious** behavior.
  5. **α2-agonists** (**CLONIDINE**) - for **attention deficit** and **hyperarousal**.
  6. **Opiate antagonists** (**NALTREXONE**) – no longer recommended.
- no evidence exists as to whether it is better to use SSRIs, antipsychotics, alpha agonists, or stimulants as first line treatment (multiple medications may be necessary for optimal management).
  - **RISPERIDONE** and **FLUVOXAMINE/FLUOXETINE** are drugs of first choice!

## **ASPERGER DISORDER**

- **milder version of autism** - much less impairment in cognitive development (generally **intellectually normal**) and no significant general delay in language development (may have abnormalities of spoken language).

- follows **familial transmission** pattern.
- **males** : females = 4 : 1

## **RETT DISORDER**

- **transmitted** as **dominant X-linked** illness with (nearly) full penetrance, with early death of most male fetuses through spontaneous abortion (i.e. almost never occurs in males)  
**MECP2** (methyl-CPG-binding protein 2) gene on Xq28 mutations are present in 80% classic Rett disorder patients;  
**CDKL5** gene mutations are present in some of **MECP2** negative cases.

Rett disorder and autism are distinct entities!

- **normal development for 7-18 months** → **rapid deterioration** of behavior and mental status, deceleration of previously normal head growth, loss of hand skills and social engagement (both of which were developing normally), appearance of poorly coordinated gait or trunk movements → severe impairment of language → **severe psychomotor retardation**.
- **abnormal sleep patterns** develop as early as age 4 months (herald change in developmental trajectory).
- diffuse generalized **atrophy of cerebrum & cerebellum**.
- nonspecific, generalized EEG abnormalities present by age 2 years.

## **CHILDHOOD DISINTEGRATIVE DISORDER**

- **normal development for at least 2 years** → **marked loss of previously acquired skills** in language, social skills, bowel or bladder control, play, and motor skills, while presenting with autistic triad of abnormal communication and social interaction and repetitive, stereotyped behavior.

- can eventually become **more severe than is typical in autism!**
- **males** : females = 4 : 1

## **PDD-NOS**

- **impairment in 2 of 3 autistic symptom clusters** (either verbal / nonverbal communication difficulties or stereotyped behaviors or interests are present), but no other specific autistic spectrum disorder can be diagnosed.

**BIBLIOGRAPHY** for ch. "Psychiatry" → follow this [LINK >>](#)