Autism
History of Autism

• **The DSM-I (1952)**
  - Although autism was recognized as a unique condition as early as 1943, it was not included in the DSM.
    - Children who exhibited autistic-like symptoms were diagnosed under the schizophrenic reaction, childhood type label.

• **The DSM-II (1968)**
  - As with the first release, autism was not included as a separate diagnostic category.
    - “the condition may be manifested by autistic, atypical and withdrawn behavior.”
    - Children exhibiting these behaviors were diagnosed as schizophrenic, childhood type.

• **The DSM-III (1980)**
  - Inclusion of autism as a separate diagnostic category.
  - Only one autism designation, entitled *infantile autism*.
    - There were only six characteristics listed
    - Each of the six symptoms must be present in order for an individual to be diagnosed with infantile autism. Due to some controversy surrounding the descriptor *infantile*, this category was changed to autistic disorder in 1987.

• **The DSM-IV (1994)**
  - The most recent complete release of the DSM, the DSM-IV, occurred in 1994.
  - Category of pervasive developmental disorders and several subtypes were added.
  - In addition to autistic disorder:
    - a diagnosis could be made under the categories of Asperger’s Disorder, Rett’s Disorder, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS).
### Historical Overview Cont’d

<table>
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<tr>
<td>Onset before 30 months</td>
<td>Onset before 36 months</td>
<td>Delays or Abnormal Functioning in 1 area (social interaction, language, or play) before 36 months</td>
</tr>
<tr>
<td>Gross Deficits in language development</td>
<td>Qualitative impairment in both verbal and nonverbal communication</td>
<td>Qualitative Impairment in communication</td>
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<tr>
<td>Pervasive lack of responsiveness to others</td>
<td>Qualitative impairment in reciprocal social interaction</td>
<td>Qualitative impairment in social interaction</td>
</tr>
</tbody>
</table>
How do we define Autistic Disorder?

• **Essential features: (The Triad)**
  • Presence of markedly abnormal, impaired, or restricted
    – development in social interaction
    – development of communication
    – repertoire of activity and interests
  • These manifestations can vary greatly depending on both chronological age and developmental level

• Other names:
  – *Early infantile autism, childhood autism, or Kanner’s autism*
Current DSM-IV-TR Criteria
Autistic Disorder (299.00)

• A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3).

SOCIAL FUNCTIONING DOMAIN

• (1)- Qualitative impairment in social interaction, as manifested by at least two of the following:
  – (a) marked impairment in the 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) a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest)
  – (d) lack of social or emotional reciprocity
Current DSM-IV-TR Criteria
Autistic Disorder (299.00)

• A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3).

COMMUNICATION DOMAIN

• (2)- Qualitative impairments in communication as manifested by at least one of the following:
  – (a) delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime)
  – (b) in individuals with adequate speech, marked impairment in the ability to initiate or sustain a 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
Current DSM-IV-TR Criteria
Autistic Disorder (299.00)

• A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3).

ACTIVITIES AND BEHAVIORS DOMAIN

• (3)- Restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:
  – (a) encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or 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
DSM-5 Diagnostic Criteria

Moved to a new category termed: Neurodevelopmental Disorders to denote its manifestation early in development & developmental deficits that impair personal, social, academic, and occupational functioning.

Diagnostic Criteria:

A. Persistent Deficits in Social Communication and Social Interaction across multiple settings

B. Restricted, repetitive patterns of behavior, interests, or activities (e.g., stereotyped or repetitive motor movements, use of objects, or speech; insistence on sameness, adherence to routines; highly restricted, fixated interests at are abnormal in intensity or focus; hyper or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment.

C. Symptoms must be present during the early developmental period.
Primary Core Symptoms

**Communication Issues**
- Often avoids eye contact
- May seem like they cannot hear you
- May develop language, then abruptly stop talking
- Failure to use spoken language, without compensating by gesture

**Activities and Exploration of Environment**
- Remains fixated on a single item or activity
- Stereotypical behaviors like rocking or hand-flapping
- May Sniff or lick toys (sensory issues)
- May show minimal sensitivity to burns or bruises
- May engage in self-mutilation
- Can be intensely preoccupied with a single subject, activity or gesture
- May show distress over change
- May Insist on routine or rituals with no purpose
- May lack fear (due to not understanding the concept)

**Social Relationships**
- May act as if unaware of the coming and going of others
- May seem inaccessible, as if in a shell
- Often fail to seek comfort from others
- Often fail to develop relationships with peers
- May have problems seeing things from another person’s perspective, which may leave the child unable to predict or understand other people’s actions
- May physically attack and injure others without provocation

DSM-IV-TR, 2000
Secondary Symptoms

- Problems with typical academic coursework
- Behavioral Difficulties
  - Aggression, disruption, self-injurious behavior, hyperactivity
- Minimal or lack of social relationships
- Sensory Abnormalities
  - Tactile and auditory are most common
- Potential inability to care for themselves
  - Depending on age and developmental level
- Disinterest or inability to participate in activities requiring verbal interaction
- Feeding difficulties (Polimeni, Richdale, & Francis, 2005)
  - Refusal, selectivity, and texture sensitivities
- Sleeping Difficulties (Polimeni et al., 2005)
- During the teen years, individuals may gain skills but still lag behind in their ability to relate to and understand others.
- Puberty and emerging sexuality may be more difficult for teens who have autism than for others this age.
GENETICS
• Increased risk of Autistic Disorder among siblings, with approximately 5% of siblings also exhibiting the condition

NEUROBIOLOGICAL
• Dysregulation of serotonergic activity
• Microcephaly and Macrocephaly
• Abnormal brain imaging
• EEG abnormalities even in absence of seizures

CORE FEATURES:
• Social Impairment
  • Impairment in use of non-verbal gestures
  • Failure to develop peer relationships
  • Lack of social or emotional reciprocity
• Impairment in Communication
  • Delay or lack of spoken language
  • Stereotyped or repetitive use of language
• Restricted repetitive and stereotyped behavior, interests, and activities
  • Motor mannerisms
  • Inflexible adherence to routines or rituals

SECONDARY FEATURES:
• Odd responses to sensory stimuli
• Temper tantrums and aggressiveness
• Hyperactivity or impulsivity
• Abnormalities in eating or sleeping
• Self injurious behaviors (head banging, wrist biting)
Prevalence

• Studies published before 1985:
  – 4 to 5 cases per 10,000 children for the autism spectrum overall
  – 2 cases per 10,000 for classic autism
• Reported rates range from 2 to 20 cases per 10,000
• More recent data suggest a prevalence rate of 10 cases per 10,000 is a reasonable estimate for autistic disorder or 1 in 1000 (Fombonne, 2003)
• The most recent data indicate a prevalence rate of approximately 13 cases per 10,000 for autism, and 66 per 10,000 for the entire autism spectrum disorder (Autism, Rett’s, Childhood Disintegrative Disorder, Asperger’s, NOS)
Male to Female Ratio

- Male-to-Female ratio of 4.3:1
  - Cases without mental retardation the sex ratio may be more than 5.5:1
  - Cases with mental retardation the sex ratio may be closer to 2:1
Age and Typical Onset

• By definition onset is prior to age 3
• In infants:
  – Indifference or aversion to affection or physical contact
  – Lack of eye contact
  – Lack of facial responsiveness
  – Failure to respond to parents’ voices
Age and Typical Onset

• **Young children**
  – May treat adults as interchangeable
  – May cling to a specific person
  – May use a parent’s hand to obtain a desired object (as if the hand rather than the person is relevant)

• **School-aged children**
  – May become more willing to be passively engaged in social interactions (parallel play)
  – Little sense of boundaries in social interactions
Duration of Symptoms and Typical Course

- Autistic Disorder follows a continuous/chronic course [unless treated successfully]
- In school age children and adolescents, developmental gains in some areas are common
  - Increased in social functioning as the child reaches school-age (cap off)
- However, some individuals deteriorate behaviorally as they reach adolescence
- Language skills and overall intellectual level are the strongest factors related to prognosis

DSM-IV-TR, 2000
AUTISM

Persons with autism may possess the following characteristics in various combinations and in varying degrees of severity.

- Inappropriate laughing or giggling
- No real fear of dangers
- Apparent insensitivity to pain
- May not want cuddling
- Sustained unusual or repetitive play; Uneven physical or verbal skills
- May avoid eye contact
- May prefer to be alone
- Difficulty in expressing needs; May use gestures
- Inappropriate attachments to objects
- Insistence on sameness
- Echoes words or phrases
- Inappropriate response or no response to sound
- Spins objects or self
- Difficulty in interacting with others
Comorbidities

- Autism often has coexisting **neuropsychiatric disorders:**
  - Attention Deficit Hyperactivity Disorder (Reiersen & Todd, 2008)
    - The DSM-IV-TR prohibits the co-diagnosis of an ASD and ADHD
    - However, clinically significant symptoms of these two conditions commonly co-occur
    - Children with both sets of symptoms may respond poorly to standard ADHD treatments, and may benefit from additional types of medications or from behavioral or other therapies
  - Affective Disorders (Matson & Nebel-Schwalm, 2005)
    - Thought to exist but literature has yet to systematically investigate the relationship
    - Ghaziuddin, Tsai, & Ghaziuddin (1992) reported comorbid depression in 2% of the cases studied
  - Anxiety Disorders: 11-84% comorbidity rate (White et al., 2009)
  - Obsessive-compulsive Disorder- differential diagnosis mandatory is proper diagnosis
    - more common for children with autism to simply display behaviors that are similar to those of OCD, but that are in fact a part of their autism symptoms
    - It is thought that autism and OCD based repetitive thoughts and behaviors are quite similar in the early stages of development, but become dissimilar over time as they often serve different functions within the two disorders.
  - Tourette Syndrome (Zafeiriou, Ververi, & Vargiami, 2007).
    - The prevalence of Tourette Syndrome among individuals with autism is estimated to be 6.5%, higher than the 2% to 3% prevalence for the general population.
    - Several hypotheses for this association have been advanced, including common genetic factors and dopamine, glutamate, and serotonin abnormalities.
- Teens with autism are at an increased risk for developing problems related to depression and anxiety (White et al. 2009)
Mental Retardation and Autism

- **Mental Retardation** (Chakrabarti & Fombonne, 2001; DSM-IV-TR, 2000; Yeargin-Allsopp et al., 2003)
  - 25-70% estimated comorbidity rate
    - Large range may be due to the difficulties in assessing intelligence in children with autism
- Chakrabarti and Fombonne (2001) assessed 26 autistic children
  - 30% with intelligence in the normal range (IQ above 70)
  - 50% with mild to moderate retardation
  - Approximately 20% with severe to profound retardation (IQ below 35).
- Interestingly, for ASD other than autism the association is much weaker: the same study reported normal intelligence in about 94% of 53 children with PDD-NOS.
- Common assumption that these go together, but it may be that the presence of both makes it more likely that the children will be assessed and diagnosed
Medical Comorbidities

• **Comorbid Medical diagnoses** - 15% to 37% of individuals with autism
  – Seizure Disorders- 25% (DSM-IV-TR, 2000; Tuchman & Rapin, 2002)
  – Immune System Dysregulation (Warren et al., 1996)
  – Gastrointestinal Disorders (Kuddo & Nelson, 2003)
Savants and Special Skills

• A rare condition in which an individual has one or more areas of expertise that are in contrast with the individual's overall limitations
  – Of 5400 children with autism, 531 were reported by parents to have special abilities (Rimland 1978)
  – 10% incidence of savant syndrome has become the generally accepted figure in autistic disorder (Treffert, 2000)
  – Savant syndrome is not limited to autism. In a survey of an institutionalized population with a diagnosis of mental retardation, the incidence of savant skills was 1:2000 (.06%) (Hill, 1977)
Savants and Special Skills

- **Music**: usually performance, most often piano, with perfect pitch; composing in the absence of performing has been reported, as has playing multiple instruments (as many as 20).
- **Art**: usually drawing, painting, or sculpting
- **Calendar calculating**
- **Mathematics**: lightning calculating or the ability to compute prime numbers, for example, in the absence of other simple arithmetic abilities
- **Mechanical or spatial skills**: capacity to measure distances precisely without benefit of instruments, the ability to construct complex models or structures with painstaking accuracy, or the mastery of mapmaking and direction-finding.
Savants and Special Skills

• There is a spectrum of savant skill
  – Obsessive preoccupation or memorization
  – Talented savants
    • Cognitively impaired persons in whom the musical, artistic, or other special abilities are more prominent and highly honed, usually within an area of single expertise, and are very conspicuous when viewed in contrast to overall disability
  – Prodigious savant
    • Extraordinarily rare individuals for whom the special skill is so outstanding that it would be spectacular even if it were to occur in a non-impaired person
    • Fewer than 50 prodigious savants known to be living worldwide at the present time who would meet that very high threshold of savant ability
Figure 1. Landscape in Poland.

Figure 5 A and B. Lake View and Church.
GENETICS
• Twin Studies
• Chromosome 7 – The RELN Gene
• Chromosome 15 – area 15q11-q13
• X-Linked Chromosome

NEUROBIOLOGICAL

Macrocephaly

Abnormalities in Cerebellar Development

Abnormalities in Frontal Lobe “Theory of Mind”

Amgydala and Hippocampal Abnormalities

CORE FEATURES:
• Social Impairment
• Impairment in Communication
• Restricted repetitive and stereotyped behavior, interests, and activities

Lack of “Central Coherence” Persistent preoccupation with parts of objects

“Joint Attention” • Impairment in use of nonverbal behaviors

• Impaired or total lack of adequate speech
• Impaired conversational skills
• Inability to understand emotions or intentions of others

SECONDARY FEATURES:
• Odd responses to sensory stimuli
• Temper tantrums and aggressiveness
• Hyperactivity or impulsivity
• Difficulty with sensory integration
• Abnormalities in eating or sleeping
• Self injurious behaviors (head banging, wrist biting)
• Seizures

Dopamine Abnormalities

Low levels of GABA

High blood Serotonin Levels

CELLULAR ABNORMALITIES

• Repetitive and self injurious behaviors

• Stereotyped behaviors
• Sensory sensitivity
• Seizures

• Repetitive behaviors and compulsions
• Difficulty showing emotion and handling sensory information

Abnormalities in Cerebellar Development

Abnormalities in Frontal Lobe “Theory of Mind”

Lack of Social or Emotional Reciprocity
• Motor Stereotypies
• Difficulty processing facial expressions
Environmental Influences

- Exposure to **congenital Rubella** (Chess, 1977) has been shown to increase the rate of autism in children
  - More common infections, like influence have not shown to be related (Dassa et al., 1995)
- Miller & Stromland (1993)- **Thalidomide Exposure**
  - 33% of cases exposed to Thalidomide between the 20-24th day of gestation went on to develop autism
- Ardinger et al. (1988)- **Gestational Valproic acid exposure**
  - 71% of children show developmental delays (specifically language development) or neurological abnormalities related to autism after exposure
- 11.4% prevalence of autism among children **exposed to cocaine in utero** was found in a retrospective chart review (Davis et al. 1992)
  - Language, play skills, social skills, and fine motor behavior were affected
  - More research is needed as 3 of these 8 children had mothers who abused multiple drugs
- **Thimerosal (Preservative in the MMR Vaccine)**
  - Thimerosal contains mercury components, leading several studies to reveal higher than recommended levels of mercury in the blood of infants who received the vaccine
  - MMR vaccine itself has not been shown to be scientifically related to the development of ASD or other PDDs, yet parents now have the option to request preservative free vaccinations
- **The role of environmental toxins remains controversial, with various speculations for possible toxic influences without substantiating evidence.**
  - These influences overall have shown to account for only minimal suspected environmental influence
Genetics

- **Twin Studies**
  - Folstein & Rutter (1977) 11 Monozygotic and 10 Dizygotic twin pairs
    - Found a 36% concordance of Autism in MZ and 0% in DZ twin pairs
    - 1 out of 10 DZ pairs had cognitive deficits- language delay (9 out of 11 in MZ - 82%)
    - Prevalence rates range from 2-10 in 10,000
Genetics

- Folstein & Rutter’s study was replicated in 1993 using ADI and Autistic Diagnostic Observation Schedule
  - 60% concordance rate for MZ and 0% for DZ
- Three other twin studies 1985-1995
  - Concordance rates range from 36-96% in MZ and 0-30% in DZ
  - Heritability for autism at 91-93% depending upon the base rates used.
<table>
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<tr>
<th>Study</th>
<th>Proband type</th>
<th>Pairs included</th>
<th>MZ pair-wise concordance</th>
<th>DZ pair-wise concordance</th>
<th>MZ concordance for social-cognitive disorder&lt;sup&gt;a&lt;/sup&gt;</th>
<th>DZ concordance for social-cognitive disorder&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
<td>Folstein &amp; Rutter,</td>
<td>Autism, atypical autism (Kanner &amp;</td>
<td>11 MZ 10 DZ</td>
<td>4/11 = 36%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0/10 = 0%</td>
<td>9/11 = 82%</td>
<td>1/10 = 10%</td>
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<td>1977</td>
<td>Rutter criteria)</td>
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<tr>
<td>Ritvo et al., 1985</td>
<td>Autism (Research Diagnostic Criteria)</td>
<td>23 MZ; 17 DZ</td>
<td>22/23 = 95%</td>
<td>4/17 = 23%</td>
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<tr>
<td>Steffenburg et al.,</td>
<td>Autistic Disorder (DSM-III-R)</td>
<td>11 MZ; 10 DZ</td>
<td>10/11 = 91%&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0/10 = 0%</td>
<td>10/11 = 91%</td>
<td>3/10 = 30%</td>
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<td>1989</td>
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<tr>
<td>Bailey et al., 1995-</td>
<td>Autism (ICD-10)</td>
<td>17&lt;sup&gt;b&lt;/sup&gt; MZ; 11 DZ</td>
<td>11/16 = 69%</td>
<td>0/11 = 0%</td>
<td>14/16 = 87%</td>
<td>1/11 = 9%</td>
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<td>New sample</td>
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<sup>a</sup>Social-cognitive disorder: diagnosis made of the basis of one or more of the following: (a) verbal or performance IQ or social quotient of 70 or below; (b) lack of phrase speech by 30 months; (c) speech-language problems requiring specialist help including grossly abnormal articulation persisting to the age of 5 years; (d) school achievement problems requiring special education measures at school.

<sup>b</sup>Includes one set of triplets resulting in three pairs; for the purpose of concordance the triplets were counted as two pairs as in the original study.

<sup>c</sup>Proband-wise concordance = 53%.

<sup>d</sup>Proband-wise concordance = 95%.
Genetics

• **Family Genetic Studies**
  – Comparing frequency of disease in relatives of an affected person with prevalence in general population

• **Bolton et al. (1991, 1993)**
  – First-degree relatives of 99 individuals with autism and 36 individuals with Down syndrome
  
  • Focused on cognitive abnormalities, social abnormalities, and repetitive stereotyped behaviors
  
  • Rates of autism in siblings was raised 3% compared to 0% in DS
  
  • 3% had clear-cut autism, another 3% has atypical syndrome of autism, and another 3% had cognitive and social abnormalities.
Genetics

• **Ritvo, Jorde, et al. (1989)** it was reported sibling recurrence risk of autism was 7% if first autistic child was male and 14.5% if was female

• 1991 study was replicated and found 3.7% (vs. 7%)
  – Researcher noted a marked fall of autism rate in 2\textsuperscript{nd} and 3\textsuperscript{rd} degree relative (.13% and .05%)
Genetics

• **Assessment of parents of children with autism:**
  
  – In 7 studies from 1988 to 2005 rates of social impairments, aloofness, and pragmatic language impairments in fathers and mothers of children with autism or Asperger syndrome range from 10-45%
  
  – Strong correlation for severity of restricted repetitive behaviors and interests in child with autism and parents with obsessive-compulsive traits or disorders
<table>
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<tr>
<th>Study</th>
<th>Proband type (N; dx criteria)</th>
<th>Control group (N)</th>
<th>Relative type (N)</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartak et al., 1975</td>
<td>Autism, males only, IQ&gt;70 (19; Rutter criteria)</td>
<td>Dysthaptic* (23), mixed* (5)</td>
<td>Parents, siblings</td>
<td>Family history method</td>
<td>In 25% of families of both the autistic and dysphasic groups parents or siblings had a history of language or speech disorder. Both groups showed a higher rate of language and speech disorder than the general population.</td>
</tr>
<tr>
<td>August et al., 1981</td>
<td>Autism (41; Rutter criteria)</td>
<td>Down syndrome (15)</td>
<td>Siblings (71)</td>
<td>Direct study</td>
<td>15.5% of siblings of autistic individuals vs. 3% of Down syndrome siblings showed cognitive disability. The family prevalence was 19.5% for autistic families vs. 7% for Down syndrome families. There was a trend toward autistic probands with a family history of cognitive disabilities to be lower in IQ.</td>
</tr>
<tr>
<td>C. Gillberg et al., 1992</td>
<td>Autism (35; DSM-III/III-R)</td>
<td>DAMP* (42), normal (21)</td>
<td>Parents (68), siblings (33)</td>
<td>Family history</td>
<td>Speech-language, reading-spelling problems were no more common in first degree relatives of children with autism than normal controls.</td>
</tr>
<tr>
<td>Ozonoff et al., 1993</td>
<td>Autistic disorder, PDD-NOS, IQ&gt;70 (18; DSM-III-R)</td>
<td>Learning disorder, IQ&gt;70(18)</td>
<td>Siblings (18)</td>
<td>Direct study</td>
<td>Control siblings performed better than autistic siblings on executive function tasks. No difference was seen in theory of mind tasks, verbal IQ, performance IQ, or full scale IQ.</td>
</tr>
<tr>
<td>Szatmari et al., 1993</td>
<td>PDD-autism, Asperger disorder, atypical autism (52; DSM-III-R/ICD-10)</td>
<td>Down syndrome (13), very low birth weight infants (20)</td>
<td>Siblings (76), parents (97)</td>
<td>Direct study</td>
<td>There were no differences on cognitive measures between relatives of different PDD subtypes. Neither mental retardation or specific cognitive deficits aggregated in families with PDD.</td>
</tr>
<tr>
<td>Plumet et al., 1995</td>
<td>Autism females only (26; DSM-III/AD)</td>
<td>Down syndrome, females only (26)</td>
<td>First-degree relatives</td>
<td>Direct study</td>
<td>Tests designed to assess subtle verbal dysfunction showed no difference between parents of autistic and Down syndrome females but significant impairment in brothers of autistic females. Relatives' performance was not correlated with the intellectual level of the proband.</td>
</tr>
</tbody>
</table>

Table III. Continued

<table>
<thead>
<tr>
<th>Study</th>
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<th>Control group (N)</th>
<th>Relative type (N)</th>
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</tr>
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<tbody>
<tr>
<td>Szatmari et al., 1995</td>
<td>PDD-autism, Asperger disorder, atypical autism (52; DSM-III-R)</td>
<td>Down syndrome (13), very low birth weight infants* (20)</td>
<td>Parents (103)</td>
<td>Family history</td>
<td>No differences on cognitive measures were identified in relatives of children with autism vs. controls.</td>
</tr>
<tr>
<td>Hughes et al., 1997</td>
<td>Autism (24; DSM-III-R/ICD-10)</td>
<td>Learning disabled (27), normal (33)</td>
<td>Parents (40)</td>
<td>Direct study</td>
<td>Parents, especially fathers, of children with autism showed impairments in executive function relative to controls. No group differences were seen in a control test of spatial span indicating that the groups did not differ on ability or motivation.</td>
</tr>
<tr>
<td>Boutin et al., 1997</td>
<td>Autism, PDD (49; DSM-III-R)</td>
<td>Mentally retarded (18)</td>
<td>First-degree relatives (156)</td>
<td>Family history</td>
<td>Rates of cognitive disorder did not differ between relatives of children with autism vs. relatives of children who are mentally retarded (17.3 vs. 16.4%). More relatives of female vs. male autistic probands had cognitive disorder, a pattern that was not seen in relatives of mentally retarded probands.</td>
</tr>
<tr>
<td>Fombonne et al., 1997</td>
<td>Autism (99; DSM-III-R/ICD-10)</td>
<td>Down syndrome (36)</td>
<td>Parents (202), siblings (159)</td>
<td>Direct study</td>
<td>No differences in cognitive measures were identified in relatives of children with autism vs. control. However, siblings with the lesser variant had lower IQ scores and poorer academic achievement than unaffected siblings.</td>
</tr>
</tbody>
</table>

*Dysphasic-uncomplicated developmental language disorder without autism.
*Mixed-autistic features but disorder regarded as atypical or partial in its manifestation.
*DAMP = Children with deficits in attention, motor control, and perception.
*1000-1500 g birth weight.
Chromosome 7

The normal chromosome 7 is on the right.

The chromosome on the left is inverted with the arrow marking the location of inversion.

This inversion is affecting the WNT2 and RELN genes was strongly associated with autistic disorder (p=.013) especially in subtests of patients with severe language delays.
The Reelin (RELN) Gene

- Reelin signaling was impaired in post mortem individual with autism.
- The RELN gene encodes a signaling protein that plays a pivotal role in the migration of several neuronal cell types and in the development of neural connections.
- 218 Caucasian families (97 control) were tested for genetic associations of RELN variants to autism. They found a repeat polymorphism in the 5’ untranslated region (5’-UTR) was the most significant association.
Chromosome 15

• The area on chromosome 15q11-q13 (a.k.a. Prader-Willi/Angelman critical area - PWARC).
  – If duplication involves the PWARC area patients are more likely to have developmental delay or autism, than if the duplication fell outside that area.
Chromosome 15

- Area on chromosome 15q11-q13
- Genes for the three receptor subunits of GABA are located on this chromosome.

Figure 15.2. Location of single nucleotide polymorphisms (SNPs) in the gamma-aminobutyric acid A (GABA) receptor subunit genes on chromosome 15 analyzed for association.
X-Linked Chromosome

• Two disorders that share symptoms with autism: Fragile X syndrome and Rett’s syndrome, are caused by genes on the X chromosome.

• The fact that more males than females have autism supports the idea that the disorder involves genes on the X chromosome.
  – Females may be able to use their other X chromosome to function normally, while males, without such a “back up” show symptoms of the condition.
Neurobiological Correlates of Autism

Cerebral cortex - a thin layer of gray matter on the surface of the cerebral hemispheres. Two-thirds of its area is deep in the fissures or folds. Responsible for the higher mental functions, general movement, perception, and behavioral reactions.

Amygdala - responsible for emotional responses, including aggressive behavior.

Hippocampus - makes it possible to remember new information and recent events.

Basal ganglia - gray masses deep in the cerebral hemisphere that serves as a connection between the cerebrum and cerebellum. Helps to regulate automatic movement.

Major Brain Structures Implicated in Autism

Brain stem - located in front of the cerebellum, it serves as a relay station, passing messages between various parts of the body and the cerebral cortex. Primitive functions essential to survival (breathing and heart rate control) are located here.

Cerebellum - located at the back of the brain, it fine tunes our motor activity, regulates balance, body movements, coordination, and the muscles used in speaking.

Corpus callosum - consists primarily of closely packed bundles of fibers that connect the right and left hemisphere and allows for communication between the hemispheres.
Neurobiological Correlates of Autism

• Brain Volume
  – Macrocephaly = having a head circumference greater than the 97th percentile.
  – Kanner (1943) described abnormal brain size in children with Autism as having “relatively large heads”.
  – A study of 137 individuals with Autism and found 23.4% had macrocephaly (not significantly different on IQ, sex, or severity of autism)
Brain Volume

• In a study 60 children with Autism (52 control) at 2-4 yrs and 5-16 yrs:
  – 90% of those with autism had larger brain volumes at 2-4 yrs (37% had macrocephaly and 18% just larger than average), but at 5-16 autism group was no larger than control.
  – Overgrowth in autism is mostly during childhood followed by a period of abnormally slow growth.
Brain Volume

• Implication of larger brain volume in young children with autism is unclear but many believe that larger volumes may be due to increased neuronal growth or decreased neuronal pruning.

• One study found volume of cerebral white matter to be disproportionately enlarged in toddlers relative to cortical gray matter but in a separate adolescent sample white matter volume was significantly diminished with no differences in gray matter.

  – Herbert et al. (2003) found cerebral white matter to be disproportionally larger in his sample of eleven, 7 yr old autistic boys.
Yellow region of brain shows the enlarged white matter of an autistic child’s brain. The red regions show the grey matter which is smaller in autistic children.
Brain Volume

- Reduction in white matter by adolescence is also found with PET scan studies showing reduced inter-regional correlations in autism participants
  - Suggests reduced functional integration and connectivity.
  - One consequence of this is reduced integration of functions is autistic individuals lack “central coherence” a cognitive process that makes integration of parts into a whole problematic (Frith, 1989).
The Cerebellum

- Implicated in multiple functions:
  - Shifting attention
  - Procedural learning
  - Language
  - Non-motor learning

- Abnormalities in this area have consistently been detected in postmortem, MRI, and PET studies
The Cerebellum

• Significant loss of Purkinje neurons in the cerebellar vermis and cerebellar hemispheres

• Enlarged total cerebellar volume and cerebellar gray matter in adults with autism
  – After controlling for IQ and overall brain volume these differences were no longer significant
The Cerebellum

- An fMRI study looked at 8 autistic subjects and 8 controls
  - Increased cerebellar activation in autism subjects during a motor task (pushing a button)
  - Less cerebellar activation during an attentional task (pushing a button in response to a target)
  - Abnormalities in cerebellar development in autism may have different implications for motor and attentional functioning
The Cerebellum

• Townsend et al. (1999) showed deficits in orienting and shifting attention.
  – The development of joint attention is a core deficit in autism

• Impaired joint attention may be central to autistic symptomatology.
  – Autistic children fail to follow gestures of others, fail to show interest in objects, and fail to shift their gaze between objects and people during interactions
The Temporal Lobe

• The Amygdala:
  – Emotional arousal and emotional learning

• The Hippocampal System:
  – Memory functions:
    • Feature binding, contextual memory, source memory, and deferred imitation
    • These memory skills are most important for forming representations of social events, semantically encoded words, and face-name associations
The Temporal Lobe

• In a study of 9 autistic children amygdala abnormalities, predominantly in cortical, medial, and central amygdala nuclei were seen in all subjects.
  – Abnormally small densely packed neurons were found in hippocampal fields, the anterior cingulated gyrus, and medial septal nucleus.

• Children who experience temporal lobe damage may develop autistic like symptoms.
The Temporal Lobe

• 6-month old monkeys with bilateral removal of the amygdala and hippocampus at birth:
  – Avoided social contact, had little eye contact, motor stereotypies, and unexpressive faces

• Structural MRI studies of the hippocampus and the amygdala has yielded mixed results:
  – Significantly greater amygdala volume and marginally decreased hippocampal volume
  – Decreased amygdala and hippocampal size
The Temporal Lobe

- fMRI studies have consistently found abnormalities in the activation of the amygdala and fusiform gyrus:
  - Three studies have shown that autism patients showed limited or no activation of the amygdala and fusiform gyrus when processing facial expressions.
  - Two of these studies have shown activation in other areas of the brain more often related to object perception.
Frontal Lobe is associated with reasoning, planning, parts of speech, movement, emotions, and problem solving.

Children with Autism: Abnormal blood flow, abnormal serotonin synthesis and reduced dopaminergic activity in the frontal lobe.
The Frontal Lobe

- Medial prefrontal lesions can lead to “theory of mind” impairments
  - Children with autism exhibit abnormal frontal activation during theory of mind tasks but not other tasks
  - “Theory of Mind”
    - Ability to attribute mental states to self and others, interpret others emotions and intentions as well as between their own knowledge and others beliefs
WATERHOUSE, FEIN, AND MODAHL

FOUR DYSFUNCTIONAL SYSTEMS
GENERATE SYMPTOMS OF AUTISM

TEMPORAL AND PARIETAL ASSOCIATION CORTEX
- TRUNCATED POLYSENSORY CIRCUITS WITH
- EXTENDED UNISENSORY CIRCUITS
OR
- DISORGANIZATION THROUGHOUT ASSOCIATION CORTEXES

NON-CAUSAL CONSEQUENT DYSFUNCTIONS
FRONTAL LOBE
FUNCTIONS DISRUPTED BY ABERRANT INPUT FROM
- AMYGDALA SYSTEM
- HIPPOCAMPAL SYSTEM
- TEMPORAL AND PARIETAL CORTEX

OXYTOCIN-OPHATE SYSTEM
- ABNORMAL SEROTONIN LEVELS
- ABNORMAL OT/BE LEVELS
- IMPAIRED RECEPTOR SITES

AMYGDALA SYSTEM
- NEURON IMMATURE
- INCREASED NEURON DENSITY

HIPPOCAMPAL SYSTEM
- NEURON IMMATURE
- INCREASED NEURON DENSITY

NON-CAUSAL ASSOCIATED DYSFUNCTIONS
CEREBELLUM
- NORMAL OR
- ENLARGED OR
- ATROPHIED

BRAINSTEM
- NORMAL FUNCTION OR
- ABNORMAL FUNCTION
### Table 2

*Autistic Behaviors and Proposed Contributing Neurofunctional Mechanisms*

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Hippocampal dysfunction</th>
<th>Amygdala dysfunction</th>
<th>Oxytocin–opiate dysfunction</th>
<th>Temporal and parietal cortex dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 diagnostic behaviors</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1. Poor nonverbal skills</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2. Without friends</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>3. Doesn’t share experiences</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>4. No emotional reciprocity</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>5. Absent/delayed speech</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>6. Impaired conversation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>7. Stereotyped speech</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>8. Lack of social play</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>9. Nonfunctional routines</td>
<td>X</td>
<td>X</td>
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<tr>
<td>10. Repeated body movements</td>
<td></td>
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<tr>
<td>11. Preoccupied one interest</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>12. Preoccupied with objects</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>10 nondiagnostic behaviors</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1. Impaired sensory integration</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Abnormal orienting/attention</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Seizures and self-injury</td>
<td>kindling sensitive</td>
<td>kindling sensitive</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>4. Abnormal attachment</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>5. Abnormal eating and sleeping</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>6. Exact pattern learning</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>7. Sensory hypersensitivity</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>8. Savant skills</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>9. Developmental regression</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Mental retardation</td>
<td>X</td>
<td>X</td>
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<td>X</td>
</tr>
</tbody>
</table>
Trouble at the Cellular Level

- **Serotonin**
- One third of those with autism have increased blood serotonin levels
  - Rates range from 25-50% higher than persons without autism
  - SSRI’s improve repetitive behaviors, compulsions, and social impairments
  - High serotonin levels may explain why persons with autism have problems showing emotion and handling sensory information, such as sounds, touch, and smells
- PET scan of 30 children with autism (≤age 5)
  - Decreased serotonin synthesis in the thalamic and frontal areas
  - Increased serotonin synthesis in contralateral cerebellar dentate nucleus
Trouble at the Cellular Level

• **Dopamine**
  - Drugs that block dopamine receptors can be helpful in reducing repetitive behaviors and self injury (Tsai, 1999; Gagliano et al. 2004).

• **GABA (Gamma-amino-butyric acid)**
  - Levels of different types of GABA compounds are abnormally low in persons with autism.
    - Low levels may contribute to autism. In studies of mice, disrupting the GABA pathway causes seizures, extreme reactions to touch and sound, and stereotyped actions—symptoms also common in autism.
    - Many persons with autism also have epilepsy and also show low levels of GABA
Table 1 Key Neurobiological Correlates of Autism across Research Areas.

<table>
<thead>
<tr>
<th>BASIC NEURAL STRUCTURES AND PROCESSES</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain Volume</strong></td>
<td></td>
</tr>
<tr>
<td>HIS Increased brain weight in childhood: ++</td>
<td>Kemper &amp; Bauman, 1998</td>
</tr>
<tr>
<td>Increased brain weight in adolescence and adulthood: ?</td>
<td>Bailey et al., 1998 (+)</td>
</tr>
<tr>
<td>SI Increased brain volume in childhood: ++</td>
<td>Kemper &amp; Bauman, 1998 (-)</td>
</tr>
<tr>
<td>Increased brain volume in adolescence/adulthood: ?</td>
<td>Comai et al., 2001</td>
</tr>
<tr>
<td>OTH Enlarged head circumference in childhood, adolescence, and adulthood: ++</td>
<td>Palmen et al., 2004 (+)</td>
</tr>
<tr>
<td>Neuronal Growth Dysregulation</td>
<td></td>
</tr>
<tr>
<td>HIS Atypical neuroanatomical structure: +</td>
<td>Casanova et al., 2002</td>
</tr>
<tr>
<td>Cell migration errors: +</td>
<td>Bailey et al., 1998</td>
</tr>
<tr>
<td>Decreased dendritic branching: +</td>
<td>Blatt et al., 2001</td>
</tr>
<tr>
<td>OTH Dysregulation of proteins associated with neural growth: +</td>
<td>Fatehi et al., 2001</td>
</tr>
<tr>
<td>Increase in neurotrophins and neuropeptides at birth: +</td>
<td>Nelson et al., 2001</td>
</tr>
<tr>
<td>Neurotransmitters</td>
<td></td>
</tr>
<tr>
<td>AN Atypical early serotonin exposure in rats can lead to morphometric/behavioural characteristics similar to those observed in autism: +</td>
<td>Whitaker-Azmitia, 2001</td>
</tr>
<tr>
<td>FI Atypical serotonin synthesis: +</td>
<td>Chugani et al., 1999</td>
</tr>
<tr>
<td>Reduced dopaminergic activity in frontal cortex: +</td>
<td>Ernst et al., 1997</td>
</tr>
<tr>
<td>OTH Increased levels of serotonin in blood: ++</td>
<td>Schain &amp; Freedman, 1981</td>
</tr>
<tr>
<td>Abnormal levels of glutamate and GABA in blood: +</td>
<td>Rolf et al., 1993</td>
</tr>
<tr>
<td>Abnormal levels of opioids in blood and cerebrospinal fluid: +</td>
<td>Gillberg et al., 1983</td>
</tr>
<tr>
<td>Decreased levels of oxytocin in blood: +</td>
<td>Gillberg &amp; Svennerholm, 1987 (+)</td>
</tr>
<tr>
<td>Increased dopamine metabolites in cerebrospinal fluid: ?</td>
<td>Launey et al. (1987) (-)</td>
</tr>
<tr>
<td>Abnormalities in beta endorphin reactivity: +</td>
<td>Leboyer et al., 1994</td>
</tr>
<tr>
<td>Serotonin re-uptake inhibitors can reduce symptoms: ++</td>
<td>Gordon et al., 1992</td>
</tr>
<tr>
<td>Dopamine blocking drugs can reduce symptoms: ++</td>
<td>Gagliano et al., 2004</td>
</tr>
<tr>
<td>Oxytocin infusions can reduce symptoms: +</td>
<td>Hollander et al., 2003</td>
</tr>
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<thead>
<tr>
<th>GROSS STRUCTURES AND DIVISIONS</th>
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<tbody>
<tr>
<td><strong>Cerebellum</strong></td>
<td></td>
</tr>
<tr>
<td>HIS Loss of Purkinje neurons in vermis and hemispheres in nearly all cases: ++</td>
<td>Bauman &amp; Kemper, 1985</td>
</tr>
<tr>
<td>Loss of cerebellar cortex granular cells in some cases: +</td>
<td>Kemper &amp; Bauman, 1993</td>
</tr>
<tr>
<td>SI Hypoplasia/hypoplasia of verbal lobules VI and VII: +</td>
<td>Courchesne et al., 1994</td>
</tr>
<tr>
<td>Increased cerebellar volume: ?</td>
<td>Hardan et al., 2001 (+)</td>
</tr>
<tr>
<td>FI Decreased blood flow in cerebellar hemispheres: +</td>
<td>Piven et al., 1997 (-)</td>
</tr>
<tr>
<td>Atrial typical cerebellar activation during attention and motor tasks: +</td>
<td>Allen &amp; Courchesne, 2003</td>
</tr>
</tbody>
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(Continued)
<table>
<thead>
<tr>
<th>Location</th>
<th>Finding</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal Lobe</td>
<td>Morphometric abnormalities in the MTL lobe in most cases: ?</td>
<td>Kemper &amp; Bauman, 1998 (+) Bailey et al., 1998 (−)</td>
</tr>
<tr>
<td></td>
<td>MTL lesions in animals lead to autism-like symptoms: ?</td>
<td>Bachevalier, 1996 (+) Amarc et al., 2003 (−)</td>
</tr>
<tr>
<td></td>
<td>Structural abnormalities in amygdala and hippocampus: ? (findings differed)</td>
<td>Aylward et al., 1999 (+) Haznedar et al., 2000 (−)</td>
</tr>
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<td></td>
<td>Atypical activation of MTL structures during theory of mind and facial processing tasks: ++</td>
<td>Baron-Cohen et al., 1999</td>
</tr>
<tr>
<td></td>
<td>Atypical activation of temporal lobe structures during language comprehension tasks: +</td>
<td>Just et al., 2004</td>
</tr>
<tr>
<td></td>
<td>Temporal lobe damage is linked to autistic symptoms: ++</td>
<td>Bolton &amp; Griffiths, 1997</td>
</tr>
<tr>
<td>Frontal Lobe</td>
<td>Thickened frontal cortices and irregular cortical laminar patterns in some cases: +</td>
<td>Bailey et al., 1998</td>
</tr>
<tr>
<td></td>
<td>Inverse correlation between frontal lobe volume and cerebral vermis lobule size: +</td>
<td>Carper &amp; Courchesne, 2004</td>
</tr>
<tr>
<td></td>
<td>Abnormal frontal blood flow in children: +</td>
<td>Zilbovics et al., 1995</td>
</tr>
<tr>
<td></td>
<td>Abnormal serotonin synthesis: +</td>
<td>Chuhan et al., 1997</td>
</tr>
<tr>
<td></td>
<td>Reduced dopaminergic activity: +</td>
<td>Ernst et al., 1997</td>
</tr>
<tr>
<td></td>
<td>FI research based on core deficits theories in autism implicates the prefrontal lobe: ++</td>
<td>Luna et al., 2002</td>
</tr>
<tr>
<td>Corpus Callosum</td>
<td>Decreased corpus callosum volume: ++</td>
<td>Egaas et al., 1995</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>Link between caudate volume and levels of stereotyped and repetitive behaviour: +</td>
<td>Scars et al., 1999</td>
</tr>
<tr>
<td>Brain Stem</td>
<td>Decreased brain stem size in some cases: +</td>
<td>Rodier et al., 1996</td>
</tr>
<tr>
<td></td>
<td>Reduced brain stem area: ?</td>
<td>Hashimoto et al., 1992 (+) Elia et al., 2000 (−)</td>
</tr>
</tbody>
</table>

Note. Type of research: HIS: histopathological research; AN: animal research; SI: structural imaging research; FI: functional imaging research; OTH: other. Extent of research support: ++ replicated research, + initial research or replicated research with some contradictory evidence; ?: mixed evidence (+/− after references indicate support/lack of support). Ratings are estimates used for illustrative purposes to show patterns of research across disciplines and support for various pathophysiological findings. References provide examples of relevant case material and are not exhaustive.
Assessment of Autistic Disorder-Screening Devices

• **Checklist for Autism in Toddlers (CHAT)**
  - Developed by Baron-Cohen, et al. (1996)
  - Nine-item Screening Tool completed by parents with toddlers as young as 18 months of age
  - Specificity and Positive Predictive Power (PPP) have been shown to be strengths of this measure (Coonrod & Stone, 2005)
    - PPP is the proportion of patients with positive test results who are correctly diagnosed.
  - Three best items: (Baird, et al., 2000)
    - Lack of eye gaze monitoring, lack of protodeclarative pointing, lack of pretend play by age 18 months
  - Also includes additional items which can be filled out by medical practitioners
Screening Devices: M-CHAT

• Modified Checklist for Autism in Toddlers (M-CHAT)
• Developed and Implemented in the US for use with 24-month old toddlers (Robins, Fein, Barton, & Green, 2001)
• Same 9 items from original CHAT as well as additional items that are likely to be present in children older than 18 months
• More time is needed to evaluate the psychometric properties of this screening instrument
M-CHAT Screener

Please fill out the following about how your child usually is. Please try to answer every question. If the behavior is rare (e.g., you've seen it once or twice), please answer as if the child does not do it.

1. Does your child enjoy being swung, bounced on your knee, etc? Yes No
2. Does your child take an interest in other children? Yes No
3. Does your child like climbing on things, such as up stairs? Yes No
4. Does your child enjoy playing peek-a-boo/hide-and-seek? Yes No
5. Does your child ever pretend, for example, to talk on the phone or take care of dolls, or pretend other things? Yes No
6. Does your child ever use his/her index finger to point, to ask for something? Yes No
7. Does your child ever use his/her index finger to point, to indicate interest in something? Yes No
8. Can your child play properly with small toys (e.g., cars or bricks) without just mouthing, fiddling, or dropping them? Yes No
9. Does your child ever bring objects over to you (parent) to show you something? Yes No
10. Does your child look you in the eye for more than a second or two? Yes No
11. Does your child ever seem oversensitive to noise? (e.g., plugging ears) Yes No
12. Does your child smile in response to your face or your smile? Yes No
13. Does your child imitate you? (e.g., you make a face-will your child imitate it?) Yes No
14. Does your child respond to his/her name when you call? Yes No
15. If you point at a toy across the room, does your child look at it? Yes No
16. Does your child walk? Yes No
17. Does your child look at things you are looking at? Yes No
18. Does your child make unusual finger movements near his/her face? Yes No
19. Does your child try to attract your attention to his/her own activity? Yes No
20. Have you ever wondered if your child is deaf? Yes No
21. Does your child understand what people say? Yes No
22. Does your child sometimes stare at nothing or wander with no purpose? Yes No
23. Does your child look at your face to check your reaction when faced with something unfamiliar? Yes No
Screening Devices-Social Communication Questionnaire

• The SCQ is a parent report measure containing 40-items
  – Designed to screen for pervasive developmental disorders as a whole in children ages 4 and older (Berument et al., 1999).
  – Two Versions: One for children 6 and under, one for children older than 6-years of age

• Items are scored as present or absent in the areas of reciprocal social interaction, language, communication, and repetitive/stereotyped behaviors

• Sensitivity, Specificity, and PPP values are high when compared to other childhood diagnoses (Coonrod & Stone, 2005)
Screening Devices—Vineland Social-Emotional Early Childhood Scales

- SEEC (Barrow, Balla, & Cicchetti, 1998) was designed to be completed in a semi-structured interview format with an adult familiar with the child’s social-emotional behavior.
- Responses are compared to a standardized sample of young children ages birth through 5 years, 11 months. (Taken from the national sample obtained for the Vineland adaptive behavior scales, (Sparrow, Balla, and Cicchetti, 1984).
- Items are grouped in the following way:
  - Interpersonal relationships
  - Play and leisure time
  - Coping skills
  - Overall social-emotional composite score is also obtained
- Takes approximately 15-25 minutes to administer (Sparrow, et al., 1998)
More in-depth Assessment of Autistic Disorder

• Diagnostic assessments would be made following:
  – the identification from a screening instrument
  – a recommendation from a pediatrician
  – a suggestion from a concerned teacher or parent

• Assessment generally includes:
  – Family input (via an interview)
  – Observation of the child
    • During both structured and unstructured activities
  – Clinical judgment of the diagnostician
Childhood Autism Rating Scale - CARS

- One of the earliest developed and most widely used assessment tools
- Items are based on the DSM-IV and 1978 National Society for Autistic Children criteria
- Fifteen items are rated on a scale from 1 (within normal limits for age) to 4 (severely abnormal use of the behavior for age)
  - Descriptions of the range of the behaviors accompany each item to assist in the scoring

Schopler, Reichler, & Renner, 1988)
### Example from the Childhood Autism Rating Scale-CARS

#### I. Relating to People

| 1      | No evidence of difficulty or abnormality in relating to people: The child’s behavior is appropriate for his or her age. Some shyness, fussiness, or annoyance at being told what to do may be observed, but not to an atypical degree |
| 1.5    |
| 2      | Mildly abnormal relationships: The child may avoid looking the adult in the eye, avoid the adult or become fussy if interaction is forced, be excessively shy, not be as responsive to the adult as is typical, or cling to parents somewhat more than most children of the same age |
| 2.5    |
| 3      | Moderately abnormal relationships: The child shows aloofness (Seems unaware of adults) at times. Persistent and forceful attempts are necessary to get the child’s attention at times. Minimal contact is initiated by the child |
| 3.5    |
| 4      | Severely Abnormal relationships: The child is consistently aloof or unaware of what the adult is doing. They almost never respond or initiate eye contact with the adult. Only the most persistent attempts to get the child’s attention have any effect. |
Gold Standards! The ADI-R and the ADOS

• **The combination of:**
  - the Autism Diagnostic Interview-Revised (ADI-R)
    • A semi-structured interview for caregivers (LeCouteur, Lord, & Rutter, 2003)
  - And the Autism Diagnostic Observation Schedule (ADOS)
    • A standardized protocol for observing the communicative and social behavior of toddlers to adults (Lord, Rutter, DiLavore, & Risi, 2001)

• Considered to be the “gold standard” of the diagnostic process of Autistic Disorder
Autism Diagnostic Interview-Revised (ADI-R)

• The ADI-R is comprised of 93 items
• Responses are sought from caregivers
• Linked to the DSM-IV and ICD-10 criteria
• Takes approximately 2 hours to complete  
  – (with an experienced interviewer!)
• Chakrabarti and Fombonne (2001) found that Interrater reliability to be excellent for the domain scores of the three subscales:
  – Communication
  – Social reciprocity
  – Restricted, repetitive behaviors
Autism Diagnostic Observation Schedule (ADOS)

- The ADOS is comprised of four modules for use with individuals of varying developmental and language levels (Lord et al., 2001; Lord & Corsello, 2005).
- Scored from 0-3
  - 0 = regular use or typical behavior
  - 3 = lack of skill or behavior
- Approved for use in non-verbal 2 years olds---verbally fluent adults
- Module 1- Pre-Verbal-Single Words
- Module 2- Phrase Speech
- Module 3- Fluent Speech
- Module 4- Activities for Daily Living, Plans, Hopes
Modules 1-4

• (1) Comprised of 10 activities
  – (e.g., Free play and response to joint attention)
• Behaviors scored include:
  – Frequency of vocalizations directed to others
  – Pointing
  – Responsive social smile
  – Showing others
  – Functional play with provided objects
• (2) Includes some activities from Module 1, with additional tasks
  • (e.g., a construction task and a picture description)
• (3) Includes creating a stories to include the themes of:
  – Friends
  – Marriage
  – Loneliness and other emotions
• (4) This module is designed for high functioning adolescents and adults
• Assesses for
  – Daily living skills
  – Plans for the future
  – Personal hopes and goals
Assessments for Educational Planning and Intervention

• Brock et al. (2006) Obtaining relevant information from a psychoeducational assessment will depend heavily on:
  – making key accommodations
  – Selecting instruments appropriate for use with individuals with autism spectrum disorder
• Prepare the Student ahead of time for the testing situation (familiarize them)
• Minimizing distractions
• Placing the assessment schedule in the student’s daily schedule
• Using powerful external rewards
• Allowing non-standard responses
Educational Planning and Intervention Assessments Cont’d.

- **Autism Screening Instrument for Educational Planning (ASIEP-2)**
  - Five standardized subtests for diagnosis, placement, educational program planning, and progress monitoring
  - Includes the Autism Behavior Checklist (ABC)
    - 57 items for teachers and parents to describe the child
    - Valuable for documenting change (Lord & Corsello, 2005)

- **Psychoeducational Profile (PEP-3)**
  - Used to identify strengths and weaknesses in the skills of individuals with autistic disorder (Schopler, Lansing, Reichler, & Marcus, 2005).
  - Age range is 6 months to 7 years
  - Strictly for the purpose of educational planning

- **Adolescent and Adult Psycheducational Profile (AAPEP)**
  - Designed to develop individual treatment goals for adolescents and adults over age 12 with autism spectrum disorders (Mesibov, Schoper, Schaffer, & Landrus, 1988)
  - Direct observation scale and two interviews which include a home scale and a school/work scale
Educational Planning and Intervention Assessments Cont’d.

• Assessment of Basic Language and Learning Skills (ABLLS-R)
  – Designed as an assessment and curriculum guide for children with autism and other developmental disabilities
  – Contains assessment and skills tracking grids
  – Also contains information that guides the development of the child’s IEP goals

• Scored from 0-4 on 554 items:
  – Basic learning
    • (e.g., cooperation, imitation, play and leisure, and ability to follow classroom routines
  – Academic skills
    • (e.g., reading, math, writing, and spelling)
  – Motor skills
    • (e.g., dressing, eating, grooming, and toileting)

Partington, 2006
Best Practice for Assessment

- Need for Psychologists to be well-trained
- Use multiple sources of information
- Include family members as an integral part of the evaluation
- All instruments should be reliable, valid, and culturally sensitive
- Use more in-depth instruments after screening devices
- Provide follow-up services
School Intervention

- **Individuals with Disabilities Education Act, IDEA**
  - All states must provide a public school education to children with disabilities from ages 3 to 21, regardless how severe their disabilities are
  - A child has the right to an educational placement that is based on an assessment and evaluation of their own special needs
    - These needs must be identified, outlined and included in an Individualized Education Program (IEP) for each child, with a clear, detailed description, of the specific services the child will receive
  - The right to a full range of educational services that may include related services
    - Counseling, special transportation, speech/language, occupational or physical therapy
  - IDEA requires that children with disabilities be educated in the "Least Restrictive Environment" (LRE)
    - A setting with children who have no disabilities, or as near to such setting as possible, with special help and modifications provided to those who need it
School Intervention

- Educational objectives for children with autism
  - Social skills
  - Expressive verbal language, receptive language, nonverbal communications skills
  - Engagement and flexibility in developmentally appropriate tasks and play
  - Fine and gross motor skills
  - Cognitive skills (symbolic play and academic skills)
  - Appropriate behaviors
  - Independent organizational skills
School Intervention

• **Area/Domain: Speech Language**

• **Measurable Annual Goal:** Will improve his expressive language skills.

  1) Will imitate words modeled by adults in 3 out of 5 opportunities

  2) Will answer questions with consistent word approximations in 3 out of 5 opportunities

    a) what is it? (label)
    b) where is it? (location: in, on, under, up, down)
    c) who is it? (persons name)

  3) Will use 10 consistent word approximations to request: food, location change, play, needs in 3 out of 5 opportunities (words to be determined as demonstrates an interest.)
School Intervention

- **Area/Domain: Social/Behavior**
- **Measurable Annual Goal:** Will increase his social interactions and appropriate behavior in a group environment.
  1) Will respond to or initiate an interaction with a peer during class time 1 time per day
  2) Will engage in turn taking activities with adults or peers throughout the school day for
     a) 2-3 turns
     b) 4-5 turns
  3) Will attend to the person/object/event that is the focus at small group time for an increasing amount of time
     a) 1-2 minutes
     b) 3-4 minutes
     c) 5-6 minutes
School Intervention

• Classroom Management

• Steps to establish a behavior plan
  1. In a behavior change plan, the behavior is first clearly defined in measurable terms.
  2. A baseline measure of the behavior is taken before the intervention procedure begins (unless the behavior is life threatening or may harm others).
  3. The intervention is established using punishment to decrease undesired behaviors and reinforcement to increase desired behaviors.

• Data is analyzed to determine the effectiveness of the intervention plan. Modifications are made in an ongoing basis to work toward the desired result.
School Intervention

- **Visual Schedules**
  - Help address child’s difficult with sequential memory
  - Assist with language comprehension
  - Schedules lessen anxiety because they clarify what activities will occur and when

- **Social Skills Training**
  - Gestures, eye gaze, facial expression
  - Body language and posture
  - Physical space
  - Attending
  - Conversational turn taking
  - Figurative language
School Intervention

- please be quiet
- nice hands
- don't touch
- stand up
- sit
- sit
- Shoes on feet
- work
- walk
- pick up
- don't kick others
- no spitting
Overview of Treatments for Autistic Disorder in Children

• No etiology-based treatment modality has been developed to cure individuals with autism.
• Comprehensive interventions are considered the gold standard:
  – Specific assessments
  – Parental counseling
  – Behavior modification
  – Special education in a highly structured environment
  – Sensory integration training
  – Speech therapy
  – Social skill training
  – Medication

• These pieces and combinations have demonstrated significant, positive, treatment effects in many individuals with autism.

Tsai, 1999
Psychopharmacotherapy

• Findings strongly suggest that neurochemical factors play a major role in autism.

• Provide the rationale for psychopharmacotherapy in individuals with autism.
Clomipramine

- (Brand name Anafranil)
- CMI affects:
  - some norepinephrine and dopamine neuronal uptake
  - most powerfully inhibits 5-HT reuptake
- Brasic et al. (1994) found that CMI seemed to reduce sporadic movements and compulsions in some young autistic children
- Contrastingly, Sanchez et al. (1996) reported that 6 of 7 children became worse on CMI in that behavioral problems increased and constipation was common side effect.
- In adults with autism, CMI showed:
  - significant improvement in social interaction
  - significant reduction in repetitive behavior
  - decrease in aggression
  - Patients tolerated the drug well and had no severe adverse effects other than dry mouth (McDougle et al. 1992; Brodkin et al., 1997)
Fluvoxamine

- (Brand name is Luvox)
- Fluvoxamine is a 5-HT uptake inhibitor
- Controlled studies of fluvoxamine in children with autism have not been reported
  - One pediatric sample reported (McDougle et al., 1998):
    - significant increase in agitation, aggression, insomnia, and other forms of behavioral activation
    - limited efficacy
- In adults with autism, fluvoxamine has been shown to have therapeutic effects:
  - reduction of obsessive-compulsive symptoms and aggression
  - increased desire to pursue social relationships
  - improved interpersonal interaction
  - less withdrawal from human contact (McDougle et al., 1990; Harvey & Cooray, 1995; McDougle, Naylor, & Cohen, 1996).
- Except for mild sedation and nausea in a few patients, fluvoxamine was well tolerated with no significant adverse effects (McDougle et al., 1996)
Sertraline & Buspirone

- (Brand Names include Zoloft, Lustral)
- **Sertraline** is a selective 5-HT uptake inhibitor
- Controlled studies of use of sertraline in children with autism have not been reported (Tsai, 1999)
- Sertraline improved (Steingard et al., 1997):
  - transition-induced anxiety and agitation in autistic children
  - symptoms of impaired reciprocal social interaction, aggression, and repetitive behavior in some adults.
  - Not controlled trials, rather, open trial studies
- Adverse side effects included headache, agitation, weight gain, and reduced appetite (Potenza & McDougle, 1997; Hellings et al., 1996).
- **Buspirone** (Brand name is Buspar) is a 5-HT1A partial agonist
- One study reported a reduction in hyperactivity and stereotypic behavior in children with autism. No adverse effects were observed (Realmuto, August, & Garfinkel, 1989).
<table>
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<th>Reference</th>
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DOPAMINE-RELATED TREATMENTS-Haloperidol

- Brand names include Haldol & Serenace
- **Haloperidol** is a dopaminergic blocking agent that has been systematically studied in large samples of hospitalized autistic children, under careful monitoring and under double-blind and placebo-controlled conditions (Anderson & Campbell, 1989, Nar et al., 1982).
- Although haloperidol did not alter the core symptoms of autism, it was reported that haloperidol, (at doses ranging from 0.25 to 4.0 mg/d)
  - improved coordination, self-care, affect, and exploratory behavior; reduced stereotypies, withdrawal, hyperactivity, fidgeting, and temper tantrums; increased social relatedness; and facilitated learning in the laboratory (Andersen & Campell, 1989).
- Within an age range of 2.3 to 8.2 years, haloperidol was more effective in older than younger children, and children with disruptive symptoms seemed to be the best responders (Locascio, 1991).
- At optimal doses, no severe side effects of haloperidol have been noted.
- Excessive sedation is most common above optimal doses or during dose regulation, followed by acute dystonic reactions, a Parkinson-like syndrome, and akathisia.
- Long-term side effects of haloperidol include weight gain, withdrawal dyskinesia, and tardive dyskinesia.
Amphetamines and Methylphenidates

- The effects of stimulants have not been extensively studied in individuals with autism.

- Aman (1982) reviewed the effect of stimulants in developmental disorders and concluded that there is no role for the use of stimulants in the autistic population.
  - However, the studies included in the reviews involved mostly lower-functioning autistic children.
  - More research needed with adolescents and higher-functioning individuals (like HFA and Asperger’s Syndrome).

- More recent reports of positive effects of stimulants in certain autistic children:
  - decreased hyperactivity and impulsiveness
  - improved attention and concentration

- Particularly those with higher-functioning autism (Quintana et al., 1995; Tsai, 1999).
Psychopharmacology Overall

• Studies in older children and adults have demonstrated effectiveness of some drugs in altering some of the most debilitating and stigmatizing symptoms of autism
  – Few well-controlled studies with young children exist.
• Additional factors that may limit use of medical interventions with this age group include:
  – the difficulties health professionals may experience in pinpointing diagnoses
  – the medical comorbidities that often accompany autism (i.e., seizure disorders, problems with sleep)
  – lack of research on the use of medication in combination with other interventions
• It is quite clear that for certain kinds of behaviors (aggression, self-injury, and repetitive behaviors) pharmacological interventions can be an important aspect of a comprehensive treatment program.
• It is much less clear that what appear to be the ’core’ deficits of autism are as effectively targeted, although some improvements may be apparent in terms of increasing availability to benefit from behavioral intervention (McDougle, 1998).
Behaviorally Based Treatments

- Lovaas (1987) held a behavioral-intervention project (starting in 1970) that sought to maximize treatment gains.
- Treatment took place almost all day, stopping only when the child was asleep.
- Focused on children below 4 years of age.
- Participants were assigned to either a control or intervention group.
  - Experimental received 40+ hours of one-on-one treatment per week.
  - Control received 10 hours of one-to-one treatment per week.
  - Treatment involved interactions with the child in the home, school, and community.
  - Both groups received treatment for at least 2 years, maximum of 3 years.
  - See Lovaas et al., 1980 teaching manual for more information.
- Follow-up:
  - Significant Intellectual Functioning differences between groups.
  - 47% of the experimental group achieved normal intellectual and educational functioning in contrast to only 2% of the control group subjects.
  - Normal was defined as children who successfully passed the 1st grade and achieved average IQ scores on the WISC-R.
  - Almost all gains were maintained after a 7 year follow-up (!!!)

- The findings from the article were pivotal in the helping families with children with autistic disorder get services in schools.
- Early intensive behavioral intervention (EIBI), AKA “Lovaas therapy,”
Applied Behavior Analysis (ABA)

- Behavior analysis is the study of behavior, behavior change, and the agents of change.
- ABA: applying what is learned from the analysis of behavior to understand the functional relationship between behavior and other conditions.
- The behavior analyst uses data review to develop hypotheses as to why a particular behavior occurs in a particular context without regard to etiology or “cause,” then creates interventions to alter identified behavior(s).
- Information obtained from behavior analysis, therefore, is used to purposefully and systematically modify behavior.

Jensen, 2002
ABA Continued

• ABA has been used to create programs for individuals with autism since the 1970’s
• These programs target specific skills in a specialized sequence
  – goals being to alter behavior so as to increase and/or improve socialization, communication, and general adaptive functioning.
• Such treatment, applied intensively in the toddler and preschool years, has been referred to as Early intensive behavioral intervention (EIBI).
• Numerous techniques are used to accomplish treatment goals. These often include traditional behavioral techniques such as functional assessment, prompting, shaping, and reinforcement, as well as techniques specifically designed for the treatment of autism (eg, discrete trial training).
• EIBI programs are based on ABA principles and typically include intensive (usually 25 to 40 hours per week), individually administered treatment interventions.
• ABA also is erroneously perceived about as a specific intervention technique (ie, “doing ABA”), rather than as an overall science and service delivery mechanism used to establish, guide, and evaluate ongoing intervention.

Lovaas, 1981; 1987; 1993
Evidence for the Efficacy of Intensive Behavioral Intervention

- Behavioral Interventions have shown **significant positive benefits** including
  - an overall increase in functional skills and cognitive performance
  - a decrease in autistic symptoms (Harris, 2000; McEachin, Smith, & Lovaas, 1993; Luiselli et al., 2000; Green, 1996; Sheinkopf & Siegel, 1998; Smith, Eikeseth, Klevstrand, & Lovaas, 1997).

- Lovaas (1987) findings suggest that these subjects were not “cured,” but many were indistinguishable from typical peers on observation and assessment.

- Despite methodologic problems in various studies, there is evidence for the efficacy of ABA-based intervention programs, particularly those that are:
  - (1) center based and/or rigorously supervised
  - (2) provide individually determined, targeted behavioral intervention for 25 to 40 hours per week,
  - (3) incorporate individual behavioral methods and the teaching of generalization throughout the child's total day.
    - (Harris & Handleman, 2000; Arnold, Luiselli et al., 2000; Green, 1996 & Leaf, 1999)

- Intervention for autism appears to be most effective when started early.
  - (Harris, 2000; Luiselli et al., 2000 & Dawson & Osterling, 1997)

- As with many types of disorders and delays, children with higher levels of cognitive functioning and/or verbal skills prior to treatment are more likely to make greater progress and to achieve levels of functioning more approximating normal peers.