Volunteers Needed For NIH Autism Center of Excellence at U. Pittsburgh: 412 246-5485

- Pregnant mom’s with child w/autism
- Infants who have older sibling w/ autism
- Any 2-4 year old with autism who can sit w/mom
- Verbal 5-18 year olds with autism or Asperger’s
- Verbal 19-45 year olds with autism or Asperger’s
- Free assessment, no costs; transportation paid
- Paid participation
- Need control volunteers also! Same benefits
Autism Spectrum Disorders (Unofficial)*
Pervasive Developmental Disorders (Official)

DSM-IV (1994): Pervasive Developmental Disorders

- Autistic Disorder
- Asperger’s Disorder
- Pervasive Developmental Disorder NOS
  - Childhood Disintegrative Disorder (4-12 yrs)
  - Rett’s Disorder (very rare; girls)
## Prevalence 1/166
### 2002-2006

<table>
<thead>
<tr>
<th>Description</th>
<th>Baird(^1)</th>
<th>Chakrabarti &amp; Fombonne(^2)</th>
<th>Brick Township, NJ(^3)</th>
<th>Chakrabarti &amp; Fombonne(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism</td>
<td>30.8/10,000</td>
<td>16.8/10,000</td>
<td>40.5/10,000</td>
<td>22.0/10,000</td>
</tr>
<tr>
<td>Other ASDs</td>
<td>27.1/10,000</td>
<td>45.8/10,000</td>
<td>26.9/10,000</td>
<td>36.7/10,000</td>
</tr>
<tr>
<td>Total for ASDs</td>
<td>57.9/10,000</td>
<td>62.6/10,000</td>
<td>67.4/10,000</td>
<td>58.7/10,000</td>
</tr>
<tr>
<td>Total for ASDs</td>
<td>1/170</td>
<td>1/170</td>
<td>1/150</td>
<td>1/170</td>
</tr>
</tbody>
</table>

\(^1\) Baird et al, 2000  
\(^2\) Chakrabarti & Fombonne, 2001  
\(^3\) Bertrand et al, 2001  
\(^4\) Chakrabarti & Fombonne et al, 2001
## Prevalence 1/150
February 2007

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism</td>
<td>60/10,000</td>
<td>38.9/10,000</td>
<td></td>
</tr>
<tr>
<td>Other ASDs</td>
<td>48/10,000</td>
<td>77.2/10,000</td>
<td></td>
</tr>
<tr>
<td>Total for ASDs</td>
<td>108/10,000</td>
<td>116.1/10,000</td>
<td>66/10,000</td>
</tr>
<tr>
<td>Total for ASDs</td>
<td>1/100</td>
<td>1/100</td>
<td>1/150</td>
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\(^1\)Kadesjo et. al. JADD Vol. 29 No. 4 327-331  
\(^2\)Baird et al, The Lancet 368; 210-215 2006  
\(^3\)ADDM Network, MMWR Feb 9, 2007; 12-28  
\(^4\)This number was 20/10,000 in 1980
Recent prevalence rates reflect autism + Asperger’s Disorder + PDDNOS; also the full spectrum of autism.

Prevalence figures from the ’70’s represented only those with moderately severe autism, not even the full spectrum.

Because early intervention resulted in better outcomes, the broader spectrum of severity associated with autism, and then the other ASDs were recognized.

These two factors greatly increased the rate of diagnosis.

Public awareness of autism (ASD) continued to improve recognition, as did regional centers & other programs.
The Changing Face of Autism

- The full spectrum within autism
- Kanner originally described a full range of severity all the way from the ‘form fruste to those who were profoundly affected
- All shared the same qualitative features
- By the 70’s, the top high of autism lost and the lowest also lost in practice
### Estimates of Expressive Language Level at Age 9

151 Autism Participants

Lord et al Arch Gen Psych 2006; 63: 694-701

<table>
<thead>
<tr>
<th>Description</th>
<th>Chicago</th>
<th>North Carolina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex sentences (ADOS Module 3)</td>
<td>40.9%</td>
<td>39.6%</td>
</tr>
<tr>
<td>Sentences but not fluent (ADOS Module 2)</td>
<td>35.3</td>
<td>28.9</td>
</tr>
<tr>
<td>Words but not sentences (ADOS Module 1; ADI-R = 1)</td>
<td>10.5</td>
<td>16.8</td>
</tr>
<tr>
<td>No or few consistent words (ADI-R=2)</td>
<td>14.3</td>
<td>14.4</td>
</tr>
</tbody>
</table>
Strange or odd, reflecting social impairment
Monotone voice, little to no facial expression
Upset by change, rituals for doing things in set ways; little scripts; evolves into #4
Obsessions w/ focus on facts or collections; memory for detail superb
Clumsy, awkward
Other Important Features of Verbal ASDs

- No hallucinations
- Onset in first three years
- Socially emotionally very young
- Very poor perspective taking if any; little empathy
- Poor face & emotion recognition
- Gullible
- Very few strategies for problem solving, no flexibility
Asperger’s Disorder vs Autism

- Absence of delayed & disordered language development
- Often precocious language development
- Fewer symptoms than for Autistic Disorder
- Inaccurate distinction between HFA, AS, PDDNOS in clinical practice
Capacity to experience, comprehend, and regulate emotions at a basic and cognitive level is severely impaired and unrecognized despite frequent abnormal imaging abnormalities of the amygdala, an emotion structure of the brain.

Most verbal ASD adults are socially-emotionally 12-18 months to 4-5 years of age. Failure to recognize this in treatment worsens behavior.
As severity spectrum of autism re-expanded, it became clear that there were variations from autism but still the same quality of deficits.

- Asperger’s Disorder: no delayed development of language and no mental retardation
- PDDNOS: symptoms not as severe for IQ as autism or not present in the communication and repetitive behavior domains as in autism
Before 1980, it was thought that almost every case of autism would have an underlying cause.

Between 1980 & 1990, it was found that only 5-10% of cases of autism were the result of infectious, chromosomal, or metabolic disorders.

Most common now are tuberous sclerosis, fragile x syndrome, chromosome 15q abnormalities.

Fetal rubella used to be common until childhood vaccinations eliminated this.

List of causes is long and most rare.
Some Etiologies of Autism Syndrome

The resulting symptoms of autism can bear a close or minimal resemblance to autism as it is seen in the 90-95% of children diagnosed with autism

- Fetal rubella infection
- Fetal cmv infection
- Herpes encephalitis
- Untreated PKU
- Xyy syndrome
- 15q syndromes
- Mitochondrial disorders
- Casper2 genetic mutation
2.27 relative risk of autism diagnosis conferred by the CC genotype MET receptor tyrosine kinase. MET signaling is involved in neocortical and cerebellar development, immune function, and gastrointestinal repair, consistent with the multi-organ symptoms reported in autism

Campbell et al. PNAS 2006, 45: 16834-16839
Autism is often thought to be a behavioral disorder. This narrow perspective omits its neurologic origin and the understanding of its origin in cognitive and brain differences.

Also, there are other manifestations:

- sleep disorders
- gastrointestinal disorders
- seizures
- genetic metabolic dis.
- chromosomal abnor.
- undx medical ills
Understanding Thinking in Autism: The Key to Success in Communication & Intervention
Studies have always shown an uneven cognitive profile:

- What do their cognitive strengths have in common?
- What do their cognitive weaknesses have in common?
- Answers to these questions provide insight into the underlying thought processes and brain mechanisms.
Altered Thinking BASED on Cognitive Differences: Intact or Enhanced Abilities & Deficits

<table>
<thead>
<tr>
<th>Intact or Enhanced</th>
<th>Cognitive Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>Complex Sensory</td>
</tr>
<tr>
<td>Sensory Perception</td>
<td>Complex Motor</td>
</tr>
<tr>
<td>Elementary Motor</td>
<td>Complex Memory</td>
</tr>
<tr>
<td>Simple Memory</td>
<td>Complex Language</td>
</tr>
<tr>
<td>Formal Language</td>
<td>Concept-formation</td>
</tr>
<tr>
<td>Rule-learning</td>
<td>Face recognition</td>
</tr>
<tr>
<td>Visuospatial</td>
<td></td>
</tr>
</tbody>
</table>
What Does The Profile Mean About Neurologic Function & Neural Circuitry?

- Simpler processing & abilities are intact/enhanced
- Information processing capacity is limited-integrative processing & higher order cognitive abilities are disproportionately impacted

Inference: higher order circuitry is under developed-they are reliant on lower order circuitry & basic cognitive abilities to function.
fMRI Activation During a Spatial Working Memory Task  (Courtesy John Sweeney)
No.
The reflect differences in the way the brain is wired or connected.
Jim was admitted for possible mania. He was agitated and had been sending money to television evangelists and became preoccupied with sin and going to hell. He carried and read from the Bible constantly. The psychiatrists attempted daily to convince him to try lithium but he refused. His reason was that he took lithium on June 4, 1978 and he got a stomach ache. He went to the clinic and a scene ensued. Staff yelled at him. No amount of REASONING worked to change his mind, until he was told and SHOWN there were now two forms of lithium - one was pink and one was blue. He took the “bad blue” before, but this time he would take the “good pink”. He immediately agreed to lithium. The deterioration in his behavior was the result of losing his job for asking a woman a question about her clothing, which was interpreted as sexual harassment. All structure was gone from his life and he became disorganized but not manic. Socially-emotionally he was three.
Detroit Learning Aptitude Test: Processing Demands of Complex Sentences

![Bar graph showing scores for Autism and Control groups in Letter Sequences, Word Sequences, and Oral Directions. The bars indicate significantly different scores with an asterisk.]
Reducing Information Processing Demands

- Reduce the amount of material to match the child
- Reduce the complexity of material to match child
- Use one information modality- visual or auditory
- Pre-process the material- provide the bottom line
- Increase processing time- say it slower, pause
- Use written instructions-Campbell soup type
- Beware hyperlexia (over-estimation of their level)
Abstract Reasoning: Concept Identification & Concept Formation

- 90 verbal individuals with autism >12 yrs
- 107 control volunteers
- Concept identification
  - Attribute identification
  - Rule-learning
- Concept formation
  - Self-initiated strategy
- Cognitive flexibility
Dissociation Between Concept Identification & Concept Formation in Autism

- **Intact** concept identification:
  - Attribute identification
  - Rule learning
- **Inflexible** in applying rules in changing contexts
- **Impaired** concept and strategy formation

Bill is a young adult with autism who decided to take figure skating lessons. His mother drove to the rink several times a week. After a while, she decided to skate while he had his lesson. Bill performed his routine, but people learned to stay out of his way. He went where his program required him to go regardless of others. One day his mother forgot to note where Bill was and he ran her over, knocking her unconscious. The emergency team was called and she was given first aide and taken to the hospital. The next day she asked Bill why he did not come to her assistance, since he was an Eagle Scout with a first aide badge. He replied “It expired.”
**Effect of dual task on memory span and tracking performance**

<table>
<thead>
<tr>
<th>People with autism</th>
<th>Digit recall</th>
<th>tracking performance</th>
<th>Mu score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>single</td>
<td>dual</td>
<td>single</td>
</tr>
<tr>
<td>Mean</td>
<td>86.19</td>
<td>&gt; 48.13</td>
<td>52.75</td>
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<tr>
<td>SD</td>
<td>7.55</td>
<td>16.77</td>
<td>10.47</td>
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<td>Controls (n = 16)</td>
<td></td>
<td></td>
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<td>Mean</td>
<td>87.25</td>
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Digit recall is expressed as a percentage of correct sequences.

**Dual task performance deficit in autism;**
*(but matched performance in single task conditions)*

Garcia-Villamisar & Della Sala, 2002 Cognitive Neuropsychiatry
What Does This Mean About Thinking?

People w/autism think differently:

- They have an enhanced awareness of details
- They have a reduced understanding of meaning & reduced capacity for conceptual reasoning in all areas
- They can only handle small amounts of *new* information
- They can only think so fast; no rapid automatic thinking
- They may use different cognitive skills to compensate
- If the information or task is visual, they understand more
- The brain is wired differently to cause these differences
Information Processing

- Overwhelmed easily, no organizing principles
- Don’t extract same meaning, harder to be part of a conversation or group when behind or there’s bottom line meaning not the same as others
- Can’t recognize faces or emotions, themes of books, movies, conversation or tell logical stories (same with “wh” questions & verbs)
- Difficulty with problem solving and common sense in real life (rules not enough) and life without externally imposed structure

- In the last three panels, SC4-SC6, the difficulty emerges as platform motion is introduced. These panels demonstrate delayed development and a failure of the autism group to achieve adult levels.
- Measures for autistic subjects (circles) and control subjects (crosses) and locally smoothed curves (solid line for autistic subjects, broken line for control subjects). R-square for fits: 0.198 (SC3), 0.164 (SC4), 0.175 (SC5), and 0.170 (SC6).
Clinical motor tests commonly find impairments
More rigorous testing rare except grooved pegboard for praxis and finger tapping
Linked to poor sign language; poor writing
Postural control impaired- due to impaired vestibular-visual-position sense; parents say they don’t know where limbs or body are in space
Sensory Impairments:
Part and Parcel of Autism

- Common
- More common in children than adults?
- Can be severely impairing
- Sound, light, tactile, taste sensitivity & aversions
- Also preoccupations with sensory
- Pain and temperature insensitivity
- Can be disabling and impact behavior
- Respect them; protect or accommodate for them
Autism is defined on the basis of abnormalities in social, communication and imaginative play, and restricted interests-repetitive behavior.

The neuropsychologic and postural findings define deficits considerably beyond this triad, suggesting a more brain-wide disturbance in information processing.

Williams et al. 2006, 12: 279-298
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- Verbal 19-45 year olds with autism or Asperger’s
- Free assessment, no costs; travel & hotel paid
- Paid participation
- Need 300 with ASD
- Need control volunteers also! Same benefits

autismrecruiter@upmc.edu
“Co-Morbidity” Or Autism

- Mental retardation: part and parcel of autism
- Hyperactivity: part and parcel of autism (60-70%)
- “ODD”: resistance to change
- “OCD”: usually restricted and repetitive behavior; rarely it is co-morbid OCD
- Seizures: 30% in autism by third decade; gene
- Anxiety: natural consequence of symptoms and comorbidity
- Depression: secondary to symptoms and/or comorbid
Brain activation during sentence comprehension in high-functioning autistic subjects

Marcel Just
Nancy Minshew
Tim Keller
Vlad Cherkassky
Jennifer Roth
Superior to age-, IQ-, gender- matched controls on word & non-word decoding, spelling, vocabulary, fluency

Inferior to controls on comprehension of sentences, idioms, metaphors, stories
Sentence reading task and comprehension probe

The player was followed by the parent

Who was following?
player       parent
Brain activation during sentence comprehension in autism
in Brain, 2004

Autism group has less activation in **Broca’s area**
• (a sentence integration area)
than the control group and more in **Wernicke’s area**
• (a word processing area)
Results are consistent with poorer comprehension of complex sentences, coupled with good word reading (spelling bee champs)
Reliably lower functional connectivity for autistic participants between pairs of key areas during sentence comprehension (red end of scale denotes lower connectivity)
Reliable differences in functional connectivity: autism group has lower functional connectivity but same rank order
Functional Underconnectivity During A Problem Solving Task: The TOL

Marcel Just
Nancy Minshew
Tim Keller
Vlad Cherkassky
Group differences in functional connectivity

Control group

Group with autism

Functional connectivity (z)

ROI pairs

LPOCG:RPOCG
LPOCG:RT
RIFG:RIPL
RPOCG:RST
RDLFPC:RIPS
LDLPC:LSPL
LIP:RIPS
LIPS:RSFG
RIP:RIPS
RIFG:RIPS
RDLFPC:RIPS
RHESL:RHP
LIFG:RIPS
RCBL:RIPS
What Does All This Mean About Low Functioning People With ASD?

- Information processing: they have little to no capacity to process information to understand information or express a response.

- Brain connectivity: no distant connections; only some local connections; in most severe cases, there is no local connectivity - no meaning is attached to sensory information.
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autismrecruiter@upmc.edu
Concept Formation Impairments Present Globally
All rely on prototype formation mechanisms

- Motor concept learning
- Memory dependent on strategies
- Story creation or theme identification
- Face recognition
- Face affect recognition
- Strategy formation, problem solving
Cognitively the problem is with prototype formation and 

*automatic processes*

as opposed to conscious, verbally mediated reasoning.
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**Dual task performance deficit in autism; (but matched performance in single task conditions)**

Garcia-Villamisar & Della Sala, 2002 Cognitive Neuropsychiatry
Infants are born with automatic mechanisms that allow them to form Prototypical Representations of Information.
Which of these is the best example of a dog?
Which of the following two faces looks more familiar to you?
Cognitive Research in 5-50 year old HFAs

- The way individuals with autism come to learn about both the world and people is different from individuals who do not have autism.
- There are core differences in the way they learn categorical information and acquire “expertise”

Gasgeb, Strauss, & Minshew. Child Dev 2006; 77: 1717-1729
Most Difficult Faces for Participants with Autism To Classify By Gender
Gender Categorization
5- to 7- Year- Old Children

Typical Hair Typical Cap Atypical Hair Atypical Cap

Control Autism

*p < .05

Strauss, M.S. et al., Child Development (under revision)
Gender Categorization
8- to 12- Year Old Children

* p < .05
Gender Categorization
13- to 17- Year Old Teenagers

Control
Autism

*p < .05
Volunteers Needed For Infant Toddler Study at U. Pittsburgh: 412 246-5485

- Pregnant mom’s with child w/autism
- Infants who have older sibling w/ autism
- Any 2-4 year old with autism who can sit w/mom
- Free assessment, no costs; transportation paid
- Paid participation
- Need control volunteers also! Same benefits- bring a friend or come with your friend
Diagnostic criteria for 299.00
Autistic Disorder

A. 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. *(on the following 3 slides)*

B. Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years:
   - social interaction
   - language as used in social communication, or
   - symbolic or imaginative play
Diagnostic criteria for 299.00
Autistic Disorder (cont’d)

1. Qualitative impairment in social interaction
   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
2. Qualitative impairment in communication
   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
3. Restricted repetitive and stereotyped patterns of behavior, interests, and activities:
   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 mannerism (e.g., hand or finger flapping or twisting, or complex whole-body movements).
   d) persistent preoccupation with parts of objects
Behavioral Expression of Social Deficit

- **Most severe:** no response to any social overture & no attempt to initiate social contact with others
- **Intermediate:** a few unvarying stereotyped ways of initiating contact, contact initiated solely for needs; not sustained; no understanding of social etiquette between people or in groups
- **Less severe:** interactions consist of monologues, extended scripts that sound original but aren't, or are dependent on others’ questions; inadvertently offensive to others but also naive and gullible; can’t chit chat
**Language & Communication Deficits**

- **Most severe:** global aphasia & apraxia (loss or impaired ability to speak or understand language); mute

- **Intermediate:** echolalic with no comprehension → a few echoed sentences used functionally to indicate needs → a few stereotyped sentences used rote with extremely limited comprehension; short scripts; talks but not to you

- **Less severe:** grammatically correct sentences but deficits in comprehension of idioms, metaphors, and stories; talk about obsessions; monologues; long scripts; unending questions; cannot chit-chat; conversation not reciprocal

- **Bottom line:** expression is greater than comprehension
Expression of Impairment in Play

- **Most severe:** complete lack of interest in toys
- **Intermediate:** interest in smell, taste, or texture of objects; preoccupation with the parts of toys (spins wheels, lines up; carries around): nonfunctional or atypical play
- **Less severe:** functional play sequences but play is stereotyped; may precisely imitate video or TV; preoccupied with game shows, letter-word games, computer, video games- advantage due to piecemeal processing & rule based
Restricted & Repetitive Behavior: Expression of Local-Global Cognitive Deficit

- **Most severe:** self-stimulatory behavior disproportionate to IQ, oblivious to change
- **Intermediate:** interest in elementary features but not whole, tantrums with change, rituals for doing things, controlling of what others do and say
- **Less severe:** tolerant of ordinary changes, narrow range of interests that are preoccupations or obsessions with a focus on details, no common sense or insight; poor concept formation, problem solving; inflexibility; rule and fact based