

How the Brain in Autism Defines the World: A Different Sense of Reality

Minot State University

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Research Participants Needed: 1/1/07-6/1/12

- High functioning individuals (IQ score of 80 or higher) and 5-45 years
- Through June 2012; no cost; participant payment; free comprehensive assessments
- Need control volunteers also! Bring a friend.

Epidemiologic Studies

	Baird et al. 2000 ¹	Chakrabarti & Fombonne ²	Brick Township, NJ ³	Chakrabarti & Fombonne ⁴
Autism	30.8/10,000	16.8/10,000	40.5/10,000	22/10,000
Other ASDs	27.1/10,000	45.8/10,000	26.9/10,000	36.7/10,000
Total for ASDs	57.9/10,000	62.6/10,000	67.4/10,000	58.7/10,000
Total for ASDs	1/170	1/160	1/150	1/170

¹ Baird et al., 2000; ² Chakrabarti & Fombonne, 2001; ³ Bertrand et al., 2001;

⁴ Chakrabarti & Fombonne et al., 2005

Epidemiologic Studies

	Kadesjo, et.al. ¹ 1999	Baird et al ² , 2006	CDC ³
Autism	60/10,000	38.9/10,000	
Other ASDs	48/10,000	77.2/10,000	
Total for ASDs ⁴	108/10,000	116.1/10,000	66/10,000
Total for ASDs	1/100	1/100	1/150

¹Kadesjo et. al. JADD Vol. 29 No. 4 327-331; ²Baird et al, The Lancet 368; 210-215 2006

³ADDM Network, MMWR Feb 9, 2007; 12-28 ⁴This number was 20/10,000 in 1980

Estimates of Expressive Language Level at Age 9 -- Percent of 151 Participants

	Chicago	North Carolina
Complex sentences (ADOS Module 3)	40.9	39.6
Sentences but not fluent (ADOS Module 2)	35.3	28.9
Words but not sentences (ADOS Module 1; ADI-R = 1)	10.5	16.8
No or few consistent words (ADI-R=2)	14.3	14.4

Classification:Neurology-Psychiatry Trade Off

- Diagnostic and Statistical Manual of Mental Disorders-4th Ed-TR
- International Classification of Diseases-10th Ed
- A neurological disorder but
- Most care provided within mental health
- Double-edged sword
- MH addresses difficult behavior
- But does so without understanding its cause

Official Category in DSM-IV: Pervasive Developmental Disorder

- Autistic Disorder
- Asperger's Disorder
- Pervasive Developmental Disorder Not Otherwise Specified
- Childhood Disintegrative Disorder (onset: 4-12 yr)
- Rett's Disorder

Informal Category Not in DSM-IV: Autism Spectrum Disorders

- Autistic Disorder
- Asperger's Disorder
- Pervasive Developmental Disorder Not Otherwise Specified

- Accurate distinctions between these outside a research setting unlikely. Need a functional definition of social, language, and adaptive abilities and problem behaviors instead.

PDD-ASD

- CDD and Rett's are rare and degenerative, may be associated with early death.
- Hence, you are unlikely to see them and they will not be discussed.
- The focus will be on ASD solely. The terms ASD and PDD can and are used interchangeably, but when used, typically refer to the first three diagnoses only and NOT CDD and Rett's.

Underlying Causes of ASDs

- 90% of ASD cases are idiopathic, e.g., there is no other cause for the symptoms besides ASD
- 5-10% have an underlying disorder causing the ASD
- Most common above chance are Fragile-X syndrome, tuberous sclerosis and chromosome 15q3 duplication/deletion syndromes
- This means all cases should have a chromosome analysis for these specific abnormalities and a Woods lamp examination for TS

Psychiatric (Behavioral) Differential Diagnosis For Children With ASD

- ADHD
- Developmental Language Disorders
- Mental Retardation
- Conduct Disorder
- Adjustment Disorder
- Oppositional Defiant Disorder
- Bipolar Disorder
- Obsessive compulsive disorder
- Anything in DSM-IV, usually multiple

Psychiatric Differential Diagnosis For Adults With ASD

- Schizophrenia
- Personality disorders
- Bipolar disorder
- Obsessive compulsive disorder
- Learning disabilities
- Mental retardation
- Anything in DSM-IV, usually multiple

Bipolar Disorder: Not

- BPD diagnosis often made because of “mood swings” or outbursts; individual says what they think unfiltered- angry at what they see as unfair or unjust- or react to bullying or to social intensity of the environment without the social filter
- Their fundamental social impairment is not recognized and no one thinks of ASD; typically not able to work or get along in social settings; not drug responsive

Recognizing ASD in Verbal Individuals

- Strange or odd: reflects social impairment
- Monotone voice: usually too loud
- Little to no facial expression
- Upset by change, rituals for doing things in set ways; scripts for saying things
- Obsessions- with collecting stuff or a topic; super memory for facts or attention to small details
- Clumsy, awkward

Other Distinguishing & Important Features

- No hallucinations
- Onset in first three years
- Socially emotionally very young: naïve, child-like
- Very poor perspective taking if any
- Poor face & emotion recognition
- Gullible
- Very few strategies for problem solving, not flexible

Asperger's Disorder vs Autism

- Absence of delayed & disordered language development now and before 5 years
- Fewer symptoms than for Autistic Disorder
- Often precocious language development
- Actual application of diagnosis: highly variable with poor distinction between HFA, AS, PDDNOS

Quick Diagnosis of ASD in LFA

- **Intermediate severity:** echolalic, few scripted stereotyped sentences; socially isolated; self-stimulatory behavior; difficulty with change; sensory issues
- **Most severe:** no language, no comprehension, no prosody, no adaptive behavior- out of proportion to IQ; direct care staff can tell who has autism vs non-autistic MR- they are highly familiar with IQ expectations

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

Social Emotional Immaturity: Disturbance in Affective Contact Not Included in DSM

- 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.

Co-Morbidity Or Autism?

- Mental retardation: part and parcel of autism
- Hyperactivity: part and parcel of autism
- “ODD”: resistance to change
- “OCD”: usually restricted and repetitive behavior; rarely it is co-morbid OCD
- Seizures: 30% in autism by third decade; gene
- Depression: secondary to symptoms or comorbid
- Dysthymia: rare but occasional very negative
- Anxiety: natural consequence of symptoms

Medical Complications of Autism

- Seizures in 30% by end of third decade
- Gastrointestinal- variety of intolerances, ulcers
- Sleep disorders into adulthood
- Inborn errors of metabolism- each one rare- fatigue, weakness, vomiting
- Chromosomal abnormalities-majority rare

Common Principles of Neurology

- Brain disturbances produce a constellation of cognitive & neurologic deficits, not a single deficit
- Multi-organ involvement is the rule in non-acquired neurologic disorders- because affected genes are in every cell in the body

Neurologic Approach to Deciphering Disease

Neurologists' approach to investigating brain dysfunction is to characterize all impaired abilities AND all intact abilities to define common principles or characteristics of the underlying disease process.

Disease Processes: Finding A Mechanism

- Trauma
- Infectious disease
- Vascular disease
- Tumor or mass
- Toxins
- Developmental processes

Developmental Processes

- Organogenesis
- Neuronal proliferation
- Glial proliferation, migration
- Neuronal migration
- Neuronal organization
- Myelination

The Cognitive & Neurologic Profile of Autism

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 cognitive and neural mechanisms

Discriminant Function Analysis: Domains Without Deficits³

Domain	Tests Passing Tolerance	Percent Correct	Kappa ¹
Attention	Letter Cancellation; Number Cancellation	66.70	0.33
Sensory Perception	Finger Tip Writing; Luria-Nebraska Sharp/Dull Tactile Scale item	64.40	0.29
Simple Language	K-TEA Reading; K-TEA Spelling WRMT-R Attack; Controlled Oral Word Association	71.20	0.42 ²
Simple Memory	CVLT Trial 1	65.20	0.30
Visuo-Spatial	WAIS-R Block Design	56.10	0.12

¹Kappa below .40 indicates poor agreement beyond chance

²Significant *Kappa* reflects superior performance by autistic subjects

³ Based on 33 individually age, IQ, gender matched pairs of subjects

Discriminant Function Analysis¹: Domains With Deficits

Domain	Tests Passing Tolerance	Percent Correct	Kappa
Motor	Grooved Pegboard; Trail Making A	75.80	0.52
Complex Language	K-TEA Reading Comprehension; Verbal Absurdities; Token Test	72.70	0.45
Complex Memory	Nonverbal Selective Reminding-Consistent Long Term Retrieval; WMS-R Story Recall-Delayed Recall; Rey-Osterrieth Figure-Delayed Recall	77.30	0.55
Reasoning	20 Questions; Picture Absurdities; Trail Making B	75.8	0.52

¹Based on 33 individually matched pairs of autistic & control subjects (Neuropsychologic Functioning in Autism: Profile of a Complex Information Processing Disorder, *JINS*, 3:303-316, 1997)

The Profile of Intact & Impaired Abilities in High Functioning Autistic Individuals

Intact or Enhanced

- Attention
- Sensory Perception
- Elementary Motor
- Simple Memory
- Formal Language
- Rule-learning
- Visuospatial processing

Cognitive Weaknesses

- Complex Sensory
- Complex Motor
- Complex Memory
- Complex Language
- Concept-formation
- Face Recognition

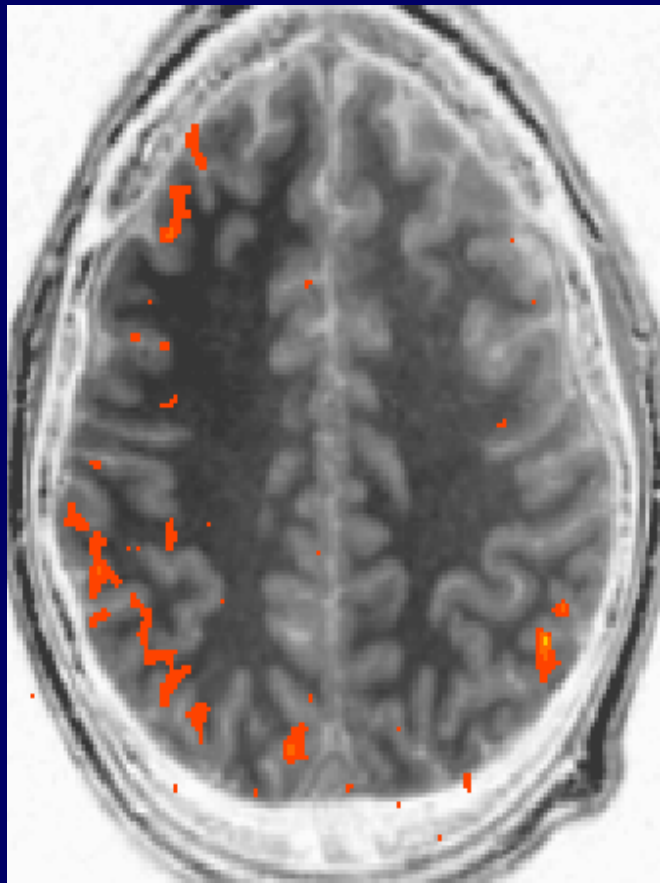
What Does The Profile Mean About Neurologic Function & Neural Circuitry?

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

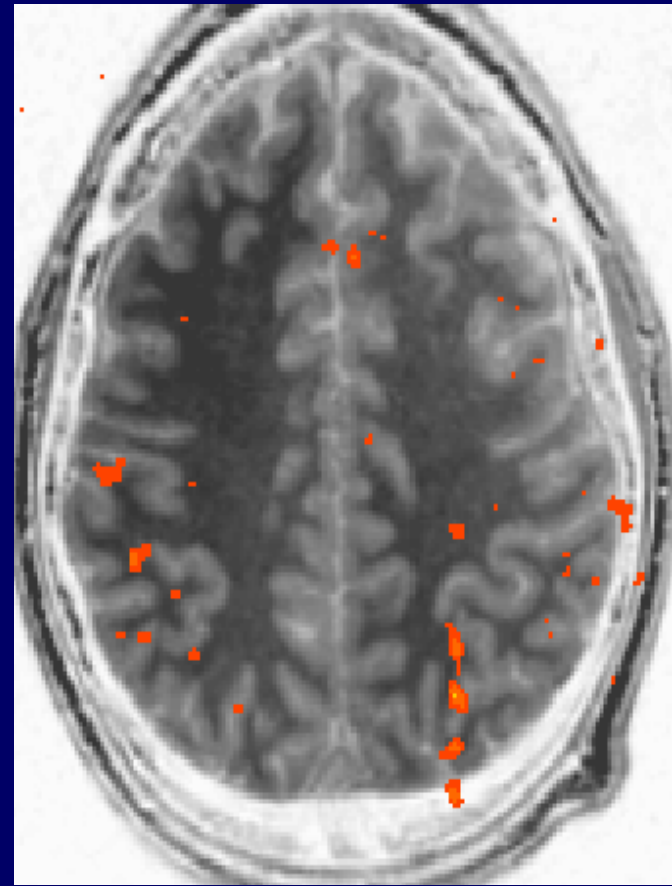
Inference: higher order circuitry is under developed- they are reliant on lower order circuitry & basic cognitive abilities to function.

fMRI Activation During a Spatial Working Memory Task

(Courtesy John Sweeney)



Healthy Group



Autism Group

Behavioral Example of Cognitive Profile: Using the Profile to Intervene

Jim was admitted for possible mania. He was agitated and had been sending money to television evangelists and became preoccupied with sin and being good, which he talked about constantly. The psychiatrists attempted daily to PERSUADE 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 the medication. 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. Socially-emotionally he was three years old. He was not reciprocal in conversation. He talked, the doctors talked.

Effect of dual task on memory span and tracking performance

	<i>Digit recall</i>		<i>Tracking performance</i>		<i>Mu score</i>
	<i>single</i>	<i>dual</i>	<i>single</i>	<i>dual</i>	
<i>People with autism (n = 16)</i>					
Mean	86.19	> 48.13	52.75	> 37.81	66.87
SD	7.55	16.77	10.47	8.22	10.74
<i>Controls (n = 16)</i>					
Mean	87.25	= 86.88	54.06	= 55.25	84.75
SD	4.81	7.58	14.61	7.39	11.52

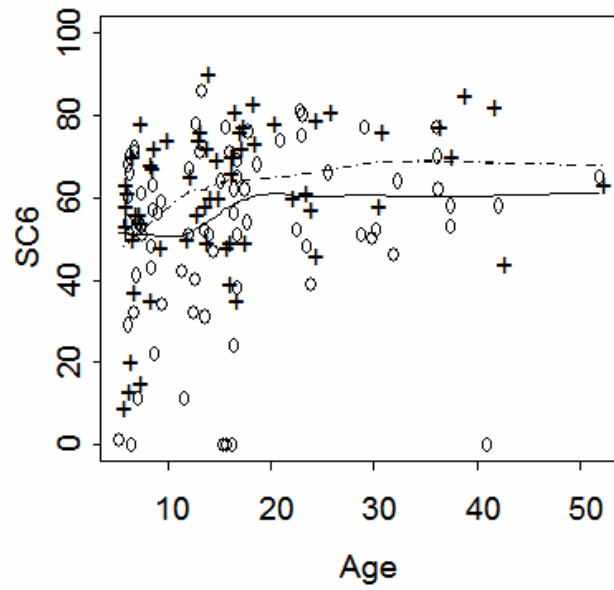
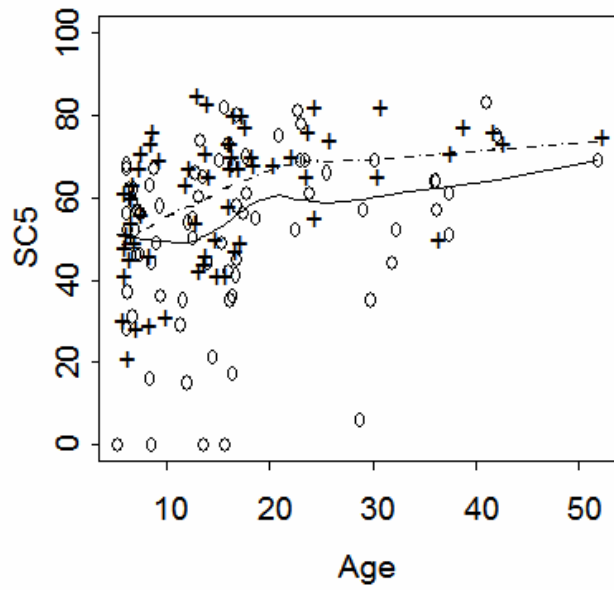
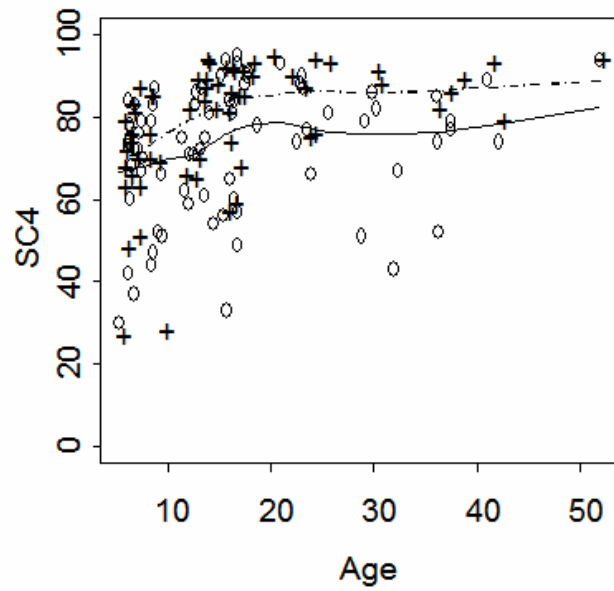
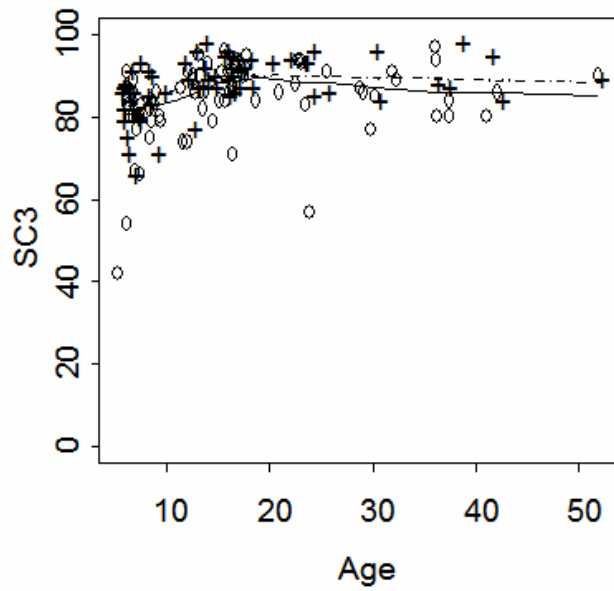
Digit recall is expressed as a percentage of correct sequences.

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

Garcia-Villamisar & Della Sala, 2002 *Cognitive Neuropsychiatry*

Minschew et al. (2004) Underdevelopment of the postural control system in autism. *Neurology*; 63:2056-2061.

- 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).



Additional Implication of Profile: Triad to Brain-Wide

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.

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
- Extent to which these were dissociable skills

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
- These two classes of abilities are dissociable in autism: do not develop simultaneously as they do in normal children

Minshew, Meyer & Goldstein, 2002, Neuropsychology 327-334.

Behavioral Example of Cognitive Profile: Rules Override Concepts

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 aid 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 aid badge. He replied “It expired.”

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

How the mind organizes information,
Or not in the case of autism

Cognitively the problem is with
prototype formation and
automatic processes
as opposed to conscious, verbally
mediated reasoning.

Pitt Infant and Toddler Development Center

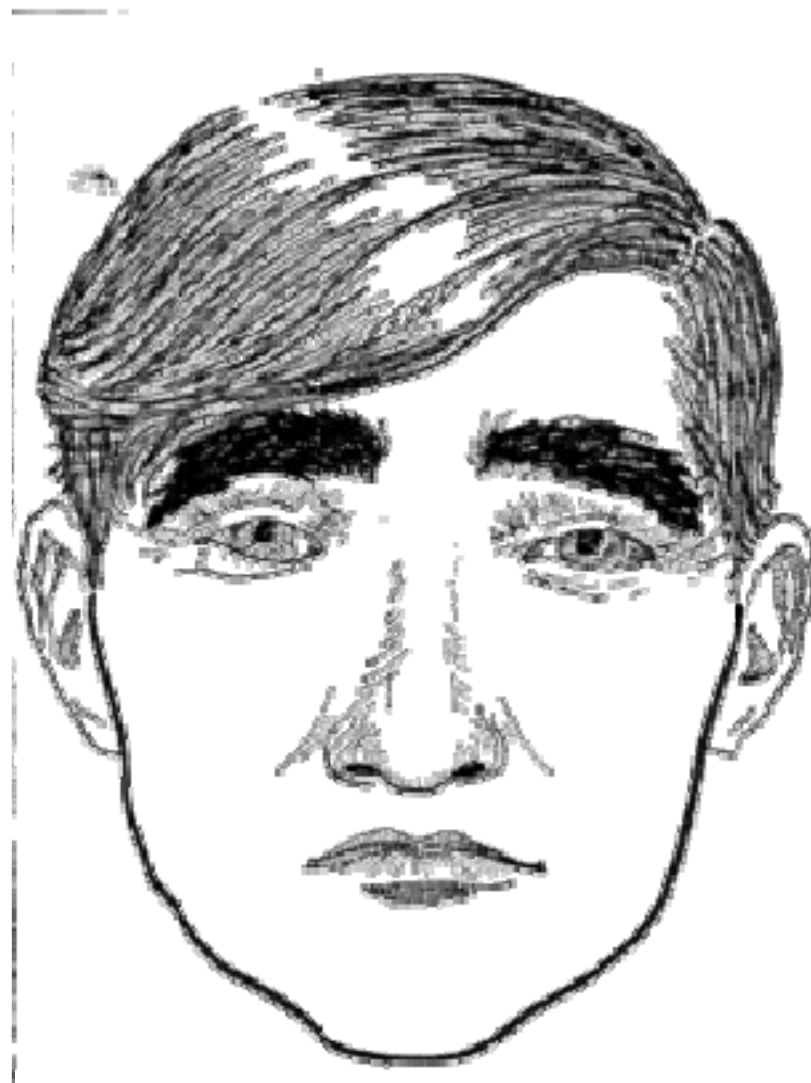
- Abilities that adults take for granted that normally develop in infancy and toddlerhood:
- For example:
 - ✓ Our abilities to recognize faces and emotional expressions
 - ✓ Our abilities to understand the difference between basic categories in the world— cats, dogs, lions ...



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?

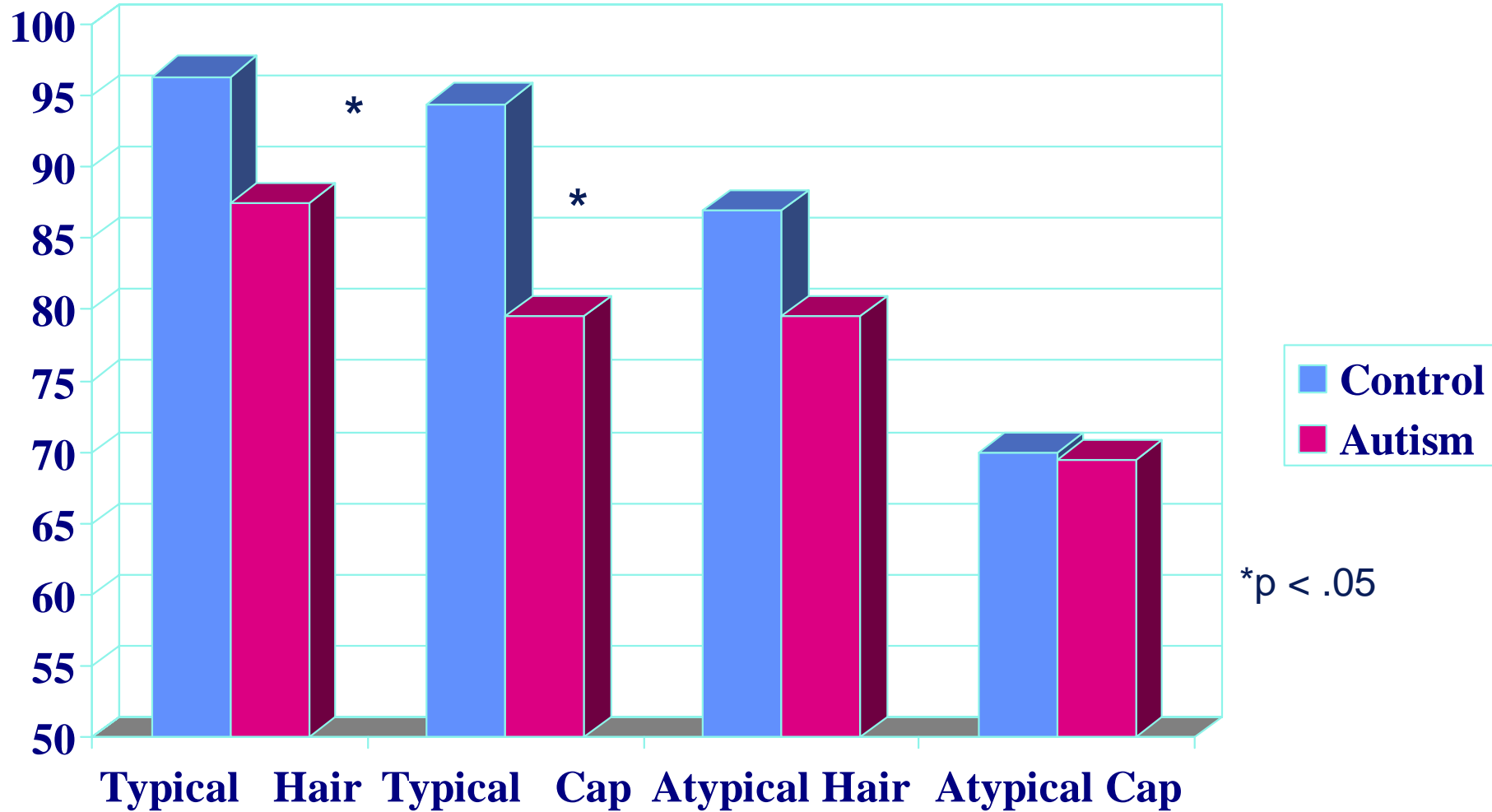


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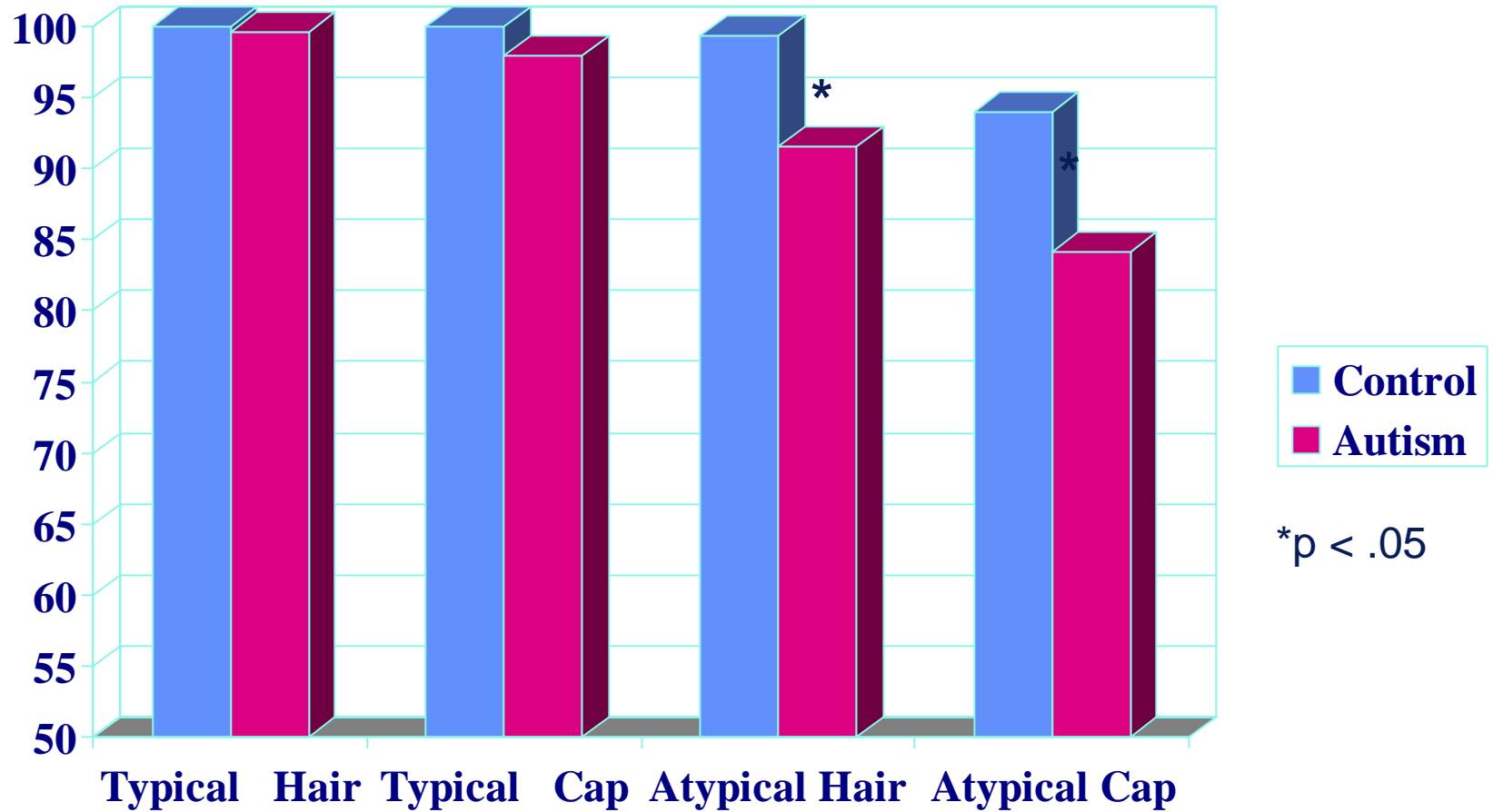


2

Gender Categorization 5- to 7- Year- Old Children



Gender Categorization 13- to 17- Year Old Teenagers





TYPICAL

SOMEWHAT TYPICAL

ATYPICAL

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