Pediatric Epidemiology Course
Autism Lecture

September 28, 2015

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The “ASD” in All People

• Autism Spectrum Disorder is defined by underdevelopment (child-like state) of skills for being social, communicating, recognizing and regulating emotions, understanding concepts, and functioning in a dynamic world.

• Most people do not have ASD but they do have problems constantly or situationally with one or more of these skills for varying reasons.

• What you learn about ASD students will be applicable to all students and people and to yourself.
Topic 1: The Latest on Prevalence
Prevalence: How Common is Autism Spectrum Disorder?

• Prevalence: 1/68, 1/50, 1/35
• Translates to: 1.5%, 2%, 2.9% of population
• Not an overestimate- probably an underestimate
Prevalence Estimates Do Not Include:

• Those with a fragment of ASD
• Those with functional social, communication and reasoning impairments due to abuse, violence, poor models, poverty, etc
• Those with social cognitive and non-social cognitive deficits but intact basic abilities-they are missed on usual autism measures, most clinicians and even parents.
The Real News:
50% have “normal” IQ scores and language

- **50% have IQ scores >85**
- **Another 23% have IQ scores of 71-85**
- In North Korea: 66% of these normal IQ ASD students are in regular classrooms and unidentified. The same is probably true here.
Topic 2: Adolescence and Adaptive Function
Adolescence As A Time of Increased Symptoms in ASD Students Who Have Relatively Intact Cognition and Language (RICLA)

- Most of the rise in prevalence is due to new diagnoses of ASD in adolescents with relatively intact cognitive and language abilities
Autism phenotype versus registered diagnosis in Swedish children: prevalence trends over 10 years in general population samples

Sebastian Lundström, Abraham Reichenberg, Henrik Anckarsäter, Paul Lichtenstein, Christopher Gillberg

Cite this as: BMJ 2015;350:h1961
doi: 10.1136/bmj.h1961
Abstract In a record-linkage study in Stockholm, Sweden, the year 2011 prevalence of diagnosed autism spectrum disorders (ASD) was found to be 0.40%, 1.74%, 2.46% and 1.76% among 0-5, 6-12, 13-17 and 18-27 year old.
Adolescence

Why might adolescence be a time when these children come to attention for the first time?

What skills do they now need that they did not have before? What is different about the world they live in as adolescents?
A Two-Hit Model of Autism: Adolescence as the Second Hit

Giorgia Picci and K. Suzanne Scherf
Department of Psychology, Pennsylvania State University

DOI: 10.1177/2167702614540646
cpx.sagepub.com
The “Second Hit” is Adaptive Behavior

Not exactly but almost.
The circuitry that supports connection of information into an integrated schema, to self and to function in a dynamic world likely starts very early in development but accelerates in adolescence. Externally imposed structure helps children to function without these skills but is inadequate in adolescence and adulthood.
Children are simpler than adolescents and life for them is simpler

- Clear rules and authority structure that they respect, value and conform to or try to
- Children value these rules and the opinion of their teachers
- They are child-like in their hearts and spirits
- They have yet to develop the cognitive capacity or desire for deception, manipulation, or retaliation, or choose not to
- In the ideal world these things are true.
Life gets much more complicated and real world-like in adolescence

- Adolescence is a time of greatly increasing social, emotional and cognitive demands.
- Students with ASD do not have the typical growth in advanced social, emotional and thinking skills that other students do.
- But you will see impaired social, emotional, communication and problem solving skills for different reasons in many non-ASD students.
Topic 3. Behavioral Hallmarks & Underlying Brain Impairments in ASD
Clinical Hallmarks of ASD

• Perceived as odd or strange
• Often expressionless face or one expression
• Poor use of eye contact for communication
• Unusual memory for details but poor concepts
• Poor common sense, poor abstraction
• Obsessions/special interests focused on details
• To them, we are illogical, erratic and scary.
• Ethan.wmv
• Adam.wmv
• Ryan.wmv
Two Basic Limitations of ASD Students

• They have lots of information in the form of details and facts but their minds do not connect them into a meaningful schema. It is like having thousands of unmatched socks.
• They don’t understand how the facts they know relate to how they would function in the external world or even what the facts mean about themselves (internal world).
Understanding what information means about and to themselves

• Brain imaging studies show that people with ASD lack a brain representation of “self”
• So social interactions like hugging others or being hugged are facts about the external world but not ones they experience in relation to themselves.
Figure 2. Posterior midline self factor location. A. Location of the voxels (circled) derived from the factor analysis of the Control Group that defined the posterior cingulate/precuneus sphere of this group’s self factor. Voxels in this cluster (with MNI x-coordinates extending from 0 to −9) are shown projected on the mid-sagittal plane. (The coordinates and radii of all 6 spheres associated with this factor are shown in Table S1 in File S1). B. Mean activation in midline brain structures for the verb hug (averaged over agent and recipient roles) for the two groups, differing in posterior cingulate/precuneus. The verb hug was chosen for illustration here because of the salience of hugging as a social interaction in autism, where enveloping pressure is sometimes desired but without physical contact between oneself with another person, as in Temple Grandin’s squeeze machine [40]. The depiction of the activation in this slice for all of the other verbs was very similar to hug, for both groups.
Lack An Integrated Schema of the World

• Brain automatically creates larger concepts to which facts/details/events are appended
• Each new experience or piece of information is automatically related to this body of information
• Not so in autism. As parents say, they just do not seem to learn from experience nor do they know what the facts mean about the world. If it is 32 degrees outside, they know that but do not know that means they should wear a coat nor do they even know when they are cold.
Adult Outcomes in ASD
Howlin et al 2004; Mazefsky & White, 2014

• Limited data- that’s a problem!
• Poor for majority with low IQ in terms of living independently, jobs, and significant social relationships
• 10 participants with IQ >70: did better than low IQ people with ASD but outcome highly variable and not predictable by IQ score
Part 4. Criteria and Deficits
HETEROGENEITY

If you know one person with autism, you know one person with autism.

Why is this true?
(Eventually you will recognize patterns.)
HUMAN BEINGS ARE COMPLEX.
THEY CHANGE RADICALLY WITH AGE.

We are just used to these changes.
THEY DIFFER GREATLY ACROSS THE IQ RANGE.

We are less familiar with this at the ends.
Commonalities Also Exist At 10,000 Feet

• Despite wide differences in behavioral manifestations, common characteristics are discernable and have resulted in diagnostic criteria that can be applied across the clinical spectrum (DSM-5)

• Genetic heterogeneity converges on a finite number of mechanisms

• Brain heterogeneity converges on altered cortical systems development and function
DSM-5 Criteria for ASD

A. Persistent deficits in social communication and social interaction across multiple contexts
   1. Deficits in social-emotional reciprocity
   2. Deficits in nonverbal communicative behaviors used for social interaction
   3. Deficits in developing, maintaining, and understanding relationships
DSM-5 Criteria for ASD

B. Restricted, repetitive patterns of behavior, interests, or activities (at least two of the following)

1. Stereotyped or **repetitive** motor movements, use of objects, or speech
2. **Insistence on sameness**, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior
3. Highly restricted, **fixated interests** that are abnormal in intensity or focus
4. Hyper- or hypo-reactivity to **sensory** input or unusual interest in sensory aspects of the environment
Lots of Leftover Pieces

• Reflected in “associated symptoms” and “co-morbidity” due to failure to understand the broad impact of ASD on the brain
• No broad appreciation by clinicians of developmental neurobiologic mechanisms eg neuronal organization, neuronal migration, and hence unable to see the larger pattern.
• Geneticists know this.
Spontaneous Mutations: Increased rate of "de novo" copy number variations: submicroscopic deletions or duplications of DNA sequences. More common in simplex than multiplex families. Opened door to two genetic mechanisms: inherited gene mutations and spontaneous copy number mutations - instability in replication of DNA.

Potential reversal of Neurodevelopmental Disorders (in Fragile X, Rett & Angelman Syndromes) in adult mice.
Associated Features

- Large gap between IQ and adaptive skills
- Intellectual impairment
- Language impairment
- Self-injury, disruptive/challenging behaviors
- Motor deficits (praxis, coordination, balance)
- Anxiety
- Depression
- Catatonia
Co-Morbidity

70% of those with ASD have one psychiatric disorder and 40% have two or more:

- ADHD
- Developmental coordination disorder
- Anxiety disorder
- Depressive disorder
- Specific learning disabilities (literacy, numeracy)
- Epilepsy, sleep problems, and GI problems
Deficits in social-emotional reciprocity (i.e., the ability to engage with others and share thoughts and feelings)...

“...intervention, compensation, and current supports may mask difficulties in at least some contexts.”

“... deficits in social-emotional reciprocity may be most apparent in difficulties processing and responding to complex social cues (e.g., when and how to join a conversation, what not to say).

Adults who have developed compensation strategies for some social challenges will struggle in novel or unsupported situations and suffer from the effort and anxiety of consciously calculating what is socially intuitive for most individuals.”
Deficits Underlying Symptoms

- Social cognition
- **Emotion regulation**
- Executive function
- Abstraction (rule-learning, concept formation)
- **Processing speed**
- Prototype learning/generalization
- Learning from experience
- Formal language, semantic pragmatic language, nonverbal language
- **Automatic versus conscious processing**
- Motor learning, motor praxis, motor coordination, motor speed
- Postural control (multi-sensory integration)
- Sensory processing
- **Adaptive function** (deficit in its own right)

Overall: lack of integration of elementary features or input to form higher order schema that support comprehension, learning/wisdom and adaptive function
Long List of Deficits Categorized by Clinical Function/Domain

• I find it more useful to think in terms of altered information processing that is present across all domains - from motor and sensory to memory and learning to reasoning

• This construct of altered information processing makes it easier to think about an approach
Part 5. Underlying Impairment in Automatic Thinking
Conscious vs Automatic Ways of Knowing Things

- Brain and mind have two broad ways of “thinking”: rapid automatic “thinking” and slow, conscious, verbally mediated thinking.
- Vast majority of thinking is automatic and non-conscious- we are not aware of it.
- We automatically know so much and assume therefore that everyone else knows and understands these things. Others are usually not thinking what you think they are.
- Check your students’ comprehension always and again and again. Watch their faces to see if it is clicking or not. Listen to what they say to hear if what they say reflects understanding.
How to Teach The Automatic

• How to know when you hit this wall: when saying it again in more detail does not work, when saying it more simply and slower as you would to a younger child does not work

• Identify the implied (Social Story method)

• Convert what you have to say to the equivalent of Campbell Soup directions (getting rid of the unnecessary, giving the bottom line)

• Ultimately it may be learning by doing- by experiencing it, keeping a diary of experiences and what was learned (what worked and what did not) and listening to others think out loud about these things in small trusted groups

- ASD group had a lack of differential activation to the artificial language condition with the frequency & stress cues and to the condition with the frequency cues alone.

- 8-month old children with typical development are sensitive to frequency and stress cues.
The brains of individuals with autism do not automatically process semantic information in the same way that controls do.

Individuals with autism may recruit more right hemisphere language areas which indicates that semantic processing is more challenging for them.
Example of Rapid Prototype Formation

Note “rapid”. Slow speed of processing is common in ASD.
• 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.
Or—Which of these is the best example of a dog?
Which of the following two faces looks more familiar to you?
Prototype formation likely to be key to face recognition and all other facial features including affect. Also a key ability for all types of learning.

Can not take for granted that the individual recognizes faces as s/he may be using clothing, hair, environment cues. Or that they know other concepts as they may be reciting facts.
Successful Face Recognition is Associated with Increased Prefrontal Cortex Activation in Autism Spectrum Disorder

John D. Herrington, Meghan E. Riley, Daniel W. Grupe, Robert T. Schultz

This study examines whether deficits in visual information processing in autism-spectrum disorder (ASD) can be offset by the recruitment of brain structures involved in selective attention. During functional MRI, 12 children with ASD and 19 control participants completed a selective attention one-back task in which images of faces and houses were superimposed. When attending to faces, the ASD group showed increased activation relative to control participants within multiple prefrontal cortex areas, including dorsolateral prefrontal cortex (DLPFC). DLPFC activation in ASD was associated with increased response times for faces. These data suggest that prefrontal cortex activation may represent a compensatory mechanism for diminished visual information processing abilities in ASD.
Supported employment improves cognitive performance in adults with Autism

D. García-Villamisar\textsuperscript{1} & C. Hughes\textsuperscript{2}

Journal of Intellectual Disability Research
Volume 51 Part 2 pp 142-150 February 2007
Implications For Treatment

• Learning from experience bridges the gap between knowledge and adaptive function (use of knowledge)
• Building cognitive over sight over behavior impulses
Part 6. Brain Basis of ASD
Brain Basis of ASD

• Alterations in cortical connections locally and globally
TOL Task: Bihemispheric Task
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 autism 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.
Group differences in functional connectivity

Control group

Group with autism

Functional connectivity (z)

ROI pairs

LPOG:RPOCG
LPPRECG:RPOCG
LPOG:RT
RIFG:RIPL
RPOG:RST
RDLPC:RIPS
LDLPC:LPSC
LIPL:RIPS
LIPS:RSFG
LIPS:LSFG
RIPS:RSFG
RIFG:RIPS
LDPFC:RIPS
RHEVEL:RIPS
LIFG:RIPS
RCEBELL:RIPS
Neural Basis of Cognitive, Affective, Language, & Neurological Deficits

- Systems level abnormalities: within and between systems connectivity
- Cortical systems
- Broad but selective (see cortical systems)
- Gray matter and white matter reflections
- Plastic and responsive to treatment in many individuals, with measureable improvements at neural level
Autism Begins in the Womb

• Epidemiologic studies are consistent in showing that environmental contributors have their impact in pregnancy
• Much of brain development is established in utero
• Long ago Dr. Margaret Bauman said that the neuropathologic changes occurred no later than 30 weeks of pregnancy
The Biggest “E” Effect in ASD is Beneficial Impact of Interventions

• Lots of evidence that human environmental influences are strong and positive
• Studies are demonstrating brain changes as a result of these interventions
• Think about “E” effects in two ways
Topic 8. Genetics of ASD

COMPLEX

Rapidly evolving.

Once cellular and molecular mechanisms defined, treatment will change radically.
Topic 9. Treatment
Treatment Frontiers

• Earlier- infants and toddlers (Early Start Denver Model- ESDM)
• Evidence base for well-developed interventions like Pivotal Response Therapy
• Mindfulness combined with cognitive strategies
• Cognitive rehabilitation approaches
• Brain stimulation- rTMS, DCS- coming soon
Fundamental News

• The brain in ASD is “plastic” or changeable at all ages.
• That is the basis of the success of behavioral, cognitive and brain stimulation approaches.