“Understanding How the Mind & Brain Think in Autism”

Bowling Green State University
June 6, 2009

Nancy Minshew, MD
Director, NIH Autism Center of Excellence
Professor Psychiatry & Neurology
University of Pittsburgh USA
Pervasive Developmental Disorders (DSM)  
*Autism Spectrum Disorders (Informal)

DSM-IV (1994): Pervasive Developmental Disorders
  *Autistic Disorder
  *Asperger’s Disorder
  *Pervasive Developmental Disorder NOS
  Childhood Disintegrative Disorder
  Rett’s Disorder

Group may vary widely depending on diagnostic instruments used-ADI-R &/or ADOS- & other exclusions; therefore findings may vary widely.
Autism is the result of alterations in how the brain processes information that alters how the mind sees the world.
Is autism a synapse-opathy?
Autism is a dysconnectivity syndrome.
Autism is a dysconnection syndrome.

And how that came to be known.
Why that is important to you.

It is the cornerstone of treatment.
It is the footprint of the cause.
My answer: what is the basis of heterogeneity?
My guess: variable genes & variable gene expression on the background of inter-human variability
Brain disturbances produce a constellation of cognitive & neurologic deficits, not a single deficit.

There is no expectation by neurologists of a single primary deficit that causes all the other deficits— that is a fiction of behaviorists.

Most neurologic disorders are multi-organ system disorder because the genes are present in all cells.
Typical Signs & Symptoms of ASD in Verbal Individuals

- Strange or odd, reflecting social impairment
- Monotone voice, little to no facial expression
- Upset by change, rituals for doing things in set ways; scripts; evolves into obsessive interests
- Obsessions w/ facts or collections; memory for detail superb
- Clumsy, awkward
Abnormalities in complex behavior
Verbal & nonverbal language impairments
60% intellectual disability (aka mental retardation)
30% seizures
Not deaf or blind (elementary sensory spared)
Subtle alterations in tone & reflexes (WM spared)
Not dysmorphic, normal growth

Interpretation: diffuse association cortex, bilateral
Brodman’s Map & Connectivity

- Primary sensory & motor cortex
- Unimodal association cortex
- Heteromodal association cortex
- Intra- and inter-hemispheric connections
Information Processing

- Acquisition abilities
- Processing of simple information
- Processing of complex information
- Auditory & visual domains
No dyslexia or visuospatial deficits—actually the opposite= no focal deficits

Language development: capacity to repeat without ability to use words originally or comprehend

Know names for objects but not meanings

Revision: distributed neural network disorder—underdevelopment of cortical connectivity
Disease Processes

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

- Organogenesis
- Neuronal proliferation
- Glial proliferation, migration
- Neuronal migration
- Neuronal organization
- Myelination
Neuronal organization refers to the events in brain development that result in the abilities that are most unique to humans.

Neuronal organizational events include the development of neuronal processes, dendritic arborizations, synaptogenesis, and the rich interconnections between neurons.
Neurologists’ characterize all impaired AND all intact abilities to identify their common characteristics linked to their shared dependence on a common underlying cause.

This approach turned out to be particularly fortuitous in autism.
# The Profile of Intact & Impaired Abilities in High Functioning Autistic Individuals

<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 processing</td>
<td></td>
</tr>
</tbody>
</table>

- Complex Sensory
- Complex Motor
- Complex Memory
- Complex Language
- Concept-formation
- Face Recognition
What Does The Profile Mean?

- Simpler abilities are intact or enhanced
- Information processing capacity is limited - & integrative processing & higher order cognitive abilities are disproportionately impaired
- Inference: higher order brain circuitry is under developed - they are reliant on lower order circuitry particularly visual circuitry to function.
fMRI Activation During a Spatial Working Memory Task  (Courtesy John Sweeney)

Healthy Group

Autism Group
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 stomachache. 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.
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 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></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><strong>People with autism</strong>&lt;br&gt;(n = 16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>86.19</td>
<td>&gt; 48.13</td>
<td>52.75</td>
</tr>
<tr>
<td>SD</td>
<td>7.55</td>
<td>16.77</td>
<td>10.47</td>
</tr>
<tr>
<td><strong>Controls</strong>&lt;br&gt;(n = 16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>87.25</td>
<td>= 86.88</td>
<td>54.06</td>
</tr>
<tr>
<td>SD</td>
<td>4.81</td>
<td>7.58</td>
<td>14.61</td>
</tr>
</tbody>
</table>

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
“Neurotypical people have a social sense right from the time they’re born.” p. 32

“My ability to function in the world & develop social relationships has been learned solely through my intellect…and use of my visualization skills. I have learned by rote how to act in different situations. Using my visualization ability, I observe myself from a distance in each situation. I call this my “little scientist in the corner”… I take note of the details that make up the situations just like a scientist observes an experiment. All that data gets put on my computer hard drive memory…
How I “tackle social situations is very much a scientific approach, based on observation, analysis, conclusions.”

She learned by reading articles and trial and error, keeping what worked and discarding what did not. She was 40 before she had enough data in her data base to improve.
Lessons of First Chapter

- Minshew, Goldstein & Williams: no single primary deficit but there is a multiple primary deficit pattern in which all deficits characterized by reduced integrative processing & decreased connectivity.

- Happe & colleagues: no cognitive explanation for deficits; reverted to deficit triad in theory of mind, executive dysfunction, and central coherence. But: omits sensory, motor, postural deficits.
The neuropsychologic profile and postural control findings define deficits considerably beyond the DSM triad, suggesting a more brain-wide disturbance in information processing and its neuronal architecture—befitting a disorder of neuronal organization.

Williams et al. 2006. 12: 279-298
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 …
Concept Formation Deficits: Search for More Fundamental Cognitive Mechanisms

- Motor concept learning
- Memory dependent on strategies
- Story creation or theme identification
- Face recognition
- Face affect recognition
- Strategy formation, problem solving
A Mechanism For Rapid Automatic Processing

- Non-conscious
- Not verbally mediated
- Flexible
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?
Attractiveness Ratings

Correlation of ratings by Controls vs. Autistics: $r = -.06$
TYPICAL

SOMEWHA TYPICAL

ATYPICAL
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
A Major Omission From All Cognitive Theories
Dr. Temple Grandin

“For some of us with ASDs, the emotional-relatedness physical or biochemical circuitry is missing—no matter how hard we try, it’s a bridge that may never be built because some of the basic building materials are missing.”

“Romantic relationships have a level of social complexity that I still don’t understand today and I consciously choose not to participate in them. My way of thinking and functioning does not describe everyone on the spectrum.”
Temple Grandin’s Perspective

“I experience the emotion of love, but it’s not the same that most neurotypical people do. Does that mean my love is less valuable than what other people feel?”

“Some people with autism don’t understand or experience any sort of emotional attachment or romantic love. I would speculate that autism involves an atypical development of the ...reward systems.”
“On June 2, 1975, I was very angry. The bottom of my stomach felt as if I had swallowed a dumbbell: I spent much of my childhood and teenage years dealing with that emotion and getting to know it intimately.”

“My autism brought me much misery and unhappiness, and in essence robbed me of a childhood. I was born with a pervasive fear that never seemed to diminish, so I spent most of my earliest years devising ways to lessen the unrelenting terror, if not get rid of the chronic dread completely. To that end, I tried to find ways to look at and take in the world that would make sense to me and
“..be less overwhelming, while at the same time, provide a measure of comfort, control, balance, and security—all of which were missing from my life. Isolating and manipulating objects while tuning out people; fixating on repetitive motions; asking the same questions over and over; developing stereotypical movements, arbitrary rules and rigid thinking; and focusing to an extreme degree on one item or event to the exclusion of every else were among the ways I found some control and security, while temporarily sidestepping my fears.”
Autism: A Disorder of Affective Contact: Part 2 of Brain Behavior Definitions

- Capacity to experience, understand & regulate emotions fundamentally altered and not appreciated
- Many verbal ASD individuals socially-emotionally as young as 12-18 months to 3-5 years of age causes major symptoms
- Studies of amygdala-cortical interactions and connectivity related to social motivation, frustration management, in progress

Social Emotional Immaturity: Also Not in DSM