Psychiatric Comorbidity in Children, Adolescents, and Adults with Autism

Janet Lainhart, MD
Professor-Department of Psychiatry
Faculty Member – Waisman Center, Laboratory for Brain Imaging & Behavior Laboratory
University of Wisconsin-Madison

The Problem: Striking Manifestations across the Lifespan, Ability and Disability, Cause Unknown
Challenge to Neuroscience

- Autism: the fastest growing developmental disability.
- There are no biological markers of autism.
- There is no way to prevent the disorder or complications of the disorder.
- There are no specific treatments based on the underlying neurobiology of the disorder because the neural basis of autism and its complications is unknown.

The Clinical Problem

Identification of infants at risk for autism and young children early in the course of the disorder is important. Providing early intensive intervention is important.

*But it is also important to understand the neural basis of autism and its complications in older children, adolescents, and adults with the disorder. The majority are currently destined to live with significant lifelong impairment. --1/3rd may worsen over time rather than remain stable or improve.
The Clinical problem

There is substantial evidence that autism is a disorder of brain connectivity.

We and others have found widespread but not uniformly diffuse microstructural abnormalities in white matter. Abnormalities of cortical and subcortical gray matter are also observed.

- Neural networks involved in social communication and social interaction and repetitive behaviors appear to be involved.
- Brain networks involved in attention, motor activity, emotional regulation and control, and compulsive behaviors may also be or become involved.
**Age Severe Tantrums Started**

- Autism: n=46
- Language-Impaired: n=9

**Age Atypical Sleep Patterns Started**

- Autism: n=46
- Language-Impaired: n=16
Age Atypical Eating Pattern Started

<table>
<thead>
<tr>
<th>Group</th>
<th>Autism</th>
<th>Language-Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-36 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37-60 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>61-96 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cumulative Percent

0 10 20 30 40 50 60 70 80

Age Self-Injurious Behavior Started

<table>
<thead>
<tr>
<th>Group</th>
<th>Autism</th>
<th>Language-Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cumulative Percent

0 10 20 30 40

Autistic children have more abnormal behaviors.
What is observed

Specific Behaviors

- Pushing
- Hitting

Underlying Deficits

From: Behavioral Issues In Autism
Plenum Press, NY

Causes of emotional and behavioral problems in autism - 1

Particularly impairing core features of the disorders

- difficulty communicating with and understanding others; social impairment; repetitive behaviors

Cognitive impairments

- deficits in complex information processing;
  - theory of mind deficits; executive dysfunction;
  - deficits in central coherence; specific learning disabilities
How to diagnose co-morbid psychiatric disorders in autistic individuals

1. Understand the core and associated features of autism well, and how their manifestation change over the lifespan.
2. Understand the other co-morbid conditions well.
3. Understand the patient’s “best baseline”, and how he/she has changed over time.
4. Get information from an informant who has known the patient well for a long time.

Causes of New or Worsened Emotional and/or Behavioral Problems in Autism - 2

MEDICAL DISORDERS
- seizures; other acute and chronic illnesses

PSYCHIATRIC DISORDERS
- depression; anxiety; attention deficit; hyperactivity; bipolar disorder; obsessive-compulsive disorder; psychotic disorders

DIMENSIONAL TRAITS (at baseline: IQ etc.)

LEARNED BEHAVIORS

LIFE EXPERIENCES
- related to autism and other life experiences
How common are other psychiatric conditions in individuals with ASD?

N=109 children with autism (community ascertained; Boston and Utah)
5-17 years (mean 9.2, s.d. 2.7), mostly males
all with at least some language
Full Scale IQs 42-141 (mean 82.5, s.d. 23.4)
Parent Interview, present and lifetime disorders, by a clinician
Impairment above and beyond core features of autism

Lifetime Prevalence of DSM-IV Disorders in the Boston/Utah Sample

- Major depressive disorder 10.1% (13.8%)
- Depression, NOS 2.8%
- Bipolar I Disorder 1.9%
- Bipolar II Disorder 0.9%
- Schizophrenia 0

(Leyfer et al., JADD, 2006)
Lifetime Prevalence of DSM-IV Disorders in the Boston/Utah Sample

- Specific phobic disorder  44.3%
- Social phobic disorder  7.5%
- Separation anxiety disorder  11.9%
- Generalized anxiety disorder  2.4% (n=41)
- Panic disorder  0

- Other Impairing Non-DSM Anxiety-like Syndromes
  - Transition-change Anxiety Syndrome
  - Focused Anxiety Syndrome

(Leyfer et al., JADD, in press)

---

Lifetime Prevalence of DSM-IV Disorders in the Boston/Utah Sample

- Obsessive compulsive disorder  37.2%

- Oppositional defiant disorder  (n = 86)  7.0% (4.6%)

- ADHD  (n=85)  30.5%  (24.7%)
  - Inattentive  20 %
  - Combined  7.0%
  - Hyperactive  3.5%

(Leyfer et al., JADD, in press)
Number of Co-morbid Lifetime Psychiatric Disorders

- Utah/Boston sample
  - Only 27.5% had no co-morbid disorder
  - 22% had 1 co-morbid disorder
  - 30% had 2 co-morbid disorders
  - 20.5% had 3 or more co-morbid disorders

Aggression

Specific Behaviors
- Pushing
- Hitting

Underlying Deficits
- Poor Social Judgment
- Unawareness of Feelings of Self & Others
- Sensory Misperceptions
- Impaired Cognitive Processing at baseline
- Major Depression
- New Psychosocial Stressor

From: Behavioral Issues In Autism
Plenum Press, NY
Do Any Medication Treat Core Features of Autism-spectrum disorders?

No medication “cures” autism or completely eliminates core features of autism. But a number of medications may have a mild to modest effect on some features of autism.
Social deficits
Communication deficits
Stereotyped repetitive behaviors

What Associated features of ASD may be helped by medication and other interventions?

Depression
Anxiety
ADD/ADHD
Other psychiatric disorders
Atypical behaviors that are not part of any co-morbid disorders
Medications Commonly Used in Autism and Side Effects

Stimulants: Attentional deficits, hyperactivity, (executive function defects)
Serotonin-reuptake inhibitors: depression, anxiety, compulsive-like repetitive behaviors incl. repetitive question-asking, transition/change-related anxiety (social behaviors, communication).
Atypical Neuroleptics: nonspecific serious behavioral problems – tantrums, aggression, self-injurious behavior.

What has gone awry in brain development in ASD?

The power of brain imaging to understand autism spectrum disorder and its complications.

Source: Abidkov & Bigler (2010)
Use variation in clinical manifestations to drive the discovery of the brain-basis of ASD and its complications.

Use variations in brain structure, microstructure, and functional connectivity to drive the discovery of new gene variants and factors involved.

Understand defects in pathways.

Develop new biology-based treatments that target molecular abnormalities, aberrant brain structure & function, and the clinical and day-to-day problems they cause.

Translational Research – hope for the future
WAISMAN CENTER Laboratory for Brain Imaging & Behavior
UNIVERSITY OF WISCONSIN

McLEAN Hospital / HARVARD UNIVERSITY Neurostatistics Lab

UNIVERSITY OF UTAH Scientific Computing & Imaging Institute (SCI) and Eccles Institute of Human Genetics

BRIGHAM YOUNG UNIVERSITY Neuropsychology, Brain Imaging & Behavior Lab

Our research is supported by:
P30 HD003352-45 (Waisman Center Core Grant) from the Eunice Kennedy Shriver, National Institute of Child Health & Human Development (NICHD)

NICHD T32 HD07489 Waisman Center Postdoctoral Training Award and The Hartwell Foundation fellowship (Brittany Travers)

RO1 MH080826, RO1 MH084795, and KO8 MH092697 from the National Institute Of Mental Health