Program Description:
The understanding of the neurobiological basis of autism has grown exponentially, primarily because of the availability of modern neuropathological procedures and structural MRI techniques that allow the study of the brain in living humans including young children with autism. Understanding of these developments is important to SLPs as they plan and implement intervention and provide education to parents of children with autism. This presentation provides an update on neuropathological and structural imaging findings particularly those relevant to language development. Implications of these findings for provision of services will be discussed.

Learning Outcomes
At the end of this presentation, you will be able to:
1. Discuss recent findings from neuropathological and structural magnetic resonance imaging research in autism.
2. Describe the impact of these neurobiological differences on the behavioral presentation of autism.
3. Apply these findings to the planning of intervention for children with autism.

<table>
<thead>
<tr>
<th>AUTISM AS A NEURODEVELOPMENTAL DISORDER</th>
<th>NOTES</th>
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<tbody>
<tr>
<td>Autism</td>
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<tr>
<td>• Is a neurodevelopmental disorder</td>
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<tr>
<td>• In autism, the way in which the brain responds to environmental input results in a cascade of problems in learning and social functioning.</td>
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<tr>
<td>Autism</td>
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<tr>
<td>• Is not simply a disorder of social functioning.</td>
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<tr>
<td>• The absence of mental retardation doesn’t mean there is an absence of cognitive differences.</td>
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<td>Neurobiologically, autism is:</td>
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<td>• A large-scale neural systems disorder with alterations in cortical systems connectivity.</td>
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<td>Abnormal connectivity occurs:</td>
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<tr>
<td>• At the level of the neuron.</td>
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<td>• Structurally in white matter pathways.</td>
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<tr>
<td>• Functionally during cognitive processing between key regions.</td>
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<tr>
<td>Profile of Cognitive Strengths/Weaknesses in Autism (Williams, Goldstein, &amp; Minshew, 2006)</td>
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<tr>
<td>Intact Abilities</td>
<td>Cognitive Weakness</td>
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<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>
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<tr>
<td>*Simple Memory</td>
<td>*Complex Language</td>
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<tr>
<td>*Formal Language</td>
<td>*Concept formation</td>
</tr>
<tr>
<td>*Rule-Learning</td>
<td></td>
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<tr>
<td>*Visuospatial Processing</td>
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<tr>
<td>• The behavioral signs suggest it is a distributed neural systems disorder.</td>
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<tr>
<td>• The neuropsychologic findings define deficits considerably beyond the traditional diagnostic triad, suggesting a more brain-wide disturbance in information processing. (Williams et al., 2006, Child Neuropsychology)</td>
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Levels of Causation in Autism

| Abnormalities in Genetic Code for Brain Development |
| Abnormal Mechanisms of Brain Development |
| Structural and Functional Abnormalities of Brain |
| Cognitive and Neurological Abnormalities |
| Behavior |

ABNORMALITIES IN THE GENETIC CODE FOR BRAIN DEVELOPMENT

**Genes and Autism**

“... emerging data support the notion that the ASDs can be conceptualized in terms of multiple genetic etiologies that disrupt the development and function of brain circuits mediating social cognition and language”

(Geschwind & Levitt, 2007, *Current Opinion in Neurobiology*)

**Genetic Research**

Study of different ASD-related syndromes and single gene risk factors support the involvement of multiple brain regions, including

1) the frontal lobes,
2) anterior temporal lobes,
3) caudate, and
4) cerebellum

Regional effects do not necessarily mean that abnormalities in these locations are the "cause" of autism.

Regional effects may be the result of asynchronous development between these regions

(Abrahas & Geschwind, 2010, *Archives of Neurology*)

Although available evidence is limited, regions implicated by imaging and pathological findings generally fit with what is known about the anatomy of social cognition and language, providing a sense of validation between genetics and brain circuits.

**Abnormal Mechanisms of Brain Development**

The most consistent neuropathological finding among the ASDs is the observation of errors in neuronal migration, particularly in frontal and temporal lobes

(Abrahas & Geschwind, 2010)

**Typical Brain Development**

Early years of a child’s life are when the brain is organized in response to environmental input.

Neonates, later diagnosed with autism, show abnormally accelerated rate of HC growth that becomes significantly larger than normal at 12 and 24 months of age (Dawson et al., 2007, *Biological Psychiatry*)

**Head Growth in Autism**

- Group mean 60-70th percentile.
- Onset accelerated growth at 12 months with 15 to 20% macrocephaly by 4 to 5 years.
- Growth decelerates and plateaus so that brain volume "normalizes" in childhood, though subset remain macrocephalic throughout life.
- Important to recognize that larger HC for Height is not universal in autism and HC=Ht and HC<Ht growth trajectories are compatible with autism.


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<tr>
<th>Trajectory of TBV in Autism Across the Lifespan</th>
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<tr>
<td>Using a dataset comprised of 259 individuals with autism and 357 controls between the ages of 12 months and 50 years, Courchesne et al. (2010) document early brain overgrowth during infancy and toddlerhood with an accelerated rate of decline or degeneration from adolescence to late middle age.</td>
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<td>(Courchesne et al., 2010, <em>Brain Research</em>)</td>
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<tr>
<th>Increased Brain Volume in Autism:</th>
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<td>Group TBV paralleled group HC findings.</td>
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<td>In early childhood, 2 to 4 years of age, the TBV of children with autism is larger than age- and gender-matched controls (Hazlett et al., 2005; Redcay &amp; Courchesne, 2005).</td>
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<tr>
<td>TBV of children with autism plateaus in adolescence, but TBV of TD children continues on an upward curve to early adulthood (Lainhart, 2006).</td>
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<tr>
<th>Importance of TBV findings</th>
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<tr>
<td>Suggests that autism is the result of a neurodevelopmental process that is under genetic control, and</td>
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<tr>
<td>Early overgrowth coincides with the onset of the behavioral symptoms providing an explanation for what behaviorally seems like a sudden onset.</td>
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<tr>
<td>At least in its initial stages, the neurodevelopmental abnormality in autism appears to be one of accelerated growth rather than a passive process such as the failure of pruning or lack of programmed cell death (Minshew &amp; Williams, 2007, <em>Archives of Neurology</em>)</td>
</tr>
<tr>
<td>Early overgrowth is also not consistent with an acquired insult to brain development after birth.</td>
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<td>Increase in TBV in autism appears to be related to intracerebral white matter and cortical gray matter depending on the method of parcellation.</td>
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<tr>
<th>STRUCTURAL ABNORMALITIES RELEVANT TO LANGUAGE DEVELOPMENT IN AUTISM</th>
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<tr>
<td><strong>Myelination Process</strong> (Pujol et al., 2006)</td>
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<tr>
<td>At Birth: Primary sensory pathways &amp; pyramidal tract</td>
</tr>
<tr>
<td>After 3 months of age: Heschl’s gyrus (for processing of auditory stimuli)</td>
</tr>
<tr>
<td>Between 5 months &amp; 18 to 24 months: Language-related areas</td>
</tr>
<tr>
<td><strong>Myelinization Process</strong></td>
</tr>
<tr>
<td>Formation of a sheath of white matter or glial cells along the axons of the neurons.</td>
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</tbody>
</table>
- Important for speed of processing and communication between different areas of the nervous system.
- Is a gradual process that begins during the latter portion of the gestational period and continues after birth
- Language-related areas are not completely myelinated until after 35 months of age.
- Outer radiate white matter is the latest region of the cortex to myelinate.

**Non-Uniform Growth Patterns of White Matter in Autism**  
Herbert et al. (2003, *Brain*) parcellated white matter into inner and outer radiate white matter:

1. Increased volume of outer intra-hemispheric short and medium range cortico-cortical connections.
2. No increase in inter-hemispheric or cortical-subcortical connections.

**GRAY MATTER: MINICOLUMN ABNORMALITIES IN AUTISM**

- **Minicolumns**  
  - The basic anatomic and physiologic unit of the cortex.
  - Composed of radially oriented arrays of pyramidal neurons, interneurons, axons and dendrites.
  - Control the flow of neurochemical information from one layer to the next.

- **Minicolumns** (Casanova et al., 2006, *Acta Neuropathol*)  
  - Organization of cells, perpendicular to the pial surface, thought to contribute to integration of neuronal information across cortical layers.
  - Minicolumns hypothesized to be smallest radial unit of information processing.

**In autism, minicolumns are:**
- Increased in number
- Narrower with reduced neuropil space
- Smaller neuron cell bodies and nucleoli

**Minicolumn abnormalities most pronounced in:**
- Dorsolateral prefrontal cortex (important for goal setting and control of cognitive processes).
- The anterior cingulate (important for attentional control).
  
  (Casanova et al., 2006, *Clinical Neuroscience Research*)

**Minicolumn Findings**
- Lend support to behavioral and ERP studies that suggest that individuals with autism have difficulty with top-down processing resources.
- Although, other research suggests an interactive combination of both top-down and bottom-up processing as problematic in autism (Behrmann, Thomas, & Humphrey, 2006).

**GRAY MATTER: VOLUMETRIC DIFFERENCES**

**Regional GM Differences in Autism** (Carper & Courchesne, 2005; Hazlett et al., 2006; Palmen et al., 2005)
- Appears to be increased in the frontal and temporal lobes.
- Occipital lobes demonstrate only small increases.
- Frontal and temporal regions are ones in which increases in volume appear to be related both to maturation and experience (Giedd et al., 1999).

**Left Hemisphere Language Areas: L Inferior Frontal Gyrus & Temporal Lobe**  
With respect to LH language areas, structural MRI studies suggest a different maturation pattern for children with ASD.

**MRI Volumetric Studies of Language Areas**
- Knaus et al. (2009) reported significant correlations between the volumetric measures of frontal language areas and language and symptom severity in children with autism ages 7 to 11.
- These findings suggest that, in autism, language development may be indexed by related changes in frontal and temporal language structures.

**IMPLICATIONS OF THE NEUROBIOLOGY OF AUTISM FOR IDENTIFICATION AND INTERVENTION**
- The effects of autism are occurring long before the behavioral signs are manifested.
- Therefore, early identification is essential for the most effective remediation of the disorder.

**Current Research:**
- Push is on to identify a “biomarker” that would allow early identification.
- Strategy is to acquire imaging data on the infant siblings of children with autism.

**Implications for SLPs Regarding Young Children**
- Early identification and early intervention is key to ameliorating the effects of the abnormal brain development.

**Basic assumption about the effect of a developmental language disorder:**
The presence of a developmental condition will interfere with the development of language because it interferes with brain development and alters the way the brain responds to environmental input.

The adult has to do the work that the brain of the child with autism doesn’t automatically carry out.

**What Work Should the Adult Do?**
- Separate speech from non-speech sounds.
- Parse words from string of language.
- Make the important information obvious.
- Clearly pair language with environmental referents.
- Provide large numbers of exemplars so that the brain has an adequate amount of input from which to learn (statistical learning).

**Implications for SLPs Regarding Older Children and Adults**
- Autism is a brain systems/network problem.
- Therefore, it will effect more than social functioning.
- Other problems with information processing are less apparent but no less real.
- Individuals with autism learn and act differently because their...
brains function differently.

- Environment can influence their learning but cannot change the underlying neurophysiological differences.

### Older children and adults with ASD

#### Compensatory mechanisms: What's changeable?

- Experiential base
- Controlled processing can be used to perform tasks that NTs do with automatic processing.
- Speed of performance can be improved with practice.

#### Individual differences:

- Need to consider the person’s individual differences
- Simply because you have autism doesn’t mean other genes are not affecting brain development.

### Conclusions

- Autism involves an abnormal maturational process that affects the development of both white matter and gray matter brain structures.
- Significant impact is seen on brain structures related to language development.
- Early identification & early intervention are important so that environmental accommodations can be implemented which will promote positive neural adaptations to optimize the behavioral outcomes.

For more information or if you're interested in participating in research:

Web:
- http://pittautismresearch.org
- http://www.ccbi.cmu.edu

Email:
williamsd2139@duq.edu

### References:


Biographical Sketch:
Diane L. Williams, Ph.D., CCC-SLP, is an Assistant Professor in the Department of Speech-Language Pathology at Duquesne University and is affiliated with the NIH-funded Autism Center of Excellence at the University of Pittsburgh/Carnegie Mellon University. She does research on social cognition, language processing, and learning in autism using functional imaging. Dr. Williams is a Board Recognized Specialist in Child Language and a certified speech-language pathologist with extensive clinical experience working with toddlers, preschoolers, school-age children, and adults with autism. She is the author of *Developmental Language Disorders: Learning, Language, and the Brain,* which presents a summary of current research on the neurological basis of these disorders and the application of this research to the learning process.