An Introduction to the Neurobiology of Autism Spectrum Disorder (ASD)

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The speaker has no conflicts of interest to report.

Learning Objectives

• Upon the completion of this presentation, the learner will be able to describe the etiology of autism spectrum disorder according to the underconnectivity hypothesis of Nancy Minshew and colleagues.

• Upon the completion of this presentation, the learner will be able to describe the etiology of autism spectrum disorder according to the social motivation hypothesis of Geraldine Dawson and colleagues.

• Upon the completion of this presentation, the learner will be able to describe the etiology of autism spectrum disorder according to the social perception hypothesis of Kevin Pelphrey and colleagues.

• Upon the completion of this presentation, the learner will be able to describe findings from recent research on the effects of intervention on the brain functioning of children with autism spectrum disorder.
DSM V and ASD

A. “Persistent deficits in social communication and social interaction across multiple contexts . . .” (p. 50, American Psychiatric Association, 2013).

B. “Restricted, repetitive patterns of behavior, interests, or activities . . .” (p. 50).

• Behaviorally defined disorder
• Neuroscience and its methodologies
• Neurodevelopmental Disorder
• Underlying Complexity

Approaches to the Neurobiology of ASD

• Social Primacy Hypotheses: Social Motivation and Social Perception
  “ASD displays great phenotypic heterogeneity and etiological diversity, but . . . social dysfunction has been it’s hallmark and unifying feature” (p. R127, Pelphrey & McPartland, 2012).

• Underconnectivity Hypothesis
  “[ASD is primarily characterized by] . . . defects in early neuronal organizational events during brain development that disrupt the connectivity of neural systems” (p. 632, Minshew, Scherf, Behrmann, & Humphreys, 2011).

Underconnectivity: Nancy Minshew and Colleagues
**ASD and Neuropsychological Functioning**

(Minshew, Goldstein, & Siegel, 1997; Williams, Goldstein, & Minshew, 2006)

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<th>Problems with Complex Information Processing</th>
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• ASD is primarily a disturbance in complex information processing

• Social information processing is just one type of complex information processing

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**Functional Underconnectivity, Complex Information Processing, and ASD**

(Just, Cherkassky, Keller, Makin, 2004; Just, Cherkassky, Keller, & Minshew, 2006)

• Complex information processing emerges from different regions of the brain collaborating together simultaneously

• Two studies assessed ASD individuals engaged in complex information processing tasks: Sentence Comprehension and Tower of London (subject groups: HFA and neurotypical)

• Activation assessed in brain regions involved in these tasks with functional magnetic resonance imaging (fMRI)

• Findings indicated that ASD subjects had a lower degree of synchronization of functional underconnectivity between brain regions compared to neurotypicals

• Functional Underconnectivity in ASD limits complex information processing

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**White and Gray Matter Tracts, Structural Underconnectivity, and ASD**

(Just, Keller, & Kanna, 2013)

• Structural underconnectivity causes bandwidth problems (limitations in the amount of information communicated in a particular time period)
Minshew and the Etiology of ASD
(Minshew & Mazefsky, 2013)

• Genetic abnormalities related to neural connectivity
• This leads to abnormal neuronal organization/brain development
• This leads to abnormal functional and structural underconnectivity
• This leads to problems with complex information processing
• This leads to behaviors typically associated with ASD

Social Motivation: Geraldine Dawson and Colleagues

Reward Processing and Social Stimuli
(Dawson, Webb, & McPartland, 2005; Dawson et al., 2005)

• Biological reward/pleasure are regulated by the mesolimbic dopamine reward circuit
• Infants are hard wired to experience biological rewards/pleasure from social stimuli (smiles, eye gaze, speech, gestures), particularly in the facial region
• From this experience of pleasure, infants learn to anticipate that social stimuli like looking at the face will bring reward/pleasure
• Consequently, infants are motivated to seek out social stimuli
Oxytocin, Mesolimbic Dopamine Circuit, and ASD  
(Dawson & Bernier, 2007; Dawson, Bernier, & Ring, 2012)

- Oxytocin is a neuropeptide that promotes prosocial behavior (bonding) in many mammals including humans
- Oxytocin influences the mesolimbic dopamine system to highlight the importance of social stimuli
- Individuals with ASD have lower levels of oxytocin
- Individuals with ASD often have variations in the oxytocin gene compared to neurotypical individuals
- Small studies indicate that intranasal administration of oxytocin improves social functioning of individuals with ASD

Reward Processing, Social Motivation, and ASD  
(Dawson, Webb, & McPartland, 2005; Dawson et al., 2005)

- Individuals with ASD don’t appear to experience to the same degree as neurotypicals, biological rewards/pleasure from social stimuli, particularly the face
- As a result, they don’t anticipate to the same degree that future social stimuli will bring reward/pleasure
- Consequently, individuals with ASD don’t seek out social stimuli to the same degree as neurotypicals

Brain Structures and Social Motivation in ASD  
(Dawson & Bernier, 2007; Dawson, Bernier, & Ring, 2012)

- Anterior Cingulate Cortex: Attention
- Orbitofrontal Cortex: Representations of reward value
- Nucleus Accumbens: Mesolimbic dopamine reward system
- Ventral Tegmental Area: Mesolimbic dopamine reward system
Dawson and the Etiology of ASD  
(Dawson, Bernier, and Ring, 2012)

- Problems with Oxytocin and Mesolimbic Dopamine System (Reward Processing)
- Less attention to social stimuli
- Less specialization of brain structures and processes devoted to social stimuli processing
- Decreased social motivation
- An interaction between genes, brain, and environment

Social Perception: Kevin Pelphrey and Colleagues

Social Perception and Biological Motion  
(Pelphrey & Carter, 2007; Pelphrey, Shultz, Hudac, & Van Derwyk, 2011; Pelphrey & Shultz, 2013)

- Biological motion is the initial social perception of another living creature's movements (eye gaze, gestures, facial expressions, walking)
- Animals (monkeys, birds) and humans are hardwired to preferentially attend to biological motion versus non-biological motion (non-living things)
- Newly hatched chicks and two day old infants will preferentially attend to biological motion
- Posterior superior temporal sulcus (pSTS) is specialized for biological motion/intention reading
Biological Motion and Toddlers with ASD
(Klin, Lin, Gorrindo, Ramsay, & Jones, 2009)

• Case study: Fifteen month old infant with autism.
• Eye tracking methodology found that an infant attended to non-biological motion stimuli versus biological motion stimuli
• Second Study: three groups of 2 year olds (ASD, developmentally delayed, and typical)
• Typical and developmentally delayed toddlers attended preferentially to biological motion but ASD toddlers did not

Biological Motion, Posterior Superior Temporal Sulcus (pSTS), and ASD
(Pelphrey & Carter, 2007; Pelphrey, Shultz, Hudac, & Van Derwyk, 2011; Pelphrey & Dukel, 2010)

• Biological motion detected by the pSTS allows people to "read" the intentions of people; intention reading is a more advanced aspect of social perception
• From eye gaze, facial movements, and actions we can draw conclusion about the ideas, beliefs, desires, and mental states that direct individuals
• In a series of studies Pelphrey and colleagues found that ASD individuals had problems with reading intentions
• ASD individuals also had abnormal activation patterns in the pSTS compared to typical controls

Brain Structures and Social Perception
(Pelphrey & Carter, 2007; Pelphrey, Shultz, Hudac, & Van Derwyk, 2011)

Fusiform Face Area
Specialized for Face Processing

Amygdala
Recognizes Emotional States by interpreting Facial Expressions

Posterior STS
Biological Motion
Intention Reading
### Pelphrey and the Etiology of ASD

(Pelphrey, Shultz, Hudac, & Van Derwyk, 2011; Pelphrey and Shultz, 2013)

- Deficit in the fundamental building block of social perception: biological motion
- Problems in the emergence of different brain structures specialized for social perception, particularly the pSTS
- This affects the ability of the individual with ASD to use social information to further develop these specialized brain structures and their interconnections
- An interaction between genes, brain, and environment

### Intervention, ASD, and Brain Function

### Early Intervention, ASD, and Normalized Brain Activity

(Dawson et al., 2012)

- RCT comparing Early Start Denver Model (ESDM) to typically available Community Intervention (CI)
- Forty-eight 18-30 months old with ASD received 2 years of treatment from ESDM or CI; plus a control group of matched typically developing children
- ESDM subjects: significant improvements in IQ, Language, Adaptive Behavior, and ASD Dx
- ESDM subjects: EEG indicated normalized functioning in the Anterior Cingulate Cortex, Fusiform Face Area, and Prefrontal Cortex
**Intervention, ASD, and Improved Brain Activity**  
(Voos, Pelphrey, et al., 2012)

- Two case studies of an evidence-based intervention: Pivotal Response Treatment (PRT) for 4 months
- Subject M (5 years, 1 month - Autistic Disorder)
- Subject CC (5 years, 5 months – PDD NOS)
- Both subjects improved social communication skills and adaptive behavior skills
- Subject M: fMRI showed increased activation in the left fusiform gyrus and left prefrontal cortex
- Subject CC: fMRI showed increased activation in the fusiform gyri, the left pSTS, and left prefrontal cortex

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**Recommendations for Practice**

- Identify ASD red flags
  
  Autism Speaks Website Visual Glossary (www.autismspeaks.org)
  
  

- Assess with screening instruments
  
  

- If the results of initial screening are positive, refer the client for a comprehensive assessment

- If diagnosed with ASD, educate families about the efficacy of intervention and refer to appropriate programs
References


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