Autism: Where is the lesion, what is the lesion and where we go from here

Evdokia Anagnostou
Bloorview Research Institute, Holland Bloorview Rehabilitation Hospital

Background/Rationale
Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits and repetitive behaviors or restrictive interests. It remains a behaviorally defined syndrome with no reliable biological markers.

Research Question
The goal of this review is to critically examine available neuroimaging / genomics data and its relevance to our understanding of the neurobiology of ASD.

Methods & Analyses
This is scoping review of imaging/genomics in ASD. Imaging and Genomics data by the Holland Bloorview / SickKids teams will be highlighted

Results:
Recent genomics work highlights the presence of genetic and phenotypic heterogeneity in ASD with a number of underlying pathogenetic mechanisms. Genomic variations however seem to cluster around certain brain pathways, such as synaptic cell adhesion, kinase activity, and genes related to CNS development.

Although there is variability in the literature on structural magnetic resonance literature (MRI), there is evidence of volume abnormalities in both grey and white matter, with a suggestion of some region-specific differences. Early brain overgrowth is probably the most replicated finding in a subgroup of people with ASD. New techniques, such as cortical-thickness measurements and surface morphometry, have begun to elucidate the patterns of abnormalities as they evolve with age, and are implicating specific neuroanatomical or neurodevelopmental processes. Functional MRI and diffusion tensor imaging techniques suggest that such volume abnormalities are associated with atypical functional and structural connectivity in the brain, and researchers have begun to use magnetic resonance spectroscopy (MRS) techniques to explore the neurochemical substrate of such abnormalities.

Conclusion
Genomics and imaging work converge to suggest an atypically connected and poorly organized brain in individuals with ASD. We now need to further clarify imaging atypicalities, and start interpreting them in the context of what we already know about typical neurodevelopmental processes including migration and organization of the cortex. Such an approach will allow us to relate imaging findings not only to behavior, but also to genes and their expression, which may be related to such processes, and to further our understanding of the nature of neurobiologic abnormalities in ASD

Relevance
Integrating Genomics and Imaging data will be critical in identifying pathways relevant to novel treatment development.

Evdokia Anagnostou

Dr. Evdokia Anagnostou is a child neurologist and a clinician-scientist at Bloorview Research institute and assistant professor at the Department of Pediatrics at University of Toronto. She is also an adjunct assistant professor at the department of psychiatry at Mount Sinai School of Medicine in New York.

Dr. Anagnostou's research focuses on psychopharmacology and neuroimaging in autism. She has been funded to run the first pediatric clinical trial of oxytocin in autism, as well studies of memantine, omega 3 fatty acids and pioglitazone. She is also funded as part of the Neurodevenet consortium to study brain-genetics-behaviors correlations, and is a PI/co-PI /co-I on several studies examining brain structure, function and neurochemistry in children and adolescents with ASD. She is also collaborating with engineering colleagues at University of Toronto to examine the biomechanical properties of functional motor skills such as handwriting in autism, and examine the use of sensors to measure physiologic arousal and test its value as an anxiety measure in autism.

She serves on the treatment advisory board of Autism Speaks, the treatment advisory board of the International Rett Syndrome Foundation, and on the scientific review committee for the Autism Treatment Network.