Neuropathology of Autism: Insights from human post-mortem brains and Shank3-deficient mice

Neha Uppal

Ph.D. Student in the Department of Neuroscience and Friedman Brain Institute, Icahn School of Medicine at Mount Sinai; Graduate Fellow of the Seaver Autism Center for Research and Treatment

Van Etten, (Room 1C-1): 11:30am, Friday, May 31st, 2013

Bio: Neha Uppal received her B.S. in Child Development and Biomedical Engineering from Tufts University in 2009. She began her doctoral work in the laboratories of Patrick Hof and Joseph Buxbaum in order to understand how the brain of a child with autism differs from a neurotypical child. Her thesis work focuses on identifying the neuropathology of areas implicated in autism at the cellular and synaptic level.

Abstract: Autism is a neurodevelopmental neuropsychiatric disorder that is increasing in prevalence, affecting 1 in 88 children, but we have yet to understand how the disorder affects the underlying cytoarchitecture of the brain. My work focuses on understanding the histopathological basis of autism through characterizing the developing autistic brain at the cellular and synaptic level, in humans and mice respectively. In our human studies, we are determining whether there are neuropathological differences in neuron number, type, and morphology in patients with autism and neurotypical controls. We focus on areas that have been implicated in autism both through its characteristic behavioral symptoms and imaging studies; the areas we are studying are the frontoinsular cortex, anterior cingulate cortex, Brodmann’s areas 44 and 45, and the posterior inferior occipitotemporal gyrus (area V4). At the molecular level, we are investigating a mouse model of autism with a variant of the gene Shank3, which encodes for a scaffolding protein found in the postsynaptic density of excitatory synapses. Approximately 1% of patients with autism have variants of Shank3, which has drawn attention to the strong possibility that these variants are one of the causes of the disorder. Using electron microscopy, we are assessing differences in synapse morphology, size, and type between wild type, Shank3 heterozygous, and Shank3 homozygous mice, which may explain the electrophysiological and behavioral impairments observed in these mice. Overall, these studies hope to improve our understanding of the effects of autism in the brain, and in turn will enhance our knowledge of potential mechanisms underlying the disorder.

Please contact: Dr. John Foxe (john.foxe@einstein.yu.edu) for information.