JOHNSON CENTER

Ted Lindsay Foundation Research Report 2013

Over the last few years, the Ted Lindsay Foundation has been supporting research at The Johnson Center for Child Health and Development to examine the effects of pre- and post-natal mercury exposure on child development. Exposure to mercury and other environmental toxicants, such as lead and polychlorinated biphenyls (PCBs), has been shown to result in behavioral and cognitive impairments in young children. While mercury exposure primarily occurs from eating contaminated fish, mercury in the form of the preservative, thimerosal, were previously included in many pediatric vaccines leading to concerns about it's possible effects on infant development. Although there has been no research directly linking vaccines to autism, the safety of thimerosal-containing vaccines has not been adequately tested.

One area of our research is therefore examining whether 'low-level' mercury exposure from thimerosal-containing vaccines affects infant development, cognition and behavior in a non-human primate model. In 2008, we initiated a five-year comprehensive non-human primate study at the University of Washington Infant Primate Research Center. We have partnered with a number of experts in the fields of neuroimaging, behavior, immunology and neuropathology, from some of the best US academic institutions, providing a framework for collaborative research and data sharing to accelerate progress. This large, multi-disciplinary study is examining the development, cognition and behavior of animals receiving different vaccines, as well as controls animals receiving saline placebo injections. Since the study is performed blinded (meaning that researchers collecting data and samples do not know what study group animals are assigned to), we are unable to complete final data analyses until the end of the study. We have, however, undertaken some preliminary analyses of primate behavior and brain pathology, which are highlighted below.

Working with collaborators at the University of Washington, Seattle, we have performed a preliminary analysis (8 animals/group) examining early developmental and behavioral measures from birth through 12 months of age. While no changes in measures of cognition, discrimination learning and social behavior were noted between vaccinated and unvaccinated animals, the full complement of 12 animals/group will be examined on completion of the study in order to solidify these preliminary observations.

We have also completed a preliminary neuropathological analyses of the same animals in collaboration with researchers at the University of Texas-Southwestern. These studies are looking at two structures of the brain: the cerebellum – the part of the brain involved in motor control, some cognitive functions such as attention and language, and in regulating fear and pleasure responses; and the hippocampus which is responsible for memory and spatial navigation. In our primate model we found that the cerebellar Purkinje were significantly larger in vaccinated versus unvaccinated animals, whereas the hippocampal CA1 neurons were significantly smaller.

We have immunostained several brain sections to look for signs of neuroinflammation, a consistent finding in autism. Using antibodies to identify astrocytes and microglia we have found excellent immunostaining in the cerebellum, neocortex, amygdala and hippocampus but did not find any qualitative indication of a neuroinflammatory response in either vaccinated or unvaccinated animals. A quantitative analyses of these data will begin soon. These preliminary data suggest that the thimerosal-containing vaccines may cause some changes to both the cerebellar Purkinje cells and hippocampal CA1 neurons but these changes are not associated with brain inflammation. We are currently entering the fifth year of this study, and anticipate that all sample collections and animal assessments will be completed by the end of 2013. Data analyses and publication will begin earnestly at that time.

A second study supported by the Ted Lindsay Foundation was initiated last year to identify biomarkers in blood samples from children with autism using a novel method of analyte profiling. Multi-Analyte Profiling (MAP) analysis enables us to screen for hundreds of altered analytes in a small blood sample and may be useful diagnostically or for targeting therapeutic interventions in autism. A recent paper published in 2010 found that adult males and females with Asperger's Syndrome (a form of high functioning autism) differed in blood biomarker profiles. Using a MAP approach, this study showed that the predominant blood biomarkers identifying males with Asperger's were increased levels of certain cytokines and other inflammatory molecules, consistent with their proposed role in autism. In contrast, females with Asperger's had altered levels of growth factors and hormones in their blood - a very different profile to males. We are using a similar approach comparing serum from young children with and without autism to determine whether gender-specific biomarker profiles can be identified for autism. Our preliminary data suggest that several inflammatory markers, as well as certain proteins involved in other conditions, such as Alzheimer's Disease, may be elevated in children with autism. Based on this data, we are are now developing an autism-specific biomarker panel that may help differentiate blood samples from children with and without autism. Identification of a panel of biomarkers that are common to children with autism may lead to the development of a novel diagnostic assay to assist in early identification. We feel strongly that this approach will provide great insight into the molecular mechanisms involved in both the etiology and development of autism, allowing us to also develop possible targets for therapeutic intervention.

Our sincere thanks for the continued support of the Ted Lindsay Foundation, and to all of you who have contributed to our research over the years. Your contributions are making meaningful differences in the autism community and will continue to do so for years to come.

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