THE JOHNSON CENTER
FOR CHILD HEALTH AND DEVELOPMENT

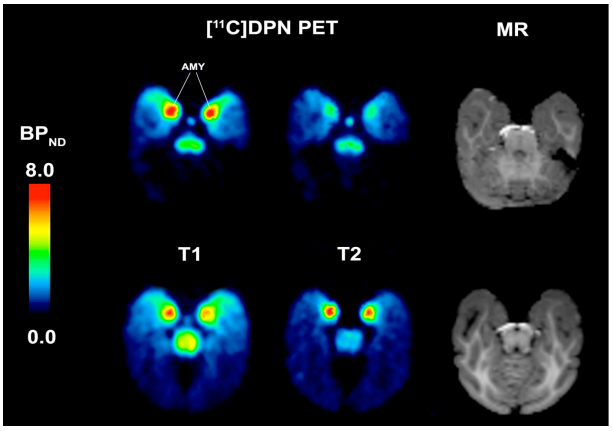
2011 Research Update from The Johnson Center for Child Health and Development

It's hard to believe that another year has gone by. We have just completed our 7th year of research, funded in part by the Ted Lindsay Foundation. One aspect of our research program is directed at trying to determine whether certain environmental exposures, or 'triggers', may result in some children developing autism. It is well established that pre- and post-natal exposures to a variety of environmental toxicants, such as mercury, lead, and polychlorinated biphenyls (PCBs) can result in cognitive impairment or behavioral problems in young children. One of the areas of research at The Johnson Center is to examine the safety of mercury-based vaccines. In order to address these concerns, we have developed a non-human primate model to examine behavior, development, brain structure and function, and intestinal health comparing unvaccinated and vaccinated animals.

This project has taken place over the last six years in two phases. The initial pilot study, performed at the University of Pittsburgh, has been completed. Data from this study has identified the following:

• A delay in the acquisition of neonatal reflexes in newborn primates receiving a thimerosal-containing Hepatitis B vaccine at birth (neonatal reflexes are critical for survival; Hewitson et al., 2010a).

• Changes in amygdala growth and amygdala opioid ligand binding in non-human primate infants after vaccination (amygdala is a small structure in the brain responsible for fear response and social behavior; its development is typically altered in children with autism; Hewitson et al., 2010b).



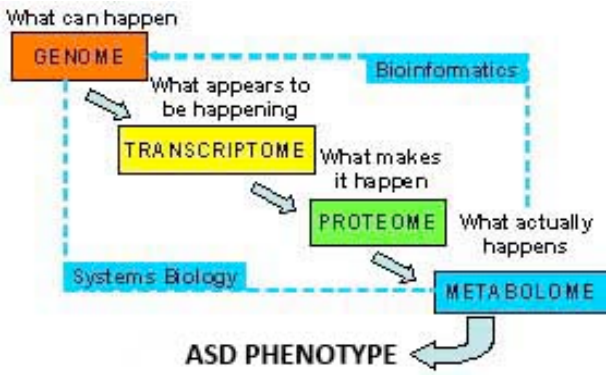
Binding of the opioid (morphine-like) receptors in the amygdala (AMY) of unvaccinated (upper images) and vaccinated (lower images) macaques. Vaccinated macaques do not show a maturational decrease in opioid ligand-binding from approximately 4 months of age (T1) to approximately 8 months of age (T2), suggesting that cumulative vaccine exposures between T1 and T2 may be affecting amygdala function.

• Increased total brain volume in vaccinated but not unvaccinated primate infants; (a larger brain volume has consistently been reported for children with autism).

• Cognitive and behavioral impairments in vaccinated infants compared to control animals; (using tasks of discrimination learning to examine emerging cognition, vaccinated animals displayed behavioral responses that are routinely observed in children with autism).

Based on the success of the pilot study, financial support from generous donors, including the Ted Lindsay Foundation, has enabled us to expand these studies to undertake a large scale, five-year, comprehensive non-human primate study at the University of Washington. We have partnered with a number of experts in the fields of neuroimaging, behavior, immunology, genomics, metabolomics, and statistics, from some of the best US academic institutions. This comprehensive research program will provide confirmatory data from some of the same analyses from Phase I studies but in a larger cohort of animals, as well as extending those investigations to other areas of clinical concern such as immune response, pathogenesis, and other emerging epigenetic factors as etiologic contributors. This study should be completed in 2013 and we hope it will provide definitive answers as to the possible role of mercury-containing vaccines and autism.

In 2009, the Centers for Disease Control and Prevention (CDC) reported that autism affects nearly 1 percent of American 8-year olds, a 57 percent increase in ASD cases compared to four years earlier. The number of children affected by autism today is likely to be much higher than that, perhaps as many as 1 in 90 boys. Autism is the fastest-growing developmental disability in the U.S. and yet autism receives less than 5% of the research funding of many less prevalent childhood diseases. As part of our research portfolio, The Johnson Center for Child Health and Development has initiated a study examining nutritional deficits in children with autism with respect to bone mineral density; and a second study investigating the efficacy of an elemental based diet for children with autism and severe gastrointestinal abnormalities. We are also working to identify biomarkers in blood samples from children with autism using genomic, proteomic and metabolomic profiling.



The '-Omics' Cascade in autism. The ability to acquire data via the technologies in the -omics cascade greatly enhances our ability to understand biological mechanisms. These tools provide autism researchers with a growing understanding of how transcribed genes and their resulting translated proteins give rise to a suite of metabolites that determine the ASD phenotype. Since an ASD diagnosis can represent such greatly different phenotypes within the autism spectrum, these tools hold great promise in providing basic biological information that may direct therapies or enhance drug development.

Through this research we hope to be able to screen and identify children with ASD who might benefit from specific treatments; develop and test biomarker profiles that form a diagnostics tool; develop and test biomarker profiles that form an instrument for monitoring the clinical course of the disease and the therapeutic response to medical

intervention; and improve the clinical well-being of affected children and increase our knowledge base of this disease.

We extend our sincere thanks for the continued support of the Ted Lindsay Foundation and their supporters. We still have much work to be done.

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Hewitson L, Houser LA, Stott C, Sackett G, Tomko JL, Atwood D, Blue L, White ER (2010a). Delayed acquisition of neonatal reflexes in newborn primates receiving a thimerosal-containing Hepatitis B vaccine: Influence of gestational age and birth weight. J. Toxicol. Environ Health, Part A, 73 (19): 1298-1313.

Hewitson L, Lopresti BJ, Stott C, Mason NS, Tomko J. (2010b) Influence of pediatric vaccines on amygdala growth and opioid ligand binding in rhesus macaque infants: A pilot study. Acta Neurobiol Exp (Wars). 70(2): 147-164.