Prenatal plastic chemical exposure, molecular programming and offspring neurodevelopment .

Abstract for seminar 26.11 (349 words)

Exposure to everyday environmental chemicals – e.g., chemicals in plastic products– during pregnancy may be harmful to brain development. One plausible mechanism for the male excess of autism spectrum disorder is via exposure to bisphenols and related chemicals that suppress cellular expression of the aromatase gene (CYP19A1), a key enzyme that converts androgens to estrogens in the developing brain. In the Barwon Infant Study (BIS) human birth cohort of 1,074 children, we show that higher prenatal maternal levels of BPA in the top quartile of prenatal maternal BPA levels were associated with higher autism spectrum ASD symptoms at age 2 and ASD diagnosis at age 9 only in males with low aromatase genetic pathway activity scores. Also, higher prenatal bisphenol A (BPA) levels were predictive of higher methylation across the CYP19A1 brain promoter 1f region measured in the cord blood of offspring.These human epigenetic findings were also demonstrated in the Columbia Center for Children's Environmental Health Mother and Newborn (CCCEH-MN) cohort. In tandem with these human studies, we provide laboratory findings across structural, functional, transcriptomic and electrophysiological domains. Thus, taken together, we find that prenatal BPA exposure is associated with impaired brain aromatase function and ASD-related behaviors and brain abnormalities in males that may be reversible through postnatal intervention with 10HDA, an estrogenic fatty acid. A human trial is being developed.

We have used the modern causal inference technique of molecular mediation to also investigate other underlying pathways between early environment plastic chemical exposure and adverse neurodevelopment, highlighting the potential adverse role of prenatal inflammation, immune disruption, epigenetics and metabolomics. We find phthalate plastics associated with a maternal metabolic shift in pregnancy towards non-oxidative energy pathways, which are inefficient compared to oxidative metabolism is associated with a higher risk of subsequent ASD symptoms and diagnosis. We investigate personalised prevention, demonstrating children with certain genetic profiles such as predisposition for low antioxidant capacity are more vulnerable to the adverse effects of chemicals. Overall, this work combining molecular biology and epidemiology aims to identify not only chemicals associated with more adverse child neurodevelopment outcomes, but the underlying biological pathways that increase risk.