Effect of developmental pyrethroid exposure in prairie voles as a model of neurodevelopmental disorders

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Neurodevelopmental disorders (NDDs) are a class of lifelong incurable disorders with few treatments are biomarkers. They share common comorbidities including deficits in communication and learning, repetitive behavior, and hyperactivity such as attention deficit hyperactivity disorder (ADHD), Autism, and Developmental disability. The incidence of NDDs has been rapidly rising affecting almost 17% of children in the US. Heritability is still a crucial factor in the etiology of NDDs, however large meta-analysis data now consider environmental impact as a major contributor. Recent epidemiological studies have shown the effect of pyrethroid pesticides on pregnant women and risk factors associated with the proper brain development in the children. Pyrethroids are common household insecticides widely used in the US and considered relatively “safe” by the Environmental Protection Agency (EPA). Despite growing evidence of the complex gene-environment interaction in the etiology of NDDs, very few environmental factors have been studied.

Previously, our lab has studied the effects of deltamethrin (pyrethroid) in mice. Our research aims to look at the effect of developmental pyrethroid exposure (DPE) in prairie voles as a model of neurodevelopmental disorders.

We exposed pregnant vole dams to 3mg/kg of deltamethrin two weeks prior to pregnancy, during pregnancy and throughout lactation. Following weaning, the offspring grow to adulthood and are subjected to a battery of behavioral tests to look at deficits in five different domains namely communication, cognition, social interaction, repetitive behavior, and locomotion. After concluding behavioral tests their brains are harvested along with other tissues for further studies.

Our results show that developmentally exposed prairie voles had deficits in communication, cognition, repetitive behavior, and locomotion (hyperactivity). Previously harvested brains from the mice study were used to look at disruptions in molecular mechanisms because of DPE. Transcriptomics and Kinomics data showed widespread disruption in two circadian rhythm genes (PER2 and CIART), MAP kinase pathway, and kinases involved in synaptic growth. Data from metabolomics showed disruption in folate metabolic pathway. This led to developing our second

hypothesis that folate supplementation during pregnancy might be a potential therapeutic strategy to reduce the effects of developmental pyrethroid exposure.

