

Folate prevent autism-relevant phenotype from developmental pyrethroid exposure in Prairie Voles

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Pesticide exposure has been linked to an increased risk of neurodevelopmental disorders (NDDs) such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), with evidence suggesting that early life exposure may be particularly harmful. Pregnant women exposed to pyrethroid pesticides are at a higher risk of their child being diagnosed with autism or other neurodevelopmental disorders. Our laboratory is investigating the effects of developmental pyrethroid exposure (DPE) to the pyrethroid pesticide deltamethrin on brain and behavior in prairie voles. In this study, we exposed female prairie voles to low doses of deltamethrin (3 mg/kg every third day), with or without supplementation with 5-MTHF, a folate vitamer, during pregnancy and lactation. We then tested the resulting adult offspring for behavioral changes relevant to NDDs and analyzed brain tissue to understand the molecular underpinnings of these effects. DPE caused changes in four behavioral domains relevant to NDDs, including communication, cognition, repetitive behavior, and locomotion (including circadian rhythms), several of which were rescued by maternal folate supplementation. In the brain, DPE impacted the expression of SHMT1, an enzyme in the folate pathway; while folate supplementation caused compensatory changes in two other folate-related proteins, FOLR1 and MTHFR. DPE also caused increases in serum and brain folate which were prevented by maternal folate supplementation. These results show the DPE causes an autism- and NDD-relevant behavioral phenotype which is prevented by maternal folate supplementation, and that direct effects on folate metabolism may be a mechanism of these effects.

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