Periconceptional Folic Acid-containing Supplements and LINE-1 DNA Methylation in the MARBLES Prospective Study of Autism Spectrum Disorder

R. J. Schmidt\(^1\), F. Crary\(^2\), A. M. Iosif\(^1\), J. E. Dienes\(^1\), and J. M. LaSalle\(^2\)

(1)Public Health Sciences, University of California at Davis, Davis, CA, (2) MIND Institute, Sacramento, CA, (3)Medical Microbiology and Immunology, University of California at Davis, Davis, CA

Background: In population-based studies, maternal periconceptional folic acid intake is associated with reduced risk for autism spectrum disorder (ASD) in the child.

Objectives: In a prospective study of high-risk families, we examined whether folic acid supplementation decreased ASD risk in siblings. We also examined relationships with LINE-1 DNA methylation as an indicator of potential epigenetic mechanisms, given the ties between folate and methylation.

Methods: Mothers in the MARBLES (Markers of Autism Risk in Babies: Learning Early Signs) study who had at least one child with ASD, and who became pregnant with another child were included. LINE-1 methylation was measured in DNA extracted from maternal whole blood samples collected during each trimester and at delivery, and in the child’s cord and peripheral blood using bisulfite conversion and pyrosequencing (averaged across 5 CpG sites). Maternal interviews collected information on prenatal vitamin and supplement intake. Final ASD clinical diagnoses were made at the MIND Institute using standardized assessments at 36 months.

Results: Children whose mothers did not report taking a prenatal vitamin and consumed no supplemental folic acid during the first month of pregnancy were several times more likely to be diagnosed with ASD. Folic acid supplementation and ASD were also associated with trends in global DNA methylation in the child.

Conclusions: Taking folic acid supplements during the first month of pregnancy could reduce risk for ASD in subsequent children, and could also affect the child’s LINE-1 DNA methylation. Additional research is needed to confirm these results and to explore dose thresholds further.

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