TEXAS Health and Human Services | Texas Department of State Health Services

Diabetes and Obesity-Related Genes and the Risk of Neural Tube Defects in the National Birth Defects Prevention Study

Neural tube defects (NTDs) are among the most common, most costly, and most deadly of all human congenital anomalies whose etiologies remain largely unknown. Two well-established risk factors for NTDs are maternal pre-gestational diabetes and pre-pregnancy obesity. Collaborators from the Dell Pediatric Research Institute, University of Texas at Austin; the Texas Birth Defects Epidemiology and Surveillance Branch, Texas DSHS, Austin; The University of Texas School of Public Health in Houston; Stanford School of Medicine; and The University of North Carolina evaluated genetic susceptibility related to diabetes and obesity as a risk factor for neural tube defects (NTDs).

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Lupo PJ, Canfield MA, Chapa C, Lu W, Agopian AJ, Mitchell LE, Shaw GM, Waller DK, Olshan AF, Finnell RH, Zhu H. Diabetes and obesity-related genes and the risk of neural tube defects in the national birth defects prevention study. American Journal of Epidemiology. 2012; 176(12): 1101-1109.

Twenty three single nucleotide polymorphisms (SNPs) among nine genes associated with type 2 diabetes or obesity were investigated. Samples were obtained from 737 NTD case-parent triads included in the National Birth Defects Prevention Study (NBDPS). Log-linear models were used to evaluate maternal and offspring genetic effects. Both spina bifida and anencephaly were investigated.

Main findings from this research

- Maternal genetic effects on NTD risk were observed among three obesity and diabetes related genes (FTO, TCF7L2 and LEP). FTO encodes a protein that is associated with body fat accumulation. Variants in TCF7L2 are known markers for type 2 diabetes; LEP encodes the hormone leptin that has a profound effect on eating behavior and metabolic rate.

- An offspring genetic effect on NTD risk was observed in the gene encoding uncoupling protein 2, which is involved in energy metabolism.

Conclusion and discussion

In one of the largest studies of its kind, our findings suggest that maternal genes involved in glucose metabolism and obesity may modify a woman's risk of having a NTD-affected pregnancy. To our knowledge, this is the first report to identify the role of maternal obesity/diabetes genes in the development of NTDs. This is important as maternal genes influence the baby's environment during pregnancy. These findings must be replicated, but eventually may help in identifying those women at the greatest risk of have a NTD-affects pregnancy.