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Advanced glycation end products and autism- Evidence for a connection

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Autism is a complex and heterogeneous neurodevelopmental disorder of unknown etiology which results from both genetic and environmental factors. Among the environmental factors associated with autism are maternal obesity and diabetes. AGEs are a heterogeneous group of macromolecules that are formed by the non-enzymatic glycation of proteins, lipids and nucleic acids. AGEs are implicated in diabetic complications and can induce oxidative stress and inflammation. Humans are exposed to two sources of AGEs: exogenous AGEs that are ingested in foods and endogenous AGEs that are formed in the body. Diets with a high glycemic index are also associated with the accumulation of AGEs in the body. To test the hypothesis that AGEs contribute to the development of autism we used BTBR mice, a genetically homogeneous inbred strain of mice that displays behavioral traits that reflect all three diagnostic symptoms of autism including abnormal social interactions, impaired communication and repetitive behavior. Adult female mice were fed either a low or high glycemic diet beginning prior to impregnation. Their offspring were fed the same diet and at 10 weeks of age male mice were tested for behavioral markers of autism. We show that the BTBR mice continuously exposed to a low glycemic diet beginning at conception showed significant reductions in multiple, autism-associated behaviors including repetitive grooming and perseveration. Overall, these data suggest that AGEs, a major consequence of diabetes, can contribute to the development of an autistic phenotype and suggest that maternal dietary modifications could have an impact on the development of autism.

Biography

Pamela Maher obtained her Ph.D. in Biochemistry from the University of British Columbia followed by postdoctoral studies at the University of California, San Diego. Over the last 10 years her research has evolved from basic studies on the mechanisms underlying nerve cell survival and death to more translationally-oriented research on the development of approaches to prevent neurological disorders. She has over 100 publications in peer-reviewed journals. Her research is currently funded by NIH.

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