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Metabolic and epigenetic alterations in patients with Alzheimer's disease

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The number of people living with dementia is estimated at 44 million worldwide, and is expected to rise to 76 million by 2030 and to 136 million by 2050. Alzheimer's Disease (AD) currently affects more than 5 million Americans, with numbers expected to grow. The pathophysiological changes in AD patients begin decades before the onset of dementia, highlighting the urgent need for the development of early diagnostic methods, novel therapeutic approaches, and methods to monitor efficacy of experimental therapeutics. Targeted metabolomics with the overall goal to determine changes in mitochondria- and energy-related metabolites was conducted in CSF and plasma from males and females with mild cognitive impairment (MCI), AD and control patients involved in the Mayo Clinic Study of Aging. Panels of metabolites that include amino acids, fatty acids, lipids and components of the TCA cycle revealed that metabolic changes in females were more pronounced and correlated strongly with the disease compared to males. Analysis of metabolic fluxes in TCA cycle in human fibroblasts from late onset AD male and female patients using Glucose and Glutamine stable isotope tracers confirmed stronger inhibition of fluxes in female patients. Epigenetic changes were also more pronounced in female patients suggesting a link to altered energy metabolism. Overall, our data demonstrate that metabolic changes associated with the development and progression of AD differ between males and females where females are affected to the greater extent.

Biography

Eugenia Trushina has completed her PhD from Saratov State University, Russia and Postdoctoral studies from Mayo Clinic College of Medicine, USA. She is an Associate Professor in the Departments of Neurology and Pharmacology at the Mayo Clinic Rochester, USA. Her scientific interests include the investigation of early molecular mechanisms of neurodegeneration, the role of mitochondria in particular. Translational aspect of her work includes the development of blood-based metabolic biomarkers and mitochondria-targeted small molecule therapeutics for Alzheimer's disease. She is a recipient of the NIH, BrightFocus, GHR, ADDF, and Mayo Clinic Research Awards.

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