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Epigenetic mechanisms linking diabetes and synaptic impairments

Giulio Maria Pasinetti

The Mount Sinai School of Medicine, USA

Abstract

Diabetes is one of the major risk factors for dementia. However, the molecular mechanism underlying the risk of diabetes to dementia is largely unknown. Recent studies revealed that epigenetic modifications may play a role in the pathogenesis of diabetes. We hypothesized that diabetes may cause epigenetic changes in the brain that may adversely affect synaptic function. We found significant elevation in the expression of histone deacetylases (HDACs) class IIa in the brains of diabetic subjects compared to control subjects, and these changes coincide with altered expression of synaptic proteins. In a mouse model of diet-induced type II diabetes mellitus (T2DM), we found that, similar to humans, T2DM mice also showed increased expression of HDAC IIa in the brain and these alterations were associated with increased susceptibility to oligomeric Aβ-induced synaptic impairments in the hippocampal formation and eventually led to synaptic dysfunction. Pharmacological inhibition of HDAC IIa was able to restore synaptic plasticity. Our study demonstrated that diabetes may induce epigenetic modifications affecting neuropathological mechanisms in the brain leading to increased susceptibility to insults associated with neurodegenerative or vascular impairments. Our study provides for the first time an epigenetic explanation for the increased risk of diabetic patients to develop dementia.

Biography

Giulio Maria Pasinetti's research on lifestyle factors and metabolic co-morbidities influencing clinical dementia, neurodegeneration and Alzheimer's disease has made him a pioneer in his field. He is the recipient of major awards such as The Alzheimer's Association's Zenith Award and the Foundation Queen Sofia of Spain Research Center Award on Alzheimer's Disease. He has received more than 30 grants and has published over 160 groundbreaking research articles. Dr. Pasinetti is a Professor of Neurology, Psychiatry, Neuroscience, and Geriatrics and Adult Development, and is Chair of the Brain Institute Center of Excellence for Novel Approaches to Neurotherapeutics at Mount Sinai School of Medicine. He also serves as Director of the Basic and Biomedical Research and Training, Geriatric Research, Education and Clinical Center at the Bronx Veterans Affairs Medical Center.