Diet and Exercise Trial to Improve Insulin Resistance, Increase Cerebral Blood Flow, Alter Metabolomic Biomarkers, and Decrease Alzheimers Disease Risk

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Research Abstract

Project Summary Metabolic syndrome (MetS) is associated with the development of diabetes and cardiovascular disease; however it is also linked with cognitive decline and dementia. We have shown that MetS is associated with lower cerebral blood flow (CBF) and memory function in late middle-aged adults at increased risk for developing Alzheimer's disease (AD). Insulin resistance (IR) is at the core of MetS, and a hallmark feature of IR is higher fasting blood glucose (FBG) as well as post prandial hyperglycemia. While we and others have demonstrated links between IR and CBF as well as cognition from an observational perspective, no studies have investigated CBF and cognition after an intervention involving exercise and a carbohydrate restricted diet (CRD) designed to improve or normalize IR and glucose homeostasis. We propose to determine the effect of improving or normalizing glucose homeostasis on CBF and cognition, through diet and exercise, in individuals with IR and at risk for the development of AD. While exercise and a CRD have been shown to improve IR and glycemic control, we have only limited knowledge of the mechanisms behind these improvements. Nutritional metabolomics, the global measurement and interpretation of metabolic profiles, assesses the interaction of diet with the endogenous gene-protein cascade and the gut microbiome. Additionally, exercise has been shown to have an impact on the human metabolome. Finally, numerous metabolites have been specifically linked to IR and impaired fasting glucose (IFG). We propose to use metabolomics to measure changes in metabolites as individuals normalize or improve IR and glucose homeostasis. Should this exploratory study reveal increased brain blood flow and improved memory in response to diet and exercise, then early treatment of these individuals at risk might offer new avenues for disease-course modification. Strategies towards early and effective risk factor management could be of value in reducing the risk of metabolic as well as cognitive decline. In addition, should this study reveal changes in metabolic abnormalities consistent with early indications of diabetes, metabolomics could be an effective approach to complement disease risk analysis in our goal toward precision care.

Further information available at:

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