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The main goal of this proposal is to study whether diabetes status (type 2 diabetes [referred to as diabetes] and pre-diabetes, compared with normal glucose tolerance [NGT]), is related to increased amyloid β (Aβ) deposition in the brain, one of the culprits of Alzheimer's disease (AD), in a community sample of 150 middle aged Hispanics with a mean age of 63 years. We will also explore whether brain Aβ mediates the association between diabetes status and memory impairment, the main early clinical manifestation of AD, and whether brain Aβ and cerebrovascular disease interact to cause memory impairment. Many studies have reported an association of diabetes with a higher risk of amnesic mild cognitive impairment (MCI) and late onset Alzheimer's dementia (LOAD), clinical manifestations of AD. The few autopsy studies that have explored whether diabetes is related to AD pathology have had conflicting results. Thus, it is not clear whether diabetes causes AD pathology. The limitations of existing studies that preclude further advance in this field include survival and selection bias related to diabetes in elderly samples, lack of concurrent measures of diabetes and cognition in middle aged cohorts, and lack of longitudinal ascertainment of diabetes and pre-diabetes. We propose to overcome these limitations and advance the field by continuing longitudinal assessments of a cohort of middle aged Hispanics with concurrent assessment of cognition and diabetes status (by history and Hemoglobin A1c [HbA1c]), by assessing the presence of brain Aβ in-vivo using 18F-florbetapir positron emission tomography (PET), and assessing the presence of cerebrovascular disease (infarcts and white matter hyperintensities [WHI]) using brain magnetic resonance imaging (MRI) in a 5-year project. Our primary hypothesis is that diabetes and pre-diabetes are related to accumulation of brain Aβ as compared to persons with NGT. Our secondary hypotheses are that brain accumulation of Aβ mediates the association of diabetes and pre-diabetes with worse memory impairment, and that the presence of brain infarcts and white matter disease increases the risk of memory impairment in the presence of Aβ. Our primary aim is to compare the presence of whole brain fibrillar Aβ measured with 18F-florbetapir PET cross-sectionally and longitudinally (with an interval of 2 years) between participants with diabetes (n=50), pre-diabetes (n=50), and NGT (n = 50). We will also examine the association of glycemia as continuous exposure, using HbA1c, with whole brain fibrillar Aβ. Our secondary aims are: 1) To explore whether differences in whole brain fibrillar Aβ measured with 18F-florbetapir PET among participants with diabetes, pre-diabetes, and NGT, mediates the association of diabetes and pre-diabetes with worse memory performance; 2) To explore if the presence of cerebrovascular disease (infarcts and WHI) moderates the mediation of Aβ in the association of diabetes and pre-diabetes with memory impairment.