F3-01-02 TYPE 2 DIABETES AND INCIDENCE OF DEMENTIA AND COGNITIVE DECLINE: WHAT ARE THE MECHANISMS?

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Background: Type 2 diabetes has been associated with higher rates of dementia and more rapid cognitive decline in a number of studies. Elevated central body obesity (CBO) and hypertension are potential mechanisms that may account for this association. CBO is known to increase insulin and related metabolites which may increase the risk of neurodegeneration. Hypertension has a direct effect on both subclinical and clinical stroke. Obesity is linked to increased risk of hypertension. A complex set of relationships exist between these factors and cognitive decline and dementia. Mexican Americans (MAs) experience a higher prevalence of obesity, type 2 diabetes and untreated hypertension than non Hispanic Whites so are at higher risk for dementia. **Methods:** In a cohort of 1789 older MAs followed over 12 years, this paper will examine how both obesity and blood pressure change over time and modify the effects of type 2 diabetes on dementia incidence and cognitive decline. Trajectories of change in both CBO and blood pressure will be modeled for their impact on cognitive function. Moderation of these effects by type 2 diabetes status will be examined. **Results:** Initial results suggest that those with an increase in BP or who maintain a high blood pressure, experience 50% more rapid decline over time. Type 2 diabetics with a high blood pressure or declining blood pressure over time experience a significantly greater rate of cognitive decline than non diabetics (P interaction between DM2 and blood pressure trajectory = 0.008). Treatment with medication attenuates this association. **Conclusions:** These findings imply that effective hypertension treatment could prevent or mitigate cognitive impairments associated with type 2 diabetes.

F3-01-03 DIABETES AND COGNITIVE IMPAIRMENT IN THE ACCORD MIND TRIAL AND IN CHRONIC KIDNEY DISEASE

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Diabetes is associated with cognitive decline and dementia, but the relation between the degree of hyperglycemia and cognitive function has been unclear. The cross- sectional and longitudinal relation between HgbA1c level and cognitive function measures in 2900 Type II diabetics from the ongoing Memory in Diabetes (MIND) substudy of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial will be described. This will include baseline and follow- up cognitive measures collected before the intensive diabetes treatment arm of the ACCORD MIND trial was halted. The second part of this presentation will address diabetes and cognitive impairment in patients with chronic kidney disease (CKD). Diabetes is the primary cause of CKD: 50-60% of CKD patients in the U.S. have diabetes. CKD is also associated with an increased risk of cognitive impairment; as renal function measured as estimated glomerular filtration rate declines, so does cognitive function. In end- stage renal disease patients on hemodialysis, more than 70% have moderate to severe cognitive impairment. The epidemiology of cognitive impairment in patients with moderate CKD or end stage renal disease will be described, including primary data from a longitudinal study in 338 hemodialysis patients in Minnesota.

F3-01-04 GLYCEMIC CONTROL AND RISK OF DEMENTIA IN A LARGE COHORT OF ELDERLY PATIENTS WITH TYPE 2 DIABETES

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Type 2 diabetes increases risk of dementia and cognitive impairment though exact mechanisms remain unclear. Lesser known is how the management and treatment of Type 2 diabetes may be associated with brain aging outcomes. Although there's been a lot of work on how glycemic changes and diabetes treatment affect cognition in children with type 1 diabetes, there's a lack of work in well characterized cohorts of elderly patients, most of who have type 2 diabetes. This presentation will report on results from the Kaiser Permanente of Northern California Diabetes Registry. The role of glycosylated hemoglobin, hypoglycemic episodes, hyperglycemia, pharmacological treatment, and diabetes-specific complications on risk of dementia in a large longitudinal cohort of well characterized patients with type 2 diabetes will be discussed.

F3-01-05 BRAIN IMAGING IN DIABETES MELLITUS: METABOLIC OR VASCULAR DAMAGE?

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Background: Type 2 diabetes (DM2) is associated with a 1.5 to 2 times increased risk of dementia (Alzheimer's disease, as well as vascular dementia) as well as with cognitive disturbances short of dementia. **Methods:** In my presentation I will give an overview of brain imaging studies in DM2 and on possible determinants of imaging abnormalities and impaired cognition. **Results:** In patients with DM2 brain imaging studies show cortical and subcortical atrophy, a larger volume of white matter hyperintesities and a more frequent occurrence of infarcts relative to controls, all of which are related to reduced cognitive performance. Studies on risk factors for cognitive decrements and abnormalities on brain imaging in DM2 have mostly been performed in non-demented individuals, mostly with a cross-sectional design. Atherosclerotic disease, cerebrovascular or other, may be an important determinant. There may also be associations with worse glycemic control, microvascular complications, hyperinsulinemia and hypertension. Longitudinal observational studies, and ultimately intervention studies, are required to fully appreciate the relevance of these risk factors for cognitive dysfunction and brain imaging abnormalities in DM2. **Conclusions:** DM2 is associated with both vascular lesions and brain atrophy. Vascular disease appears to be an important determinant. Further longitudinal observational studies, and ultimately intervention studies, are required to fully appreciate the etiology of cognitive dysfunction and brain imaging abnormalities in DM2.

F3-01-06 THE EFFECTS OF DIABETES MELLITUS ON NEUROPATHOLOGIC FINDINGS AT AUTOPSY: THE VANTAA 85+ STUDY

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Diabetes mellitus has been identified as a risk factor for dementia and its main subtypes, Alzheimer's disease (AD) and vascular dementia (VaD). The mechanisms underlying these associations are still unclear and much remains unknown about the effects of diabetes on brain pathology. Studies of postmortem neuropathology can provide insight into the role that diabetes may play on cerebrovasculature and Alzheimer's disease associated neurodegeneration. The talk today will cover findings from the Vantaa 85 + Study and the role of diabetes on cerebral infarction, tangle burden, and amyloid burden. Interactions with APoe4, hypertension, hypercholesterolemia, myocardial infarcts, and ApoE4 status will be discussed.