Background: Neurogranin, a postsynaptic protein mainly localized in dendritic spines of neurons within associative cortical areas, is a physiological marker of synaptic plasticity mechanisms. We examined the diagnostic accuracy of cerebrospinal fluid (CSF) concentrations of neurogranin in distinguishing patients with Alzheimer’s disease (AD) dementia from cognitively healthy controls (HC) and frontotemporal dementia (FTD). We also tested the classificatory performance of CSF neurogranin using a novel unbiased biomarker-guided descriptive categorization system for AD, the “A/T/N” scheme. This approach includes three binary biomarker categories reflecting AD pathophysiology, where “A” refers to “amyloid-beta (Aβ) pathology,” “T” to “tau pathology,” and “N” to neurodegeneration.

Methods: We quantified CSF neurogranin in a multicenter cross-sectional study retrospectively conducted in a convenience series from three independent European academic expert memory clinic centers including a total of 108 participants classified as clinical AD dementia patients (n=35), FTD patients (n=9), mild cognitive impairment (MCI) subjects (n=41), and cognitively HC (n=23), according to clinical diagnostic criteria (“Level I”). Using the biomarker-based classification system (“Level II”), we categorized subjects as AD pathophysiology-negative (n=15), tau pathology-positive only (n=15), Aβ pathology-positive only (n=13), AD pathophysiology-positive (n=33), FTD (n=9), and HC (n=23). An in-house developed ELISA was used to measure CSF neurogranin concentration (LLOQ=125 pg/mL). AUROCs were computed through logistic regression within a discriminatory performance of neurogranin. Results: At Level I, neurogranin discriminated AD dementia patients from HC individuals [AUROC=0.72 (95% CI, 0.58-0.86)] and FTD patients [AUROC=0.76 (95% CI, 0.55-0.96)]. At Level II, neurogranin distinguished tau pathology-positive and AD pathophysiology-positive patients from HC [AUROC=0.77 (95% CI, 0.60-0.94) and 0.85 (95% CI, 0.74-0.95), respectively] and AD pathophysiology-positive patients from FTD [AUROC=0.85 (95% CI, 0.64-1.00)].

Conclusions: CSF neurogranin consistently distinguishes AD dementia patients from HC. Because neurogranin helps discriminate AD from FTD, its increased CSF concentration seems to be AD-characteristic at the clinically phenotyped group level. Moreover, the “A/T/N” dissection model allows improving the diagnostic accuracy of neurogranin in distinguishing cognitively impaired patients with AD pathophysiology and, to a lesser degree, tau pathology from HC as well as AD pathophysiology from FTD.

Poster Presentations: Monday, July 17, 2017

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GHRELIN, AMYLIN, GASTRIC INHIBITORY PEPTIDE AND COGNITION IN MIDDLE-AGED HIV-INFECTED AND UNINFECTED WOMEN: THE WOMEN’S INTERAGENCY HIV STUDY

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Background: HIV infection is becoming a chronic infection of aging, along with other aging-related conditions, such as cognitive impairments. Hormones secreted by the gut have been shown to interact with the brain and regulate feeding behavior and energy balance. Amylin, pancreatic islet amyloid polypeptide (PIAPP), has been compared to brain amyloid-beta and may be dysregulated in HIV infection. We explored the gut-brain axis by examining gut hormone levels and cognitive test scores in women with (HIV+) and without (HIV-) HIV infection. Methods: Participants included 356 women (248 HIV+, 108 at risk HIV-) in the Brooklyn Women’s Intergency HIV Study (WIHS) with measured levels of ghrelin, amylin, and gastric inhibitory peptide (GIP), also known as glucose-dependent insulinotropic polypeptide. Cross-sectional analyses using linear regression models estimated the relationship between gut hormones and Trails A, Trails B, Stroop interference time, Stroop word recall, Stroop color naming and reading, and Symbol Digit Modalities Test (SDMT) with consideration for age, HIV infection status, Wide Range Achievement Test score (WRAT), CD4 count, insulin resistance, drug use, and race/ethnicity. Results: Among women at mid-life with HIV infection for at least 10 years, or among those at risk, better performance on cognitive tests was generally associated with higher ghrelin, amylin and GIP levels. However, the strength of association varied, as did significance level by HIV status. Conclusions: Previous analyses in WIHS participants have suggested that higher BMI, waist, and WHR are associated with better cognitive function among women at mid-life with HIV infection. This study indicates that higher gut hormone levels are also associated with better cognition. Gut hormones may provide additional mechanistic insights regarding the association between obesity and Type 2 diabetes and cognition in middle-aged HIV+ and at risk HIV- women. In addition, measuring these hormones longitudinally would add to the understanding of mechanisms of actions of these hormones and their use as potential clinical tools for early identification and intervention on cognitive decline in this vulnerable population.

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ASSOCIATION OF PLASMA NEUROFILAMENT LIGHT CHAIN PROTEIN WITH BRAIN AMYLOID STATUS IN A PRECLINICAL COHORT OF SUBJECTIVE MEMORY COMPLAiners: THE INSIGHT-PREAD STUDY

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