Impact of Cerebrovascular Risk Factors on Brain Function and Structure in HIV-infected Individuals

Neda Jahanshad[1], Cecilia M. Shikuma[2], Kalpana Kallianpur[2], Beau Nakamoto[2], Victor G. Valcour[3], Paul M. Thompson[1]

1 Laboratory of Neuro Imaging (LONI), UCLA School of Medicine, Los Angeles, CA ; 2. Hawaii Center for AIDS, Univ. of Hawaii, Honolulu, HI; and 3. Memory and Aging Center, UCSF, San Francisco, CA

Objective: In the general population, cardio-cerebrovascular disease (CVD) is associated with cognitive dysfunction and with white matter disease on brain MRI, and adds substantively to the cognitive disease burden in co-morbid neurodegenerative diseases such as Alzheimer's Disease. HIV *per se* carries a substantial risk of cognitive dysfunction. It is estimated that mild cognitive dysfunction can be found in greater than 30% of HIV-infected individuals even in the era of highly active antiretroviral therapy (HAART). Traditional CVD risk factors such as dyslipidemia, hypertension, diabetes, and smoking are high in this population. To date, the impact of CVD risk factors on cognition in the HIV infected population has not been extensively evaluated, so we examined their effects on cognition and white matter integrity in a pilot study.

Methods: Within the 250 HIV+ participants of a 5-year longitudinal cohort study [Hawaii Aging with HIV Cohort (HAHC)], we examined the relationship between the presence or absence of CVD risk factors (hypertension, smoking [current or past], hypercholesterolemia, and diabetes) and neuropsychological (NP) test performance by logistic regression, using summary age-adjusted z scores, including composite scores for the domains of memory, psychomotor, motor and working memory/concentration/attention and a composite summary z-score. In a separate cohort of 30 HIV+ subjects, voxel by voxel fractional anisotropy (FA) and mean diffusivity (MD) maps were assessed using whole-brain diffusion tensor imaging (DTI) in individuals with and without various CVD risk factors. After nonlinear registration of all subjects' data to a mean image template, voxelwise regressions were performed for all CVD risk factors with adjustments for multiple comparisons.

Results: Significant differences in NP testing by presence or absence of CVD risk factors were found for hypertension on the working memory, attention, and concentration subscore (NPZwmca) [mean (SD) -0.19 (0.68) vs. -0.49 (0.71), $p<0.01$], smoking on the global (NPZ8) [-0.28 (0.60) vs. -0.61 (0.92), $p<0.01$]; psychomotor (NPZpm): [-0.14 (0.75) vs. -0.70 (1.16), $p=0.03$]; and motor (NPZmotor): [-0.28 (0.62) vs. -0.58 (0.86), $p=0.02$] subscores, and diabetes on NPZ8: [-0.44 (0.82) vs. -0.99 (0.94), $p=0.02$]; NPZpm: [-0.32 (1.03) vs. -0.83 (1.19), p=0.05]; and NPZmotor: [-0.42 (0.78) vs. -0.95 (0.87), $p=0.007$] subscores. In the preliminary DTI analyses of this pilot cohort, subjects with and without CVD risk factors did not differ; however metabolic syndrome, smoking and glucose intolerance showed trends for being associated with fiber integrity (MD) in the corpus callosum and frontal lobes.

Conclusions: Traditional CVD risk factors contribute to cognitive dysfunction in HIV infected individuals. Trends suggesting an impact of these risk factors on brain microstructure were observed by DTI, suggesting the promise of this neuroimaging technique for investigating the impact of CVD on brain structure and function in larger cohorts of HIV-infected subjects.