

## Correlation of MRS markers with HIV DNA in Patients Well-controlled on HAART

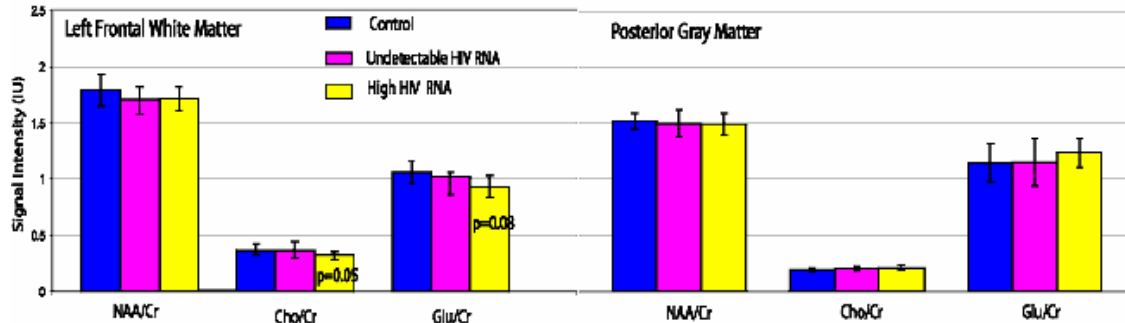
N. Sailasuta<sup>1</sup>, V. Valcour<sup>2</sup>, B. Shiramizu<sup>2</sup>, A. McMurtray<sup>2</sup>, J. Taylor<sup>2</sup>, K. Kallianpur<sup>2</sup>, and C. Shikuma<sup>2</sup>

<sup>1</sup>HMRI, Pasadena, CA, United States, <sup>2</sup>U of Hawaii, Honolulu, HI, United States

**Purpose:** Controversy exists as to whether neurocognitive impairment (NCI) in HAART-treated individuals is due to an active process, co-morbidity, or pre-HAART brain injury. Our previous findings that intracellular HIV DNA correlates to NCI in this setting suggest there is active brain injury. To test this hypothesis, we completed Magnetic Resonance Spectroscopy (MRS) on patients with detectable vs. undetectable HIV DNA among subjects on HAART with undetectable plasma viral load (HIV RNA).

**Methods:** Seventeen HIV seropositive subjects (1 female, age  $55.4 \pm 7$  years, 7 with high HIV DNA) and seven healthy subjects (1 female, age  $44.0 \pm 9$  years) underwent proton MRS examination on a 3T MRI clinical scanner with the approval of the institutional review board and in compliance with HIPAA regulations. Three brain regions were chosen: left basal ganglia (BG) left frontal white matter (FWM) and posterior cingulate gyrus gray matter (PGM). Two sets of MRS scans were acquired from each region, water suppressed and unsuppressed with 32 echo times data acquisition were employed with starting TE of 35ms and ending at 195ms. The voxel size was  $2 \times 2 \times 2 \text{ cm}^3$ . LCModel was used for spectral quantification using the unsuppressed water as internal reference. HIV DNA copy numbers were assayed from peripheral blood mononuclear cells and measured by real-time PCR (high levels:  $>100$  HIV DNA copies/ $10^6$  cells; low:  $<100$  HIV DNA copies/ $10^6$  cells)

**Results:** In the combined group of HIV ( $n=16$ ) and controls ( $n=7$ ), Glu/Cr is significantly lower in the FWM ( $p=0.05$ ). Glu/Cr ( $p=0.08$ ) and Cho/Cr ( $p=0.05$ ) were lower in patients with high HIV DNA compared to controls, while a trend toward decreased NAA was noted in HIV compared to controls irrespective of HIV DNA. No significant differences in the posterior cingulate gyrus gray matter were observed in controls and HIV-infected patients with undetectable HIV DNA.



**Conclusions:** This study identifies MRS abnormalities suggestive of active brain injury in patients on HAART with high HIV DNA. This finding supports an active process underlying HAART-era NCI and a need to search for modifiable therapies to address the peripheral reservoir of mononuclear cell infection. One of us (1) recently reported significant reduction in WM Glu with normal NAA suggesting that Glu may be an earlier and therefore can be used as neuronal marker of NCI. This present study extend this observation by defining a new marker, high DNA, thus supports our hypotheses that intracellular HIV may contribute to NCI in otherwise successfully treated HIV patients.

References: 1. Sailasuta et al. Evidence of Reduced Glutamate in the Frontal Lobe of HIV Seropositive Patients, NMR in Biomed, in press