

## Whole-brain MR Spectroscopic Imaging in Adults Perinatally-infected with HIV

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**INTRODUCTION:** HIV infection is known to alter the concentration of proton MR-observed brain metabolites, and such metabolite changes in individuals with behaviorally-acquired HIV are extensively studied. However, the long term impact of a persistent reservoir of HIV in the CNS and the potential toxic effects of long term use of some of its antiretroviral therapeutics on the brain metabolites are not characterized completely. Though metabolite changes can be expected to occur throughout the brain, predominantly in certain regions and subtly in other regions in sync with the anatomical distribution of the viral load, previous studies have evaluated metabolite changes only in few select brain anatomical regions. In this study, a unique whole-brain MRSI method is used to quantitate changes in brain metabolites, N-acetyl aspartate (NAA), total-creatine (Cre) and total-choline (Cho), in a group of adults perinatally-infected with HIV in comparison to a matched community control sample.

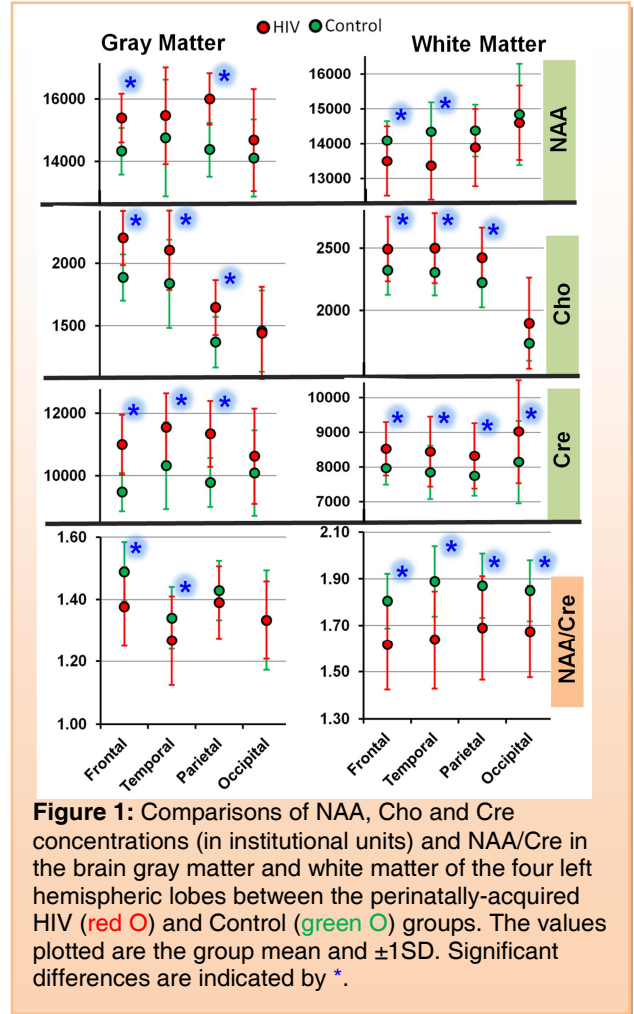
**METHODS:** MRSI data were acquired at 3T from 20 individuals with perinatally-acquired HIV (mean age: 20.5±1.8 years, age range: 18-23 years, 11 males) and 20 controls (mean age: 20.8±1.9 years, age range: 18-23 years, 8 males) using our volumetric spin-echo EPSI sequence (TR/TE=1710/70 ms, 135 mm slab, T<sub>acq</sub>= 26 min.; details in [1]). Data were processed using the MIDAS package [2, 3]. Briefly, the gradient echo (TE=6.3 ms) water signal reference EPSI data acquired in an interleaved fashion was used for the metabolite signal normalization. The signal normalized individual-subject MRSI data (64x64x32 mm<sup>3</sup>; ~1mL voxel volume) and segmented tissue type (white matter and gray matter) and CSF partial volume maps were then spatially registered with the MNI single-subject T1-MRI template. Using a 9-region atlas (frontal, temporal, parietal and occipital lobes in the left and right side, and cerebellum) defined in the template space, data were selected for analysis. The quality of data picked for analysis was controlled by including only spectra from voxels with tissue volumes of ≥70% and fitted spectral linewidths of ≤ 12 Hz. The metabolite concentration corresponding to 100 % of the gray matter (GM) or white matter (WM) in each of the 8 lobar regions was calculated by regressing the tissue partial volume against the metabolite concentration and extrapolating it to 100% of GM or WM. NAA, Cre and Cho values (in institutional units) and NAA/Cre were compared between the groups using ANCOVA with age and gender as covariates. A p-value of <0.05 was considered significant.

**RESULTS AND CONCLUSIONS:** In Figure 1 are shown the metabolite concentrations and NAA/Cre in the GM and WM of both the groups in the left hemispheric lobar regions, i.e., frontal, temporal, parietal and occipital lobes. The observed trends in the HIV group across the lobes are: a) increased NAA, Cho (except in the occipital lobe) and Cre in the GM, b) decreased NAA, and increased Cho and Cre in the WM, c) decreased NAA/Cre in the GM and WM. Significant differences observed in the HIV group in comparison to the control group include GM NAA in the frontal and parietal lobes, GM Cho and Cre in the frontal, temporal and parietal lobes, GM NAA/Cre in the frontal and temporal lobes, WM NAA in the frontal and temporal lobes, WM Cho in the frontal, temporal and parietal lobes, and WM Cre and NAA/Cre in all the lobes. In the cerebellum of the HIV group, significantly decreased NAA and NAA/Cre were observed (data not shown). Similar results were obtained for the metabolites in the right lobes (data not shown). Gender was found to have a significant influence on the metabolite differences.

Further studies are needed to understand the widespread increased metabolite concentrations in the HIV group. Specifically, measuring T2 of the metabolites and tissue water in both the groups will allow us to evaluate whether the increased metabolite concentrations are due to T2 differences between the groups, a real increase in the concentration or issues in our signal normalization method. The results of this study show that significant alterations of proton MRS-observed metabolites occur in the whole brain of adults perinatally-infected with HIV and these alterations can be quantified relative to age-matched control group values using atlas-guided analysis methods. The neuroimaging methodology described here will be useful in evaluating the biological substrates underlying HIV-associated neurocognitive disorders (HAND) prevalent in this patient population.

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**REFERENCES:** [1] Govind V et al. *J Neurotrauma* 27:483-496 (2010); [2] Maudsley AA et al. *NMR Biomed* 19:492-503 (2006); [3] Maudsley AA et al *Magn. Reson. Med.* 61:548-559 (2009).



**Figure 1:** Comparisons of NAA, Cho and Cre concentrations (in institutional units) and NAA/Cre in the brain gray matter and white matter of the four left hemispheric lobes between the perinatally-acquired HIV (red O) and Control (green O) groups. The values plotted are the group mean and ±1SD. Significant differences are indicated by \*.