7T BRAIN MRS IN HIV INFECTION: EFFECTS OF SEROSTATUS AND COGNITIVE IMPAIRMENT

Mona A Mohamed[1], Peter B Barker[1], Richard L Skolasky[2], Heidi Vornbrock Roosa[3], and Ned Sacktor[3]

[1]*Radiology, Johns Hopkins Medical Institutions, Baltimore, MD, United States,* [2]*Orthopedic Surgery, Johns Hopkins Medical Institutions, MD, United States,* [3]*Neurology, Johns Hopkins Medical Institutions, MD, United States*

Target Audience: Researchers and clinicians who have interest in HIV infection and its neurological sequelae.

Purpose: HIV has been extensively studied using magnetic resonance spectroscopy (MRS) at field strengths of 1.5, 3.0 and 4.0 Tesla (T) (1- 4). Higher magnetic field strengths (such as 7.0T) allow increased sensitivity and chemical shift dispersion and more reliable determination of brain metabolites, particularly for some of the smaller signals in the spectrum. The current study was undertaken to investigate the utility of 7.0T MRS in 5 brain regions for evaluating HIV^+ patients with asymptomatic neurocognitive impairment (ANI) versus symptomatic HIV associated neurocognitive disorder (HAND) [mild neurocognitive disorder (MND) and HIV associated dementia (HAD)].

Methods: Twenty two HIV^+ subjects were stratified into 2 groups according to their HIV associated neurocognitive disorder (HAND) cognitive status, using the Frascati criteria (5). Ten HIV^+ individuals with ANI (6 male with mean age of 62.3 ± 7.53) and 12 with symptomatic HAND, (9 male with mean age of 59.8 ± 5.4) were evaluated. Unlike symptomatic HAND, the cognitive impairment in ANI does not interfere with everyday functioning, although it is also characterized by cognitive impairment in at least two ability domains (5). All subjects were receiving combination antiretroviral therapy. Four HIV-controls (3 male with mean age of 67.7 ± 8.4) were also included. Using a 7.0T Philips 'Achieva' scanner and 32-channel head coil, brain MRI and single voxel STEAM spectra (TR/TE=3000/14 msec) were acquired from the left frontal white matter (FWM), basal ganglia (BG), Precuneus (PC), Posterior cingulate cortex (PCC) and hippocampus (Hippo) with and without water suppression. The voxel sizes ranged from 8 to 15 cc (Figure 1). Spectra were analyzed using LCModel (6) and quantified in millimolar (mM) concentrations, i.u. relative to the unsuppressed water signal. Metabolite concentrations and ratios relative to creatine (Cr) were calculated for the 2 groups. The data was not normally distributed; therefore, comparisons of the groups' medians and interquartile (IQR) ranges were evaluated for significant differences using non-parametric median test.

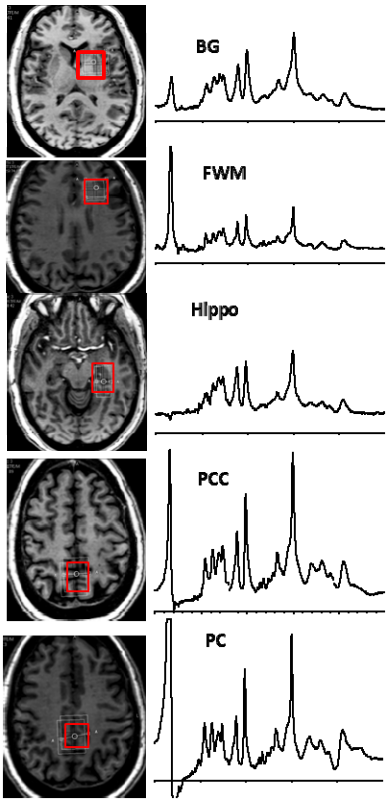

Figure 1: showing the 5 brain regions and their corresponding spectra from an HIV+ subject.

Results: There was a significant increase in BG total choline (tCho = GPC+PCh) between HIV^+ and seronegative controls [median (IQR) = 1.71 (1.15-12.0) and 1.6 (1.48-1.6) mM respectively], P= 0.03. There were no significant differences in other brain regions metabolites in regards to serostatus. In regards to cognitive impairment, there were significant differences in the FWM and PC NAA/Cr ratio which was lower in the symptomatic HAND [(median (IQR) =1.19 (1.17-1.24) for FWM NAA/Cr and 1.11 (1.05-1.21) mM for PC NAA/Cr] versus ANI [median (IQR) =1.29 (1.16-1.35) for FWM NAA/Cr and 1.24 (1.22-1.3) mM for PC NAA/Cr], P= 0.025 and 0.017 respectively. Furthermore, Glu/Cr was significantly lower in the FWM and PCC in the symptomatic HAND [median (IQR) =1.08 (0.98 -1.13) for FWM Glu/Cr and 1.07 (1.03-1.2) mM for PCC Glu/Cr] versus the ANI [median (IQR) = 1.15 (1.12-1.24) for FWM Glu/Cr and 1.24 (1.23-1.26) mM for PCC Glu/Cr], P= 0.025 and 0.005 respectively. The Hippo and BG showed no significant differences in metabolites between ANI and symptomatic HAND.

Discussion and Conclusion: Several studies performed at 3.0 T reported reduced FWM NAA, Glu/Cr and increased *myo*-inositol (mI) in symptomatic HAND as compared to ANI HIV^+ patients (3, 7). At 7T, improved separation of Glu from glutamine is possible. Furthermore, reduced Glu uptake has previously been demonstrated to occur *in vitro* in astrocytes exposed to HIV (8). The current study confirms some of these findings namely reduced FWM NAA/Cr, and it adds new findings in other brain regions namely reduced PC NAA/Cr and decreased PCC Glu/Cr reflecting neuronal impairment in association with symptomatic HAND. This study failed to demonstrate significant differences in FWM mI; however, it showed increased BG tCho in HIV^+ versus HIV^- reflecting glial cell proliferation with change in serostatus. In conclusion, 7T MRS metabolites measurement of Glu/Cr, NAA/Cr can be reliable biomarkers for assessment of symptomatic HAND in patients with HIV.

References: (1) Chang, L, Ernst, T, *et al.*, Antivir Ther 2004; 9(3):431-40; (2) Barker, PB, Hearshen, DO, *et al.*, Magn Reson Med 2001; 45(5):765–769; (3) Mohamed, M, Barker, PB et al. MRI, 2010; (4) Young, AC et al., Neurology 2014; 83(18):1592-600; (5) Antinori et al., *Neurology* 2007;69:1789–1799; (6) Provencher, SW, Magn Reson Med 1993; 30(6):672-9; (7) Sailasuta, N, Shriner, K, et al, NMR Biomed 2009; 22:326-31; (8) Wang, Z, Pekarskaya, O, *et al.*, Virology 2003; 312(1):60-73.