INFECTION WITH HIV AND HCV IS ASSOCIATED WITH NEUROMETABOLIC COMPROMISE: A 3T MAGNETIC RESONANCE SPECTROSCOPY STUDY

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Introduction: Co-infection with Human Immunodeficiency Virus (HIV) and Hepatitis C (HCV) is a common, though understudied, clinical condition affecting approximately 300,000 adults in the United States. Both viruses are capable of crossing the blood-brain barrier via infected macrophages/microglia resulting in neuropathological changes and brain inflammation. Compared to mono-infected patients, HIV/HCV co-infected patients perform worse on neurocognitive testing and demonstrate greater pathology on neuroimaging (1,2). In an effort to further define the nature of the neurophysiological abnormalities associated with HIV/HCV co-infection, this study examined cerebral metabolic changes among HCV mono-infected, HIV/HCV co-infected, and healthy controls using proton magnetic resonance spectroscopic imaging (^{1}H MRSI).

Methods: Participants consisted of ten HCV mono-infected, (mean age 56.6 years), 10 HIV/HCV co-infected (mean age 47.1 years), and ten healthy controls (mean age 46.7 years) who underwent MRI/MRS using 12 channel head receive coil. The entire protocol was approved by the institutional review board (IRB), and informed consent was obtained from each subject. Volume-selective, two-dimensional ^{1}H-MRSI was performed on a 20 mm slab superior to the ventricles [point-resolved spectroscopy (PRESS) localization; TE = 30 ms, TR = 2000 ms. The nominal voxel size was 2.82 cm^3 (16 × 16 phase encode steps over an 18X20 cm^2 FOV). Scan time was 10 minutes including the manual shim. For each voxel, metabolites were quantitated using the frequency-domain fitting routine LC-Model algorithm which analyzes the in vivo brain spectrum as a linear combination of individual in vitro metabolite spectra that constitute a basis set (3).

Results and Discussion: Figures 1 and 2 illustrate significant metabolic spectra (normalized to creatine) as processed using the LC- model. All the multivoxel spectra were quantified by LC model algorithm. Statistically significant differences were observed in metabolite ratios between the groups in the frontal white (FW), medial frontal grey (MFG) and parietal white (PW) regions. Increased myo-inositol (Ins) and decreased total N-acetylaspartate (NAA+NAAG) concentrations ($p<0.05$) were observed in the HCV mono-infected patients in FW, MFG and PW regions compared to healthy controls. Compared to controls, co-infected subjects demonstrated increased Ins and total choline (GPC+PCh+Cho) in FW, MFG and PW as well as decreased glutamate and glutamine (Glx) in FW regions.

Fig.1. Metabolites ratio of HCV mono-infected patients and healthy controls

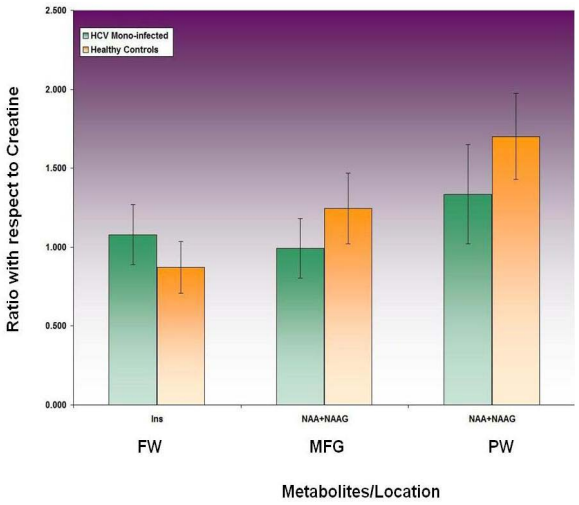
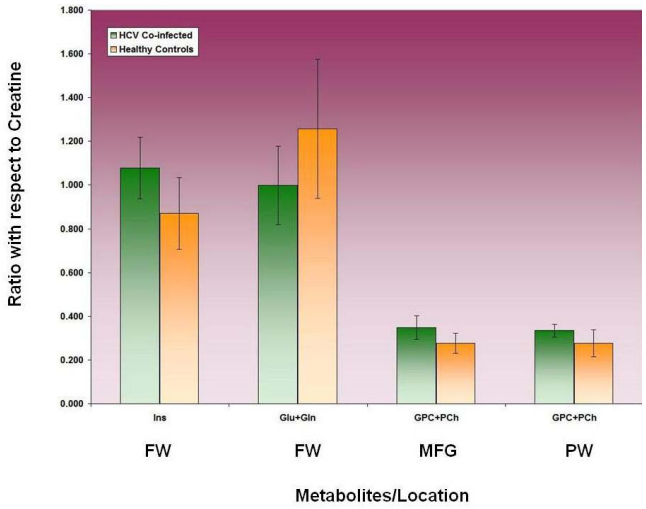


Fig.1. Metabolites ratio of HCV co-infected patients and healthy controls



Conclusion: While preliminary in nature, this study suggests that HCV infection results in neurometabolic abnormalities. Lower levels of NAA coupled with significantly higher levels of choline among the HCV mono-infected subjects provides support for the hypothesis that HCV infection gives rise to neuronal injury. The decrease in Glx among HIV/HCV co-infected patients relative to HCV mono-infected subjects supports the contention that co-infected patients experience greater neural injury and inflammation than mono-infected patients. Our laboratory is currently conducting ongoing studies to extend these findings and link them with data from other imaging techniques such as diffusion tensor imaging (DTI) as well as sophisticated neurocognitive methods. Albeit preliminary, our findings are consistent with those previously reported by Bokemeyer et al. (4) and Weissenborn et al (5) and provide increasing evidence that untreated, advanced HCV infection is associated with neurophysiologic decline.

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