3 Tesla MR Spectroscopy Reveals Decreased Glutamate and Glutamine Levels in Frontal White Matter in HIV-associated Dementia

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Introduction

The pathophysiology of HIV-associated dementia (HAD) has been extensively studied in the past using MR spectroscopy (MRS) at field strengths of 1.5 Tesla (1). At higher magnetic field strengths (such as 3.0T), increased sensitivity and chemical shift dispersion allow for more reliable determination of compounds such as glutamate (Glu) and glutamine (Gln) compared to 1.5T (2). The current study was therefore undertaken to investigate the utility of 3T MRS in the evaluation of patients with and without HAD.

Material and Methods

Forty HIV+ subjects were stratified into 2 groups according to their cognitive status using the Memorial Sloan Kettering (MSK) dementia severity score: 28 with normal cognitive function (8 females, age 46.1±5.8 years), and 12 with HAD (2 females, age 47.4±7.0 years). Single voxel spectra (TR/TE=2000/45 msec) were acquired from the left frontal white matter (FWM) and the left basal ganglia (BG) with and without water suppression using a 3.0T Philips Intera scanner with SENSE-head coil reception. The voxel size was 2.2x2.2x2.2 cm^3. Spectra were analyzed using the LCModel (3) and quantified (in mM concentrations) relative to the unsuppressed water signal, as well as ratios relative to creatine (Cr). Between group differences were evaluated using ANOVA. The level of statistical significance was set at $P < 0.05$.

Results

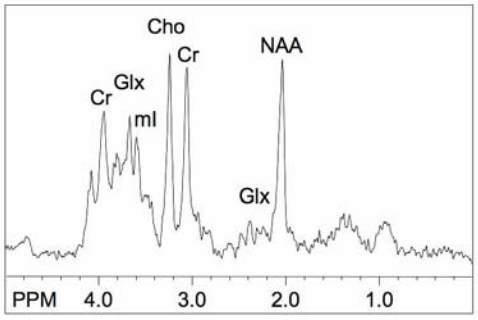

Figure 1. Frontal white matter MR spectrum of a HIV+ 47 y.o. male with HAD (MSK 2).

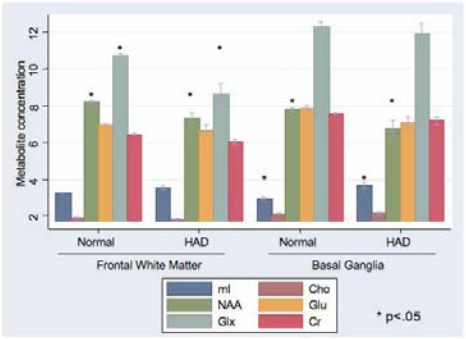

Figure 2. Metabolite Concentrations in FWM and BG in HIV+ patients with and without HAD.

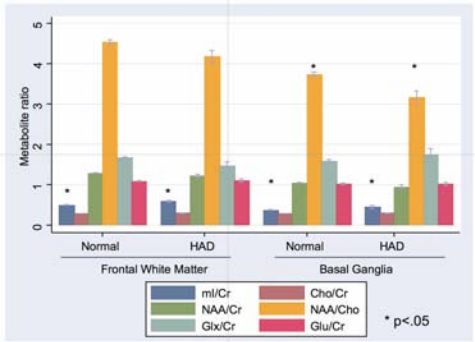

Figure 3. Metabolite ratios in FWM and BG in HIV+ patients with and without HAD.

Figure 1 shows a FWM spectrum from a patient with HAD. Results of the MRS analysis are shown in Figures 2 and 3. Combined glutamate and glutamine (Glx, predominantly Glu) was significantly lower in FWM in HAD (8.6±2.9 mM) as compared to the subjects with normal cognitive status (10.7±1.3 mM) ($P = 0.004$). In addition, consistent with prior 1.5T studies, there was a significant decrease in the concentration of FWM and BG N-acetyl aspartate (NAA) in the HAD group ($P = 0.019$ and 0.015 respectively), and significant increases in the FWM and BG myo-inositol (mI)/Cr ratios in the HAD group ($P = 0.012$ and 0.013 respectively).

Discussion

Several studies performed at 1.5T have previously reported reduced FWM NAA and increased mI/Cr levels in HAD, suggesting neuroaxonal loss or dysfunction, and glial proliferation, respectively (1). In addition, the current study performed at 3 Tesla reveals significant reductions in FWM Glx in HAD compared to HIV+ patients with normal cognition. Glx was also lower in the BG in the HAD group, but did not reach statistical significance. Reduced Glu uptake has previously been demonstrated to occur *in vitro* in astrocytes exposed to HIV as detected by Northern blot analysis and immunoblotting (4). However, it is not clear how this finding relates to the total pool of brain Glu as determined by *in vivo* MRS.

3T MRS with phased-array head coil reception allows more sensitivity detection of MRS metabolites (in particular compounds such as Glx), and it appears that Glx (consisting of mainly Glu) is abnormal in FWM of patients with HAD. The Glx signal, alone or combined with NAA, may be a useful indicator or neuronal loss/dysfunction in patients with HIV.

Acknowledgement

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References

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