LONGITUDINAL MULTI-SLICE SHORT-TE 1H MRSI REVEALS ONGOING BRAIN METABOLITE INJURY IN TREATED HIV+ PATIENTS AND IN CHRONIC HEAVY DRINKERS

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Introduction

Multi-slice short-TE 1H MR spectroscopic imaging has been used to study the separate and interactive brain effects of HIV infection and chronic active heavy drinking, an immunosuppressing habit more common in the HIV-infected than general community. Our recent cross-sectional studies showed frontal N-acetylaspartate (NAA) loss in chronic active heavy drinkers and higher thalamic myo-inositol (mI) and temporal white matter creatine (Cr) in patients infected by HIV and on antiretroviral treatment, and a positive interaction for Cho and mI in parietal white matter, suggesting that heavy drinking may exacerbate HIV effects. These cross-sectional effects were relatively subtle and it is unclear if they are premorbid or a function of drinking or HIV infection. Therefore, we performed longitudinal 1H MRSI studies to test the hypothesis of ongoing brain damage in heavy drinkers and in HIV patients, who are not treated or have high viral loads despite antiretroviral therapy.

Background

On a Siemens Vision 1.5 T, we studied 94 participants in 4 groups twice over a 2-year period: 54 HIV- individuals ((38 light drinkers (LD), 16 heavy drinkers (HD)) and 40 HIV+ patients (30 LD and 10 HD). The LD individuals drank < 20 alcoholic drinks/mo over lifetime, HD drank > 100 alcoholic dri/mo within 3 years prior to baseline and were matched on drinking severity. Both HD groups continued to drink at their respective levels during the scan interval. The HIV+ groups had a similar degree of immunosuppression at baseline (LD: CD4 353 ± 195, blood log viral load 2.58 ± 160; HD: CD4 357 ± 182, blood log viral load 2.72 ± 1.46). After routine DSE and T1w MRI, three-slice 1H MRSI (TR/TI/TE=1800/170/25ms) acquired within 30 min metabolite information from the main brain lobes, subcortical nuclei, brainstem and cerebellar vermis. Spectroscopic images were co-registered with the MPRAGE data set (TR/TE/TI = 10/4/300 ms), which had been segmented into gray matter (GM), WM, and CSF of major lobes, subcortex, cerebellum, and brainstem using probabilistic segmentation and atlas-based non-linear transformation. Lobar and regional concentrations of NAA, Cho, Cr, and mI were calculated at both time points as previously described. Main outcome measures were the annual rates of metabolite concentration change. Statistical analyses used a 2x2 ANOVA to test for main effects and interactions of HIV (positive or negative) and drinking (light or heavy). Additional analyses also used antiretroviral therapy (ART: yes or no) and viremia (viral load >400: yes or no) as main factors. Age was used as covariate where appropriate.

Results

Main effects of continued heavy drinking: Over 2 years, NAA and mI decreased in frontal WM, occipital WM, and cerebellar vermis (all $F>4.7$, $p<0.03$) and Cho decreased in the cerebellar vermis ($F=4.5$, $p=0.04$).

Main longitudinal HIV effects: In 9 HIV+ patients never treated with ART, parietal WM NAA decreased at 11±8%/yr compared to a rate of 1±6%/yr in 54 HIV- individuals ($F=13.8$, $p<0.0005$) and NAA tended to decrease in par GM and in frontal lobe (all $F>2.5$, $p<0.11$). In the entire HIV+ sample, thalamic and vermian mI increased (both $F>3.8$, $p<0.05$), while parietal NAA in WM ($F=3.7$, $p<0.06$) and GM ($F=2.7$, $p<0.10$) tended to decrease.

Interactive heavy drinking and HIV effects: No positive interactions but some negative interactions (temporal GM Cho, frontal WM Cr, occipital WM mI (all $p<0.05$)) suggest opposing effects of heavy drinking in LD (decrease) and HIV in HD (increase) on Cho and mI, but no additive or synergistic effects.

24 LD+ on ART showed lower rates of frontal GM and parietal WM NAA loss than 6 LD+ off ART ($F>5.8$, $p<0.03$). However, even the 13 virally suppressed LD+ (i.e., those on "successful" ART) had NAA decreases in temporal WM at a rate of 4±6% compared to 9 viremic patients on ART at 0±3% ($F=3.1$, $p=0.09$). Temporal Cho ($F=6.2$, $p=0.02$) and lenticular Cho levels decreased ($F=3.8$, $p=0.07$) in viremically suppressed patients on ART.

Discussion

To our knowledge, this is the first longitudinal study of brain metabolite effects of chronic heavy drinking and HIV disease progression, and the first to use short-TE multi-slice 1H MRSI successfully in a clinical setting. While continued heavy drinking at >100 drinks/month over 2 years is associated with widespread axonal damage and astrocytic alterations, heavy drinking does not appear to exacerbate ongoing adverse metabolite effects of HIV infection. Untreated HIV infection presents with ongoing neuronal injury, in particular in parietal WM. HIV patients on ART show less severe longitudinal brain metabolite damage than those off ART, but even virally suppressed HIV+ patients tend to have ongoing regional NAA loss. These results demonstrate the ability of 1H MRSI to detect longitudinal metabolite changes due to chronic heavy drinking and HIV infection.