2D CSI ^{1}H MR Spectroscopy of Lactate and Cerebral Metabolites in HIV+ Dementia

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INTRODUCTION

HIV dementia has been associated with localized cerebral metabolic changes in frontal white matter and subcortical grey matter regions, such as the basal ganglia [1-6]. Within these regions of interest (ROI), N-acetylaspartate (NAA), choline (Cho), and creatine (Cr) have been studied using single voxel ^{1}H MR spectroscopy (MRS). Previous studies have shown reduced NAA/Cr and NAA/Cho but increased Cho/Cr ratios in HIV+ patients [1, 4, and 6]. More recently, 2D CSI ^{1}H MRS has been developed and allows for focused localization of previously studied cerebral metabolites as well as lactate (LAC). Alterations in the LAC profile due to abnormalities in brain oxidative metabolism have been observed in HIV+ patients with opportunistic infections [7,8] but have not been obtained in HIV dementia patients without structural abnormalities. LAC levels may be elevated as HIV affects both macrophages and microglia and could lead to increases in anaerobic metabolism. The purpose of this study was to report high field multi-voxel 2D CSI ^{1}H MRS cerebral metabolite levels within the basal ganglia (BG) and subcortical white matter (SWM) in a spectrum of HIV+ patients.

METHODS

Subjects: Forty-four HIV+ patients (31 males, 13 females, 41 ± 2 yrs) and 10 seronegative healthy subjects (4 males, 6 females, 47 ± 2 yrs) participated in the study. Each patient underwent physical, neurological and neuropsychological evaluation and was classified by the Memorial Sloan-Kettering system for HIV associated dementia complex (ADC). To maximize statistical power, HIV+ patients were further grouped into two categories: relatively asymptomatic (ADC 0 (n=15) and ADC 0.5 (n=9)) and symptomatic (ADC 1 (n=10), ADC 2 (n=10), and ADC 3 (n=1)). 15 of the 24 asymptomatic HIV+ patients and 16 of 20 symptomatic patients were on antiretroviral therapy. All subjects provided informed consent as required by the Human Subjects Institutional Review Board at the University of Pennsylvania.

MRS: MR imaging and spectroscopy was performed in all subjects on a 3T MR scanner equipped with the standard clinical quadrature head coil provided by the manufacturer. Axial T1 weighted MPRAGE images were acquired to identify anatomical structures (TR 1620ms , TE 3.87ms, 1mm slice thickness, FOV 25x25cm). Spectroscopy imaging was performed using a SE with 2D phase encoding and outer volume saturation pulses for lipid suppression sequence (TR 2000ms, TE 135ms, n=3, 20mm slice thickness, FOV 20x20cm, voxel size 12.5 x 12.5 x 20). Voxels overlapping regions BG and SWM on both hemispheres were analyzed (Figure 1). Quantification of absolute concentrations of metabolites could not be obtained due to unknown T1, T2 relaxation times during MRS data acquisition. The area under the peak was measured for relative quantification of metabolites and calculated ratios of NAA/Cr, NAA/Cho, Cho/Cr were determined. Metabolic ratios were compared between HIV+ groups (asymptomatic, symptomatic) compared to controls by Student's t-test (* = $p<0.05$). LAC was considered present if a peak was observed 1 standard deviation above the noise. A chi square analysis was performed to determine significance across groups for the presence of LAC (** = $p<0.05$).

RESULTS

Differences in several cerebral metabolites abnormalities were observed in the HIV+ groups compared to controls (Table 1). The percentage of visible lactate peaks in BG was significantly greater in HIV+ groups compared to controls. Although not significant in SWM, visible lactate peaks were more prominent in HIV+ groups. In both BG and SWM the NAA/Cho and NAA/Cr ratios were reduced in asymptomatic HIV patients and was significantly dimished in HIV+ symptomatic patients compared to controls ($p<0.05$). In contrast, no consistent trends were observed in the Cho/Cr ratio for either ROI.

DISCUSSION

Our results demonstrate that high field multi voxel 2D CSI ^{1}H-MRS provides a more accurate understanding of cerebral metabolite changes compared to single voxel technique previously used to evaluate HIV+ patients. Neuronal mitochondrial dysregulation (reduction in NAA/Cr) and not gliosis (no changes in Cho/Cr) were observed within the ROIs of HIV+ dementia patients. The presence of the LAC was more significantly observed within the BG in both HIV+ patient groups compared to normals. LAC may reflect the presence of macrophages due to HIV infection and/or a derangement in neuronal mitochondrial metabolism. Within SWM, LAC was more frequently observed across all groups though this may be due to contamination from CSF. The use of 2D CSI ^{1}H-MRS, particularly in detecting LAC within BG, may serve as a biomarker in classifying HIV+ dementia.

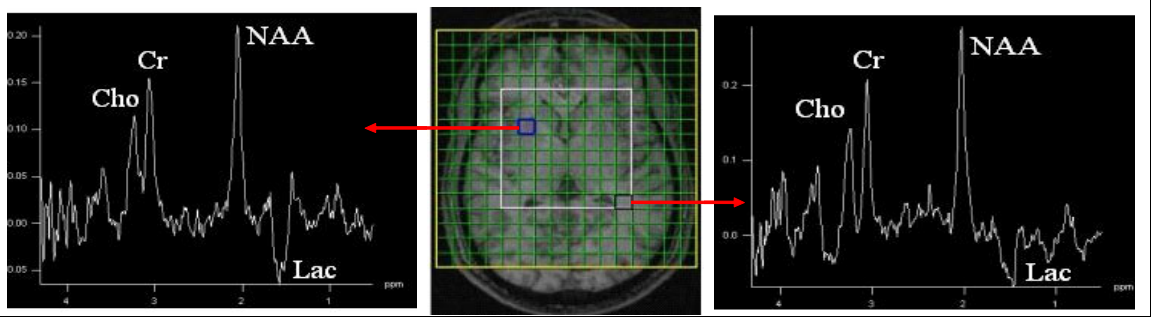

Figure 1. Basal ganglia (blue voxel) and subcortical white matter (black voxel) regions of interest and corresponding 2D CSI ^{1}H-MRS spectra from a characteristic HIV+ symptomatic patient.

Table 1. Mean Values of Metabolite Concentrations of Healthy Controls, HIV+ Asymptomatic Patients, and HIV+ Symptomatic Patients.

	NAA/Cr	Cho/Cr	NAA/Cho	% Lac
Bilateral BG – Average all voxels				
Controls	1.61 ± 0.20	0.87 ± 0.09	1.80 ± 0.26	5
HIV+ Asymptomatic	1.45 ± 0.14	1.00 ± 0.15	1.46 ± 0.14	21 **
HIV+ Symptomatic	1.54 ± 0.26	0.98 ± 0.14	1.38 ± 0.21 *	26 **
Bilateral SWM – Average all voxels				
Controls	2.22 ± 0.20	1.11 ± 0.07	2.03 ± 0.15	20
HIV+ Asymptomatic	2.10 ± 0.20	1.14 ± 0.09	1.83 ± 0.15	26
HIV+ Symptomatic	1.70 ± 0.30 *	0.97 ± 0.14	1.49 ± 0.23 *	35

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