Validation of accelerated TE-Averaged Echo-Planar Spectroscopic Imaging in Healthy and HIV youths

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Target Audience: Basic scientists interested in Compressed Sensing (CS) reconstruction of 3D-localized TE-Averaged echo-planar spectroscopic imaging; clinical researchers interested in regional metabolite differences in perinatally HIV-infected youths.

Purpose: There have been a number of single voxel based MR Spectroscopy (MRS) reports focusing on metabolite differences in human immunodeficiency virus (HIV) infected patients [1,2], however there are only a few studies that have examined metabolite changes in perinatally HIV-infected youths [3]. A versatile method for observing changes in glutamate (Glu) and other metabolites is TE-averaging, which averages several TE increments to eliminate glutamine (Gln) signal [4]. Using this technique for spectroscopic imaging of a single slice allows for greater spatial coverage [5]. In order to reduce scan time for spectroscopic imaging, an echo-planar readout can be used to obtain a spatial and spectral dimension simultaneously in a single TR [6]. Also, non-uniform undersampling (NUS) schemes can be used on the incremented dimensions (k_y,k_z,t_1) to further reduce scan time [7,8]. A new method, called accelerated TE-Averaged echo-planar Spectroscopic Imaging (TEA-EPSI), is capable of obtaining TE-averaged spectroscopic images from multiple slices in a clinically feasible scan time. This is accomplished by utilizing an echo-planar readout in combination with NUS schemes and post-processing using CS reconstruction. The purpose of this study is to use accelerated TEA-EPSI to examine regional metabolite changes between healthy youths and perinatally HIV-infected youths.

Methods: Seven healthy youths (mean age = 20.3 years) and eight perinatally HIV-infected youths (mean age = 19.9 years) were scanned using the 5D NUS echo-planar J-resolved Spectroscopic Imaging (5D EP-JRESI) sequence combined with a maximum-echo sampling scheme[8]. The following scan parameters were used: initial TE = 30 ms, TR = 1200 ms, bandwidth = 1190/1000 Hz, t_2 points = 256, t_1 increment = 64, Δt_1 = 1ms, FOV = 24x24x12 cm^3, and resolution = 1.5x1x5x1.5 cm^3. The echo-planar readout is used to encode k_x (32 points - oversampled) and t_2 (256 points) simultaneously in a single TR. The other two spatial dimensions are encoded using 16 points (k_y) and 8 points (k_z). The scans were acquired using an acceleration factor of eight (8X), which resulted in a 20 minute scan time. A separate, 3 minute unsuppressed water scan was acquired for a single t_1 point for eddy current corrections, which were applied after the data were fully reconstructed. After acquisition, the data were processed to have a double incremented J-resolved spectral scheme by applying a frequency-dependent linear phase correction, bringing the total TE increment time to 2ms. Additionally, regions outside of the 1.2 – 4.3 ppm range were set to zero. The data were then reconstructed using a modified split Bregman algorithm to minimize total variation (TV) [7, 8]. Once the data were fully reconstructed to the (x-y-z-F_2-F_1) domain, the data were transformed into the (x-y-z-F_2-t_1) domain. For all spectra (all spatial locations and all t_1 points), the N-acetylaspartate (NAA) peak was shifted to 2.0 ppm to correct for any frequency drifts. Finally, all of the t_1 points were averaged together, resulting in TE-Averaged spectra (TE = 30-156ms) in three spatial dimensions. The healthy youth and HIV youth had five different regions identified: Frontal White (FW), Frontal Gray (FG), Basal Ganglia (BG), Occipital White (OW), and Occipital Gray (OG) based on spatial location and known regional metabolite differences [9]. Peak integration was used to quantify four different metabolites for all healthy subjects and patients after chemical shift displacement error (CSDE) was accounted for (~1 pixel/ppm shift along the readout direction). No T1 corrections were performed.

Healthy	FW	FG	BG	OW	OG
NAA/Cr	1.93 ± 0.56	1.66 ± 0.58	1.51 ± 0.44	1.81 ± 0.23	2.04 ± 0.29
Glu/Cr	0.18 ± 0.09	0.22 ± 0.17	0.20 ± 0.12	0.23 ± 0.07	0.31 ± 0.05
Ch/Cr	0.83 ± 0.35	0.80 ± 0.21	0.81 ± 0.06	1.01 ± 0.17	0.97 ± 0.15
mI/Cr	0.33 ± 0.20	0.27 ± 0.16	0.26 ± 0.14	0.28 ± 0.13	0.24 ± 0.11

Table 1. Metabolite Ratios (mean ± standard deviation) of five different regional areas in healthy youths with respect to Creatine (Cr).

HIV	FW	FG	BG	OW	OG
NAA/Cr	1.54 ± 0.33	1.61 ± 0.16	1.47 ± 0.15	1.80 ± 0.30	1.77 ± 0.23
Glu/Cr	0.18 ± 0.07	0.31 ± 0.08	0.19 ± 0.07	0.25 ± 0.06	0.41 ± 0.07*
Ch/Cr	0.77 ± 0.21	0.69 ± 0.18	0.99 ± 0.18*	0.95 ± 0.09	0.89 ± 0.12
mI/Cr	0.30 ± 0.13	0.24 ± 0.19	0.29 ± 0.07	0.29 ± 0.06	0.22 ± 0.04

Table 2. Metabolite Ratios (mean ± standard deviation) of five different regional areas in HIV-infected youths. (* p<0.05 significance from healthy youths using a two-tailed t-test).

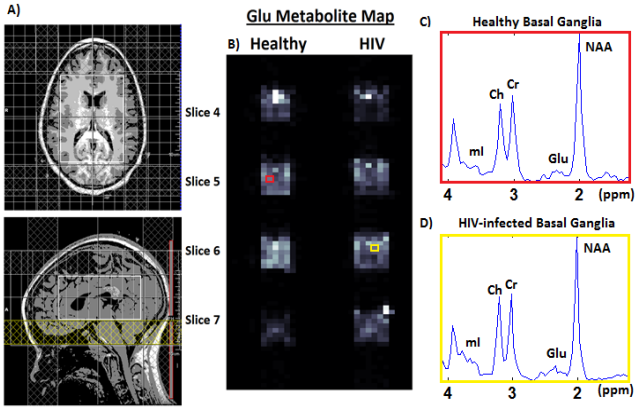

Figure 1. MRI localization (axial and sagittal) is shown (A) for a HIV-infected youth (age = 19 years). (B) Glutamate metabolite maps for 4 slices are shown for both healthy and HIV-infected youths (age for both = 19 years), as well as full spectra (C and D) corresponding to the colored regions on the metabolite maps.

Results: Table 1 shows the metabolite ratios of NAA, glutamate (Glu), total choline (Ch), and myo-Inositol (mI) with respect to Creatine (Cr) for healthy children in five different regions of the brain. Table 2 shows the same information for HIV-infected youths. A two-tailed t-test was performed for each metabolite in each region, and the significant ($p<0.05$) differences are noted with an asterisk. Figure 1 shows in vivo glutamate metabolite maps (Fig. 1B) and full spectra (Fig. 1C and Fig. 1D) from a healthy (age = 18 years) and HIV (age = 18 years) youth. A total of 8 slices are obtained, however only the four slices containing signal are displayed for the glutamate map.

Discussion: The results show a significant difference between the healthy and HIV youths for certain brain regions: increased Glu/Cr in the OG, and increased Ch/Cr in the BG. Although not significant, there is a strong trend for decreased NAA in the FW region. Decreased NAA and increased Ch are consistent with previous findings [1]. Glu differences between healthy and HIV subjects are still controversial, and opposite trends have been reported in the literature using single voxel techniques [2,3]. These opposite findings could possibly be attributed to the differences in the mean age of the two studies.

Conclusion: Accelerated TEA-EPSI has been validated in a pilot group of perinatal HIV and healthy youths. The study shows metabolite changes that are consistent with previous findings, and demonstrates the usefulness of this technique to acquire multi-slice TE-Averaged spectroscopic images. Future work will focus on quantifying metabolite concentrations using prior knowledge fitting.

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