Voxel-Based Morphometric Analysis of Gray and White Matter in Perinatally HIV-infected Youth

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Introduction: Human immunodeficiency virus (HIV) remains a major health problem worldwide. HIV in adults and children has become a chronic illness and there is a critical need to develop noninvasive, reliable techniques to detect sub clinical involvement of the brain by HIV. In our study we have compared a group of perinatally HIV-infected youth with a control group, matched for sex and age, using voxel-based morphometry (VBM), a method that allows averaging high-resolution MRI on subjects and hence comparisons at the group level. VBM has proved to be a powerful method in detecting regional differences in cerebral structure in various disorders. It provides the opportunity for an unbiased general search of abnormalities in the whole brain volume (1) and allows the detection of highly localized differences across the whole brain, even in areas where the region of interest analysis would be difficult. VBM procedures are used to quantify abnormalities in a variety of clinical conditions where routine imaging does not show any visible abnormality (2, 3). The objective of the study is to identify the gray-matter (GM) and white-matter (WM) changes that are associated with perinatal HIV infection. Statistical analysis was performed to determine the regional differences in the two groups.

Methods: Nine HIV infected patients (age 15.8y± 3.1) and nine healthy controls (age 17.6y± 2.5) were recruited for the study. All subjects gave informed consent according to an institutionally approved research protocol. A Siemens 3T Trio-Tim MRI scanner (Siemens Medical Solution, Erlangen, Germany) was used and a 3D structural MRI was acquired on each subject using a T1-weighted MPRAGE sequence (TR = 2200 msec; TE = 2.34 msec; inversion time = 900 msec; FA = 9°; matrix size = 320 x 320; FOV = 230 mm x 230 mm; slice thickness = 0.9 mm; number of slices = 192) for evaluation of structural brain abnormalities.

We have used SPM5 (statistical parametric mapping software) to preprocess and analyze our data (4-6). Image preprocessing was carried out according to the optimized protocol described by Good et al. (7) using the VBM toolbox. The high-resolution T1-weighted MRI data sets were first normalized to a standard template. The procedure then entailed a segmentation of the normalized images into GM, WM and CSF. The resulting GM/WM images were then smoothed with a Gaussian kernel of 12 mm fullwidth at half-maximum (FWHM). Voxel-by-voxel analysis of covariance was used to detect GM/WM differences between the groups with age, sex and total intracranial volume as covariates. To avoid edge effects around the border between GM and WM, we excluded all voxels with a GM/WM value < 0.1 and used an explicit mask of mean GM/WM image. Brain areas with increased or decreased metabolic patterns in HIV-infected were compared with the controls, and calculated by using 2 different contrasts, [1 -1] and [-1 1], respectively. We onset our results at a height threshold of $p < 0.001$ uncorrected and, additionally, at an extent threshold of 10 voxels (cluster level) (8). Normalized MPRAGE images from all patients and control subjects were averaged to create a mean image. Regions with significant GM/WM differences were overlaid onto the mean MPRAGE image for structural identification.

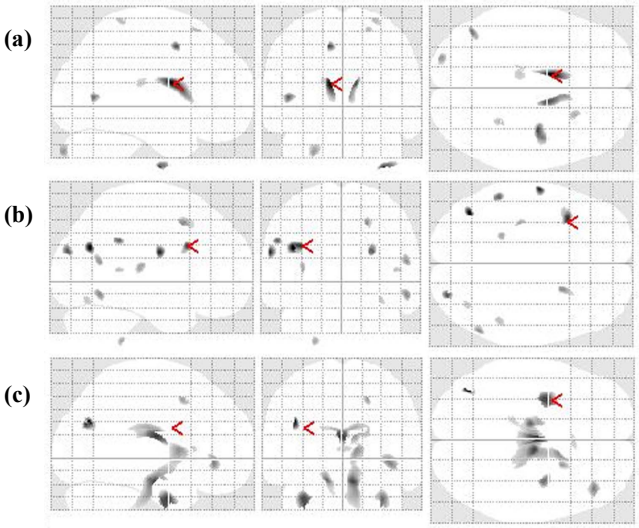

Fig. 1: Two-dimensional MIP glassbrain representation showing areas of (a) relative GM volume decrease, (b) relative GM volume increase and (c) relative WM volume decrease in HIV-infected group, compared with controls.

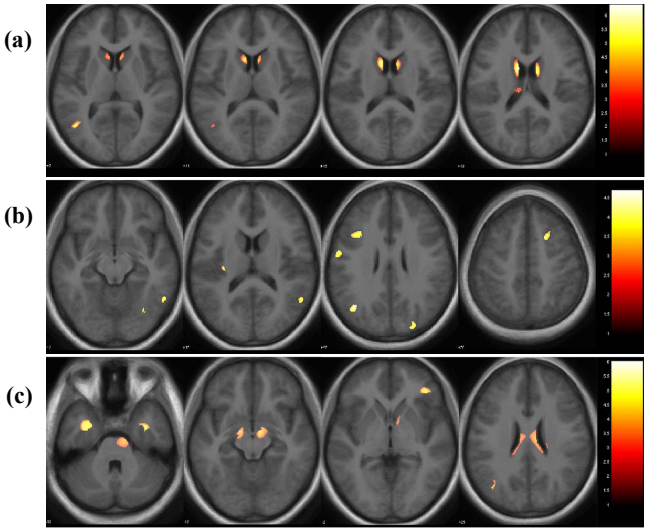

Fig. 2: Regions with significantly (a) decreased GM, (b) increased GM and (c) decreased WM overlaid over mean MPRAGE image (The neurological convention is adopted for image display).

Results and Discussion: Three views of regions appear in glass brain 2D panels and show brain regions with significant decrease (Fig. 1a) and increase (Fig. 1b) of gray matter volume (GMV) in HIV patients compared with control subjects. Fig. 2a shows decreases in GMV for the caudate nucleus bilaterally and the left parietal lobe. Increases were found (Fig. 2b) in the frontal lobe, posterior temporal lobe and parietal lobe.

Two-dimensional glass brain panels show regions with decreased white matter volume (WMV) for HIV patients compared to control subjects (Fig. 1c). Reduced WMV were visible in the temporal lobe, pons, right pre-frontal area, corpus callosum and the junction of the thalamus and mid brain (Fig. 2c). No regions displayed significant increase in WMV for HIV patients versus controls.

Conclusion: This study measured volume changes in cerebral structures resulting from perinatal HIV infection. By using VBM, we identified gray and white matter changes in the caudate nucleus, parietal lobe, frontal lobe, temporal lobe, corpus callosum and other brain regions. Further studies will be required to validate and elaborate these findings, however, this study suggests the utility of VBM in evaluating gray and white matter volume abnormalities in HIV-infected youth to evaluate the severity of the damage to the brain.

References:

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