Cross-sectional and longitudinal brain morphometry in HIV associated cognitive impairment

Y. Wu[1], P. Storey[2], B. Cohen[3], L. Epstein[4], R. Edelman[2], and A. Ragin[5]

[1]Department of Radiology, Evanston Northwestern Healthcare; Feinberg School of Medicine, Northwestern University., Evanston, IL, United States, [2]Evanston Northwestern Healthcare; Feinberg School of Medicine, Northwestern University., IL, United States, [3]Department of Neurology, Feinberg School of Medicine, Northwestern University., IL, United States, [4]Department of Pediatrics and Neurology, Feinberg School of Medicine, Northwestern University., IL, United States, [5]Department of Radiology, Feinberg School of Medicine, Northwestern University., IL, United States

INTRODUCTION: Individuals infected with HIV are vulnerable to cognitive deterioration and progression to dementia. However, there are no laboratory markers to determine the degree of brain involvement in individual patients. Quantitative MR strategies based on automated brain segmentation may provide direct, yet noninvasive evidence of brain tissue alterations associated with ongoing injury. This investigation exploited novel brain segmentation algorithms to derive comprehensive volumetric measurements of brain parenchyma, volume fractions for specific tissue types (white matter, gray matter and CSF), as well as the rate of longitudinal change. Volumetric measurements were determined in HIV and control subjects at baseline and one year follow-up. The volumetric measurements were also evaluated for patterns of relationship to clinical dementia severity.

METHODS: 10 well-characterized, medically stable HIV patients (mean age: 47.4 ± 7.5; 9 males, 2 females) and 7 healthy control subjects without history of neurologic illness (mean age: 45.57 ± 7.6; 5 males, 2 females) were evaluated with MR at baseline and a follow-up scan, approximately one year later. The groups did not differ significantly in age or education. CD4 counts for the HIV subjects ranged from 24 to 427/mL at baseline; plasma viral load ranged from undetectable to 154,938 copies/mL. Dementia severity was determined according to operationalized criteria based on the Memorial Sloan Kettering (MSK) rating scales [(1-2)]. ***MR Imaging:*** Imaging studies were performed on a 1.5T MR unit (GE, Milwaukee, USA). The MR protocol included dual echo T_2- and proton density-weighted images acquired with TR/TE = 3300 / 85 msec. ***Image Processing*:** Quantitative image analysis was performed offline on a Linux workstation. Quantitative volumetric measures were generated using automated segmentation software packages of FAST, SIENA and SIENAX in FSL (Oxford Center for Functional Magnetic Resonance Imaging). White matter, gray matter and CSF volumes were determined with FAST [(3)]. Four-class tissue segmentation was performed using two-channel (dual echo) MR. The tissue volume measures were then divided by the total brain volume to determine the tissue fractions (white matter, gray matter and CSF fractions). The normalized brain parenchyma fraction (NBPF) was determined with SIENAX [(4)], which corrects for variation in individual brain size in MNI152 standard space. The ventricular CSF fraction was also derived with SIENAX. The percent brain volume change across one year (PBVC), a measure of the rate of longitudinal atrophy, was determined with SIENA [(4)]. T2 weighted images were used for both the SIENAX cross-sectional normalized brain parenchyma fraction (NBPF) and for the SIENA longitudinal percent brain volume change.

RESULTS: Initially, the normalized brain parenchyma, normalized ventricular CSF and brain tissue volume fractions (WM, GM and CSF) were compared in HIV and control groups at each time period (Figure 2, 4). Significant differences were obtained for white matter (baseline: p=.016; follow-up: p=.046), CSF (baseline: p=.012; follow-up: p=.098), normalized ventricular CSF fraction (baseline: p=.013; follow-up: p.=.016) and normalized brain parenchyma fraction (baseline:p=.006; follow-up: p=.056). The gray matter fraction was also generally reduced in the HIV patients, however the difference was not significant at either timepoint (Figure2). The degree of brain atrophy measured across one year with SIENA was not significantly different in the two groups. Significant or nearly significant correlations were identified between the brain volumetric measurements and the average MSK dementia severity ratings for the study period .

Figure 1

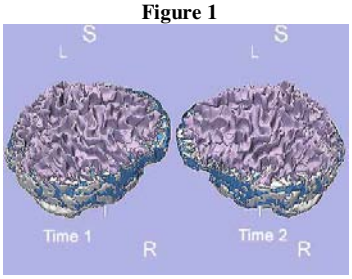

Figure 2

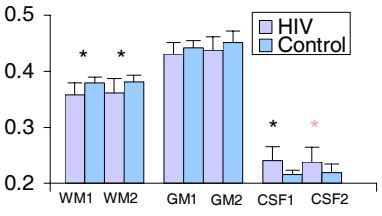

Figure 3

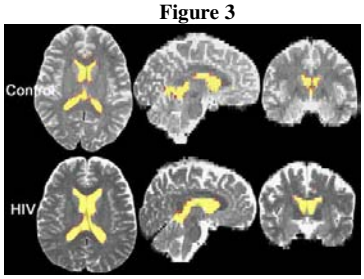

Figure 4

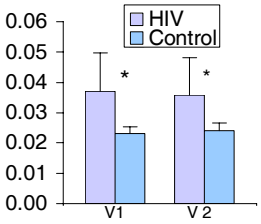

*Figure 1: 3D rendering of the FAST segmentation results of one brain two time points. Gray matter (in white color) and CSF (in blue color) were truncated to show the white matter (in purple color). Figure 2: comparison of tissue fraction in HIV and controls. * p<0.05. * p=0.098. Figure 3: segmentation results of ventricular CSF using SIENAX of one control case (the upper row) and a HIV case (the lower row). Figure 4: normalized ventricular CSF fraction of HIV and control group at both time points. * p<0.05.*

Table: Relationship between MRI tissue volumetric measurements and dementia severity

		WMF 1	GMF 1	CSFF 1	NBPV 1	NVF 1	WMF 2	GMF 2	CSFF 2	NBPV 2	NVF 2
MSK	CC	-0.53	-0.42	0.6	-0.35	0.64	-0.37	-0.54	0.53	-0.44	0.47
	p	0.01	0.06	0.004	0.11	0.001	0.13	0.02	0.02	0.06	0.05

Abbreviations: MSK= average Memorial Sloan Kettering rating across the study period; CC= Spearman correlation coefficients; WMF= white matter fraction; GMF= gray matter fraction; CSF = CSF fraction; normalized brain parenchyma fraction; NVF= normalized ventricular CSF fraction; V= ventricular CSF; 1= time 1; 2= time 2.

DISSCUSSION: Other investigators have identified parenchyma fraction changes in HIV infected patients using quantitative, volumetric MR strategies [(5-6).] This comprehensive volumetric study utilized SIENAX, a highly integrated algorithm that normalizes each individual brain into a standard space to overcome the problem of head size variation. In addition, SIENA was used to correct for changes in imaging geometry across different scan sessions for more accurate determination of the degree of brain atrophy measured in longitudinal investigations. These fully automated segmentation algorithms also minimize operator-introduced variation. The investigation indicates consistent findings of brain atrophy in HIV infected patients, including abnormally reduced normalized brain parenchyma, reduced white matter and increased CSF volume fractions, at both studied time points. These findings indicate brain shrinkage, with more prominent white matter tissue loss in HIV subjects. Volumetric measurements determined with automated segmentation algorithms also demonstrated a general pattern of significant relationships with clinical dementia severity at both assessments. While HIV patients demonstrated clear loss of brain tissue, the degree of change observed across a one year period was not significantly different in the two groups. This pattern is consistent with the protracted evolution of brain injury in HIV patients.

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