Increased brain diffusion in the genu of HIV patients at one-year follow-up

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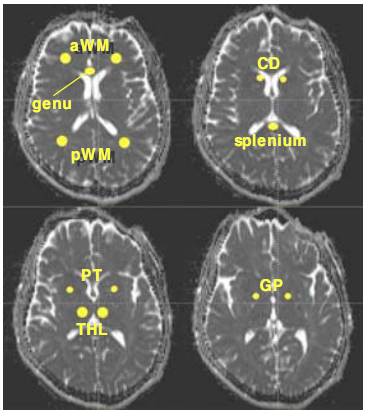
INTRODUCTION: MR diffusion tensor imaging (DTI) is able to detect cerebral white matter inflammatory changes and demyelination associated with HIV-1 infection.[1-5] Previous cross-sectional studies found increased mean diffusivity (MD) and decreased fractional anisotropy (FA) in multiple brain regions of HIV subjects compared to control subjects, most consistently in the genu of the corpus callosum. In this current study, DTI changes in the brain were evaluated at baseline and at one-year follow-up in a group of medication-stable HIV subjects and in HIV-seronegative controls.

METHODS: Participants included 23 HIV-1 positive subjects (HIV+, aged 49±2*, 36-67 years) and 15 HIV-seronegative controls (SN, aged 44±4, 22-72 years). Each subject was evaluated clinically and with neuropsychological tests at baseline and at one-year follow-up visit. MR scans were performed on a 3T Siemens Trio scanner, using a spin-echo DTI sequence (EPI, TR/TE = 3700/88 ms, b=[0,1000] s/mm^2, 12 directions). Apparent diffusion coefficient (ADC) and FA maps were calculated and regions of interest (ROIs) were manually drawn in a standardized fashion using DTI-Studio version 2.03 (**Figure 1**).[6] ROIs included the genu and splenium of the corpus callosum, anterior (aWM) and posterior white matter (pWM), thalamus (THL), caudate (CD), putamen (PT), and globus pallidus (GP). Repeated measures ANOVA was used for group comparisons.

Figure 1: Regions of Interest for MD and FA Measurements



RESULTS: Clinical: HIV+ subjects had similar clinical status at baseline and one-year follow-up: mean CD4+ cell count: 431±49 vs. 474±53/mm^3, nadir CD4+ cell count: 187±27 vs. 183±27/mm^3, plasma viral load was undetectable in 14 subjects at baseline and 17 subjects at one-year follow-up, HIV dementia scale 14.7±0.4 vs. 14.5±0.4, Karnofsky score 93.9±2.1 vs. 90.5±2.3, and clinical AIDS dementia stage 0.20±0.06 vs. 0.25±0.07. We also computed a global composite cognitive score (1-9; 1=no deficit, 9=severe deficits) for each subject based on neuropsychological tests: SN 4.1±1.0 vs. 2.9±0.7, HIV+ 5.8±0.6 vs. 4.4±0.6. Center for Epidemiological Scale-Depression score: SN 5.7±1.5 vs. 6.9±1.9, HIV+ 10.5±1.9 vs. 13.5±1.9. **DTI:** ***MD:*** The ANOVA revealed a main effect of time (p=0.020) in MD across all subjects, showing significantly increased MD from baseline to one-year. In a further analysis by region, the genu showed a significant time by HIV-status interaction, in that the MD increased 2.4% in the HIV+ subjects over time, but decreased by 0.9% in the SN controls (p=0.028) (**Figure 2**). The frontal white matter showed a significant main effect of HIV-status (p=0.017), with a greater MD in HIV+ subjects as compared to SN controls, but no interaction with time. ***FA:*** The ANOVA did not reveal a main effect of time or HIV-status across all ROIs. The frontal (p=0.048) and posterior white matter (p=0.009) showed a significant main effect of HIV-status, with a lower FA in HIV+ subjects as compared to SN controls, but no interaction with time. Although the time by HIV-status interaction was not significant in the genu, the FA decreased by 1.4% over time in the HIV+ subjects relative to the unchanged SN controls (p=0.30) (**Figure 3**).

DISCUSSION: Over one year, HIV+ subjects showed significantly increased MD in the genu relative to SN controls, while all other regions did not show interactions. This finding suggests that the genu is most sensitive to white matter changes associated with HIV infection, and that these changes can be detected within a one-year follow-up period. One recent cross-sectional study that included a relatively large number of HIV+ subjects (N=60) also found significantly higher MD and lower FA in the genu without significant differences in other brain regions.[4] Another study focusing on the corpus callosum showed significant abnormalities in the genu but not in the splenium when comparing HIV+ and AIDS patients.[2] The sensitivity of the genu in detecting white matter damage associated with HIV infection suggests the potential for early detection of HIV-associated dementia using DTI techniques, and the use of these techniques to monitor disease progression or treatment effects.

Figure 2

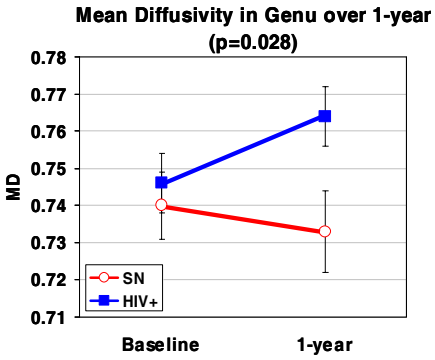
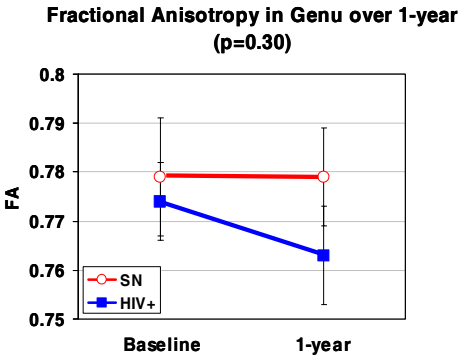


Figure 3



ACKNOWLEDGEMENTS: Study supported by NIMH and NIDA (2R01MH61427; K24-DA16170; K02-DA16991). We would like to thank Kenneth Yue, PhD; Daniel Alicata, MD, PhD; Kylie Abe, BA; Kalpana Kallianpur, PhD; and Renat Yakupov, MS for their assistance.

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* Means and standard errors are reported throughout.