Greater attentional modulation in HIV patients: A one-year follow-up study

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INTRODUCTION: Prior fMRI studies show increased brain activation during working memory and attention tasks in HIV patients with or without cognitive impairment.[1-3] Stable antiretroviral treatments may control the viral replication and partially restore immune function; however, at least 20% of HIV-infected individuals continue to demonstrate cognitive deficits, which may worsen with increasing age. A prior study demonstrated age-related increases in BOLD activation (compensatory response) during attention tasks in neuroasymptomatic HIV patients, but those with cognitive deficits showed age-related decline in brain activation in the parietal regions, possibly due to their inability to compensate.[4] The current study further evaluates the aging effect on brain function in HIV and control subjects at baseline and after one-year.

METHODS: All 46 HIV-infected and 32 seronegative controls (SN) were evaluated clinically and with fMRI at baseline and one year later. The two groups had similar ages (48±1.3, 28-67 years vs. 47±2.3, 21-71 years) and education (14.9±0.4 vs.15.5±0.4 years)]. Each subject performed fMRI during a set of visual-attention tasks with increasing levels of difficulty (tracking 2, 3, or 4 amongst 10 moving balls).[2,4] fMRI was performed at 3 T (Siemens Trio) , using single-shot gradient-echo EPI (TE/TR=30/3000ms, 3 mm slices, 1 mm gap, typically 42 axial slices, 64^2 matrix, 20cm FOV, 126 NEX). Task performance and subject motion were monitored in real-time during fMRI, to assure accuracy >80% and motion <1mm-translations and <1°-rotations. Motion and distortion corrections were performed on the scanner. After spatial normalization to the Talairach frame and spatial smoothing, activation maps and changes from baseline vs. 1-year in each group, as well as group differences for brain activation changes after one year (aging effect), were calculated with SPM2.

RESULTS: Clinical: All except 7 HIV subjects at baseline, and 3 of these HIV subjects at one-year, were treated with antiretroviral medications. Compared to baseline measurements, HIV subjects at one-year had relatively unchanged CD4 counts (412±32 vs. 456±35/mm^3), slightly lower nadir CD4 (158±20 vs.151±19), unchanged plasma viral load (Log 2.6±0.2 vs. 2.3±0.2 copies/mL), unchanged HIV dementia scales (14.3±0.2 vs. 14.4±0.3) and stable Karnofsky scores (93±1.2 vs. 91±1.2). **fMRI:** Task performance during fMRI was unchanged from baseline to 1-year follow-up on both % accuracy (>85% for all tasks) and reaction times in either subject group. All subjects showed similar activation patterns during the attention tasks. However, over 1 year, HIV subjects showed only increases in BOLD signals in the prefrontal and posterior parietal cortices (regions associated with load effects) bilaterally for all three tasks, while SN subjects showed decreased activation in the attention network for only the 3-ball task (Figure, Left). As a result, HIV subjects showed significantly greater increases after 1 year than SN controls (Figure, Center). Extracted BOLD signals from three regions of interest (ROIs) with group differences are shown in bargraphs (Figure, Right).

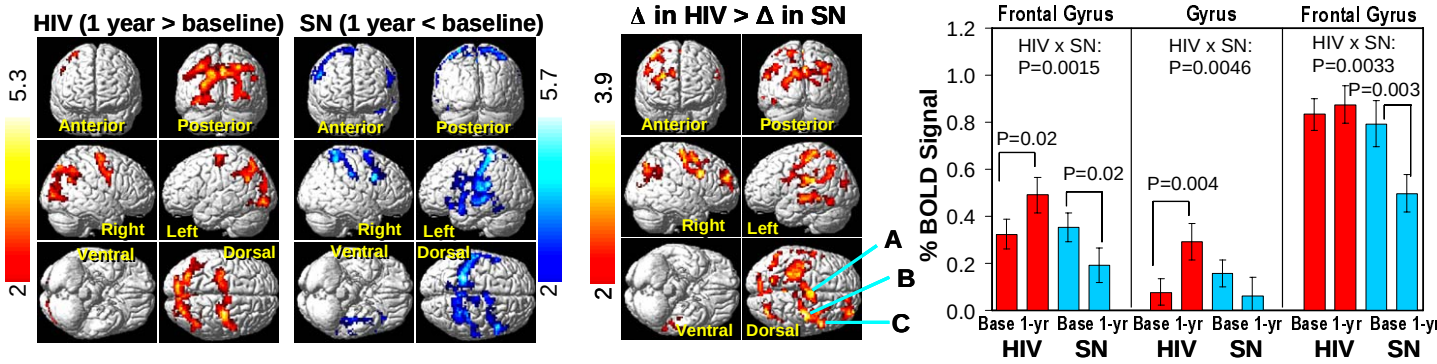

Figure: *Left*: Surface maps for the 3-ball tracking task show increased brain activation in SN controls (red regions) but decreased activation in HIV subjects (blue regions) after one-year (T ≥ 2.0, p<0.024, k>200 voxels). *Center*: Brain regions that show group differences in activation after one-year (T ≥ 1.67, p<0.05, k>200 voxels). *Right:* Bargraphs from ROIs at three cluster maxima (A: superior frontal gyrus, B: precentral gyrus, C: middle frontal gyrus) that showed group differences in BOLD signals after one-year.

DISCUSSION: In a group of clinically stable HIV subjects, we found increased brain activation in the load-associated regions of the attention network during a set of visual attention tasks over one year, while SN controls showed either no change or decreased brain activation within the attention network. These findings suggest greater attentional modulation, or a compensatory response, to maintain performance in the HIV subjects, while the SN controls probably demonstrated practice effect on some of the tasks after one-year. This suggests that HIV subjects do not become more efficient with repeat testing, unlike the control subjects, but appear to require greater usage of the brain reserve with aging even during a relatively short follow-up period of one-year. We will further evaluate the effects of cognitive functioning at baseline on longitudinal brain activation changes in HIV subjects.

ACKNOWLEDGMENTS: Studies were supported by the NIH (2R01-MH61427; K24-DA16170; K02-DA16991; 5P20-RR11091; G12-RR003061) and the ONDCP. We thank our research participants, and Drs. Cyril Goshima and Drew Kovach for subject referrals.

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