Abnormal Functional MRI in Cognitively Asymptomatic HIV Patients

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ABSTRACT: This study aims to determine whether HIV-1 positive patients with normal cognitive function show increased brain activation. Functional MRI (fMRI) was performed in 10 HIV-patients and 10 seronegative subjects, using three working memory tasks of increasing difficulty (0-back, 1-back, and 2-back). Compared to control subjects, HIV-patients showed greater % signal changes ($p \leq 0.001$) and increased activated volumes (450%, $p = 0.035$) in the lateral prefrontal cortex (LPFC), but not in other activated brain regions. Increased fMRI response in HIV-positive subjects with normal cognitive function precedes cognitive deficits, indicating preclinical injury to the neural substrate.

INTRODUCTION

Cognitive abnormalities occur in 20-40% of patients with AIDS (1). In a previous study, we observed pronounced increases in brain activation on fMRI in patients with early HIV dementia when compared to HIV-negative control subjects (2). We hypothesized that increased brain activation on fMRI may be present even in patients with normal cognitive function.

METHODS:

Subjects and tasks: fMRI was performed in 10 HIV-positive patients (age: 36.3 ± 7.9 years) and 10 seronegative subjects matched for age, education and handedness (age: 36.1 ± 6.8 years). The HIV patients had the following clinical characteristics: CD4 count: 375 ± 187/mL; log plasma HIV viral load: 3.36 ± 1.3 copies/mL; log CSF HIV viral load: 2.92 ± 1.2 copies/mL; Karnofsky score: 93 ± 5 (normal function = 100); HIV-dementia scale: 15.6 ± 0.6 (maximum 16). All HIV patients had normal cognitive function (ADC stage 0) and did not differ from control subjects on a battery of neuropsychological tests sensitive to HIV-CMC (3).

MRI-scans were performed at 1.5 T (GE SIGNA 5.8; SR 120). After aquiring high-resolution anatomic scans, fMRI was performed using single-shot gradient-echo EPI (TR 2500 ms, TE 60 ms, 16 slices, resolution 3*3*8 mm). Four periods of 30 s stimulation and 30 s rest were scanned twice for each subject and each task.

Data processing: SPM99 was used to create activation maps and BOLD difference maps (HIV patients minus control subjects; $T \geq 3.1$). Also, the number of activated fMRI voxels ($T \geq 3.1$) was determined for each subject in eight spherical VOIs (50mm Ø) in the L&R LPFC, L&R posterior parietal cortex (PPC), caudate, thalamus, SMA, and occipital cortex. The log-transformed volume data were analyzed using repeated measures ANOVA.

Table: Performance during fMRI (reaction times and % accuracy) on n-back tasks, and p-values (HIV+ vs. control subjects)

	0-back	1-back	2-back
HIV+ subjects	331±61 ms 99.3 ± 2.4 %	1471±98 ms 98.9±2.5 %	2402±126 ms 92.6± 5.3 %
Control subjects	337±41 ms 99.9±0.4 %	1481±47 ms 99.7±1.0 %	2532±154 ms 88.3±7.6 %
p-value	n.s./n.s.	n.s./n.s.	n.s./n.s.

RESULTS

1. HIV patients showed normal performance on all neurological and cognitive tests, as well as during the fMRI scans (see Table).
2. All subjects showed similar patterns of activation with each task, in the LPFC, PPC, caudate, thalamus, SMA, and the occipital cortex.
3. HIV patients showed significantly greater % signal changes compared to the control subjects predominantly in the LPFC ($p \leq 0.001$).
4. HIV patients showed increased activated brain volumes in the LPFC relative to controls (450%, $p = 0.035$). This increase in activated volume showed no significantly different dependence on task difficulty or hemisphere; see Figure.

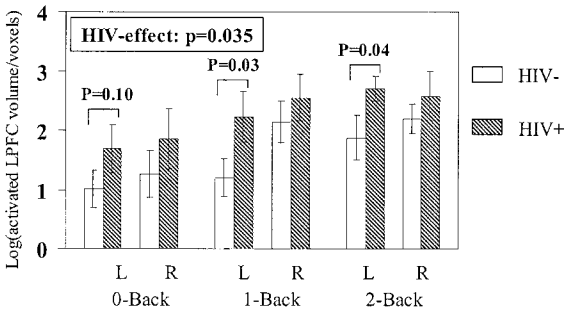

Figure: Activated brain volumes (log-transformed) in the left and right LPFC of HIV-positive and seronegative subjects. HIV patients show increased activation throughout the n-back tasks (p=0.035).

DISCUSSION

1. Increased brain activation in HIV patients with normal cognitive function may be interpreted as increased usage of brain reserve capacity in order to maintain normal working memory and other cognitive function.
2. Injury due to HIV in the neural substrate may have to reach a threshold before cognitive abnormalities can be detected clinically or on cognitive testing.
3. BOLD fMRI appears to be more sensitive than clinical evaluations or neuropsychological tests for detecting early neural deficits associated with HIV brain injury.
4. Future studies will focus on anitiretroviral medication-naïve HIV subjects, and evaluate the effect of HIV treatment longitudinally.

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