Longitudinal study of brain atrophy and lesions in HIV-infected patients

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Synopsis

Two sets of MRI scans were performed at an interval of approximately one year in eight HIV-infected patients and seven control subjects. The images were reviewed by a clinical neuroradiologist, and analyzed quantitatively for the volumes of brain parenchyma and CSF. Significant reductions in the percentage of brain parenchymal volume (PBV) were found in the HIV patients relative to the controls at both time points, and PBV measures were significantly correlated with clinical markers of neurological impairment. The rate of atrophic change across the one-year time period however did not differ significantly between the groups.

Introduction

Brain atrophy and white matter lesions are well-recognized characteristics of HIV dementia [1]. Results reported in this same subject cohort at the 2003 meeting of the ISMRM [2] showed a significantly lower percentage of brain parenchymal volume in the HIV-infected patients than in age-matched control subjects ($p<0.001$), and a significant correlation with Karnofsky performance status in the patients ($p<0.05$). To evaluate longitudinal changes in brain volume, a second set of scans was performed approximately one year after the first. The comparison between the two time points is the focus of the present report.

Materials and Methods

Imaging was performed in patients drawn from the Northeast AIDS Dementia Cohort Study [3], a longitudinal investigation of the natural history of neurologic impairment in HIV infection. Nine patients were enrolled in the MRI study, and all were in advanced stages of HIV infection, as determined by serology and CD4 counts. They all met the criteria for AIDS on the basis of a history of AIDS-defining illnesses, and were receiving antiretroviral therapy. They ranged in their degree of neurological impairment from 0 (normal) to 2 (probable dementia), on the scale defined by the AAN dementia classification. They had a mean age of 45.7 years (std 6.8, range 36 – 57), and included 2 blacks, 1 Asian and 6 whites, 2 women and 7 men. Nine control subjects were chosen to match the patients approximately in terms of age, ethnicity and gender. They had a mean age of 40.0 years (std 9.4, range 23 – 51) and included 2 blacks and 7 whites, 2 women and 7 men. Drug and alcohol use were not treated as exclusion criteria in either group. Of the original 18 subjects, 15 returned for a second scan, one of the patients having died, and two of the controls being unable to participate. The interval between scans was 394 ± 35 days (mean $\pm$ std).

Imaging was performed on a GE Medical Systems 1.5T Signa Infinity Twinspeed system using a fast spin echo sequence. Forty-four contiguous 3.5mm axial slices were used to cover the whole brain. Two images were acquired of each slice, with echo times of 25ms and 85 ms, resulting in different degrees of T_2-weighting. Other imaging parameters included: TR=3300ms, BW= ±20.83 kHz, echo train length = 10, NEX = 2, FOV = 24cm, matrix size = 256 x 256 with a phase FOV of 0.75.

The images were reviewed by a clinical neuroradiologist (JM), who qualitatively assessed lesions and brain atrophy (relative to the subjects' ages). The images were also analyzed quantitatively, as described earlier [2], to determine volumes of brain parenchyma and CSF, from which the PBV was calculated according to $\mathrm{PBV} \equiv V_{\mathrm{brain}} / \left(V_{\mathrm{brain}} + V_{\mathrm{CSF}}\right)$. To estimate the measurement uncertainty associated with the positioning of the slices (which in all cases covered the entire brain), one of the control subjects was imaged on different days within a two-week interval, providing a total of 4 data sets with varying slice placement.

Results

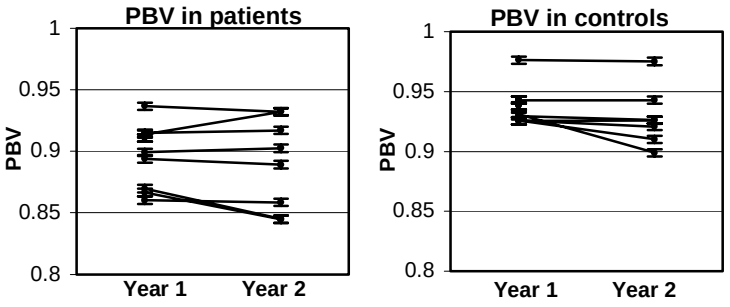
NEURORADIOLOGY FINDINGS

One of the control subjects showed a few punctate hyperintensities in the subcortical white matter, which appeared slightly more pronounced in the second year. Mild atrophy was noted in another control subject, but was reported to be stable between the first and second time points.

Of the patients, one was found to have moderate brain atrophy, and three to have mild atrophy for their age. In one with mild atrophy, the brain volume was reported to increase at the second time point, and in the others it was deemed stable. Lesions were found in four patients, three showing white matter hyperintensities, one having encephalomalacia, and one exhibiting chronic ischemic changes in the basal ganglion and subinsular region. No changes in the lesions were noted across the timepoints.

QUANTITATIVE ANALYSIS

Results of the quantitative estimates of PBV in the patient and control groups are shown in the graphs. The error bars indicate the measurement uncertainty in PBV associated with slice positioning, which was found to be about 0.003. Two of the patients showed large reductions in PBV (-0.022 and -0.025) while two others showed a small decrease (-0.005 in each case). The quantitative analysis confirmed the neuroradiologist's finding of a brain volume increase in one patient (0.018). Medical records show that this patient had temporarily stopping taking antiretroviral medications at the time of the first scan, and may have been taking steroids during that period for chronic obstructive pulmonary disease or HIV-related pneumonia. In the control group, two subjects were found to have large reductions in PBV (-0.032 and -0.016). The control subject with the largest reduction had reported marijuana dependence and alcohol abuse. One control subject who had begun chemotherapy treatment between the two time points showed a small decrease in PBV (-0.005).



The longitudinal PBV values for the HIV and control groups were submitted to repeated-measures analysis of variance. This showed a significant main effect for HIV-status ($F(1,13)=8.23$, $p=.01$), indicating reduced PBV values for the HIV subjects across both time points. The reduction in PBV in the patients relative to the controls was also statistically significant at each of the time points considered individually. There was however no significant interaction between HIV-status and brain volume change across the one-year time period. Examination of concurrent clinical measures of neurological impairment showed that PBV was significantly correlated at both time points with dementia severity (MSK stage) and Karnofsky performance status (a measure of the subject's ability to carry out activities of daily living). A correlation was also found with Beck depression scores, although this reached statistical significance only at the first time point. The volume measures were not significantly correlated with the degree of immune suppression in the HIV subjects (CD4 counts).

Discussion

While our results showed significantly lower PBV values in the HIV patients than the control subjects at both time points, there was no significant difference between the groups in the degree of brain volume loss over a one-year period. This may be due to the efficacy of the antiretroviral therapy, which has been associated with a reduction in the incidence of cognitive sequelae. Further study of the time course of atrophic changes in HIV should consider factors such as drug and alcohol use.

References

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