

## Frontal Lobe Atrophy Correlates with Nadir CD4+ Counts in HIV/AIDS: A Tensor-Based Morphometry Study of 210 Patients

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**Background:** 40% of HIV/AIDS patients experience minor to severe cognitive impairments, but the brain changes underlying this cognitive decline are still poorly understood. Using tensor-based morphometry (TBM), we set out to map, in 3D, the patterns of brain atrophy in a large cohort of 210 patients with HIV. We hypothesized that brain atrophy would be associated with nadir CD4+ counts; we also assessed associations with age, sex, education, viral load, and clinical measures of disease burden.

**Methods:** T1-weighted brain MRI scans were acquired from 210 AIDS patients scanned by the HIV Neuroimaging Consortium (mean age: 48.6±8.4 years; 175 men/35 women). A high-resolution average brain template was created to represent common anatomical features for the study population. All individual brains were non-linearly aligned to the brain template, using an inverse-consistent elastic intensity-based registration algorithm, to quantify 3D patterns of volumetric deviation. Maps of volumetric brain atrophy were created to illustrate regions of volume deficit or excess relative to the brain template, reflecting, in part, profiles of neurodegeneration. At each voxel within the brain, linear correlations were assessed between regional brain volume and (1) demographic variables: age, sex, education, and race; (2) clinical and immune system measures: ADC stage, current and nadir CD4+ T-cell counts, plasma HIV RNA, and duration of illness at the time of the MRI scan.

**Results:** After controlling for age, female patients showed greater frontal lobe atrophy than men, by 5-10% (FDR critical P=0.02). After controlling for both age and sex, non-Caucasian patients showed greater brain atrophy than Caucasian participants (FDR critical P=0.03). Lower nadir CD4+ count was associated with greater atrophy, in a broad region encompassing the frontal lobe white matter bilaterally (FDR critical P=0.03); for each 25-point reduction in nadir CD4+, there was a 2% greater deficit in frontal white matter volumes. Statistical effects of education and other clinical measures of HIV disease progression did not pass FDR correction for multiple comparisons.

**Conclusion:** TBM analysis of brain MRI provides a noninvasive measure of HIV-associated brain atrophy. Frontal brain atrophy was associated with immunosuppression,

suggesting one possible basis for impaired executive function in patients. These modulators of brain atrophy may be of interest for clinical trial design.