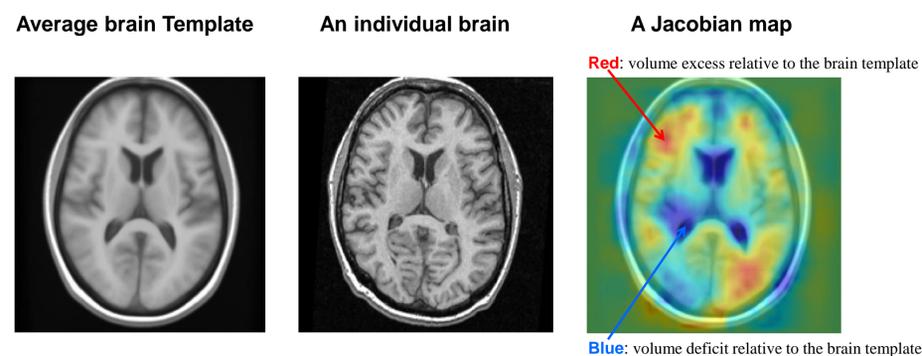


Introduction

Forty percent of HIV/AIDS patients experience minor to severe cognitive impairments, but the brain changes underlying this cognitive decline are still poorly understood. In patients with HIV/AIDS, cerebral metabolite abnormalities are known to correlate with total gray matter but not white matter volume (Cohen et al., 2010a). Nadir CD4+ T-cell counts have also been associated with total white matter volumes (Cohen et al., 2010b). To examine brain atrophy in greater detail, we used tensor-based morphometry (TBM) to map 3D patterns of brain atrophy in 210 patients with HIV. We hypothesized that regional white matter volumes would be associated with nadir CD4+ counts and brain metabolite measures of N-acetylaspartate (NAA), suggesting a link between prior immunosuppression and brain integrity.

Materials and methods

T1-weighted brain MRI scans were acquired from 210 patients with HIV/AIDS 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 (Leow et al., 2005). Maps were created to show regions of volume deficit or excess relative to the brain template, reflecting, in part, profiles of neurodegeneration. At each voxel in the brain, multiple regression was used to assess associations between regional brain volumes and (1) demographic variables: age, sex (2) immune system measures: current and nadir CD4+ T-cell counts (cells/μl), and (3) brain metabolite levels measured by proton magnetic resonance spectroscopy: NAA concentrations in the frontal white matter and basal ganglia in absolute units.



Results

Regression coefficient maps showing that Nadir CD4+ count is correlated with regional white matter volumes (FDR $q=0.05$, critical $P=0.03$)

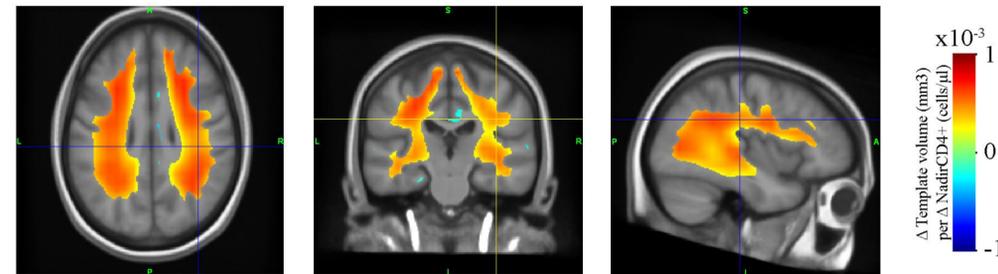


Figure 1. In brain regions where nadirCD4+ counts are significantly associated with white matter volume, the regression coefficients are shown at each voxel. These values represent the estimated degree of tissue deficit or excess at each voxel (in cubic millimeters relative to the template) that is associated with the measure of nadirCD4+ (cells/μl), after controlling for effects of age and sex on brain structure. Images are in radiological convention.

Regression coefficient maps showing that NAA levels in the frontal white matter are correlated with regional white matter volumes (FDR $q=0.05$, critical $P=0.03$)

a. Regression coefficient maps showing that NAA levels in the frontal white matter are correlated with regional white matter volumes (FDR $q=0.05$, critical $P=0.03$)

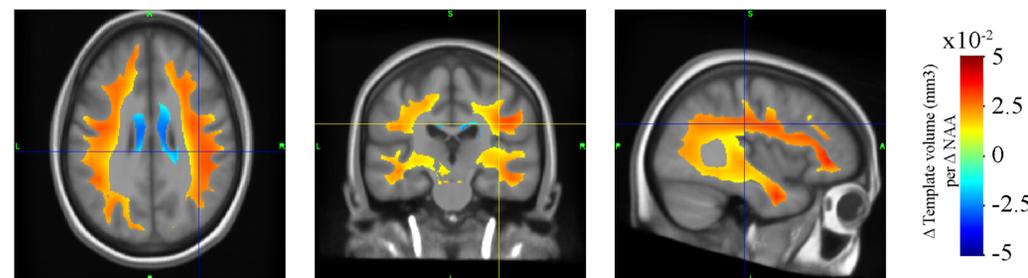
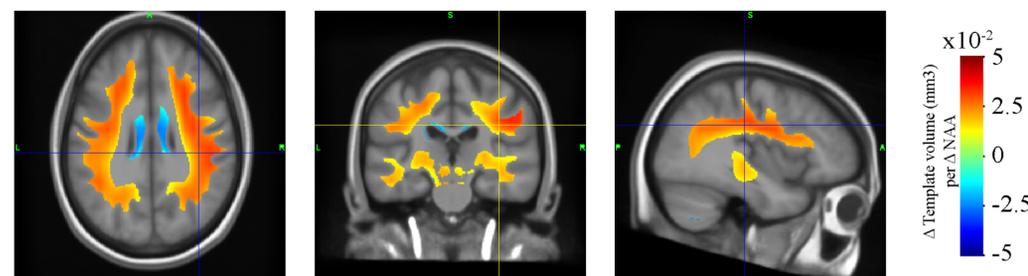


Figure 2. In brain regions where the absolute NAA concentrations are significantly associated with white matter volume, the regression coefficients are shown at each voxel. These values represent the estimated degree of tissue deficit or excess at each voxel (in cubic millimeters relative to the template) that is associated with the levels of NAA concentrations (in absolute units) in the frontal white matter (a) and basal ganglia (b), after controlling for effects of age and sex on brain structure. Images are in radiological convention and same slices are shown for (a) and (b).

b. Regression coefficient maps showing that NAA levels in the basal ganglia are correlated with regional white matter volumes (FDR $q=0.05$, critical $P=0.02$)



Conclusion

TBM analysis of brain MRI provides a noninvasive measure of HIV-associated brain atrophy. Brain white matter atrophy was associated with immunosuppression and a detectable disruption in brain metabolites that reflect neuronal integrity. These correlates of brain atrophy may be of interest for monitoring anti-retroviral treatment effects.