The Effects of Age and Study Cohort on Brain Structure Among Men with HIV Disease

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ABSTRACT

Background: Chronic HIV infection and advancing age are associated with decreased brain volume. However, as the HIV epidemic has changed since the introduction of combination antiretroviral therapy (CART), it is important to evaluate the effects of calendar period cohort recruitment on these relationships.
Methodology: 328 men (age: 50-75) enrolled in the MRI study of the Multicenter AIDS Cohort Study (MACS) underwent high resolution anatomical brain imaging (MP-RAGE at 3T field strength). The brain images from 281 met QC standards and were processed using a non-parametric correction of intensity non-uniformity (N3). Standard voxel-based morphometry (VBM) methods were run using Statistical Parametric Mapping (SPM5). Brains were segmented into grey matter, white matter and CSF compartments. The voxel-level analysis controlled for total intracranial volume and for MACS site.
Results: At the whole brain level, the HIV-infected men had significantly lower grey matter volumes (adjusted for intra-cranial volume) compared to the uninfected men (beta= -.16). Age was significantly associated with decreased grey matter volume (beta= -.20); there was no HIV-by-Age interaction. Figure 1 shows the VBM results projected onto the standard Colin27 template. The significant brain regions are shown with the t-statistics, thresholded at a False Discovery Rate of p<.05 (100 voxel extent threshold). Age was significantly associated with decreased brain volume across both cortical and subcortical regions (yellow areas in Fig. 1), including the caudate nucleus, ventral putamen, and the insular cortex. HIV disease was associated with atrophy in the basal ganglia, especially the putamen (marked in blue). The men who enrolled in the MACS in 2001/2003 had decreased brain volume in the anterior cingulate gyrus (red) relative to men who enrolled in the mid-late 1980s. There was no interaction between HIV Disease and cohort, and there was no interaction between Age and HIV Disease.
Conclusions: Although there are significant differences in brain volumes based on calendar period recruitment cohort, these effects did not interact with HIV serostatus. Within this study sample, the effects of age on brain volumes are more extensive than those associated with HIV Disease, suggesting that with survival to older age, more attention needs to be paid among infected individuals to age-associated risks for brain tissue loss.

BACKGROUND

Chronic HIV infection and advancing age are associated with decreased brain volume. However, as the HIV epidemic has changed since the introduction of combination antiretroviral therapy (CART), it is important to evaluate the effects of calendar period cohort recruitment on these relationships.

MATERIALS & METHODS

328 men enrolled in the MRI study of the Multicenter AIDS Cohort Study (MACS) underwent high resolution anatomical brain imaging (MP-RAGE at 3T field strength). The brain images from 281 met QC standards and were processed using a non-parametric correction of intensity non-uniformity (N3). Standard voxel-based morphometry (VBM) methods were run using Statistical Parametric Mapping (SPM5). Brains were segmented into grey matter, white matter and CSF compartments. The voxel-level analysis controlled for total intracranial volume and for MACS site.

SAMPLE CHARACTERISTICS

56.7% of the sample was HIV infected. 52.1% of the men who enrolled in the 19870s were HIV+, and 68.9% of the men who enrolled in 2001/2003 were infected at the time of the scan. The average age of the men was 57.5 years, with the men in C1 slightly older (58.5 yrs.) than the men in C2 (54.7 yrs.). 72.4% of the entire sample was Caucasian, with 90.3% of the men in C1 Caucasian, and 36.7% of the men in C2.

RESULTS

At the whole brain level, the HIV-infected men had significantly lower grey matter volumes (adjusted for intra-cranial volume) compared to the uninfected men (beta= -.16). Age was significantly associated with decreased grey matter volume (beta= -.20); there was no HIV-by-Age interaction. Figure 1 shows the VBM results projected onto the standard Colin27 template. Age was significantly associated with decreased brain volume across both cortical and subcortical regions, including the caudate nucleus, ventral putamen, and the insular cortex. HIV disease was associated with atrophy in the basal ganglia, especially the putamen. The men who enrolled in the MACS in 2001/2003 had decreased brain volume in the anterior cingulate gyrus relative to men who enrolled in the mid-late 1980s. There was no interaction between HIV Disease and cohort, and there was no interaction between Age and HIV Disease. However, regions of the anterior and posterior cingulate gyrus were particularly affected by these factors (lower right axial image, Fig. 2), with significant additive effects on the integrity of the cortical grey matter.

Figure 1: Effects of Age, HIV Disease and Cohort on Grey Matter
Masked Image

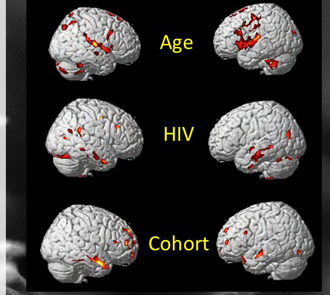
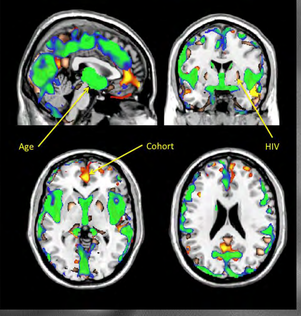


Figure 2: Overlapping Effects of Age, HIV Disease and Cohort



DISCUSSION

Although there are significant differences in brain volumes based on calendar period recruitment cohort, these effects did not interact with HIV serostatus. Within this study sample, the effects of age on brain volumes are more extensive than those associated with HIV Disease, suggesting that with survival to older age, more attention needs to be paid among infected individuals to age-associated risks for brain tissue loss.

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