Abnormal Lung Function Associated with Abnormal Brain Structure and Function in HIV

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Background

Cognitive deficits and alterations in brain structure are associated with chronic obstructive pulmonary disease (COPD). Both cognitive impairment and COPD are non-AIDS-associated co-morbidities that are increased in HIV-infected individuals, but whether lung function abnormalities have an additional impact on brain function in HIV is unknown.

Materials & Methods

Study design: Prospective cohort study

Subjects: Multicenter AIDS Cohort Study (MACS) participants with pulmonary function and brain magnetic resonance imaging (MRI)

Methods: Participants underwent measurement of lung function, brain magnetic resonance imaging, and neuropsychological functioning. Pre-and post-bronchodilator spirometry and measurement of diffusing capacity of the lung for carbon monoxide (DLco) were performed in accordance with American Thoracic Society standards. Standard reference equations for predicted values were used for spirometry and DLco; DLco was corrected for hemoglobin and carboxyhemoglobin. Three-dimensional anatomical brain images were segmented by tissue type, and the whole brain gray matter analyzed using Voxel-Based Morphometry. All participants completed: 1) neuropsychological screening tests (Trailmaking and Digit-Symbol Substitution Task (DSST), 2) the MACS neuropsychological test battery, and 3) additional tests to aid in the classification of HIV-Associated Neurocognitive Disorder.

Analyses: Multivariate models were constructed to examine impact of HIV and lung function on brain atrophy and cognitive function. Abnormal lung function was indexed by DLco (<70% predicted) and forced expiratory volume in one second (FEV_1) (<80% predicted).

Table 1: Characteristics of Study Subjects

	HIV-infected	Uninfected Controls
Number	31	28
Education (Years)	18.5 (15.1)	16.5 (2.1)
Site (% Pitt)	58.8	28.6
Race (% Cauc)	80.1	85.7
Ever smoked (% Yes)	58.1	35.7
Diffusing capacity (mean % predicted)	.87 (.17)	.82 (.15)
Forced Expiratory Vol. (mean % predicted)	1.04 (.15)	.99 (.12)

Table 2: Characteristics of Study Subjects

	DLCOPP Abnormal	DLCOPP Normal
Number	10	49
Education (Years)	16.2 (2.0)	17.8 (12.0)
Site (% Pitt)	0.00	51.0
Race (% Cauc)	80.0	83.7
Ever Smoked (% Yes)	60.0	44.9
HIV Infected	55.1	40.0
Diffusing Capacity (mean % predicted)	.61 (.08)	.89 (.13)
Forced Expiratory Vol. (mean % predicted)	.94 (.18)	1.03 (.13)

59 men had both pulmonary function and MRI performed (**Table 1**). Individuals with and without abnormal lung function were similar in demographics with a tendency for those with abnormal lung function to be more likely to have smoked (**Table 2**).

The brain structural images were processed and analyzed using Statistical Parametric Mapping and Voxel Based Morphometry (VBM8). Linear regression models were used to identify the regions whose volumes were associated with lung function, age and HIV status, controlling for study site.

Results: **Figure 1** shows the areas of brain whose volumes were affected by age and lung function. Age had its most extensive impact on the integrity of the thalamus and nucleus accumbens, while FEV_1 had its effects in the caudate nucleus. There was no significant impact of HIV disease on brain structure. Numbers in Figure 1 are the β weights from secondary regression analyses.

We then extracted the volumes of these brain regions using a region-of-interest approach with FSL's subcortical segmentation routine (FIRST). Linear regression models of these volumes revealed that while HIV disease had a weak effect on caudate volume, age and FEV_1 were more important. Age and DLco were independently associated with the volume of the nucleus accumbens.

Figure 2 shows the relationships among the lung function, brain volumes and cognitive functions. Numbers in Figure 2 are the β weights from linear regression analyses. The Global Domain score and the Worst Domain score were both predicted by brain regional volumes – higher Domain scores mean greater impairment. Thalamic integrity is linked to the Global Domain, while n. accumbens volume is associated with the Worst Domain score. DLco is linked to *both* brain regions, while FEV_1 has an independent effect on the volume of the thalamus.

Results

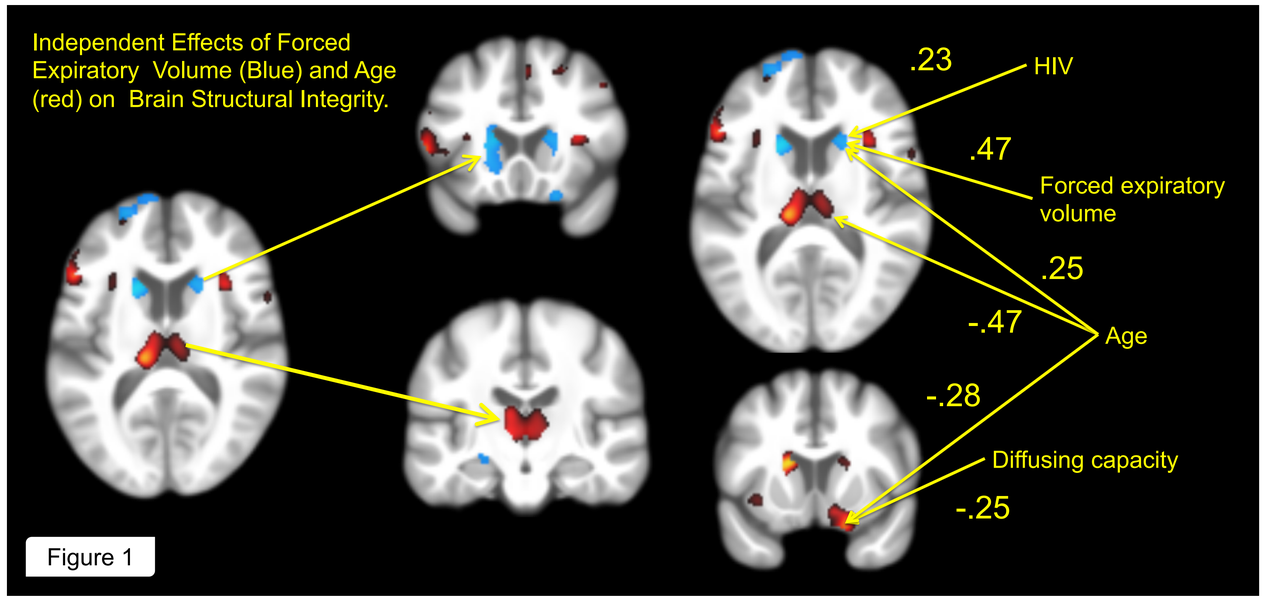


Figure 1

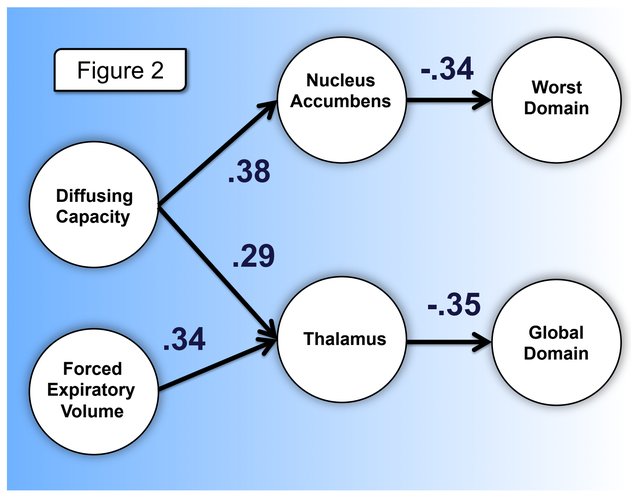


Figure 2

Conclusions

- Abnormal lung function is associated with significant brain regional atrophy, regardless of HIV serostatus.
- Decreased FEV_1 affects the volume of the thalamus, which in turn is associated with the global rating of cognitive function.
- Decreased DLco is linked to the integrity of the nucleus accumbens, which in turn affects both overall cognitive functions, and the extent of cognitive abnormality (regardless of cognitive domain).
- These data indicate that different aspects of measured lung function may have different effects on brain structural integrity.
- These data also add to the growing body of evidence that among HIV-infected individuals with access to appropriate medical care, the impact of HIV disease on brain structure is less than in the pre-cART era, and may be no more than that expected by lifestyle-associated comorbidities.

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