



LONGITUDINAL ASSESSMENT OF REGIONALLY SPECIFIC BRAIN VOLUMES IN TREATED HIV+ PATIENTS

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BACKGROUND

Combination antiretroviral therapy (cART) has transformed HIV from a fatal illness to a chronic condition. However, HIV-associated cognitive impairment remains prevalent [1]. The etiology of this brain dysfunction remains unclear because prior work has failed to determine whether the changes occur before starting cART or reflects ongoing injury [2].

RESEARCH OBJECTIVE

In this longitudinal study, we sought evidence of ongoing brain injury over two years from structural MRI and neuropsychological (NP) tests in treated HIV+ patients with well-controlled infections and good immunological recovery compared to demographically similar HIV- controls.

METHODS

Subjects

- 46 HIV+ and 31 HIV- participants.
- HIV+ subjects were on cART with well-controlled infections and no comorbid conditions.
- T1-weighted brain MRI and NP testing administered to all participants approximately 2 years apart.

Neuropsychological testing

- NP battery covered 6 cognitive domains with 8 standard tests.
- Standardized z-score for each test was calculated. NP summary score (NPZ8) was created by averaging z-scores across 8 tests.

Magnetic resonance imaging

- MRI data was processed with a robust longitudinal pipeline [3].
- Tensor-based morphometry (TBM) characterized local brain volumes at both visits.

Statistical Analysis

- Mixed effects models assessed the effect of HIV on brain volumes and NP performance with data from both visits, and determined if the infection had an effect on changes in brain volume and NP performance over time.

RESULTS

Table 1: Baseline demographics and clinical characteristics of participants.

	HIV+ (n=46)	HIV- (n=31)	p value
Age [years, mean (SD)]	47.3 (13.5)	51.2 (12.9)	0.23
Sex [n (% male)]	24 (52)	15 (48)	0.75
Ethnicity [n (%)]			0.10
White	15 (32)	16 (52)	
African-American	31 (68)	15 (48)	
Education [years, mean (SD)]	13.5 (3.3)	14.5 (2.1)	0.13
Current CD4 [cells/μl, median (IQR)]	641 (495, 885)		
CD4 Nadir [cells/μl, median (IQR)]	200 (40, 304)		
Estimated Duration of HIV infection [years, median (IQR)]	13.5 (5.3, 20)		
CPE Score [median (range)]	7.5 (5, 13)		

Neuropsychological Performance

- HIV+ patients had significantly worse NPZ8 scores at both visits compared to the HIV- group, with weaker scores in tests of executive function, attention and working memory and speed of information processing ($p<0.001$) (Figure 1).
- Change in NPZ8 over time was not significantly different between groups.
- Change in memory z-score over time reached trend level difference between the groups ($p=0.02$), where the HIV+ group had greater improvements than the HIV- group.
- HIV+ patients had significant decline in executive function over time ($p<0.001$), but the difference in change in executive function did not reach significance between the groups ($p=0.08$).

Brain Volumes

- TBM revealed significant volume reductions in thalamus, caudate, putamen, globus pallidus and midbrain in HIV+ patients at both visits ($p<0.05$) (Figure 2).

- No brain regions in the HIV+ group had significantly different rates of volume change compared to the HIV- group.
- Lower CD4 nadir correlated at trend level with smaller putamen, globus pallidus and thalamus volumes ($p<0.1$).

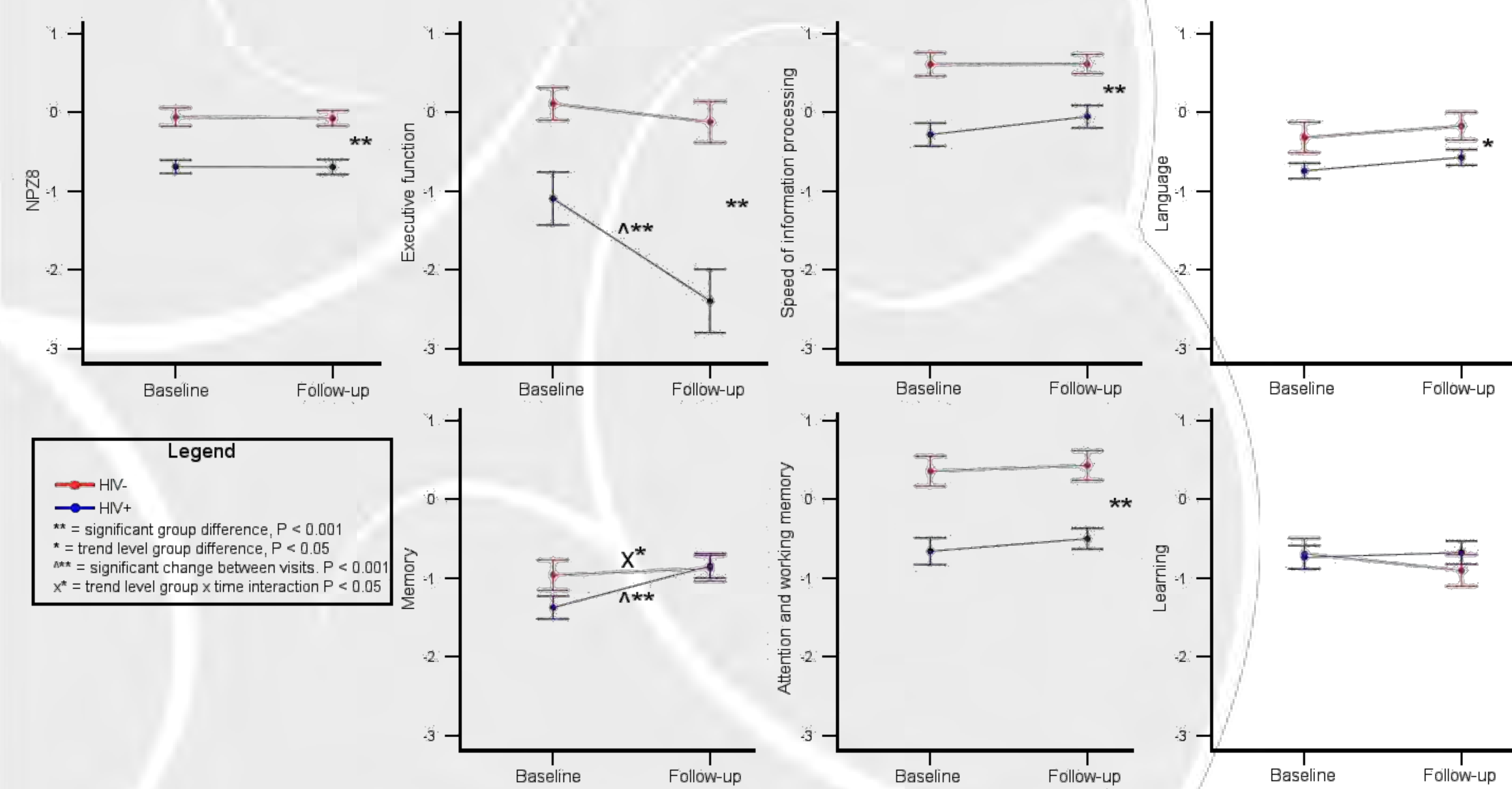


Figure 1: Neuropsychological performance in HIV+ and HIV- participants at baseline and follow-up visits.

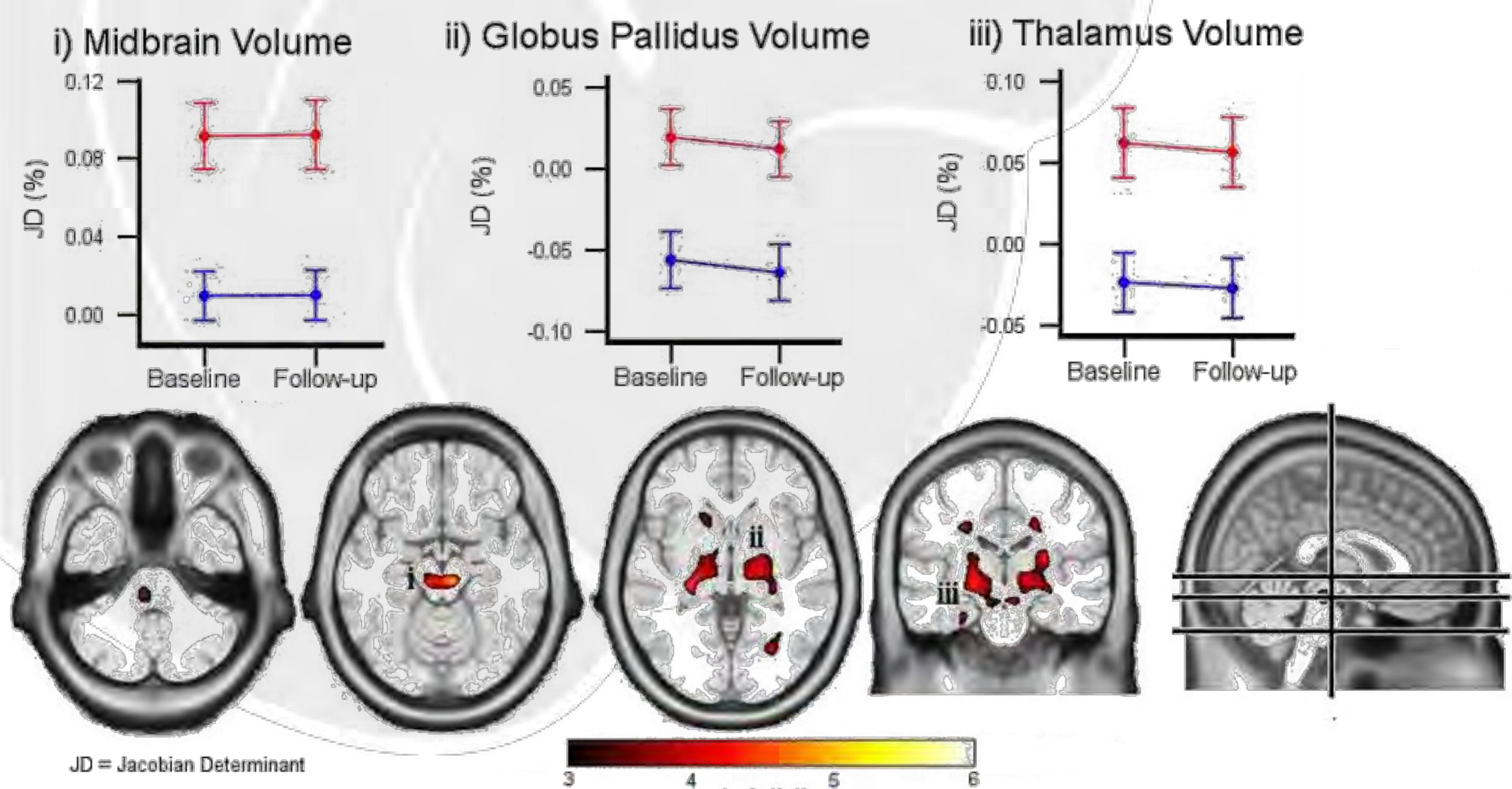


Figure 2: Subcortical volume reductions in HIV+ patients compared to HIV- individuals at both visits. The change in brain volume was comparable between the HIV+ and HIV- group over the study period.

DISCUSSION

- Regionally specific subcortical volume reductions and poorer cognitive performance were observed in the treated aviremic HIV+ group compared to demographically similar HIV- controls at both visits.
- No evidence of ongoing brain injury or overall cognitive decline were detected. The changes in brain volumes and cognition were comparable between the HIV+ and HIV- group over the study period.
- These results emphasize the importance of achieving full viral suppression to prevent the progression of brain atrophy in HIV and mitigate further brain dysfunction.
- These findings support the hypothesis that cognitive and structural brain differences in HIV+ patients most likely occurs during the period of untreated infection suggesting a possible neurocognitive benefit from early cART initiation.
- Further longitudinal studies with longer study periods and more diverse HIV+ cohorts are required to verify the results.

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