Brain Functional Connectivity Changes over 18 Months in Persons with Acute and Chronic HIV Infection

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BACKGROUND

- HIV enters the central nervous system soon after infection and produces long term effects, even in the cART era, especially for persons who remain untreated for a long period of time.
- Longitudinal evidence on functional connectivity changes in the course of HIV infection are limited, especially considering changes instigated by cART initiation.
- In this study we evaluate pre-post cART changes in treatment-naïve persons with acute or chronic HIV infection.

METHODS

- Newly diagnosed persons with HIV were prospectively enrolled in this study, excluding those with comorbidities relevant to brain or cognitive damage.
- Participants underwent a comprehensive neuropsychological evaluation covering 7 cognitive domains and
- resting-state functional MRI brain imaging at baseline and 18 months on a Philips Achieva 3.0 Tesla TX MRI scanner.
- Composite z scores per cognitive domain were calculated by averaging individual test scores (Learning/memory: GVLT/BVMT, Speed: TMTA/SDMT, Executive: TMTB/Stroop interference, Fluency: Phonemic/Semantic, Attention: Spatial Span, Letter-Number sequencing, Visuospatial: JLO, Motor: Grooved pegboard).
- Acute HIV was defined as evidence of seroconversion up to 6 weeks before diagnosis.
- Neuroimaging functional data pre-, post-processing and statistical analyses (statistical threshold: cluster level <0.05 FWE; voxel level <0.001 uncorrected) were performed using the CONN toolbox of Matlab. For between groups, pre-post analysis 2x2 mixed group factorial ANOVA was used.

RESULTS

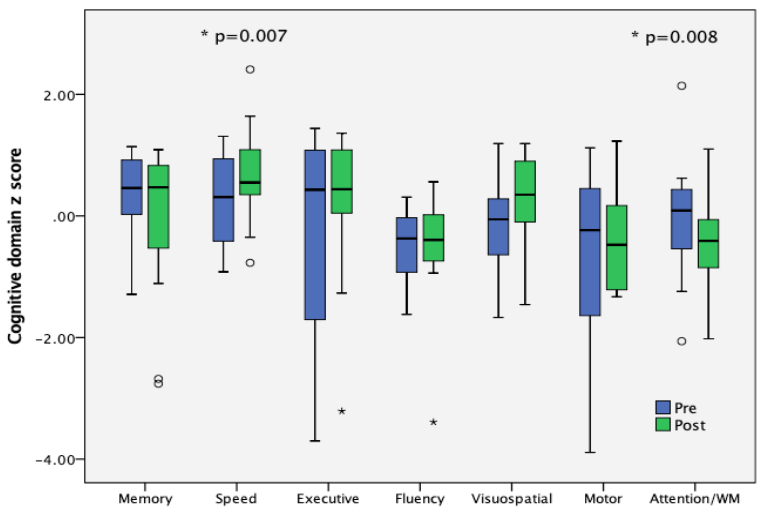
- 15 individuals (14 males) of white ethnicity with a mean (±SD) age of 36 (±10) years were enrolled (**Table 1**).
- Six persons showed evidence of acute HIV infection.
- At baseline CD4 count was 441 (±153) and log viral load 5.26 (±1). At follow-up, all patients had undetectable viral load.
- Significant changes from baseline to follow-up were detected for speed of processing (z-score 0.25 vs 0.69, p=0.007) and attention (-0.06 vs -0.46, p=0.008) (**Fig. 1**).

Table 1. Baseline characteristics

	Acute	Chronic	p value
Baseline demographics HIV infection characteristics	n= 6	n= 9	
Age (years)*	33.7 (±12.4)	37.9 (±8.9)	0.491^
Male (%)	5 (83.3)	9 (100)	
Typical education (years)*	14 (12-18)	15 (14-19)	0.394#
MSM (%)	5 (83.3)	9 (100)	
CDC Classification, n (%)			
0	6 (100)	-	
1	-	2 (22.2)	
2	-	6 (66.7)	
3	-	1 (11.1)	
CD4⁺ count (cells/μL)*	513 (421-710)	351 (289-487)	0.059#
CD8⁺ count (cells/μL)*	1752 (357-3140)	1024 (620-1446)	0.409#
CD4⁺/ CD8⁺ ratio*	0.34 (0.18-1.21)	0.36 (0.25-0.59)	1.0#
HIV RNA (log_{10} copies/ mL)*	5.8 (5.4-7.0)	4.6 (4.2-5.2)	0.013#
INSTI-based cART, n (%)	5 (83.3)	8 (88.9)	
Protease-based cART, n (%)	1 (16.7)	1 (11.1)	

Mann-Whitney U test; ^ Independent samples t-test

Figure 1. Pre-post cART neurocognitive changes in 7 cognitive domains over 18 months.



RESULTS (continued)

- Looking into intrinsic functional networks of the whole group, we found longitudinal alterations only in the **Dorsal Attention network**.
- The subgroup of chronic HIV did not show significant changes, whereas analysis between groups and across time identified functional differences in the **Salience**, **Dorsal Attention**, and **Frontoparietal networks**, that was driven from changes in the subgroup of acute HIV (**Fig. 2, Fig. 3**).

Figure 2. Pre-post cART functional connectivity changes between acute and chronic HIV, in the Salience (red), Frontoparietal (blue), and Dorsal Attention (magenta) networks.

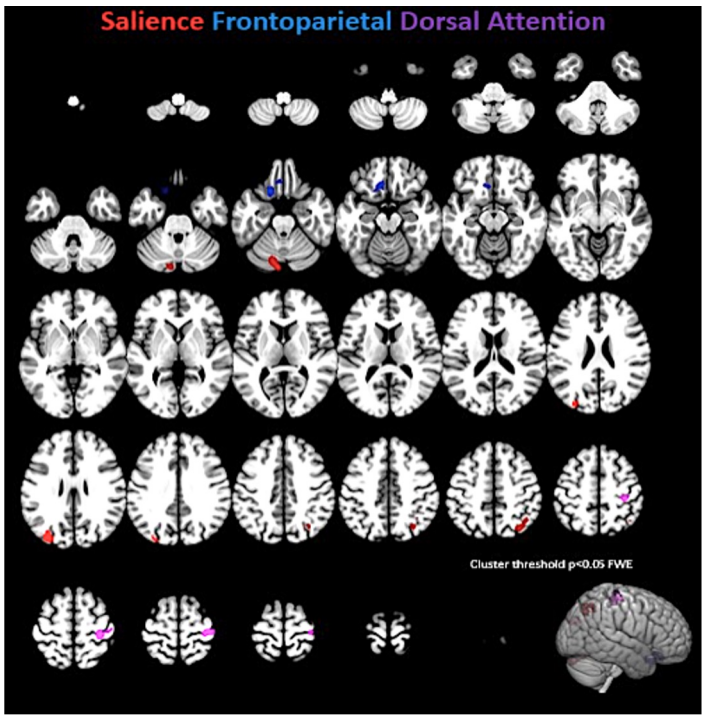
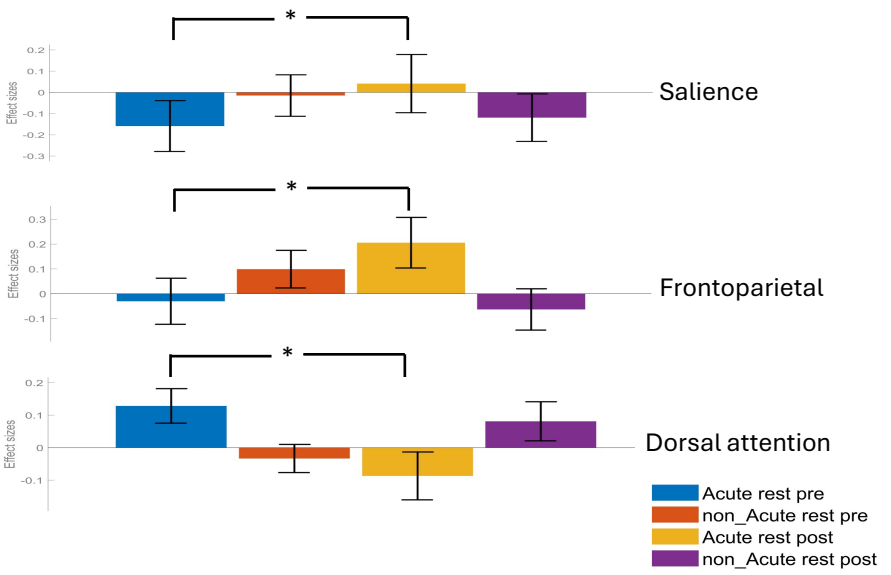


Figure 3. Pre-post cART functional connectivity effect sizes between acute and chronic HIV (pre-cART acute, blue; pre-cART chronic, red; post-cART acute, orange; post-cART chronic, magenta). *Statistically significant differences.



CONCLUSIONS

- **18 months after cART initiation, neuropsychological evaluation showed improvement in speed of information and decline in attention / working memory domains.**
- **After cART initiation, fMRI showed increased functional connectivity in salience and frontoparietal networks, and decreased connectivity in dorsal attention network in people with acute but not with chronic HIV infection.**
- **Data may suggest that in acute HIV infection cART should be started as soon as possible.**