4 Episodic Memory Deficits and Fronto-Limbic Correlates in Older Adults Living with HIV: Comparison to Parkinson's Disease and Normal Aging

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Objective: The prevalence of mild to moderate cognitive impairment, including episodic memory deficits, in people living with HIV (PLWH) remains high despite the life-extending success of antiretroviral pharmacotherapy. With PLWH now reaching near-normal life expectancy, questions concerning a potential synergy between age- and HIV disease-related effects, including degradation in fronto-limbic circuits, neural systems also compromised in Parkinson's disease (PD), have emerged.
Participants and Methods: This cross-sectional study examined the similarities and differences in component processes of verbal episodic memory and their neural correlates in 42 PLWH, 41 individuals with PD, and 37 controls (CTRL) (all participants aged 45-79 years). Learning over five trials, short-delay (SD) and long-delay, (LD), free-recall (FR) and cued-recall (CR) indices were assessed using the California Verbal Learning Test-2. Retention scores for FR and CR were derived adjusting for Trial 5 performance. All memory scores were age- and education-corrected based on the control group and reported as Z-scores. Regional brain volumes were calculated using 3T MRI data and the SRI24 atlas to delineate frontal (precentral, superior, orbital, middle, inferior, supplemental motor, and medial) and limbic (hippocampus, thalamus) regions. Brain volumes were age- and head-sized corrected based on 238 controls (19-86 years old).
Results: Compared with the CTRL group, the HIV and PD groups were impaired on learning across trials and on SD and LD free- and cued-recall, with no group difference between the HIV and PD groups on any score. All three groups benefited similarly from cues compared with free-recall. The HIV and PD groups did not differ from CTRL on retention scores. Regarding brain volumes, the HIV group had smaller middle frontal volumes than the PD or CTRL groups and smaller thalamic volumes than the PD group. Correlational analyses (Bonferroni correction for 8 comparisons, $p<.01$) indicated that fewer total number of words recalled on Trial 5, learning over Trials 1-5, total words recalled on SD-CR, LD-FR, and LD-CR were associated with smaller orbitofrontal volume in the HIV but not the PD group; the correlations between orbitofrontal volume and memory scores were significantly different between the HIV and PD groups. In PD, but not HIV, lower retention scores on SD-FR and LD-CR correlated to smaller hippocampal volume.
Conclusions: Impairment in learning and cued recall performance indicate that both encoding and retrieval processes are affected in PLWH and PD. Neural correlates of verbal memory differed between groups, with orbitofrontal volume associated with learning and recall in PLWH, whereas hippocampal volume was associated with retention scores in PD. Together, these results suggest that different nodes within the fronto-limbic mnemonic circuitry underlie the mutual verbal episodic memory deficits observed in older PLWH and PD.
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5 Combining Neurophysiology and Behavioral Measures to Identify Biomarkers of Clinical and Preclinical Hippocampus-Dependent Memory Dysfunction

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