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

Rosemary Fama[1,2], Eva M. Müller-Oehring[1], Taylor F. Levine[3], Edith V. Sulivan[1], Priya Asok[2], Stephanie A. Sassoon[2], Helen M. Bronte-Stewart[1], Kathleen L. Poston[1], Kilian M. Pohl[1], Adolf Pfefferbaum[1], Tilman Schulte[4]
[1]Stanford University School of Medicine, Stanford, CA, USA. [2]SRI International, Menlo Park, CA, USA. [3]Washington University in St Louis, St. Louis, MO, USA. [4]Palo Alto University, Palo Alto, CA, USA

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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Correspondence: Rosemary Fama, Ph.D., Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, rfama@stanford.edu

5 Combining Neurophysiology and Behavioral Measures to Identify Biomarkers of Clinical and Preclinical Hippocampus-Dependent Memory Dysfunction

Elizabeth Espinal[1,2], Akash Mishra[2], Evangelia G Chrysikou[1], Ashesh Mehta[2], Stephan Bickel[2]

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[1]Drexel University, Philadelphia, PA, USA. [2]Feinstein Institutes for Medical Research, Manhasset, NY, USA

Objective: Memory is a critical piece of the human experience and impairments in neural memory networks can have devastating consequences for the affected person. A subtype of memory, episodic memory generates context for the present based on past experience and allows us to make predictions about the future. Episodic memories become stable fixtures through long-term memory consolidation. It is believed that consolidation of episodic memory requires a dynamic interplay between connected hippocampal-cortical networks, mainly during sleep. Sleep oscillations, slow oscillations and thalamocortical spindles, coupled with hippocampal sharp wave ripples (SWR) is proposed to be mechanistically involved in establishing the crucial cortical-subcortical dialog. The current study aimed to determine alterations in typical sleep oscillations and oscillation coupling in patients with and without structural hippocampal damage and correlate them with neuropsychological measures believed to be sensitive to hippocampal dysfunction, i.e., Rey Auditory Verbal Learning Task (RAVLT) and Verbal Paired Associates (VPA-II).
Participants and Methods: We used intracranial electroencephalography (iEEG) in 14 patients with epilepsy to directly record hippocampal and neocortical oscillations and neuropsychological measures obtained prior to implantation. Half of the participants were diagnosed with mesial temporal sclerosis (MTS) in the left hippocampus and healthy tissue in the right hippocampus. The other half did not have MTS and had either mesial temporal epilepsy without MTS or extra-temporal seizures. We analyzed hippocampal SWR output from both hippocampi and characterized neocortical slow oscillations and spindles and their coupling for each participant. We correlated electrophysiological data with behavioral results of neuropsychological testing in order to characterize the clinical relevance.
Results: SWR analysis revealed significant differences in the frequency, $t(7639) = 15.52$, $p>.001$, $p > .001)$, amplitude, $t(7664) = -23.93$, $p > .001$, and waveforms ($p > .001$) of SWR in the sclerotic versus healthy hippocampi. Patients with a sclerotic hippocampus but relatively preserved verbal memory scores (RAVLT, VPA-II) showed increased SWR amplitudes in the contralateral hippocampus compared to patients with low verbal memory scores. Additionally, we found differences between hemispheres in phase amplitude coupling of SWRs to spindles and SOs ($p > 0.001$). Results of our correlational analysis were variable and dependent upon additional factors, such as age of onset and diagnosis duration.
Conclusions: Results from this work will aid in establishing a criterion for characterizing a relationship between subcortical and cortical oscillations as they relate to memory performance. Besides aiding our understanding of the neural mechanisms underpinning memory consolidation this will ideally help with developing neurophysiological biomarkers that may predict possible memory decline in resective or ablative neurosurgery absent of structural lesion. In addition, this work may potentially provide first evidence of a neurophysiological biomarker directly recorded from the human hippocampus to support possible reorganization of memory functioning in the non-sclerotic hippocampus.

Categories: Neurophysiology/EEG/ERP/fMRI
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Correspondence: Elizabeth Espinal, Drexel University, ee396@drexel.edu

6 Kynurenine/Tryptophan Ratio Moderates the Relationship Between Adiposity and Verbal Memory in Midlife

Cherry Youn[1], Barbara Strasser[2], Dietmar Fuchs[3], Hirofumi Tanaka[1], Andreana P Haley[1] [1]The University of Texas at Austin, Austin, Texas, USA. [2]Sigmund Freud University Vienna, Vienna, Austria. [3]Innsbruck Medical University, Innsbruck, Austria

Objective: Tryptophan is an essential amino acid and precursor to several compounds of neurobiological significance, including serotonin, melatonin, and nicotinamide adenine dinucleotide. However, the tryptophan-kynurenine metabolic pathway exhibits “double-edged sword” effects on neurons with

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