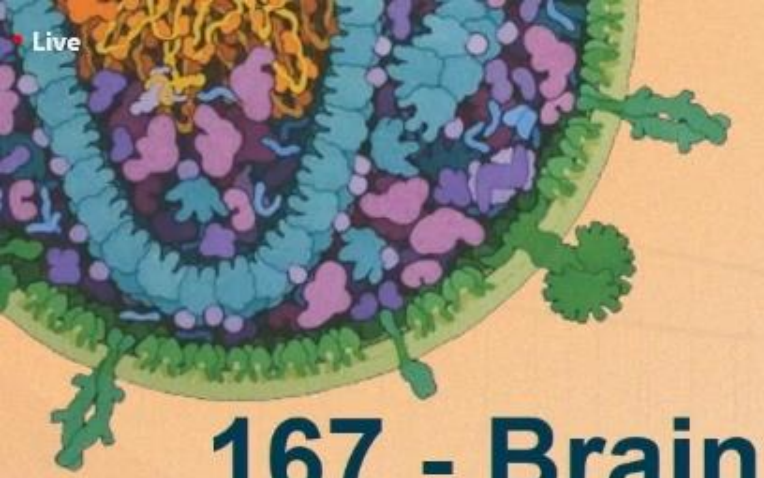

Oral Abstract Session-09

Wednesday, March 12, 2025

167 - Brain Volume Normalization After 96 weeks of ART Started During Acute HIV Infection

Robert Paul

University of Missouri St Louis, St Louis, MO, USA

Disclosure: Dr Paul has no financial relationships with ineligible companies to disclose.

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Authors and Affiliations

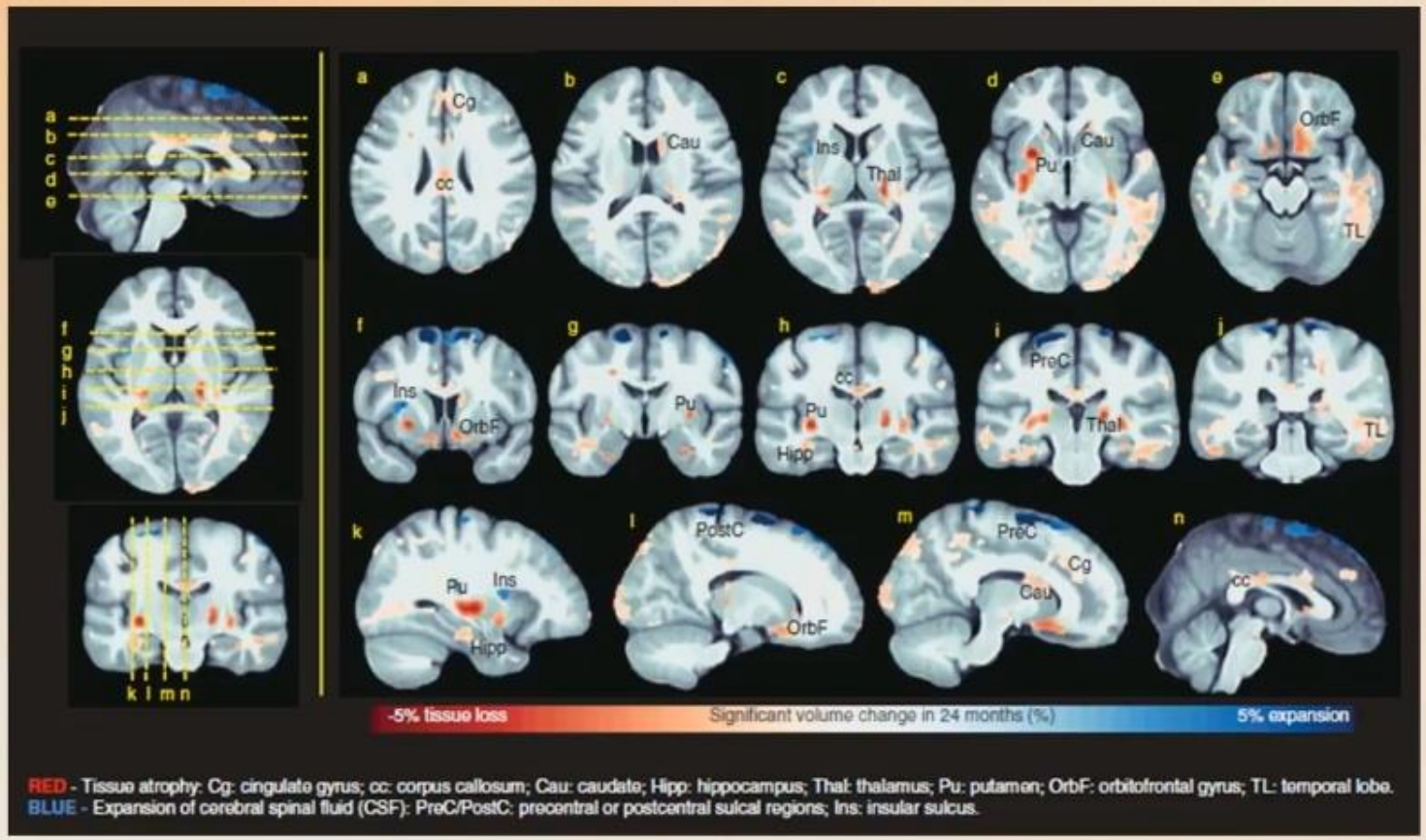
Robert Paul[1], Jacob Bolzenius[1], Phillip Chan[2], Carlo Sacdalan[3,4], Eugène Kroon[3,4], Pathariya Promsena[3], Donn Colby[5,6], Somchai Sriplienchan[3], Pom Sailasuta[7], Sandhya Vasan[5,6], Lydie Trautmann[5,6], Victor Valcour[8], Serena Spudich[2], on behalf of the RV254/SEARCH 010 Study Team

1. Department of Psychological Sciences, University of Missouri-St. Louis, St. Louis, MO, USA
2. Department of Neurology, Yale University School of Medicine, New Haven, CT, USA
3. Yale Center for Brain and Mind Health, Yale University School of Medicine, New Haven, CT, USA
4. SEARCH Research Foundation, Bangkok, Thailand
5. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD, USA
6. Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA
7. John A. Burns School of Medicine, University of Hawaii
8. Department of Neurology, Weill Institute for Neurosciences, University of California, San Francisco

Background

- Published findings from RV254/SEARCH 010 revealed atrophy in the putamen, caudate, and thalamus after 96 weeks of ART initiated during acute HIV infection (AHI)

  Kallianpur et al. AIDS, 2020



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Density of PSGL-1-expressing inflamma tory (CD14+CD16+) monocytes correlated with putamen atrophy.

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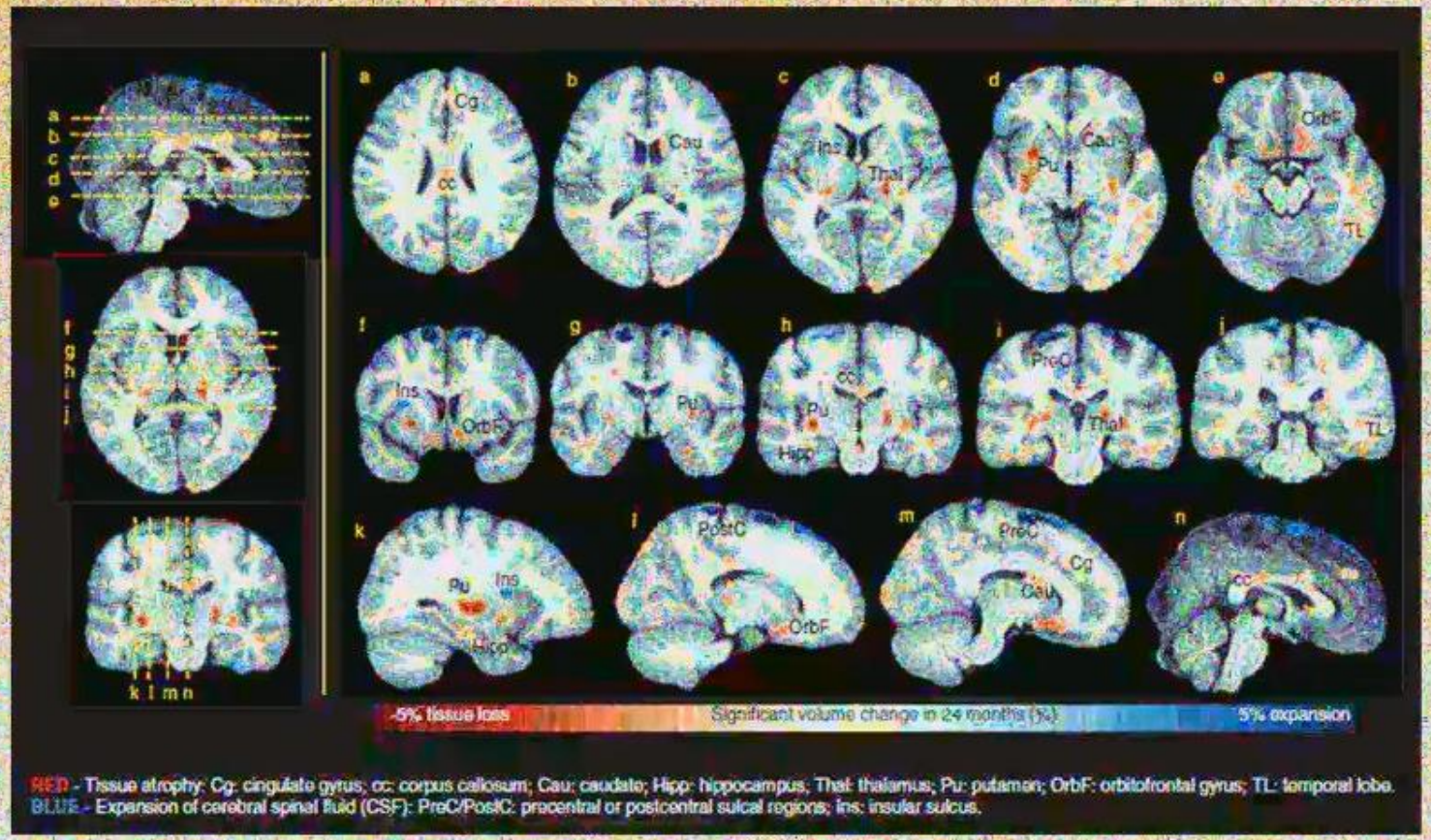


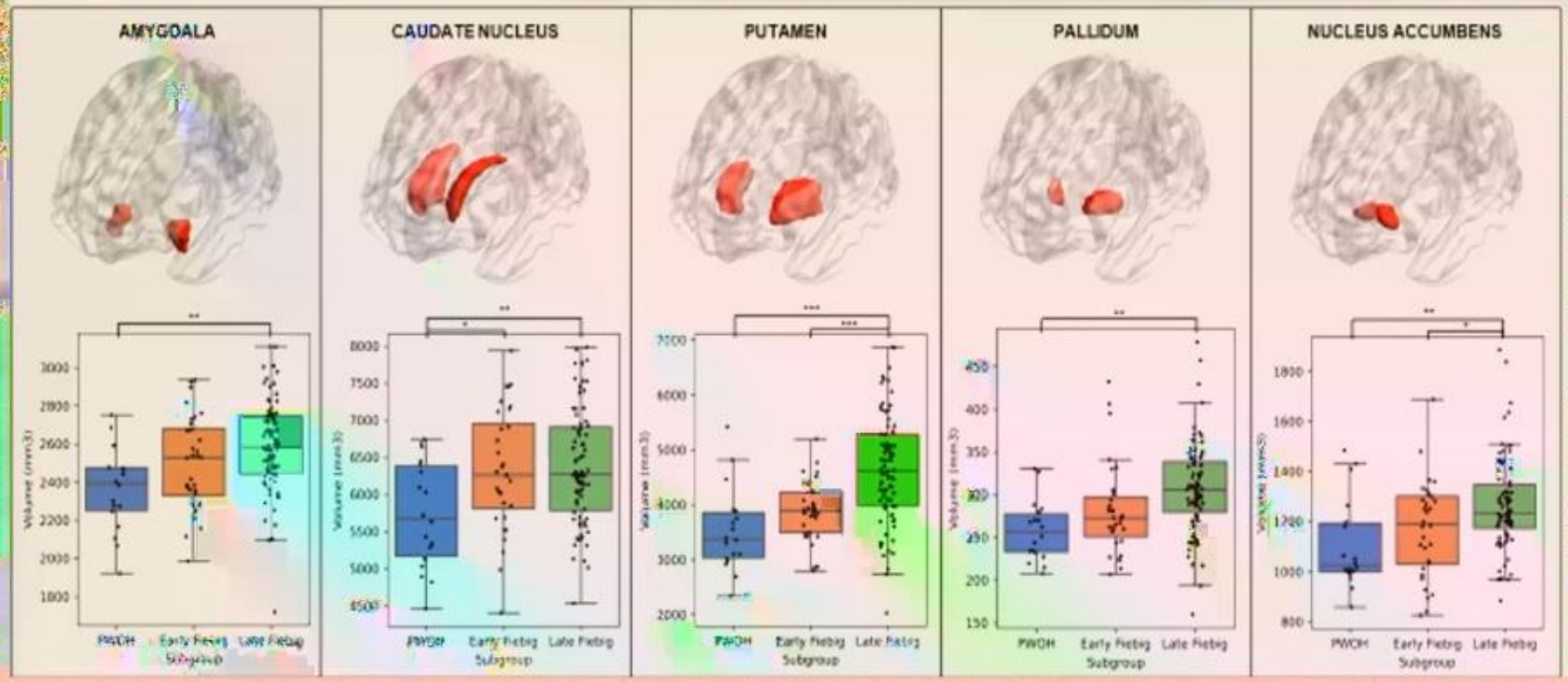
RED - Tissue atrophy: Cg: cingulate gyrus; cc: corpus callosum; Cau: caudate; Hipp: hippocampus; Thal: thalamus; Pu: putamen; OrbF: orbitofrontal gyrus; TL: temporal lobe.
BLUE - Expansion of cerebral spinal fluid (CSF): PreC/PostC: precentral or postcentral sulcal regions; Ins: insular sulcus.

Higher frequency of P-selectin glycoprotein ligand-1 expressing total monocytes correlated with caudate atrophy.

Density of PSGL-1-expressing inflammatory (CD14+CD16+) monocytes correlated with putamen atrophy.

- No comparison group
- Inconsistent with better cognition after ART initiated during AHI.

- Follow-up study revealed larger regional brain volumes during later Fiebig (III-V) compared to early Fiebig (I-II). **Bolzenius et al., 2023**



Possible that immune perturbations during later Fiebig result in brain hypertrophy during acute infection that normalize after ART.

Present analysis: Determine if brain volumes normalize or atrophy after ART when compared to demographically similar people without HIV.

Methods

- 3T MRI at week 0 (time of enrollment into RV254) and after 96 weeks of viral control following ART initiated during AHI.
- Volumes were quantified using voxel-based morphometry of170 ROIs summed across hemispheres.
- Repeated measures compared volumes within and between groups. We also examined associations between brain volumes with indices of mood and cognition at each time point as well as change over time.

Results

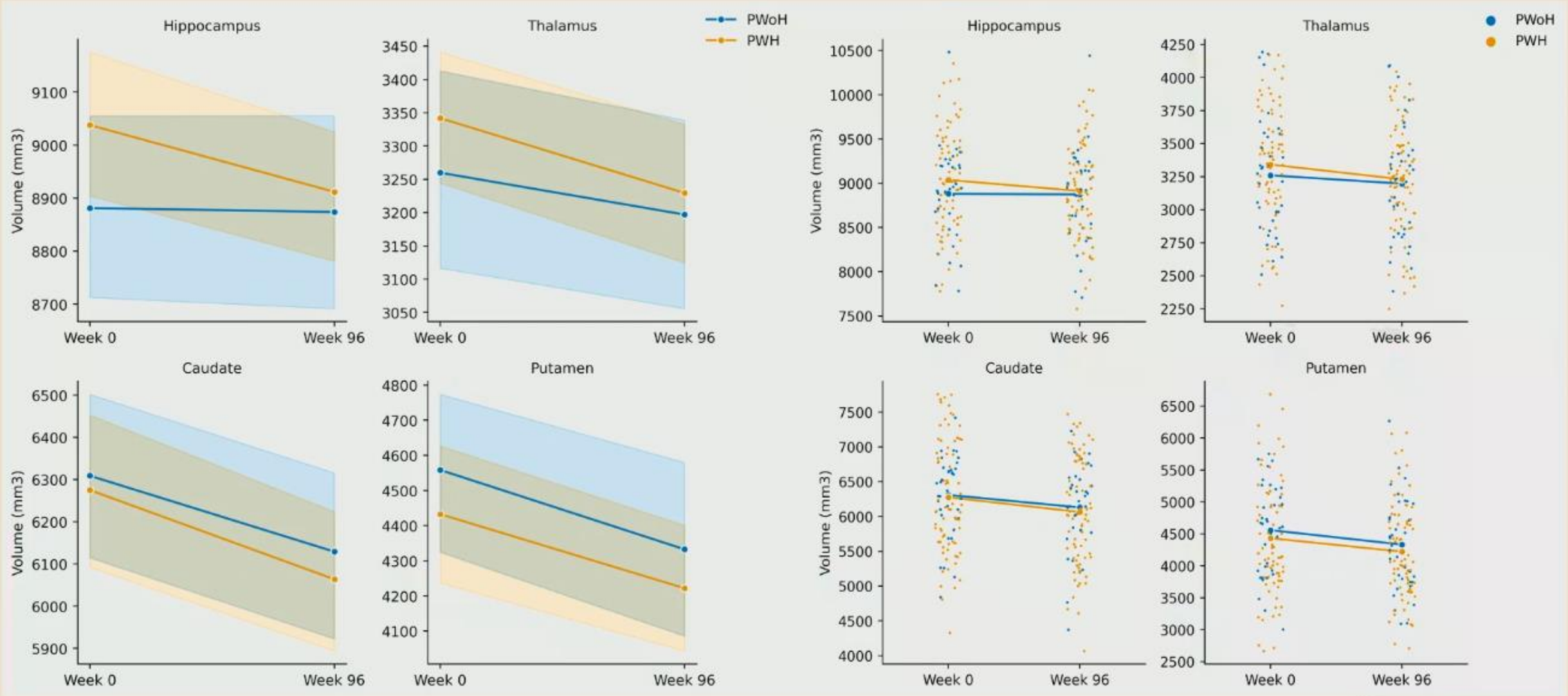
N = 109	PWH (n=74)	PWoH (n=35)
Age; M (SD)	28.82 (7.65)	28.91 (5.97)
Education; n (%)		
Secondary school or less	4 (6.3%)	0 (0%)
High school/technical school	20 (21.2%)	6 (19.4%)
Bachelor's degree or higher	40 (62.5%)	25 (80.6%)
Baseline viral load, log10; Median [IQR]	6.13 [5.43-6.79]	n/a
Baseline CD4 count; Median [IQR]	344 [246-477]	713 [600-924]
Baseline CD8 count; Median [IQR]	610 [341-879]	656 [537-844]
Fiebig I-II; n (%)	25 (33.8%)	n/a
Fiebig III-V; n (%)	49 (66.2%)	n/a
"Chem Sex"; n (%)	18 (24.3%)	n/a
PHQ-9; M (SD)	8.53 (4.88)	0.26 (0.85)

Change in brain volumes by serostatus

Region	PWH (n=74)	PWH Δ	PWoH (n=35)	PWoH Δ	Serostatus over time
Caudate	-211.2 (361.3)	<.001	-179.8 (226.0)	<.001	.740
Putamen	-210.9 (622.5)	.005	-225.8 (387.1)	.002	.449
Pallidum	-7.5 (34.4)	.068	-7.9 (31.0)	.141	.942
Hippocampus	-125.8 (200.1)	<.001	-7.4 (172.5)	.802	.388
Amygdala	+26.2 (134.8)	.099	-31.7 (98.0)	.064	.073
Thalamus	-112.4 (176.0)	<.001	-62.9 (130.5)	.007	.524
Nucleus Accumbens	-2.9 (125.9)	.844	-41.5 (94.9)	.014	.248

Values represent change (i.e., negative number=decrease, positive number=increase). Volume in mm^3.

Brain volume slopes by serostatus



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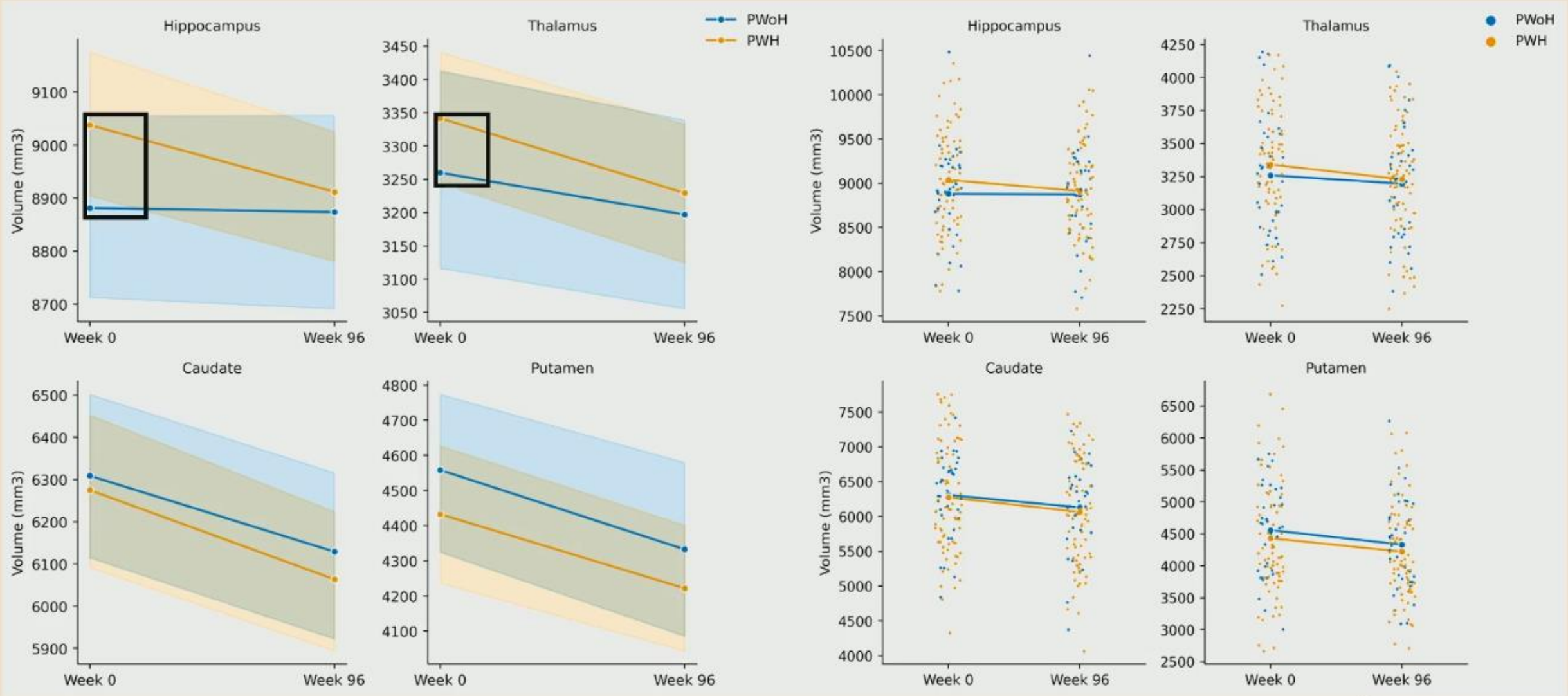
Brain volume slopes by serostatus



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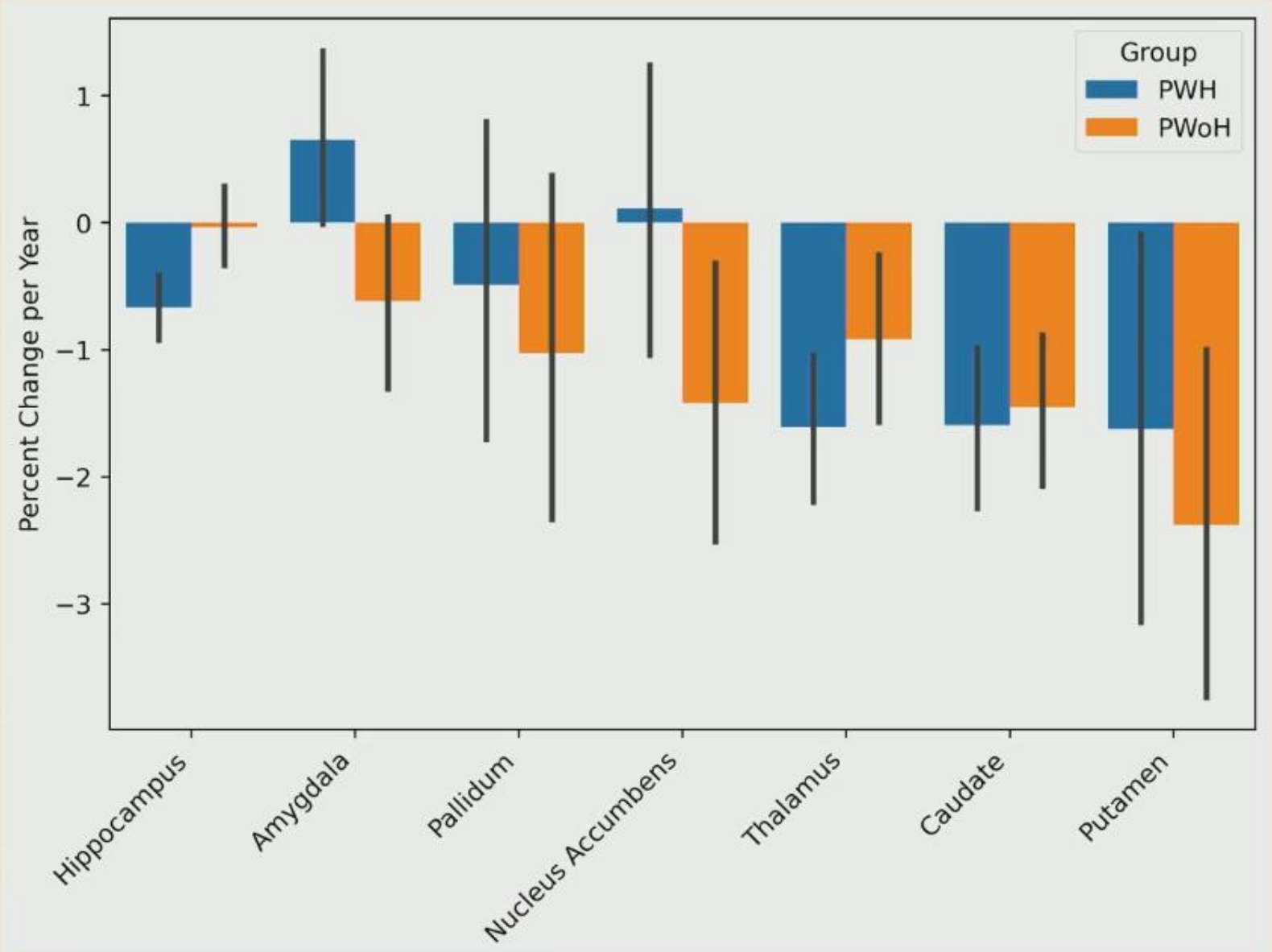
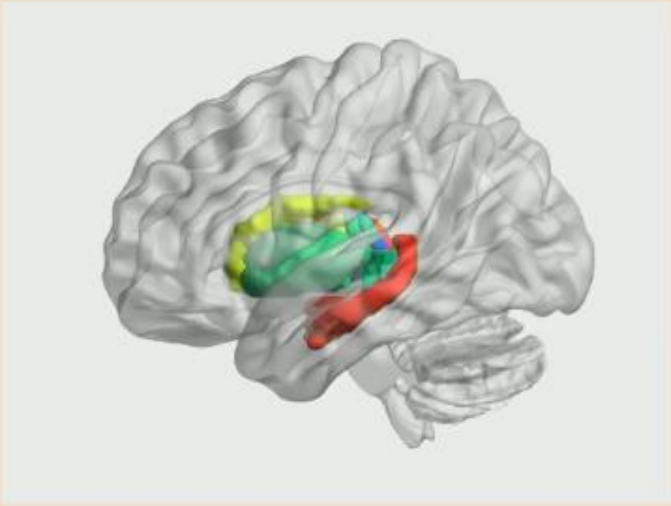
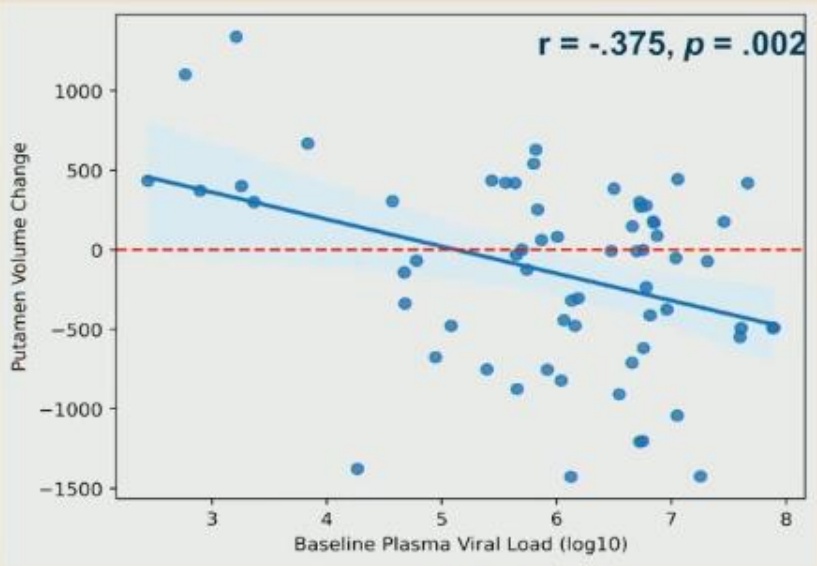
Percent Change by Serostatus







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Discussion

- No evidence of progressive brain atrophy over 96 weeks of ART initiated during acute HIV.
- Hypertrophy in brain regions during AHI “normalize” after ART, possibly reflecting resolution of early inflammatory processes prior to treatment onset.
- Normalization of brain hypertrophy (i.e., “pseudoatrophy) after treatment is observed in other neurologic conditions such as multiple sclerosis **(Vidal-Jordana et al. 2013., De Stefano et al., 2015, Cortes et al., 2023., Nakamura et al., 2024)** and Alzheimer’s disease **(Belder et al. 2024).**
- Analyses are ongoing to identify associations with HIV immune markers and clinic al outcomes before and after ART initiated during acute infection.