Brain Volumetrics Differ by Fiebig Stage in Acute Infection

419

Jacob Bolzenius[1], Pom Sailasuta[2], Andy Belden[1], Phillip Chan[3], Carlo Sacdalan[3], Julie Ake[4], Somchai Sriplienchan[3], Khunthalee Benjapornpong[3], Denise Hsu[4,5], Sandhya Vasan[4,5], Torie Tsuei[6], Serena Spudich[7], Victor Valcour[6], Robert Paul[1,8], for the SEARCH 010/RV254 and SEARCH 013/RV304 Study Teams

[1]Missouri Institute of Mental Health, University of Missouri, St. Louis, St. Louis, MO, USA; [2]Department of Tropical Medicine, Medical Microbiology and Pharmacology, University of Hawaii, Honolulu, Hawaii, USA; [3]SEARCH, Institute of HIV Research and Innovation (IHRI), Bangkok, Thailand; [4]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD, USA; [5]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, Maryland, USA; [6]Memory and Aging Center, Department of Neurology, University of California San Francisco, San Francisco, CA, USA; [7]Department of Neurology, Yale University School of Medicine, New Haven, CT, USA; [8]Department of Psychological Sciences, University of Missouri, St. Louis, St. Louis, MO, USA

BACKGROUND

Neuroimaging studies of primary and chronic HIV infection report lower brain volumes compared to uninfected individuals, especially in subcortical regions. No studies have investigated brain volumetrics in acute HIV (AH) compared to people without HIV (PWOH). Research has demonstrated the importance of early disease dynamics, with worse outcomes among individuals who initiate treatment after Fiebig II. Structural brain differences by Fiebig stage have not been examined in people with AH (PWAH).

We examined brain volume by Fiebig stage in a large sample of PWAH compared to demographically similar PWOH.

METHODS

- 112 Thai male PWAH and 18 male and age-matched Thai PWOH were included as part of RV254/SEARCH 010 and RV304/SEARCH 013, respectively.
- PWAH were stratified into early (Fiebig I-II; n=32) vs. late (Fiebig III-V; n=80) acute HIV.
- T1-weighted scans were acquired using a 3T Philips Ingenia MRI performed within 5 days of ART initiation.
- Volumes for the caudate, putamen, pallidum, thalamus, amygdala, hippocampus, and nucleus accumbens were summed between hemispheres, corrected for differences in head size, and compared across groups.
- Group comparisons were performed using ANOVAs with false discovery rate to correct for multiple comparisons.

Subcortical brain volumes were *larger* in acute HIV compared to people without HIV. Individuals in later Fiebig stages had *larger* volumes than those in early Fiebig stages.

RESULTS

- Early AH individuals had similar median CD4 T cell count (326 vs. 319 cells/mm^3), but significantly lower median CD8 T cell count (366 vs. 648 cells/mm^3) and lower average plasma viral load (5.31 vs. 6.42 $\log_{10}$ copies/mL) than late AH individuals (both ps < .01; see **Table**).
- Late Fiebig individuals exhibited significantly larger volumes in the caudate (11% larger), putamen (31%), pallidum (19%), amygdala (9%), and nucleus accumbens (15%) compared to PWOH (all ps < .05; see **Figure**).
- Late AH individuals exhibited significantly larger putamen (19% larger) and nucleus accumbens (8%) volumes compared to early AH individuals (both ps < .05).

CONCLUSIONS

- Brain volume in AH varies as a function of infection progression, indicated by Fiebig stage.
- Larger volumes in later Fiebig stages may reflect underlying neuroinflammatory processes during acute infection.
- Longitudinal research is needed to determine whether differences in brain volume persist or resolve after sustained use of ART.
- Examination of immune markers and/or brain metabolites using spectroscopy may help characterize relationships between brain structure and immune responses after acute infection.

N=130	Fiebig I-II (n=32)	Fiebig III+ (n=80)	HIV- Control (n=18)
Age; M (SD)	27.47 (5.69) Range 20-44	27.79 (6.51) Range 20-46	28.50 (7.03) Range 18-40
Sex	100% Male	100% male	100% male
ART Regimen; N (%)			
Efavirenz	12 (44.4%)	31 (46.3%)	n/a
Dolutegravir	15 (55.6%)	36 (53.7%)	n/a
Days Infected M (SD)	17.15 (8.18) Range 5-49	24.03 (8.71) Range 7-47	n/a
Days on ARV Prior to MRI M (SD)	0.31 (1.47) Range -2 to 3	0.64 (1.46) Range -2 to 5	n/a
CD4 T cell count Median (IQR)	326 (279-563)	319 (229-432)	902 (694-1084)
CD8 T cell count Median (IQR)	366 (256-493)	648 (391-995)	673 (467-1028)
Plasma HIV VL copies/mL ($\log_{10}$); M (SD)	5.31 (1.23)	6.42 (0.95)	n/a

Table. Clinical characteristics by subgroup.

ACKNOWLEDGEMENTS

We would like to thank the study participants who committed so much of their time for this study. The participants were from the RV254/SEARCH 010, which is supported by cooperative agreements (WW81XWH-18-2-0040) between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the U.S. Department of Defense (DOD) and by an intramural grant from the Thai Red Cross AIDS Research Centre and, in part, by the Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institute of Health (DAIDS, NIAID, NIH) (grant AAI20052001). Antiretroviral therapy for RV254/SEARCH 010 participants was supported by the Thai Government Pharmaceutical Organization, Gilead Sciences, Merck and ViiV Healthcare.

DISCLAIMER

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army, the Department of Defense, the National Institutes of Health, the Department of Health and Human Services, or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. The investigators have adhered to the policies for protection of human subjects as prescribed in AR-70-25.

FUNDING

These studies were supported by NIH grant R01MH113560 and DoD grant W81XWH-18-2-0040 and by additional funds contributed by the National Institute of Mental Health.

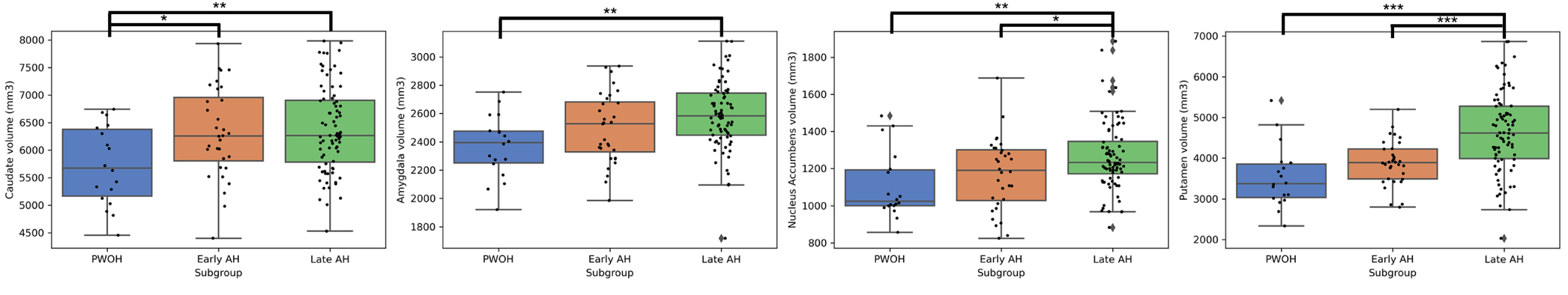

Figure. Brain volumes in select regions of interest stratified by subgroup.

Note: Post-hoc group comparisons where *p < .05; **p < .01; ***p < .001.