Childhood Trauma Modifies Brain Morphology and Cognition in People With HIV

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BACKGROUND

- Growing evidence suggests a combined detrimental effect of childhood trauma (ChT) and HIV on brain morphology and neurocognition.
- ChT in people living with HIV (PLWH) has been associated with larger bilateral (BL) amygdala, lower psychomotor & processing speed[1]; smaller right (R) anterior cingulate cortex, corpus callosum, BL caudate, BL putamen, and BL hippocampi[2]; and lower verbal fluency[3].
- **Limitations of current evidence:** untreated HIV/lack of viral suppression, lack of socio-demographic representation

AIMS

- **Aim 1:** To evaluate the effect of ChT on neurocognition, daily functioning, and brain morphology
- **Aim 2:** To explore how brain morphology modifies the relation between ChT and neurocognition and daily functioning

METHODS

- **ALLHANDS Study:** National Institutes of Health (NIH) and Department of Defense (DoD)
- Community-dwelling participants from DC, and military beneficiaries (DC; San Diego, CA)
- **Eligibility:** PLWH > 18 years, on ART AND viral load (VL) < 200 c/mL ≥ 1 year
- **Exclusion:** Hx of adult-onset trauma only and not ChT (n = 50) and failed Medical Symptom Validity Test (n = 8).
- **Statistical plan:**

Sample characteristics & covariate selection: Mann-Whitney U, chi-square or Fisher's exact test, and ANCOVA

- **Covariates for neurocognition:** cohort, duration of untreated HIV
  Covariates for daily functioning: cohort, age, gender, education, White race, duration untreated HIV

Main analyses: Regression (linear, negative binomial, logistic)

- Regress neurocognition and daily functioning on ChT, brain volume, cohort, and ChT x brain volume interaction **+ covariates**

Construct	Measure
ChT	Client Diagnostic Questionnaire[4] or intake questionnaire (≥ 1 flagged): •Physical abuse •Sexual abuse •Witnessing violence as a child
Volumetrics	•MRI scan on a 3T Philips Achieva scanner •FreeSurfer (https://surfer.nmr.mgh.harvard.edu)
Neurocognitive impairment (NCI)	Global deficit score[5] ≥ 0.5
Cognitive domains[6] (demographically adjusted T-score)	•Attention/Working Memory •Executive Functioning •Information Processing •Verbal Fluency •Learning •Memory •Psychomotor Speed
Daily functioning	•Texas Functional Living Scale (T-score) •Patient's Assessment of Own Functioning •Independent Activities of Daily Living Scale

67.5% of PLWH experienced childhood trauma

Better cognition and daily functioning was associated with greater basal ganglia volume, total gray matter volume, and cortical thickness for ChT-PLWH, **but not for ChT+ PLWH.**

RESULTS: *AIM 1*

- ChT+ PLWH had worse learning (47.8 v. 50.4, $p = 0.029$) and greater functional difficulties (all *ps* < 0.031). Other cognitive domains n.s. (all *ps* > 0.05).
- ChT+ PLWH had less average cortical thickness, total white matter, total gray matter, pallidum, hippocampal, and amygdala volumes (all *ps* < 0.05) than ChT- PLWH.
- After adjusting for demographics, cohort, and intracranial vault, univariate differences in brain morphology became n.s. (all *ps* > 0.40).

	Childhood Trauma			
	No (n = 81)	**Yes (n = 164)**	**Total (N = 245)**	***p*-value**
Cohort, count(%)				**0.011**
NIH[a]	30(37.0)	89(54.3)	119(48.6)	
DoD[b]	51(63.0)	75(45.7)	126(51.4)	
Male sex	75(92.6)	117(71.3)	192(78.4)	**<0.001**
Enrollment age (yrs), M(SD)	47.5(10.8)	49.3(9.6)	48.7(10.0)	0.127
Race, count(%)				0.019[c]
Caucasian/White	46(56.8)	67(40.9)	113(46.1)	
African American/Black	27(33.3)	82(50.0)	109(44.5)	
Other	8(9.9)	14(8.6)[d]	22(9.0)	
Education degree, count(%)				0.196
Less than 12th grade	4(4.9)	24(14.6)	28(11.4)	
12th grade/GED	15(18.5)	32(19.5)	47(19.2)	
Some college	26(32.1)	50(30.5)	76(31.0)	
Bachelor's degree	19(23.5)	29(17.7)	48(19.6)	
Higher degree	17(21.0)	27(16.5)	44(18.0)	
NCI, count(%)	14(17.3)	41(25.0)	55(22.4)	0.173
Years of untreated HIV, M(SD)	2.8(5.4)	4.8(7.1)	4.1(6.6)	**0.044**

Notes. [c]White vs. non-White. [d]Race was missing in one ChT+ participant.

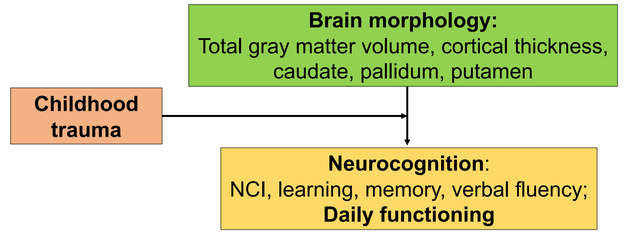
RESULTS: *AIM 2*

Interaction effects (ChT x brain morphology):

- There were significant interactions for NCI, learning, memory, verbal fluency, and daily functioning.

Simple effects analyses (ChT- vs. ChT+):

- ***For ChT- PLWH,*** greater total gray matter (OR = 0.98, $p = 0.012$) and cortical thickness (OR = 0.02, $p = 0.012$) **decreased odds** of **NCI**.
- ***For ChT- PLWH,*** greater total gray matter was related to better **learning** (B = 0.05, $p = 0.010$) and **memory** (B = 0.05, $p = 0.003$); greater putamen was marginally related to better **memory** (B = 2.02, $p = 0.062$) and verbal fluency (B = 1.91, $p = 0.069$).
- ***For ChT- PLWH,*** greater cortical thickness was related to fewer **functional declines** (B = -2.29, $p = 0.031$), but this interaction was not significant in the adjusted model.
- ***For ChT+ PLWH,*** greater caudate was related to worse **learning** (B = -2.14, $p = 0.012$), greater pallidum to worse **memory** (B = -3.11, $p = 0.048$), and greater total gray matter to worse **verbal fluency** (B = -0.02, $p = .026$).
- All other associations were n.s. (*ps* > 0.05).



CONCLUSIONS

- Better learning, memory, verbal fluency, and daily functioning were related to greater brain volumes and cortical thickness for ChT- PLWH, but not for ChT+ PLWH.
- In ChT+ PLWH, there was an inverse relationship between basal ganglia volume and memory and learning without any change in psychomotor speed; however, more detailed studies are needed to assess motor function. This relationship is possibly related to inflammation.
- Though well-controlled HIV mitigates neurocognitive deficits, ChT may still stunt benefits of increased gray matter volume and cortical thickness in PLWH.

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