Poster #: 0395

Effects of Anticholinergic Medications on Brain Integrity in Older HIV-positive and HIV-negative Adults

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Background

- The aging population of people living with HIV (PLWH) has resulted in an increase of comorbidities requiring treatment with medications.[1]
- Anticholinergic (AC) medications are linked with greater risk of cognitive dysfunction and dementia in older adults (HIV-negative and PLWH).[2,3]
- AC effects on brain structure (volumes) are not well-established.

Aims

- To examine the cross-sectional relationships between AC medication burden and brain volumes and cognition in HIV-negative controls (HC) and PLWH aged ≥40 years
- To assess the change in brain volumes and cognition over a two-year follow-up in older HC and PLWH

Methods

- **Participants** (cross-sectional):
  - 105 HC and 219 PLWH (with undetectable viral load <50 copies/mL) (Table 1)
- Participants (longitudinal - 2 year follow-up):
  - 30 HC and 94 PLWH who had no change in AC burden from baseline
- AC burden determined from medications listed in the medical records or self-reported use.
- The **Anticholinergic Cognitive Burden Scale (ACB)**[4] was used to assign a value (1-3) to each AC medication taken by participants and then summed to classify individuals as high (score >3), low (score 1-3), or no (score 0) AC burden.
- **Neuropsychological testing**:
  - Participants completed a 15-test NP battery that incorporated tests from executive function (EF), learning (L), delayed recall (DR), and psychomotor/processing speed (PM) domains
  - Raw scores converted into demographically-corrected Z-scores and averaged to create domain Z-scores
- **Neuroimaging**:
  - 3T Siemens Tim Trio MR scanner
  - FreeSurfer software (v5.3) determined frontal, parietal, temporal, occipital, total gray matter (GM), subcortical GM, cortical, and total white matter volumes.

Methods (continued)

- Statistical Analyses:
  - Differences in demographics by HIV status were assessed using T-tests or chi-square
  - A chi-square test compared the rate of high AC burden in HC and PLWH
  - General linear models tested the main effects and interaction of HIV status (HC vs PLWH) and AC burden (none, low or high) on each cognitive domain and brain volume.
  - Secondary linear mixed models tested for interactions of HIV status and AC burden on change in cognitive domains and brain volumes over time (none and low AC combined vs high).
  - Spearman's correlation assessed relationships between significant changes in brain volumes and changes in cognition

Table 1: Participant demographic and clinical characteristics

	HC (n=105)	PLWH (n=219)	P-value
Age in years; M (SD)	58.2 (8.1)	57.0 (6.6)	.22
Sex (% males)	56%	79%	**<.001**
Race (% AA)	55%	65%	.50
Education in years; M (SD)	13.8 (2.2)	13.6 (2.6)	.55
Recent CD4 T-cell count; median (IQR)	-	544 (381,802)	-
Nadir CD4 T-cell count; median (IQR)	-	177 (383, 800)	-
AC burden (% high ACB score)	12%	25%	**.002**

Results

Table 2: ACB score rates in older HC and PLWH

	HC	PLWH
No AC burden (ACB score=0)	70%	48%
Low AC burden (ACB score 1-3)	18%	27%
High AC burden (ACB score >3)	12%	25%

Results

- Older PLWH have a significantly higher rate of high AC burden compared to HC (p=.002) (Table 2).
- Significant main effects of higher ACB score and HIV on worse cognition (EF and PM domains) and smaller brain volumes (all except total white matter) (p-values <.05), but no significant interactions (p-values>.05).
- Smaller GM brain volumes were associated with lower EF and PM Z-scores (p-values <.05).

Figure 1: Representative plots of brain volumes by ACB score and HIV serostatus

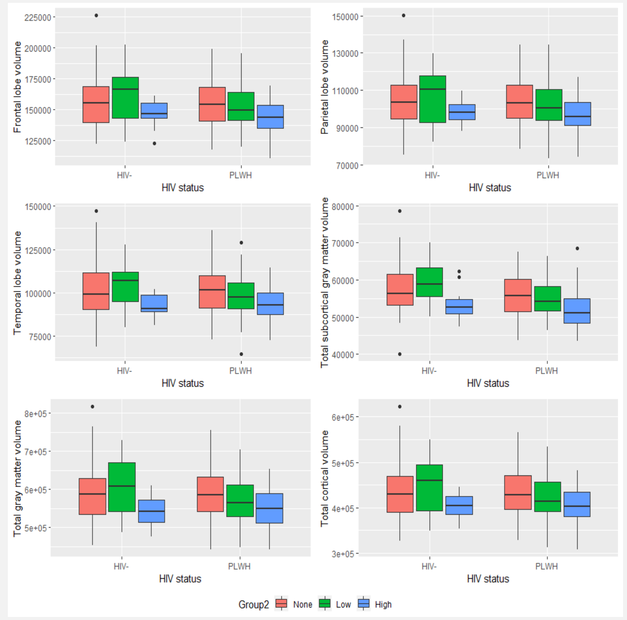


Figure 2: Change in subcortical gray matter over two years by group

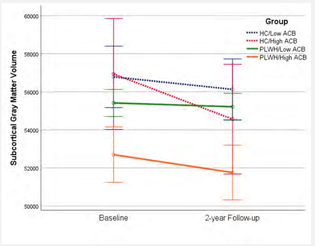
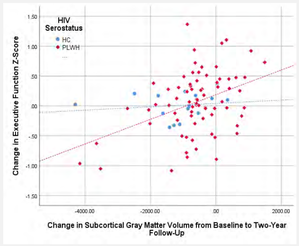


Figure 3: Change in subcortical GM and EF performance



Results

- Significant main effects of time, HIV serostatus, and ACB group on change in cognitive performance (EF and PM domains), but no significant interactions.
- Significant main effects of time, HIV serostatus and ACB group were identified for change in subcortical GM volume. The interactions between time x HIV status and time x ACB group were also significant (p<.05).
- Change in subcortical GM volume significantly correlated (r=.32, p=.005) with change in executive function performance over a two-year period (Figure 3).

Conclusions

- Older PLWH take AC medications at a higher rate than HC
- Higher AC burden is associated with both worse cognitive performance and lower brain gray matter volumes, suggesting potential neurotoxicity of AC medications
- Over a two-year period, higher AC burden was associated with greater reduction in subcortical GM volume, which in turn was associated with greater reductions in EF performance.
- AC medication burden and HIV status did not interact, suggesting that older HCs and PLWH are affected similarly by AC medications.

References

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