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Anticholinergic Burden is Associated with Depressive Symptoms in Persons with HIV

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HNRP HIV NEUROBEHAVIORAL RESEARCH PROGRAM

Objectives

- To determine how the anticholinergic (AC) effects of prescribed drugs relate to depressive symptoms and neurocognitive (NC) performance in people with HIV (PWH) who are taking effective antiretroviral therapy (ART).

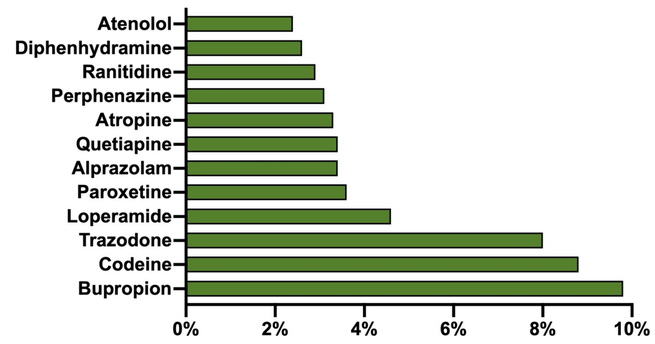
Background & Significance

- PWH have a higher risk of depression[1] and NC impairment (NCI)[2] than the general population.
- PWH are also at greater risk for polypharmacy[3], which increases the risk of drug-drug interactions and adverse reactions.
- Many prescribed drugs have AC effects, which are a risk factor for depression and NCI in the general population[4] and could contribute to the risk of these conditions in PWH.

Methods

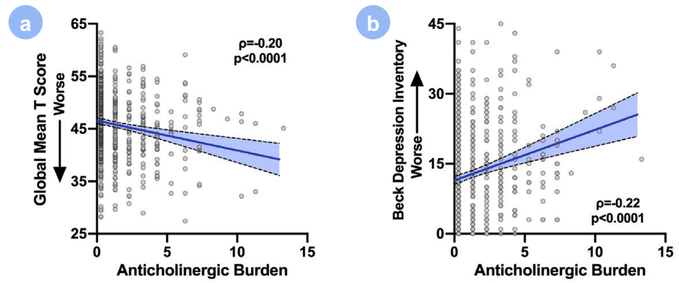
- **Design:** Retrospective cross-sectional analysis of data from 613 PWH who a) were assessed in a neuroHIV cohort in San Diego, b) reported taking ART, and c) had plasma HIV RNA ≤ 200 copies/mL.
- **Methods:** All participants underwent comprehensive assessments, which included collecting demographic, medical, NC, and psychiatric data. Depressive symptoms were assessed by the Beck Depression Inventory (BDI): values 14-19 mild depression, 20-28 moderate depression, and ≥ 29 severe depression. Global and domain-specific NC performance was summarized by a demographically corrected T scores. NC impairment was defined using the deficit score method. AC effects were summarized by the AC burden (ACB) method (range: 0-15).[5]
- **Data Analysis:** Analytical methods included correlation, analysis of variance, and multivariable regression that assessed demographic, disease, and ART characteristics as well as medical, psychiatric, and addiction diagnoses. The best multivariable model was determine using the Akaike Information Criterion and backward selection.

Figure 1: Most Commonly Reported Anticholinergic Drugs



Results

Figure 2: Correlation of Anticholinergic Burden with a) Global Mean T Score and b) Beck Depression Inventory.



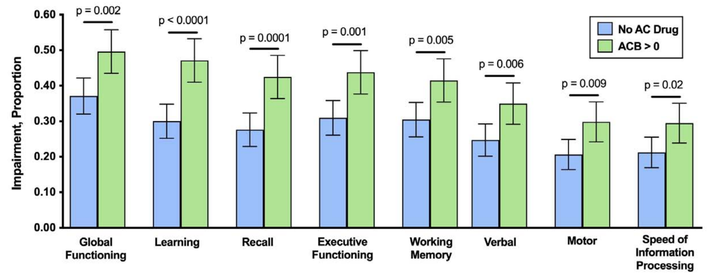
- Participants were mostly middle-aged (mean 44.7 years), European ancestry (55.5%) men (85.3%) who had taken ART for more than 4 years (53.2%) and whose current CD4+ T-cell count was >500/μL (55.4%).
- Median global T-score was 46.1 (interquartile range [IQR] 41.6-50.3). Median BDI was 11.0 (IQR 4-19).
- 260 (42.4%) took at least one AC drug. **Figure 1** displays the most common ones in this combined cohort. Among those who used at least one AC drug, the median ACB value was 2 (IQR 1-4).
- **Figure 2** displays the correlations between higher ACB and either worse Global T score (ρ=-0.20, p<0.0001) or BDI (ρ=0.22, p<0.0001).
- Higher ACB correlated with worse performance in all seven NC domains (p range 0.006 to <0.0001), particularly Recall (ρ=-0.21, p<0.0001), Learning (ρ=-0.19, p<0.0001), and Executive Functioning (ρ=-0.17, p<0.0001).

Table 1: Univariable and Multivariable Associations of BDI Value

	Univariable		Multivariable	
Variable	β estimate	p value	β estimate	p value
Anticholinergic Burden	1.08	< 0.0001	0.83	0.0006
Current Psychiatric Diagnosis	7.37	< 0.0001	5.71	< 0.0001
Lifetime Psychiatric Diagnosis	4.44	< 0.0001	2.53	< 0.0001
Lifetime Substance Use Diagnosis	2.02	< 0.0001		
Current Substance Use Diagnosis	2.35	0.0004	1.68	0.063
Number of Prescribed Drugs	0.29	0.003		
Serum Triglycerides	0.006	0.009		
Serum Glucose	0.02	0.06		
Serum High Density Lipoprotein	-0.06	0.09	-0.05	0.053

Variables with p values >0.10 in screening univariable analyses included age, sex, race/ethnicity, AIDS diagnosis, estimated duration of HIV, nadir and current CD4+ T-cell count, duration of ART, number of ART drugs, HIV RNA in plasma and CSF, serum creatinine, serum total protein, serum albumin, serum total cholesterol, serum LDL cholesterol, hemoglobin, platelets, HCV serostatus, diabetes mellitus, cancer, hypertension, hyperlipidemia, and chronic obstructive pulmonary disease.

Figure 3: Using at Least One Anticholinergic Drug was Associated with Worse Performance in all Neurocognitive Domains



- **Figure 3** displays the associations between use of at least 1 AC drug and global and domain-specific NCI. Use of any AC drug was also associated with having a BDI value ≥14 (at least mild depression, relative risk 1.43, p<0.0001).
- In multivariable regression models that included demographic, disease, and treatment characteristics as candidate covariates, ACB remained associated with worse BDI (p=0.0001, model R^2=0.41, p<0.0001, **Table 1**) and trended toward association with Global T score (p=0.07, model R^2=0.21, p<0.0001).
  - Addition of the total number of prescribed drugs to models weakened the association of ACB with Global T score below statistical significance (p=0.73) but not with BDI (p=0.003).
- The AC drugs most strongly associated with BDI were paroxetine, trazodone, atropine, olanzapine, and hydroxyzine (all p values<0.05).

Conclusions

- **AC drugs were associated with more depressive symptoms, even after accounting for several influential characteristics, including psychiatric and substance use diagnoses.**
- **This cross-sectional analysis cannot establish causality but avoiding or deprescribing AC drugs may improve depressive symptoms.**

Acknowledgements & References

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