Prescribed Drugs Distinguish Data-Driven Cognitive Profiles in People with HIV (PWH)

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Raha Dastgheyb[1], Yanxun Xu[1], Alison Buchholz[1], Donald Franklin[2], Ronald J. Ellis[2], Susan Morgello[3], David Clifford[4], Benjamin B. Gelman[5], Christina M. Marra[6], Robert K. Heaton[2], David J. Moore[2], Scott Letendre[2], Qing Ma[7], **Leah H. Rubin[1]**
[1]The Johns Hopkins University, Baltimore, MD, USA, [2]University of California San Diego, La Jolla, CA, USA, [3]Mt Sinai School of Medicine, New York, NY, USA, [4]Wahsington University in St. Louis, St. Louis, MO, USA, [5]University of Texas at Galveston, Galveston, TX, [6]University of Washington, Seattle, WA, [7]University of Buffalo, Buffalo, NY, USA

BACKGROUND

- PWH have more age-associated medical and psychiatric comorbidities than the general population, even when treated with antiretroviral therapy (ART).
- These comorbidities have been associated with poorer cognition, but less is known about the cognitive effects of the treating medications

METHODS

- Leveraged cross-sectional data collected between 2015-2019 from 1122 virally-suppressed PWH enrolled in CHARTER, NNTC, or UCSD neuroHIV cohorts with available count data on 226 non-ART drug classes gathered contemporaneously with neuropsychological testing.
- Drug classes were reduced using a principal components analysis of the counts with a varimax rotation and the number of components that accounted for at least 75% of the overall variance.
- To identify subgroups of PWH with similar cognitive deficit profiles, we used a pipeline consisting of dimension reduction with Self-Organizing Maps on domain-specific cognitive deficit scores followed by clustering using Gaussian mixture models.
- Random Forest(RF) models were created to determine the degree to which the PC drug classes distinguished cognitive profiles, along with sociodemographic variables and comorbidities. RF models contained an ensemble of 1000 trees with a 70/30 training/testing set for validation. Model performance was evaluated based on metrics, and the models with a receiver operating characteristic value of >0.65 were further evaluated with variable importance measures to identify the top 10 contributing variables**.**

RESULTS

- Clustering Pipeline of the 1122 participants resulted in 10 cognitive profiles
- Class counts of 226 non-ART drug classes were reduced to 16 principal components.
- 6 of the 9 RF models comparing to the unimpaired cluster validated with >0.65 ROC in the testing set

Prescription drugs are strong predictors of cognitive impairment profiles in PWH even in the context of their underlying psychiatric & medical comorbidities.

Fig1. Boxplots of T-Scores for each cognitive domain faceted by cluster.

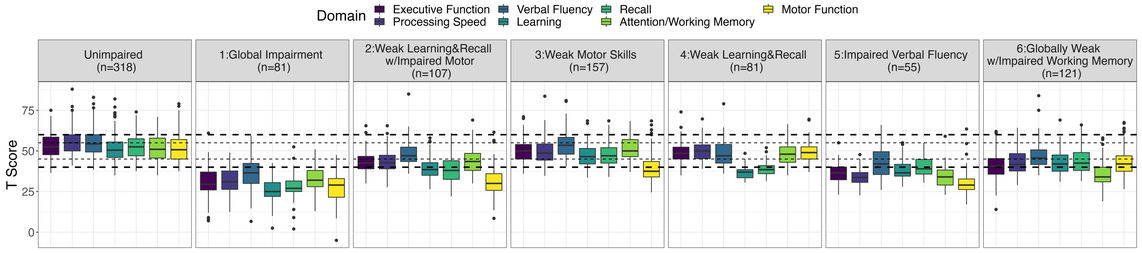


Fig2. PCA loading plot of the drug components used in the RF models. Highlighted bars show the highest loadings that are used to interpret the component. Only PCs that were top predictors in the RF models are shown.

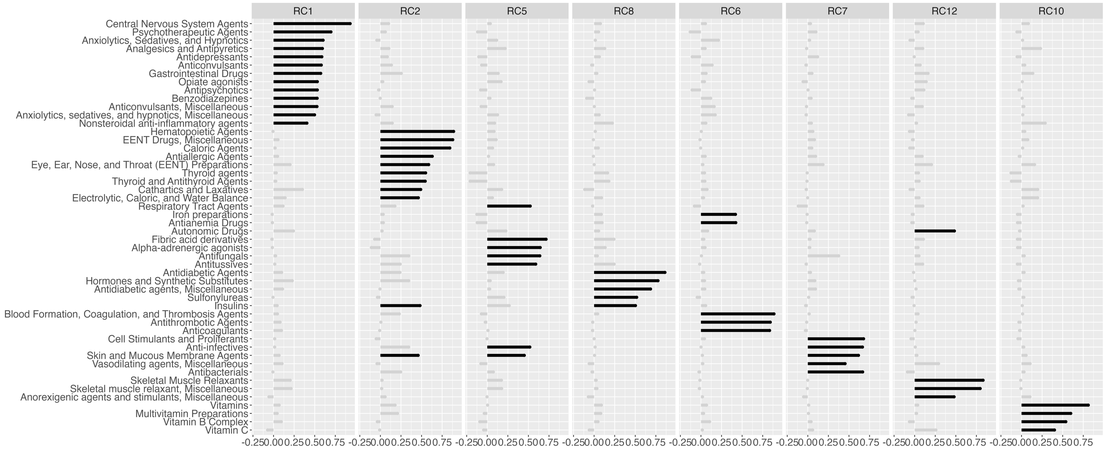


Fig3. ROC curves for each RF model as compared to the unimpaired group on the testing dataset.

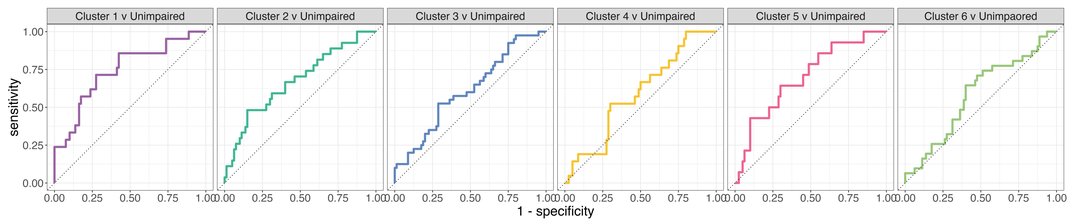
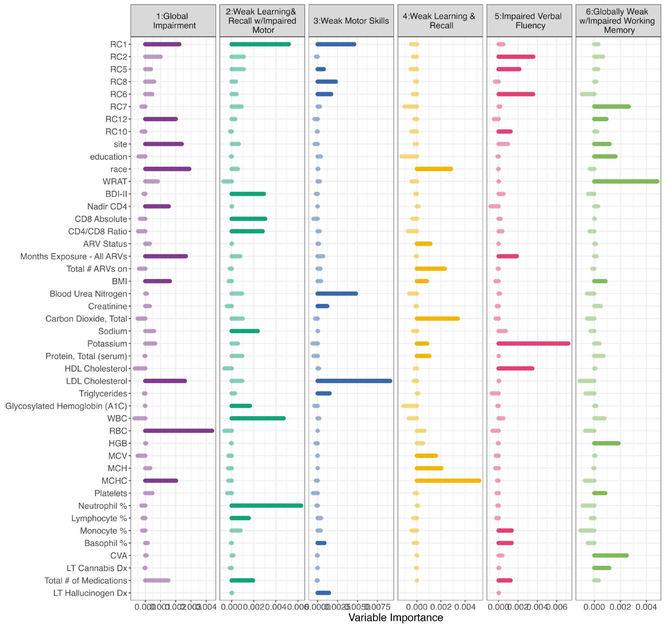


Fig4. Variable importance plot for each of the included RF models. The highlighted bars show the top 10 contributing variables for each model. Only variables that were included in the top 10 contributing factors for at least one model are shown in the Figure.



CONCLUSIONS

- Different combinations of drug classes were associated with different cognitive profiles, suggesting that the drug combinations may differently affect underlying neurobiological pathways.
- Further investigation is needed to account for the underlying conditions for which the drugs were prescribed and to understand the risks/benefits associated with different drug combinations and cognition in PWH.

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CONTACT INFORMATION

lrubin@jhu.edu; rdastgh1@jhu.edu