Plasma Microbiome Composition Among Neurobehavioral Phenotypes (NBPs) in People With HIV (PWH)

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Mohammadsobhan S. Andalibi [1,2,3], Lora Khatib [3,4], Bin Tang [2], Donald Franklin [2], Robert Heaton [2], Rob Knight [3,5,6], Scott L. Letendre [2,7], Ronald J. Ellis [1,2]

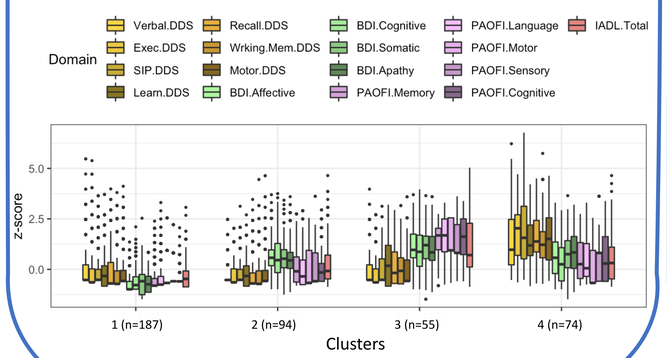
[1]Department of Neurosciences, University of California San Diego, La Jolla, CA, USA, [2]Department of Psychiatry, University of California San Diego, La Jolla, CA, USA, [3]Department of Pediatrics, University of California San Diego, La Jolla, CA, USA,[4]Neurosciences Graduate Program, University of California San Diego, La Jolla, California, USA, [5]Department of Computer Science and Engineering, University of California San Diego, La Jolla, CA, USA, [6]Center for Microbiome Innovation, University of California San Diego, La Jolla, CA, USA, [7]Department of Medicine, University of California San Diego, La Jolla, CA, USA

BACKGROUND

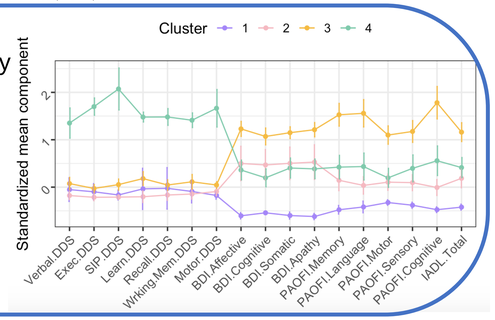
- Neurobehavioral disorders and gut dysbiosis continue to occur in treated PWH, but the relationship between the plasma microbiome and NBPs has not been investigated. Plasma microbiome analysis offers unique insights into systemic microbial translocation and immune responses. This study aimed to investigate this association using 16S rRNA amplicon sequencing of plasma samples.

METHODS

- **410 PWH** who were taking antiretroviral therapy and had plasma HIV RNA ≤ 200 copies/mL underwent comprehensive neuromedical and neurobehavioral assessments and provided plasma for 16S rRNA amplicon sequencing.
- As previously described, **17** neurobehavioral features, including **cognitive domains**, **depression subscales**, and **daily functioning**, defined 4 NBPs using dimension reduction with a self-organizing maps (SOM) followed by k-means clustering methods: NBP1:
  - ❖ healthy (n=187),
  - ❖ NBP2: depression-dominant (n=94),
  - ❖ NBP3: unhealthy in all features (n=55), and
  - ❖ NBP4: cognitive impairment-dominant (n=74).



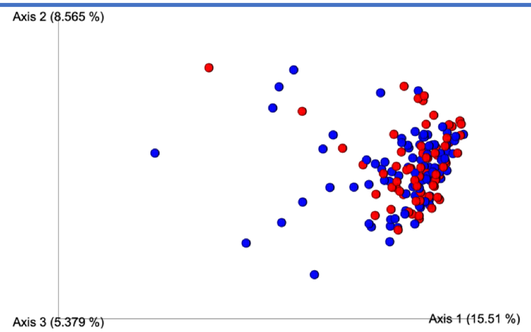
- Alpha and beta diversity were measured using diversity metrics. Differential species abundance was analyzed using Bayesian Inferential Regression for Differential Microbiome Analysis (BIRDMAn), adjusting for age and gender.



Plasma microbiome composition differs by neurobehavioral phenotype in PWH, with *Actinomycetospora*, *Mycobacterium*, and *Flavobacteriaceae* more abundant in NBP4 (cognitive impairment) than NBP2 (depression)

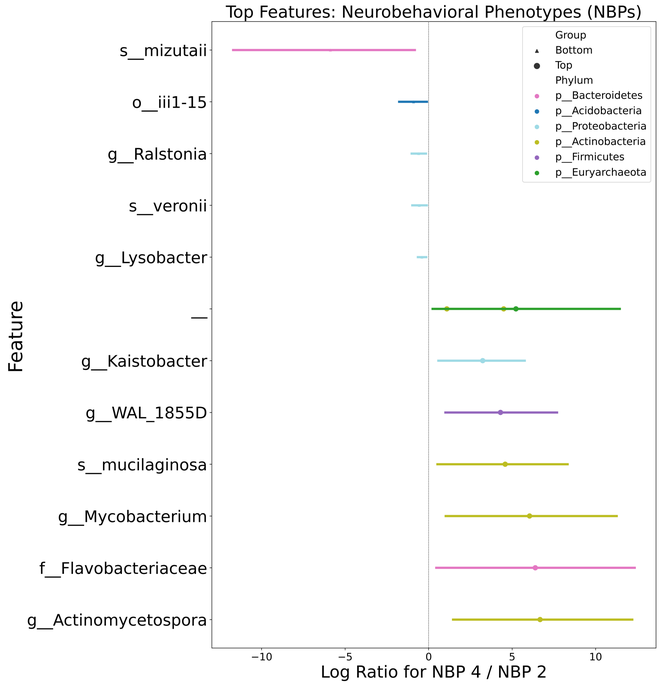
RESULTS

- Cohort characteristics:
  - ❖ mean age 42.7 ± 8.9 y,
  - ❖ 16.3% female,
  - ❖ 44.9% Black,
  - ❖ 59.3% AIDS,
  - ❖ mean CD4+ T-cells 467.5/μL.



PCoA plots based on the weighted UniFrac distance matrix show a significant difference in β-diversity between NBP4(cognitive impairment-dominant) and NBP2 (depression-dominant) in PWH (p = 0.03)

Genus ***Actinomycetospora*** and ***Mycobacterium***, ***Flavobacteriaceae*** family, and species ***mucilaginosa*** were more abundant in people with NBP4 than NBP2, potentially contributing to the observed clinical differences.



Species were differentially abundant in people with NBP4 compared to NBP2

CONCLUSIONS

- The findings of this study may occur in part by modulating immune responses:
  - ❖ Mycobacteria can induce proinflammatory immune responses and Flavobacteriaceae produce anti-inflammatory short-chain fatty acids.
- These results are provocative, but the cross-sectional design limits causal inference.
- Understanding these complex interactions support development of personalized, microbiome-based interventions to improve brain health in PWH.