00585

Functional Brain Network Changes Among Virally-Suppressed People with HIV

Jacob L van Doorn[1], Leah H Rubin[2], Farah Naaz[2], Liuyi Chen[2], Seble G Kassaye[3], Lakshmi Goparaju[3], Raha M Dastgheyb[2], Asante R Kamkwalala[2], Hannah Lee[2], Arianna Konstantopoulos[2], Joan Severson[4], Olusola A Ajilore[1], Alex Leow[1], and Pauline Maki[1]

[1]University of Illinois at Chicago, Chicago, IL — [2]Johns Hopkins University, Baltimore, MD — [3]Georgetown University, Washington, DC — [4]Digital Artefacts, LLC, Iowa City, IA

Background

- Over half of VS-PWH experience **cognitive difficulties** [1], but the reason for why is poorly understood, unexplained directly by regional activation.
- The **global network properties** of functional connectivity of brain networks provide insights into the organization of brain functioning at a global level.
- Global network metrics are widely studied in neurological and psychiatric conditions under a variety of task demands [2], but have not yet been evaluated in **virally-suppresesed people with HIV (VS-PWH)**.

Aims and Hypothesis

1. **Main Aim**: To determine what **topological differences** exist in the brain of VS-PWH compared to otherwise similar controls.
2. **Hypothesis**: Brain networks of VS-PWH appear **more random than controls**, i.e. a lower clustering coefficient (CC) and higher characteristic path length (CPL).
3. *Exploratory Aim*: Differences in global efficiency (GE), modularity (Q), and average node strength (ANS).

Methods

We examined global brain network organization in VS-PWH under **three functional MRI conditions** including resting state MRI (rsfMRI) and the performance of verbal memory and go/no-go tasks.

- N = 56 participants (69.6% VS-PWH; 51.7% female, 69.6% black) completed the MRI session and performed a battery of cognitive tests.
- Global functional brain network metrics were computed in the **weighted positive network** to yield assortativity, CPL, CC, GE, Q, and ANS.
- Multiple regressions and Pearson correlations were performed to determine serostatus effects and associations with cognitive performance, adjusting for sex, age, race, ethnicity and education.

References

1. Heaton, R. K. *et al.* HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. *Neurology* **75,** 2087–2096 (2010).
2. Bassett, D. S. & Bullmore, E. T. Small-World Brain Networks Revisited. *Neuroscientist* **23,** 499–516 (2017).

Virally-suppressed people living with HIV show a **less optimized** global functional brain network organization compared with otherwise similar controls. The cognitive performance may be **less coupled** with functional network organization in VS-PWH.

Global Functional Brain Network Differences

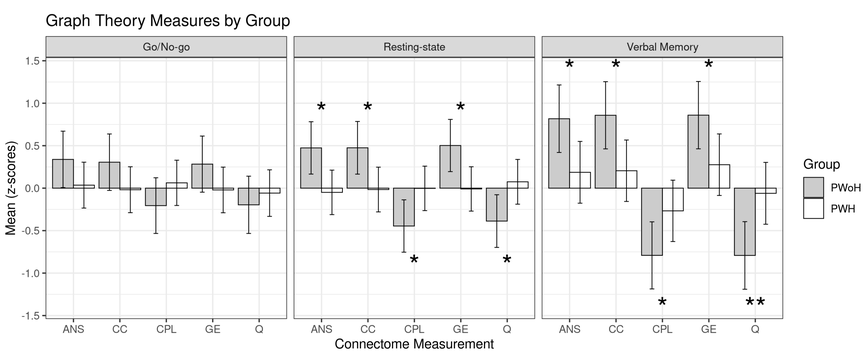


Fig. 1: The differences between groups in the clustering coefficent (CC), characteristic path length (CPL), global efficiency (GE), modularity (Q), and average node strength (ANS). The differences between CC, CPL, GE, Q, and ANS were significantly different in the resting-state and verbal memory scans but not the go/no-go scans.

Main Conclusions

- During both the resting state and performance of a verbal memory task, VS-PWH show less efficiently organized network structure (GE), less small-world network structure (CC, CPL), and less distributed connectivity (Q and ANS).
- These metrics relate to a number of cognitive processes including processing speed, working memory, and visual spatial learning.
- Graph theory metrics may serve as biomarker for VS-PWH to monitor disease progress and to evaluate new therapeutics.

Correlates with Global Network Properties

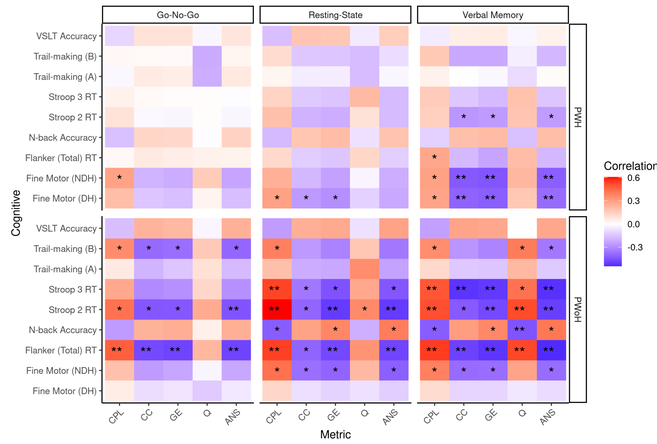


Fig. 2: Cognitive correlations with the network topology measures of the functional brain network. While there were strong correlations between several cognitive measures and the topological measures in the controls, these disappear in the VS-PWH group.

Results of Statistical Analyses

- **Resting-state**: VS-PWH showed **lower** CC (p=.03), GE (p=.02), and ANS (p=.02) and **higher** CPL (p=.04) and Q (p=.04), compared to controls.
- **Verbal Memory**: VS-PWH showed **lower** CC (p=.01), GE (p=.02), and ANS (p=.01) and **higher** CPL (p=.04) and Q (p=.005), compared to controls.
- *Go/No-go: No significant assocations in this task.*
- **Correlations**: CPL, CC, GE, and ANS with **processing speed** (reaction time on Flanker, Stroop, Trail Making, and Fine Motor Skills tasks), **working memory** (accuracy on n-back) and **visual spatial learning** test.

Funding and Acknowledgements

- Funded by NIH Grant 5 R01 MH 119947 (Rubin, Maki, multi-PI)
- We would like to thank the significant contributions made by the MACS and WIHS research participants.