

Manifold Component Analysis Improves Sensitivity In Spatial Profiling Of Longitudinal Tau-PET

Gleb Bezgin, Seyyed Ali Hosseini, Etienne Aumont, Arthur Macedo, Nesrine Rahmouni, Jenna Stevenson, Lydia Trudel, Joseph Therriault, Brandon Hall, Tevy Chan, Aurélie Lebrun, Jaime Fernandez Arias, Delphine Oliva-Lopez, Yansheng Zheng, Paolo Vitali, Jean-Paul Soucy, Serge Gauthier, Pedro Rosa-Neto

Montreal Neurological Institute, McGill University, Montreal, QC, Canada

PRN is also at: North Texas Alzheimer's Disease Research Center, Dallas TX, USA

Key take away: Manifold Component Analysis is a novel approach designed to help researchers and clinicians to have a “snapshot” of the disease progression at a given stage, based on the spatial extent and load of the misfolded protein in the brain. In this poster, we aim to track subtle longitudinal changes of tau tangle accumulation in the brain across the AD spectrum, focusing on the subjects with multiple visits. MCA can serve as an analytical approach for researchers as well as a lookup tool to select subjects with appropriately assigned stages for clinical trials.

BACKGROUND

- Tau tangle accumulation in the brain across the Alzheimer's Disease (AD) spectrum has intricate spatiotemporal continuum [1].
- The traditional Braak stage approach often uses heterogeneous regions which may blur the measurements and miss important associations with various manifestations of the disease [2,3,4].
- Recently, we developed the Manifold Component Analysis (MCA), to individually profile tau-PET data across topologically defined subdivisions of stage regions [5].

METHODS

- Used TRIAD and ADNI to profile tau-PET data as acquired via 18F-MK6240 and 18F-AV1451, respectively; only considered subjects with at least four visits.
- 16 images for 27 subjects in TRIAD (11 females, mean[s.d.] baseline age 70.1[4.5] y.o.); 245 images for 57 subjects in ADNI (31 females, mean[s.d.] baseline age 73.5[7.0] y.o.). Used MCA to compute spatial tau-PET profiles. Subject-wise profiles were evaluated for average uptake and substage-wise change between visits, including correlations with MoCA scores and cross-correlations across visits.

Fig.1. MCA: from discrete stages to continuous map

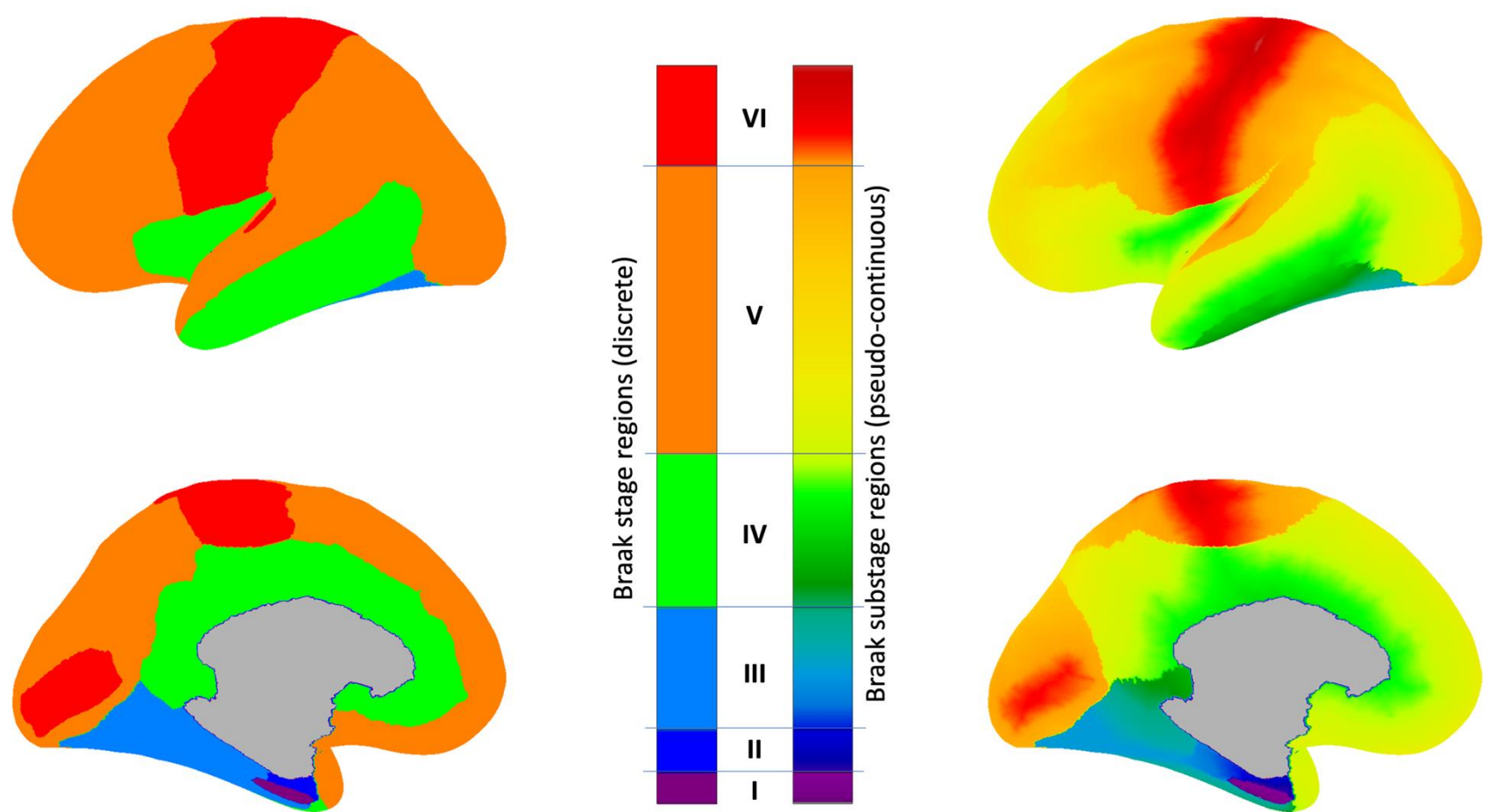
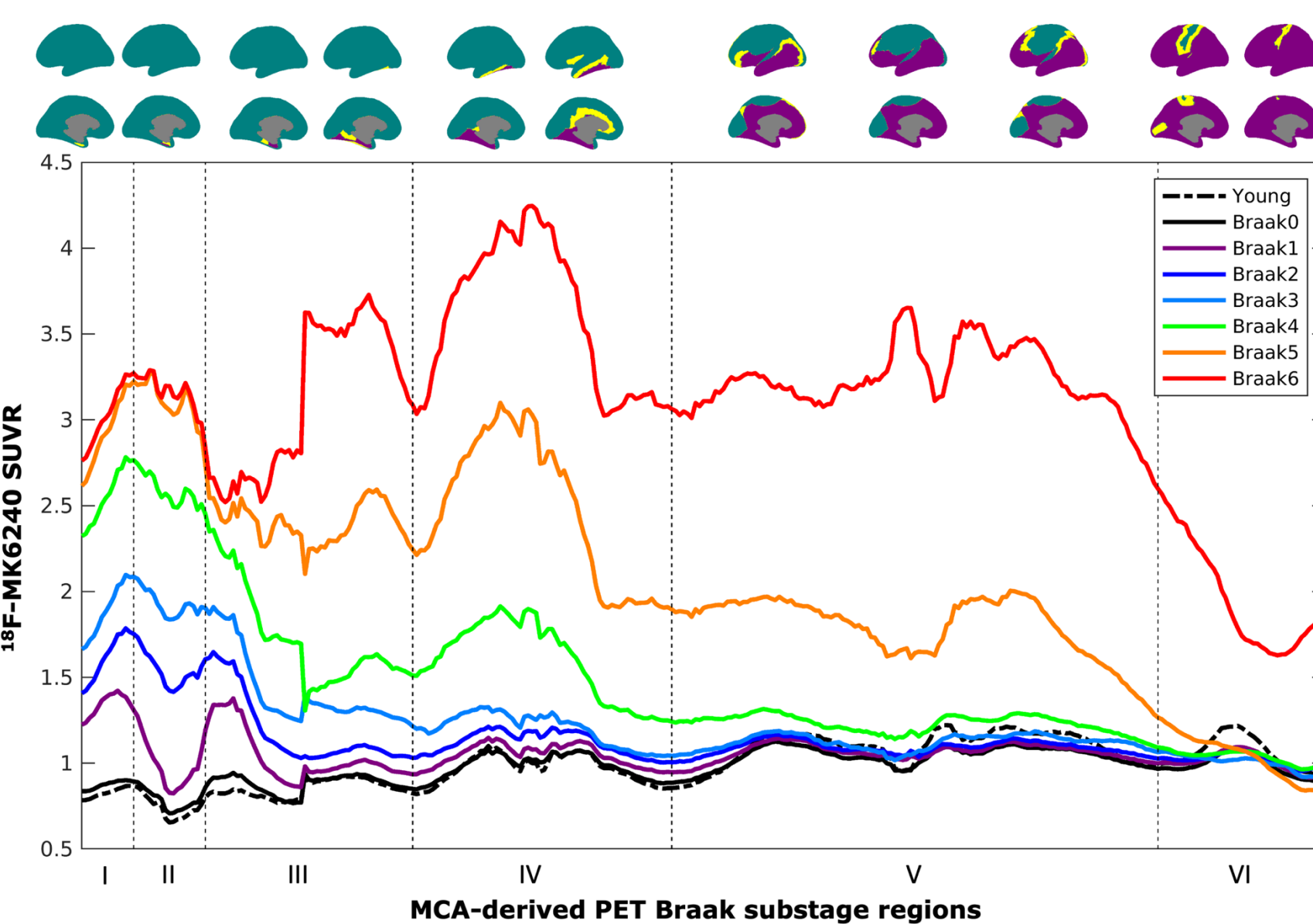


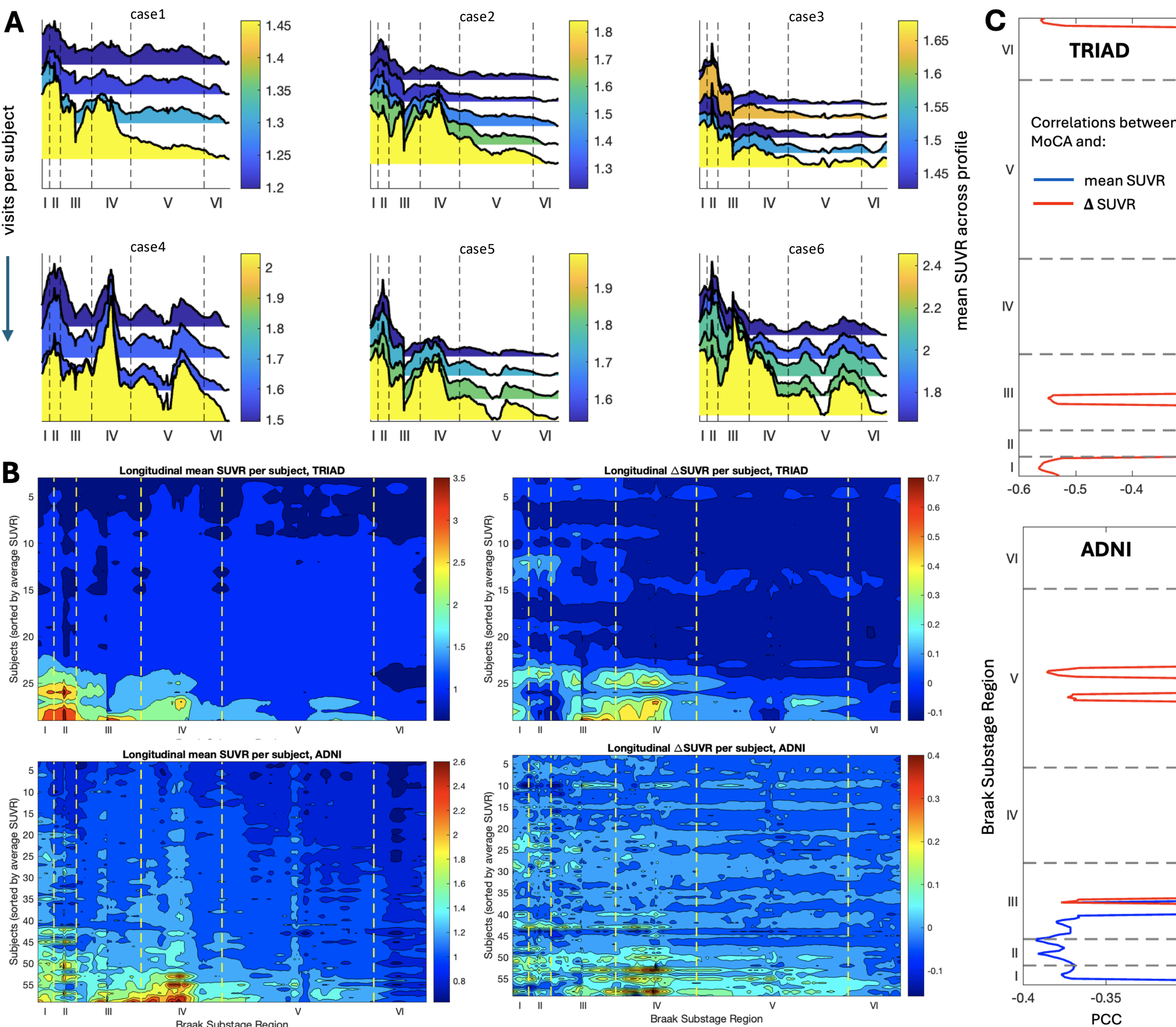
Fig.2. MCA profiles per Braak stage



RESULTS

- Tau accumulation was higher at newer visits (Fig.3A). Average profiles and inter-visit changes in SUVR showed higher uptake in Braak IV and latter Braak III (Fig.3B). Correlations between MoCA and inter-visit SUVR change appeared significant in both TRIAD and ADNI across the spectrum (Fig.3C, red). Correlations between MoCA and SUVR change using the traditional Braak-ROI approach only appeared significant in TRIAD for Braak I ROI.

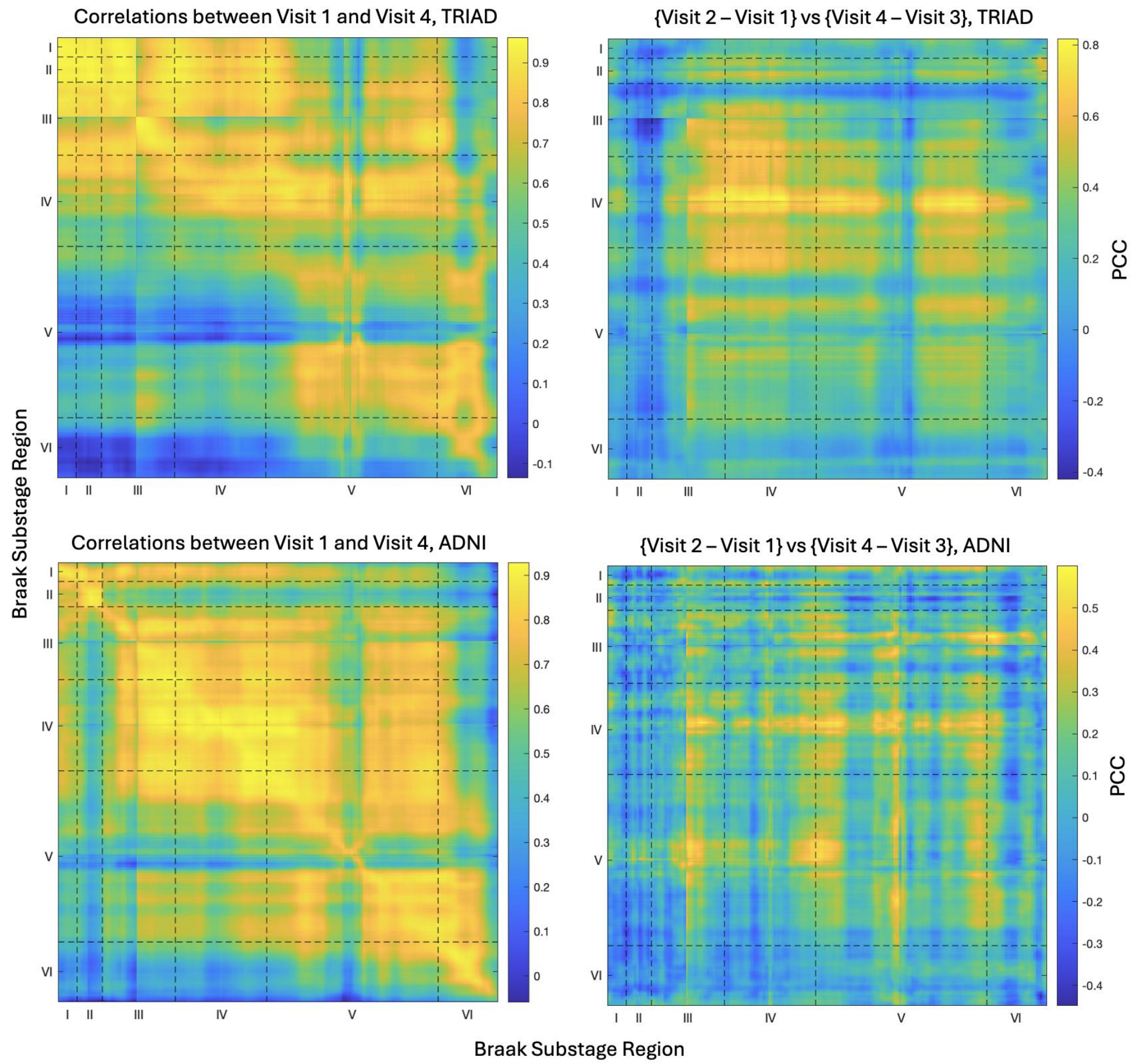
Fig.3. Longitudinal changes in tau accumulation



- The cross-correlations of SUVR (changes) across visits suggested that accumulation in Braak III and IV anticipates future higher order accumulations (Fig.4). In particular, first quantifiable changes around the topological centre of Braak IV region predicted later changes observed from that stage onward, pertaining to changes between later visits.

Fig.4 (right). Subject-wise inter-visit correlations between MCA profiles and longitudinal changes thereof.

Top row: TRIAD; bottom row: ADNI. Left column: correlations between the earliest visit and the latest visit; right column: correlations between the {visit2-visit1} and {visit4-visit3} differences.



CONCLUSIONS

Longitudinal changes in neurodegenerative diseases are important metrics that are often hard to estimate, in part due to complexity and spatial heterogeneity of the pathogenesis. MCA offers such possibility by dividing stage regions into spatially consistent substages, providing enough granularity to capture regions in question. Having tested this approach on two different cohorts with different tau-PET tracers suggests generalizability and opens avenues for evaluating novel tracers in Alzheimer's research and clinical trials.

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Disclosures

The authors declare no competing interests. All the data collected under the TRIAD cohort is governed by the policies set by the Research Ethics Board Office of the McGill University, Montreal and the Douglas Research Center, Verdun. Researchers can access the TRIAD data for research purpose by submitting a data share request via <https://triad.tlm-mcgill.com/contact-us/>. PRN and the MCSA team acknowledge Canadian Institutes of Health Research (CIHR) [MOP-11-51-31; RFN 152985, 159815, 162303], Canadian Consortium of Neurodegeneration and Aging (CCNA; MOP-11-51-31 -team 1), Weston Brain Institute, the Alzheimer's Association [NIRG-12-92090, NIRP-12-259245], Brain Canada Foundation (CFI Project 34874; 33397), the Fonds de Recherche du Québec – Santé (FRQS; Chercheur Boursier, 2020-VICO-279314).



For further information, contact Gleb Bezgin: gleb.bezgin@mcgill.ca