

# INVESTIGATING HERITABILITY ACROSS RESTING STATE BRAIN NETWORKS VIA HEAT KERNEL SMOOTHING ON PERSISTENCE DIAGRAMS

Arman P. Kulkarni<sup>1</sup>, Moo K. Chung<sup>1</sup>, Barbara B. Bendlin<sup>1</sup>, Vivek Prabhakaran<sup>1</sup>

<sup>1</sup>University of Wisconsin, Madison, USA

**Introduction** The brain’s topological differences in resting state functional connectivity (rsfc) via resting state fMRI (rsfMRI) may provide important insight into brain function and dysfunction if heritable. Topological data analysis (TDA) is one such tool, robust to noise, for analyzing how the data’s topological properties vary, and typically operates via filtration of the data and construction of a persistence diagram (PD). Therefore, the purpose of this study was to compute PDs to determine TDA-based heritability of static brain network topological features.

**Methods** The pipeline in Fig.1 was followed. 130 monozygotic (MZ) twin pairs (56M, 29.2±3.3yrs) and 74 dizygotic (DZ) twin pairs (30M, 29.1±3.5yrs) ICA-FIX rsfMRI scans from the Human Connectome Project (HCP) [2] underwent typical standardized processing. Twin groups were gender, education and age matched (p>0.15). Each scan was de-meaned and normalized by the standard deviation of each run, and HCP’s Glasser Parcellation [1] and subcortical FreeSurfer scheme (360+19 parcels, respectively) was employed. Two rsfMRI scans from one session were then concatenated, followed by generation of correlation matrices from each parcellated time series:  $\mathbf{x}_i$  for each twin as  $\rho_{ij} = \text{corr}(\mathbf{x}_i, \mathbf{x}_j)$ . Each correlation matrix was transformed into  $w_{ij} = \sqrt{1 - \rho_{ij}}$ . A graph filtration [3] was applied to each subject’s transformed data, and PDs were constructed. For all PDs, the values were interpolated onto a matrix  $G = (g_{ij})$  of grid size (300,300). Nonzero values were mirrored across  $i = j$ . Heat kernel smoothing [4] with bandwidth  $\sigma = 10$  was applied to each PD to smooth out topological noise and match PDs across subjects. The mirrored data were then removed. The final

PDs were correlated in a pairwise permuted fashion across all sets of all twin pairs within zygosity per pixel. The resulting group matrices of correlations per zygosity were denoted as  $C_{MZ} = (g_{ij}^{MZ})$  and  $C_{DZ} = (g_{ij}^{DZ})$ . The heritability index (HI) map was computed as  $HI = 2(C_{MZ} - C_{DZ})$ . The highest HI per pixel with corresponding  $C_{MZ}$  and  $C_{DZ}$  values were reported.

**Results** The most heritable regions of HI (HI=1) were clustered at distance locations (Fig.2): (0.25, 0.69), (0.36, 1.08), (0.5, 0.82), and (0.85, 0.97) [ $C_{MZ} > 0.49, C_{DZ} < 0$ ].

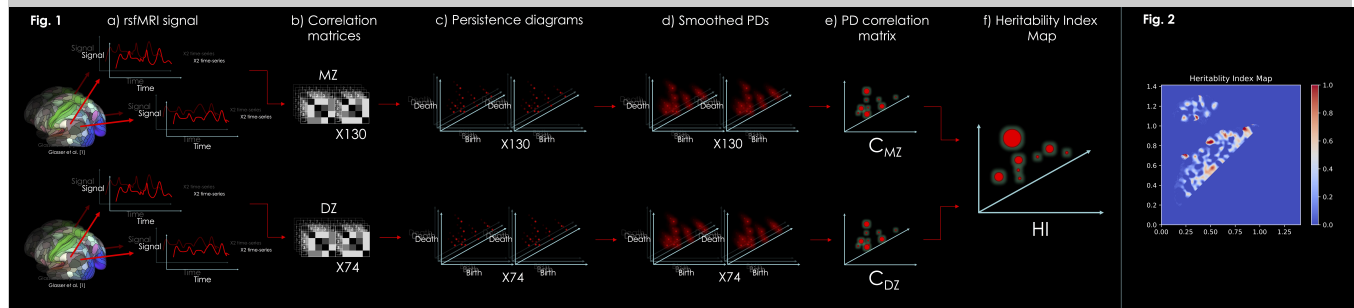
**Conclusion** An approach to investigate HI across smoothed PDs derived from graph filtration across rsfc was presented. We determined that certain topological features are heritable in rsfc. These findings may serve as further points of interest in 1) backprojection of the data for interpretation of heritable brain networks or 2) statistical inference.

## 1. REFERENCES

- [1] M.F. Glasser, T.S. Robinson, E.C. Hacker, C.D. Harwell, J. Yacoub, E., ... & S.M. Smith, “A multi-modal parcellation of human cerebral cortex,” *Nature*, vol. 536, pp. 171-178, 2016.
- [2] D.C. Van Essen, S.M. Smith, D.M. Barch, T.E. Behrens, E. Yacoub, K. Ugurbil, & Wu-Minn HCP Consortium. “The WU-Minn human connectome project: an overview,” *Neuroimage*, vol. 80, pp. 62-79, 2013.
- [3] M.K. Chung, H. Lee, A. DiChristofano, H. Ombao, and V. Solo, “Exact topological inference of the resting-state brain networks in twins,” *Network Neuroscience*, vol. 3, pp. 674–694, 2019.
- [4] S. Seo, M.K. Chung, and H.K. Vorperian, “Heat kernel smoothing using Laplace-Beltrami eigenfunctions,” *MICCAI*, pp. 505–512, 2010.

54 pt  
0.75 in  
19.1 mm

54 pt  
0.75 in  
19.1 mm



**Fig. 1 & 2.** Fig. 1: The pipeline of the proposed method is shown for creating heritability index via heat kernel smoothing on PDs based on rsfMRI data. Fig. 2: HI Map demonstrating the most heritable regions of HI clustering around distance locations (0.25, 0.69), (0.36, 1.08), (0.5, 0.82), and (0.85, 0.97).