

# Optimal Distances for Edge-Wise Reliability in the Functional Connectome

Aki Nikolaidis<sup>1</sup>, Xiaoning He<sup>1</sup>, Ting Xu<sup>1</sup>, Joshua Vogelstein<sup>2</sup>, Michael Milham<sup>1,3</sup>

1- The Child Mind Institute, 101 East 56<sup>th</sup> Street, New York, NY 10022  
 2- Johns Hopkins University, Baltimore, MD 21218  
 3- Nathan Kline Institute for Psychiatric Research, Orangeburg, NY 10962

## Summary

**Background:** Functional connectivity is one of the most important measurement techniques of the human brain. Recently, the field of neuroimaging has focused issues of reliability and reproducibility of the functional connectome<sup>1</sup>. While Pearson's correlation is the commonly used to assess the relationship between the functional timeseries in different parts of the brain<sup>2</sup>, relatively little is known about its reliability compared to other commonplace distance metrics.

**Current work:** In the current work we conducted an extensive evaluation of the univariate reliability of eight commonplace distance metrics. We assessed the differences in reliability of these distance metrics across a different atlas resolutions, scan times, and sparsity levels. We examined the cortical spatial variability of functional connectivity and ICC between the 10 atlases for each distance metrics as well.

**Results:** We found that Pearson's correlation had significantly lower edge-wise ICC than other distance metrics, and these differences were exacerbated by higher numbers of regions in an atlas, greater scan time, and thresholding all but the top 5% of edges.

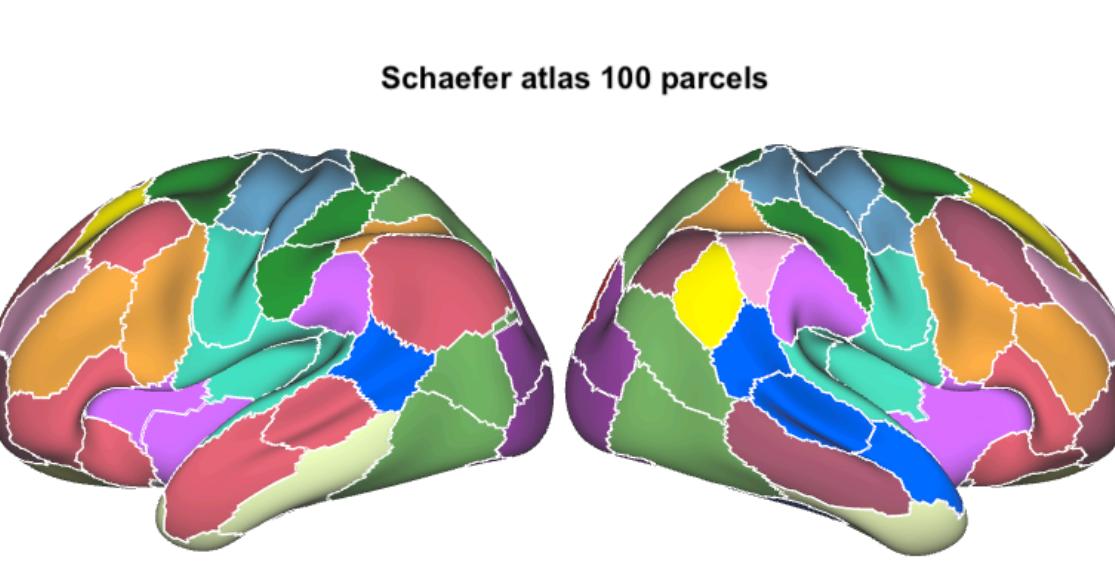
**Conclusions:** Spatial distribution of mean connectivity and ICC is highly conserved across distances. Pearson's correlation seems suboptimal for maximizing edge-wise ICC. Further evaluation is required.

## Approach

**Data:** HNU1 Test Retest<sup>3</sup>: 30 young adults; Ten, 10 min rs-fMRI.

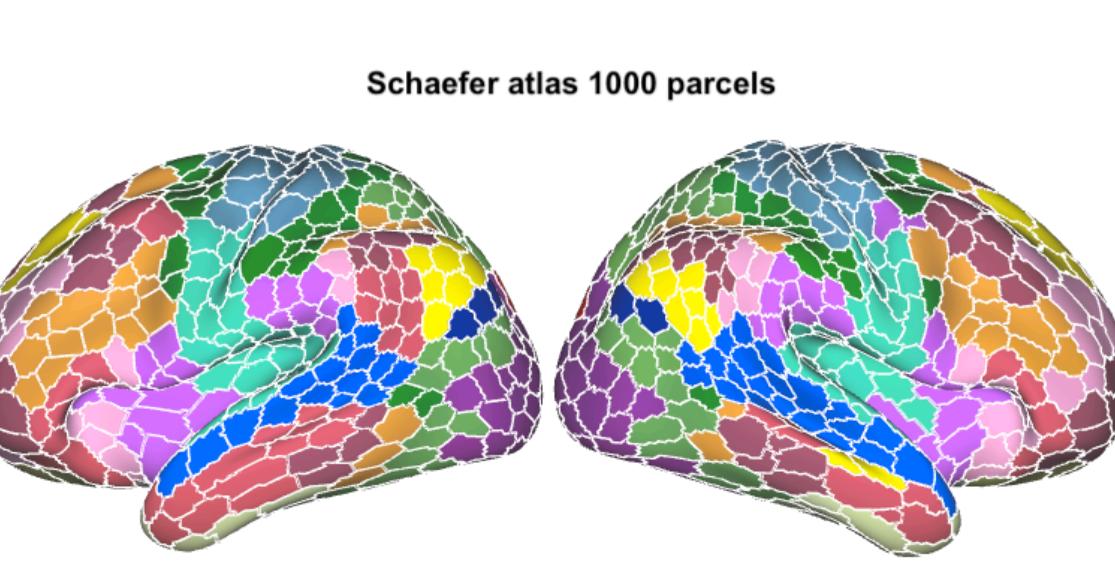
**C-PAC Preprocessing:** Skull stripping with AFNI. preprocessed to 2mm, White matter and CSF regression. No GSR, bandpass filtering 0.01-0.1, CompCor- 5 component. White matter and CSF regression, Spike regression.

**Data Extraction:** 10 sessions were concatenated into test and retest datasets with 5-50 minutes of scan time in 5-minute increments. Timeseries were extracted for the ten 100-1000 region Schaefer atlases<sup>4</sup> in volume space in increments of 100 regions.

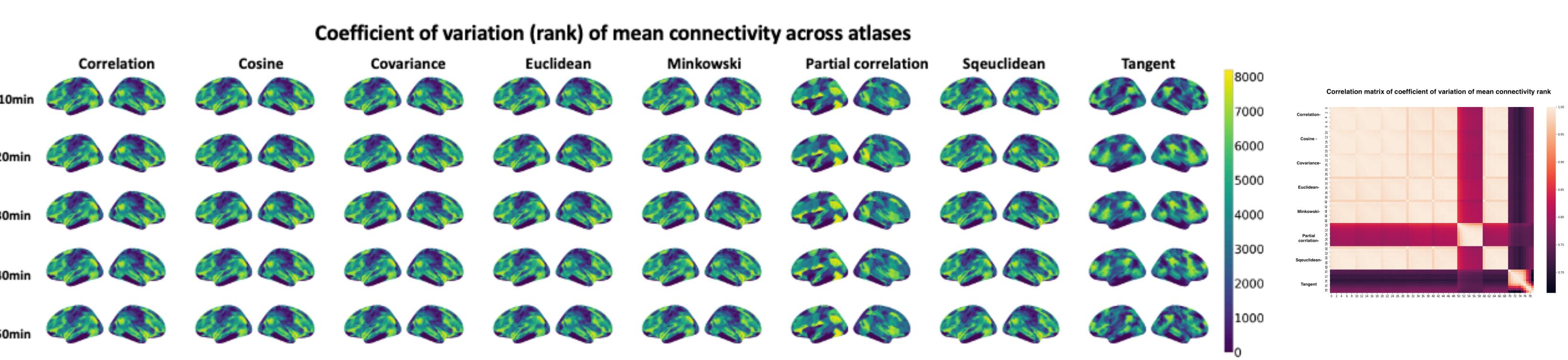
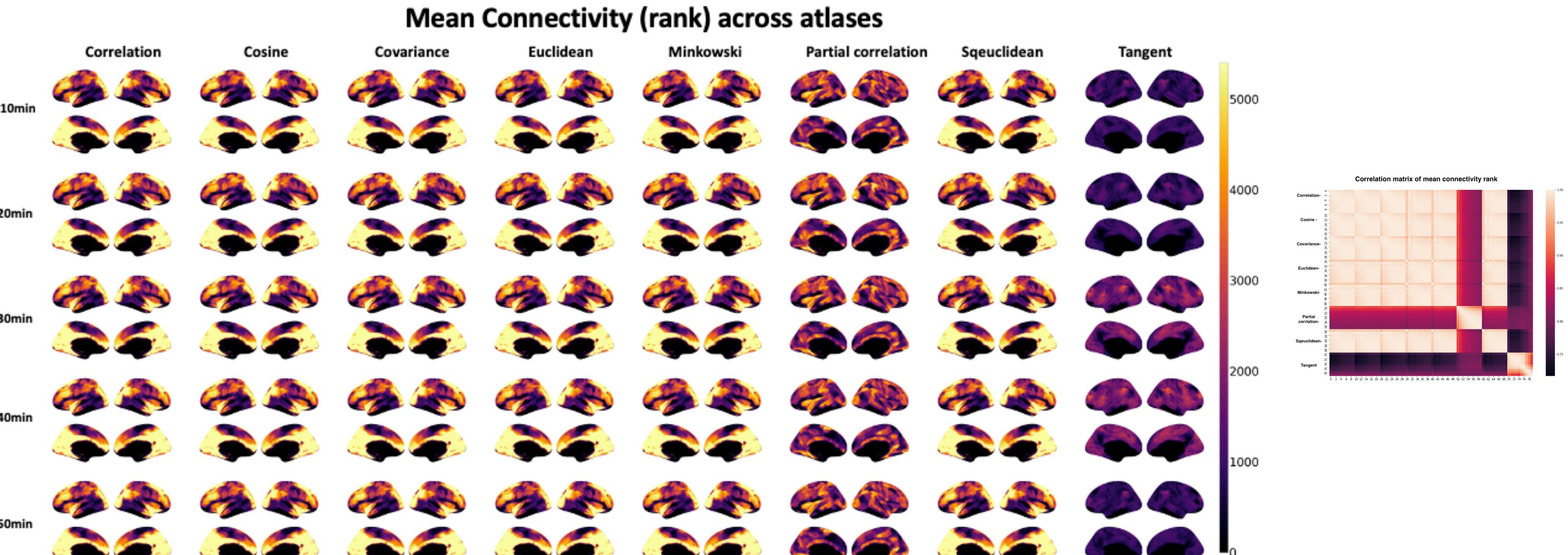


**Distance Metrics:** Scipy was used to derive our library of distances, including: Pearson's correlation, cosine, covariance, Euclidean, Minkowski, partial correlation, squared Euclidean, tangent correlation. All distances were standardized and subtracted from 1 to create a corresponding similarity metric.

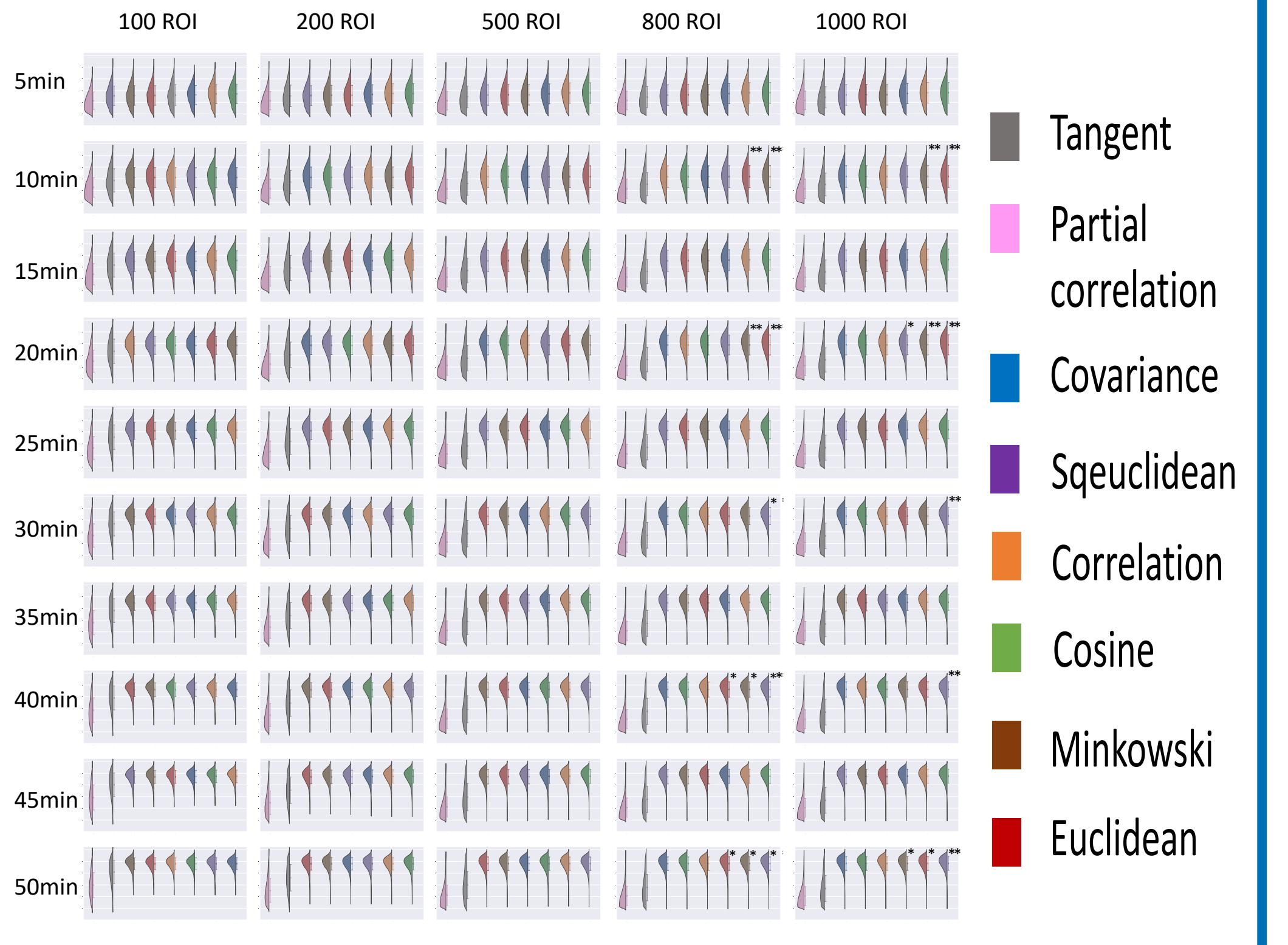
**Reliability:** We assessed univariate reliability of the individual edges through intraclass correlation coefficient (ICC)<sup>5</sup>



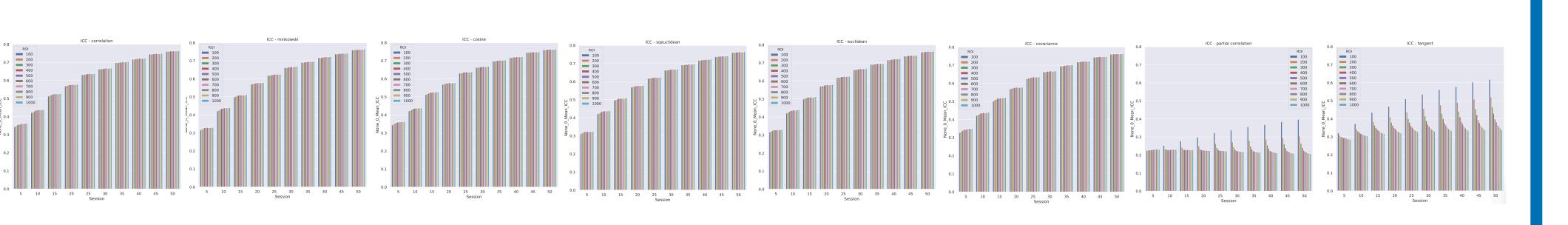
## Mean Connectivity and Coefficient of Variability Across Atlases



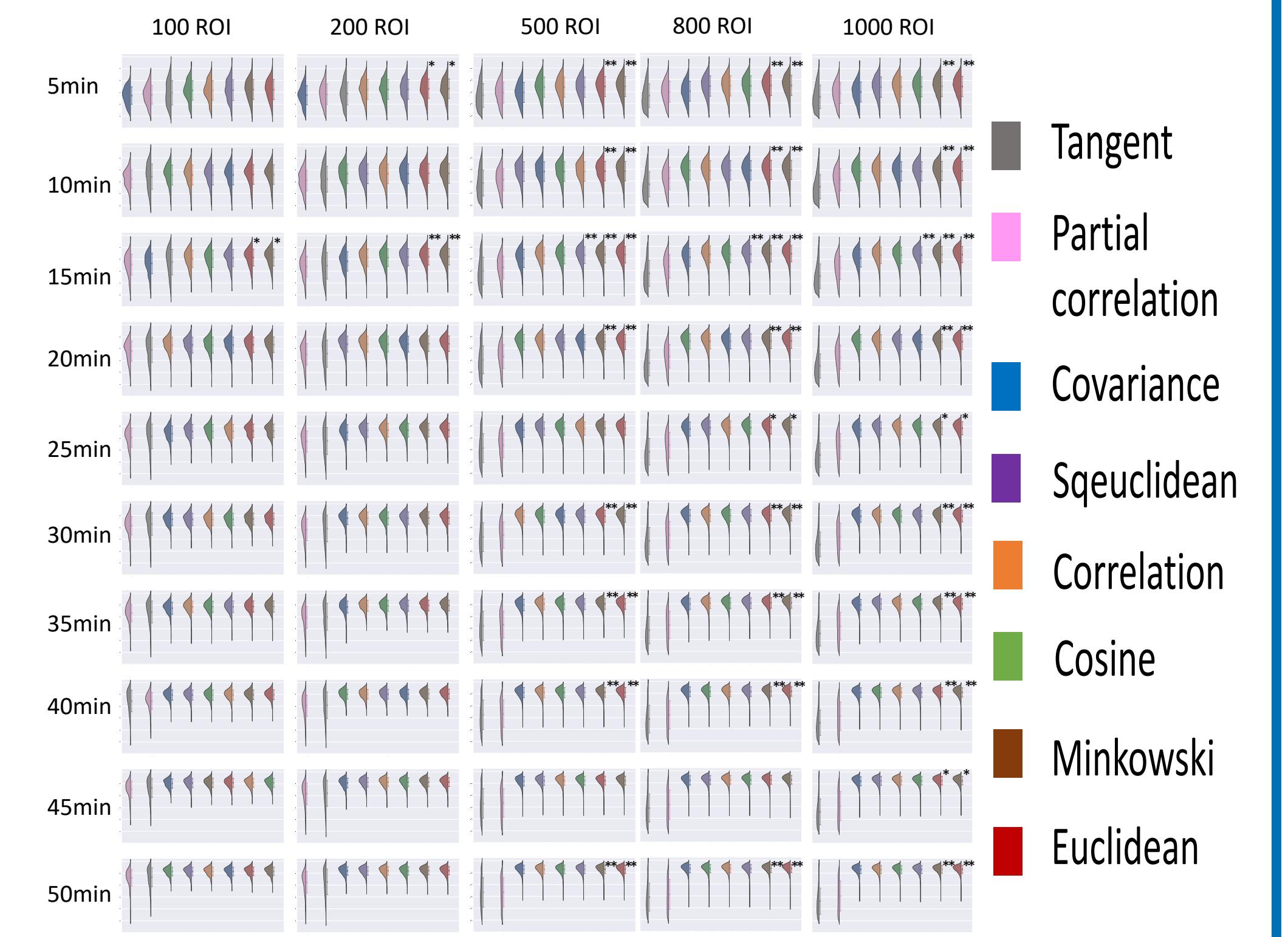
## Dense Connectome Edge-Wise ICC



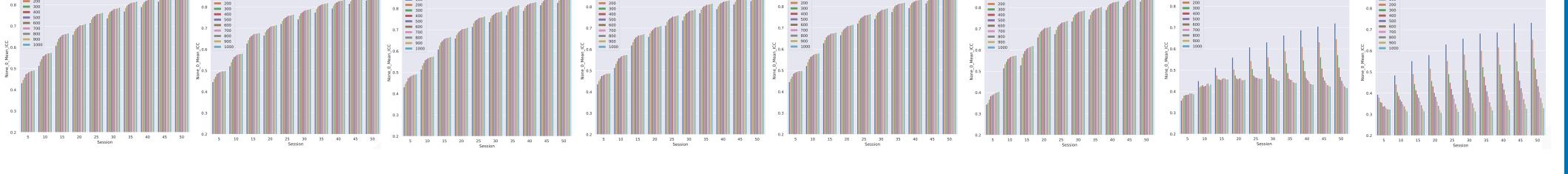
## Dense Connectome Mean ICC



## Sparse Connectome Edge-Wise ICC



## Sparse Connectome Mean ICC

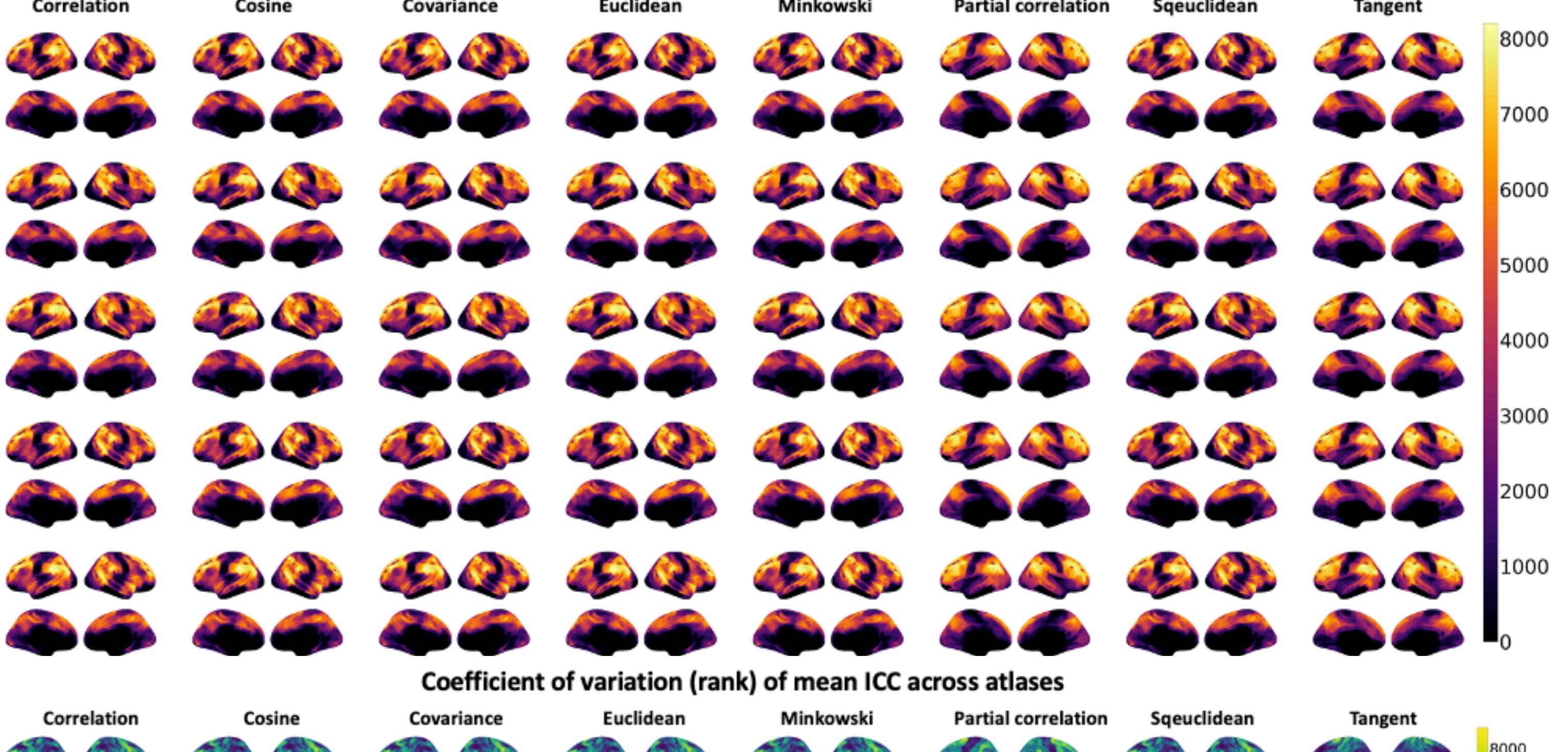


## References

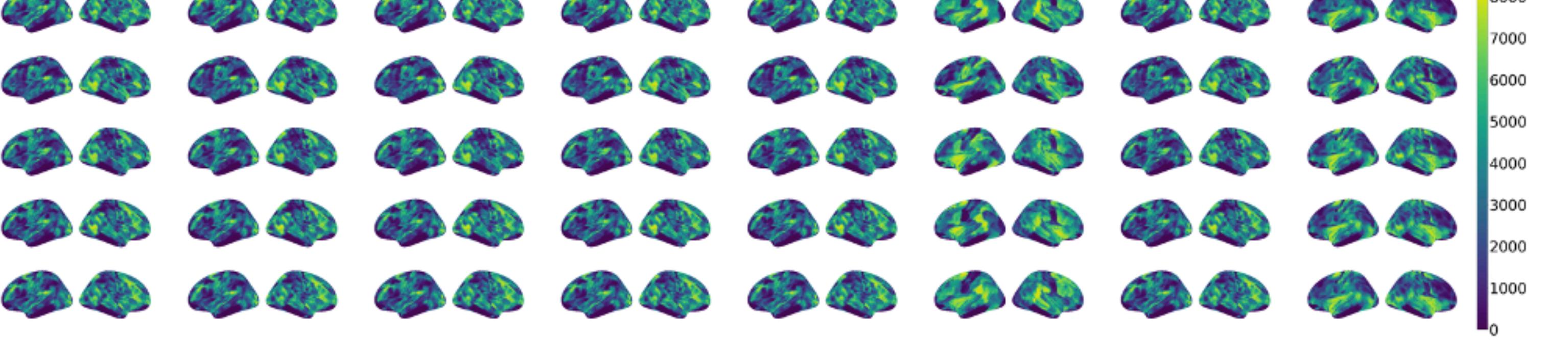
- Zuo, X. N., Xu, T., & Milham, M. P. (2019). Harnessing reliability for neuroscience research. *Nature human behaviour*, 3(8), 768-771.
- Zalesky, A., Fornito, A., Cocchi, L., Gollo, L. L., & Breakspear, M. (2014). Time-resolved resting-state brain networks. *Proceedings of the National Academy of Sciences*, 111(28), 10341-10346.
- Zuo XN, et al (2014). An open science resource for establishing reliability and reproducibility in functional connectomics. *Scientific Data*, 1.
- Schaefer, A., Kong, R., & Yeo, B. T. T. (2016). Chapter 1 - Functional connectivity parcellation of the human brain. In G. Wu, D. Shen, & M. R. Sabuncu (Eds.), *Machine Learning and Medical Imaging* (pp. 3-29). Academic Press.
- Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations—uses in assessing rater reliability. *Psychological Bulletin*, 86(2), 420-428.

## Spatial Distribution of ICC by Time and Distance

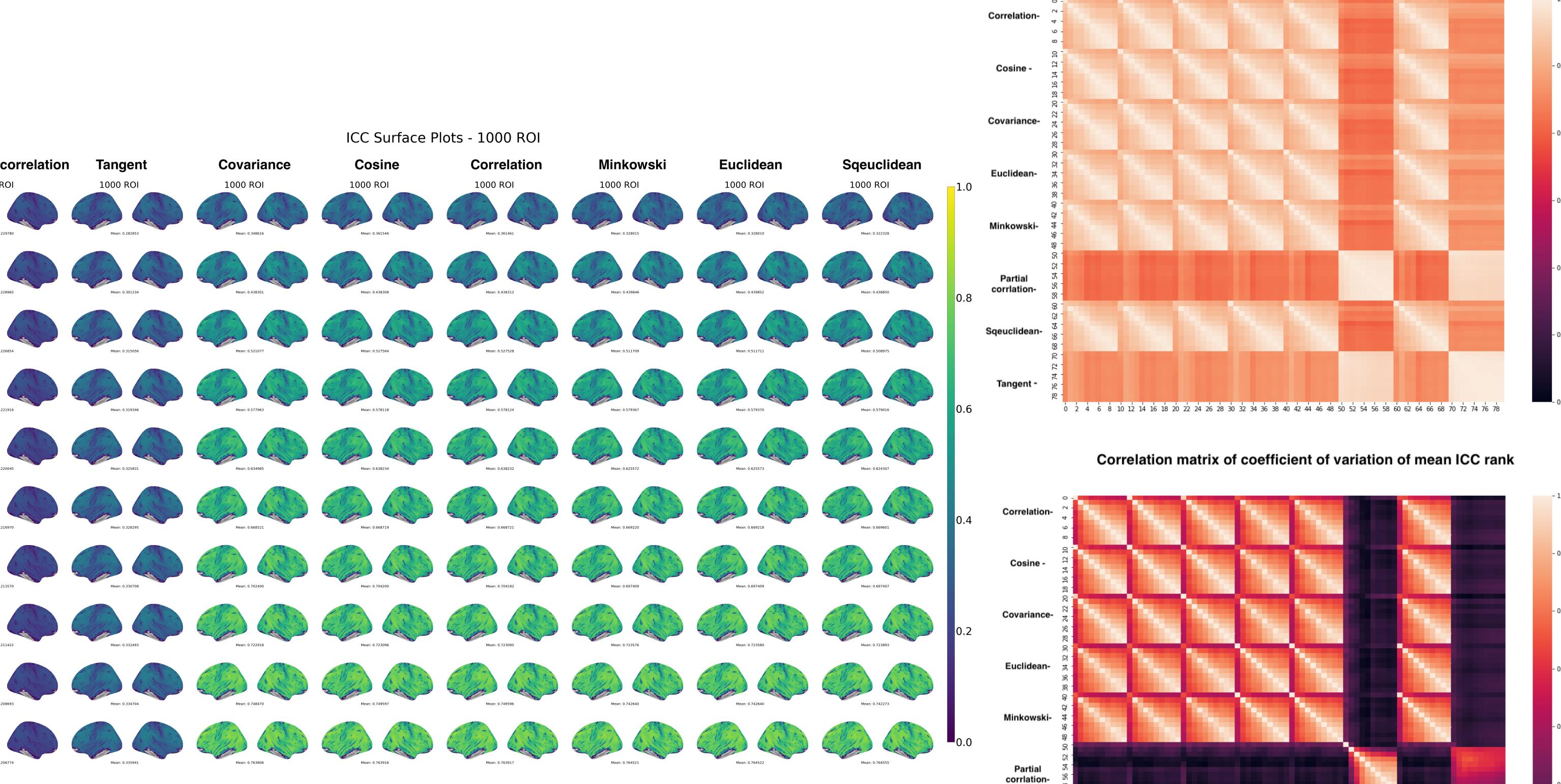
### Mean ICC (rank) across atlases



Coefficient of variation (rank) of mean ICC across atlases



Correlation matrix of mean ICC rank



Correlation matrix of coefficient of variation of mean ICC rank



## Conclusions

- Euclidean, Minkowski, Squared Euclidean, and Cosine distances tend to outperform Pearson's correlation with respect to univariate edge-wise ICC
- Univariate methods perform quite differently compared to univariate approaches (Partial & Tangent Correlation)
- Spatial distribution of mean connectivity and ICC highly conserved
- Node-wise heterogeneity in connectivity and ICC highly conserved
- Longer scans and greater numbers of ROIs associated with higher ICC
- Highest node-wise ICC heterogeneity: Lingual Gyrus, Temporal Fusiform Cortex, Occipital Pole, Cingulate Gyrus, Middle frontal gyrus, Frontal Pole