Evaluating Tangent Spaces, Distances, and Deep Learning Models to Develop Classifiers for Brain Connectivity Data

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Presentation Outline

1. Introduction and Background
2. Methods
    - Dataset
    - Post-processing Methods
    - Classifiers
3. Results
    - Task Identification
    - Twin and Subject Identification
4. Discussion

Introduction and Background

Introduction to fMRI

- **F**unctional **M**agnetic **R**esonance **I**maging
- Non-invasive neuroimaging technique
- Very high spatial resolution[6]

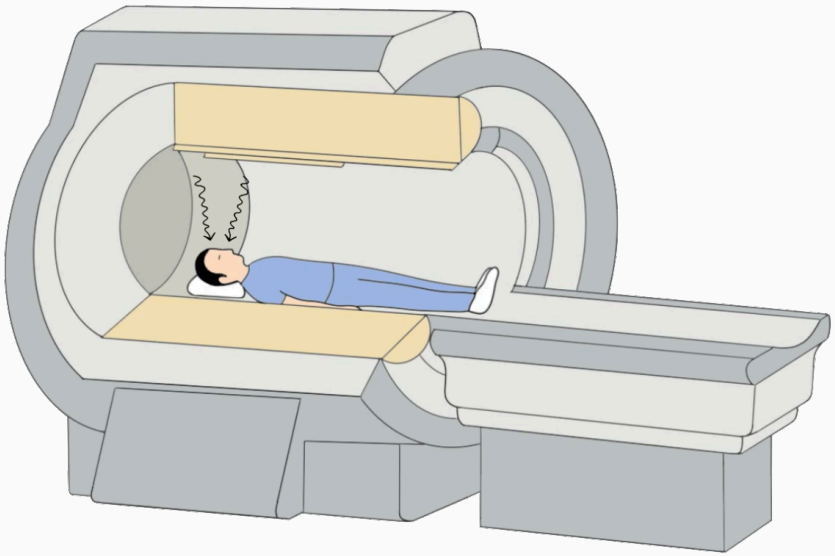


Figure 1: fMRI Scanner

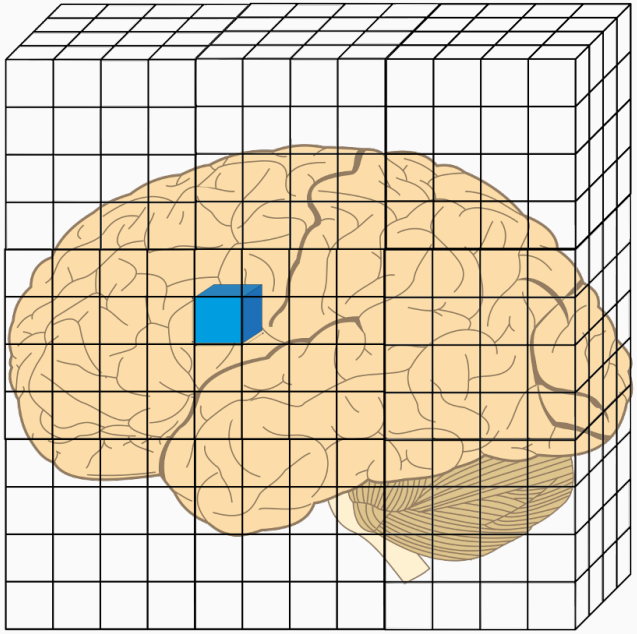
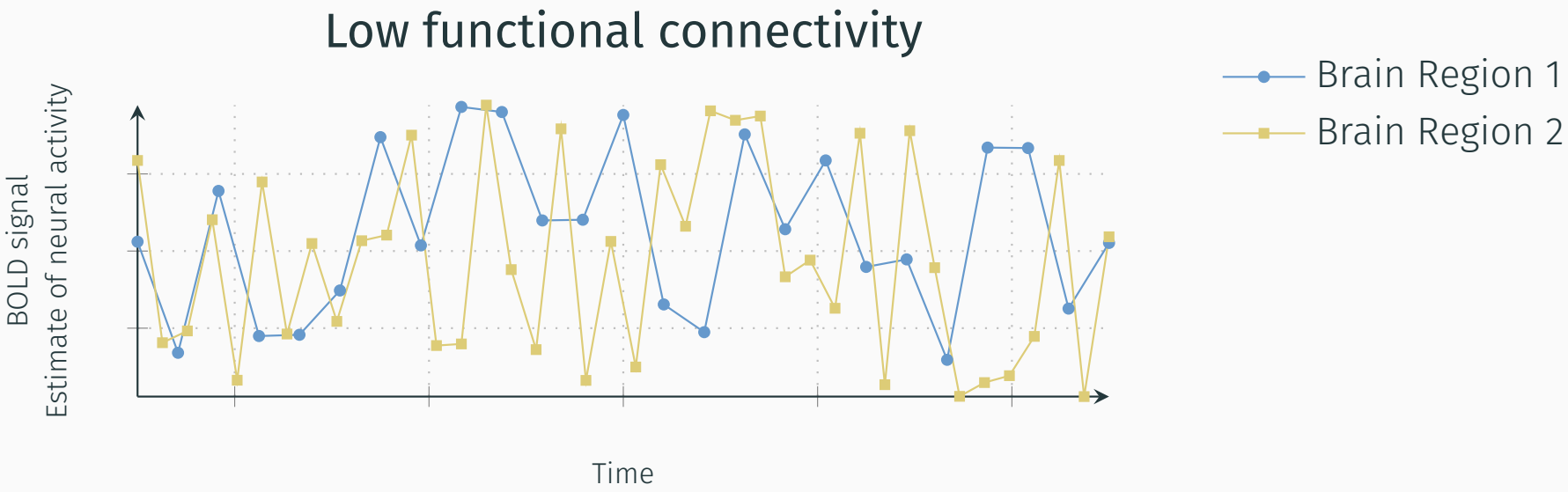
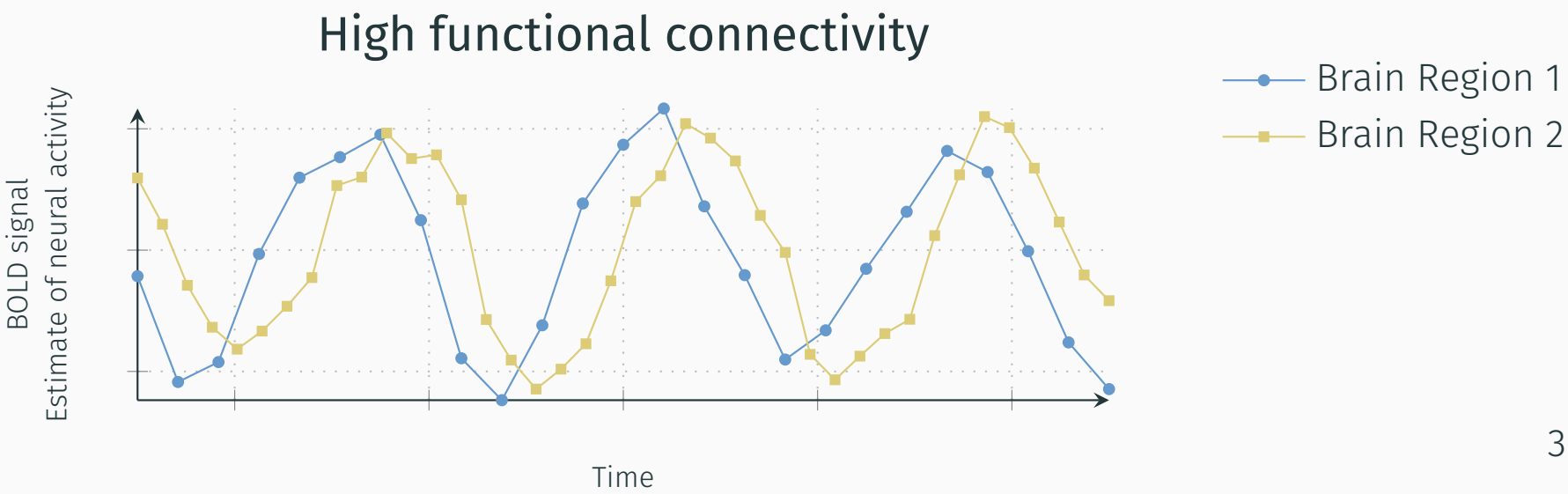


Figure 2: 1mm^3 Voxels

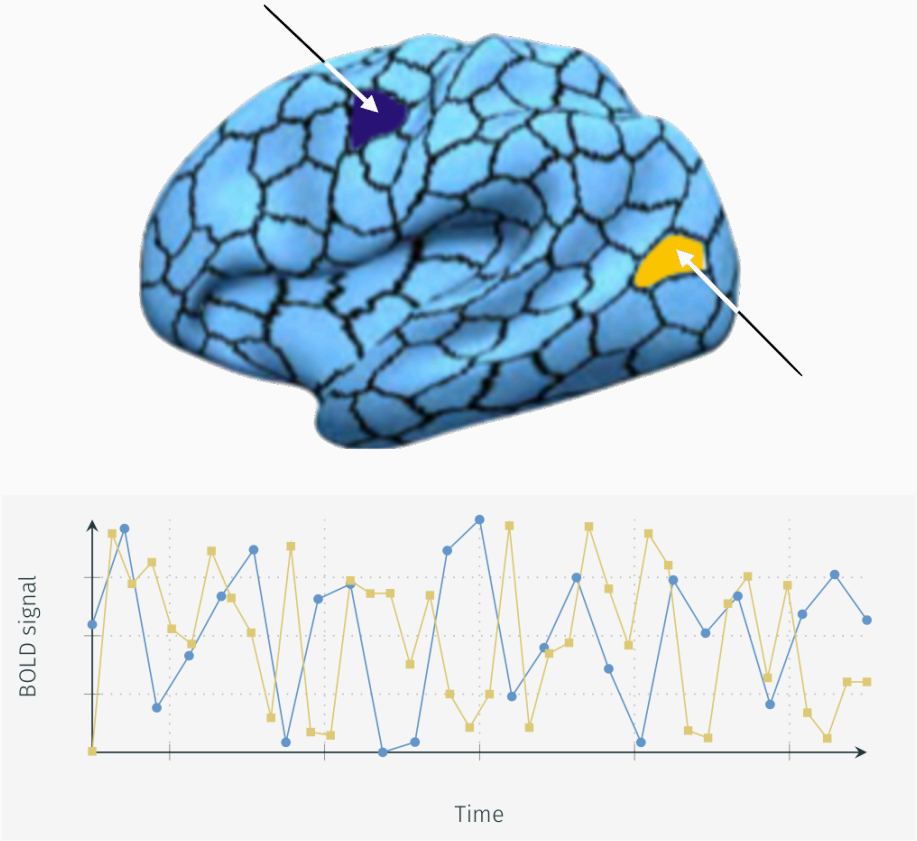
Graphic obtained from 2 Minute Neuroscience

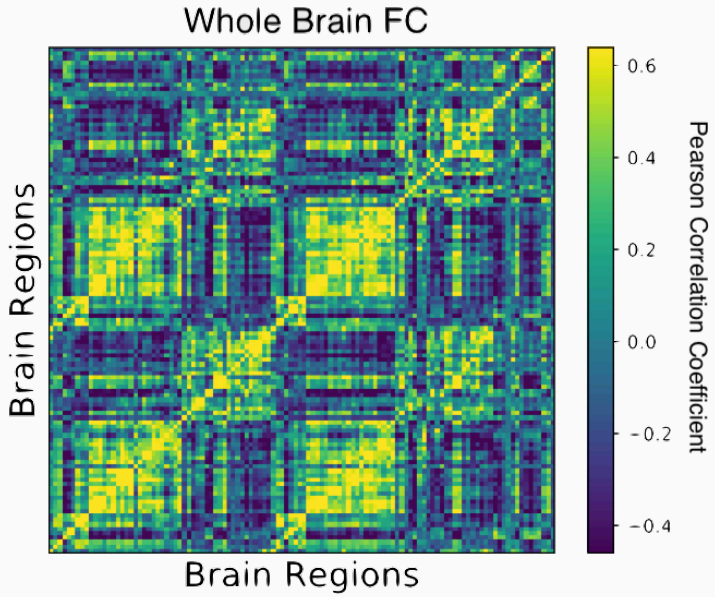
Example of Low and High Correlations of BOLD Time Series





Example Estimation of a Subject's Functional Connectome





Previous Work

- PCA reconstruction of functional connectivity (FC) improves subject-level identifiability[3]
- Geodesic distance, unlike Euclidean distance, preserves FC geometry and improves predictive power.[11]
- Deep Neural Networks have achieved a task identification rate of 0.937 in HCP 8-task fMRI classification.[12]
- Support Vector Machines have achieved MZ and DZ twin identification rate of 0.64 and 0.22, respectively.[5]

Research Motivation and Question

Motivation

- Absence of a gold standard pipeline for analyzing functional connectivity[8]
- Clinical application of fMRI is very limited[10]
- Recent data frameworks for functional connectivity have shown to increase predictive power[2, 11]
- The explosion of publicly available neuroimaging datasets has made deep learning viable[8]

Research Question

- How can we best process and project functional connectivity data for task and twin identification?

Monozygotic (MZ) and Dizygotic (DZ) Twins

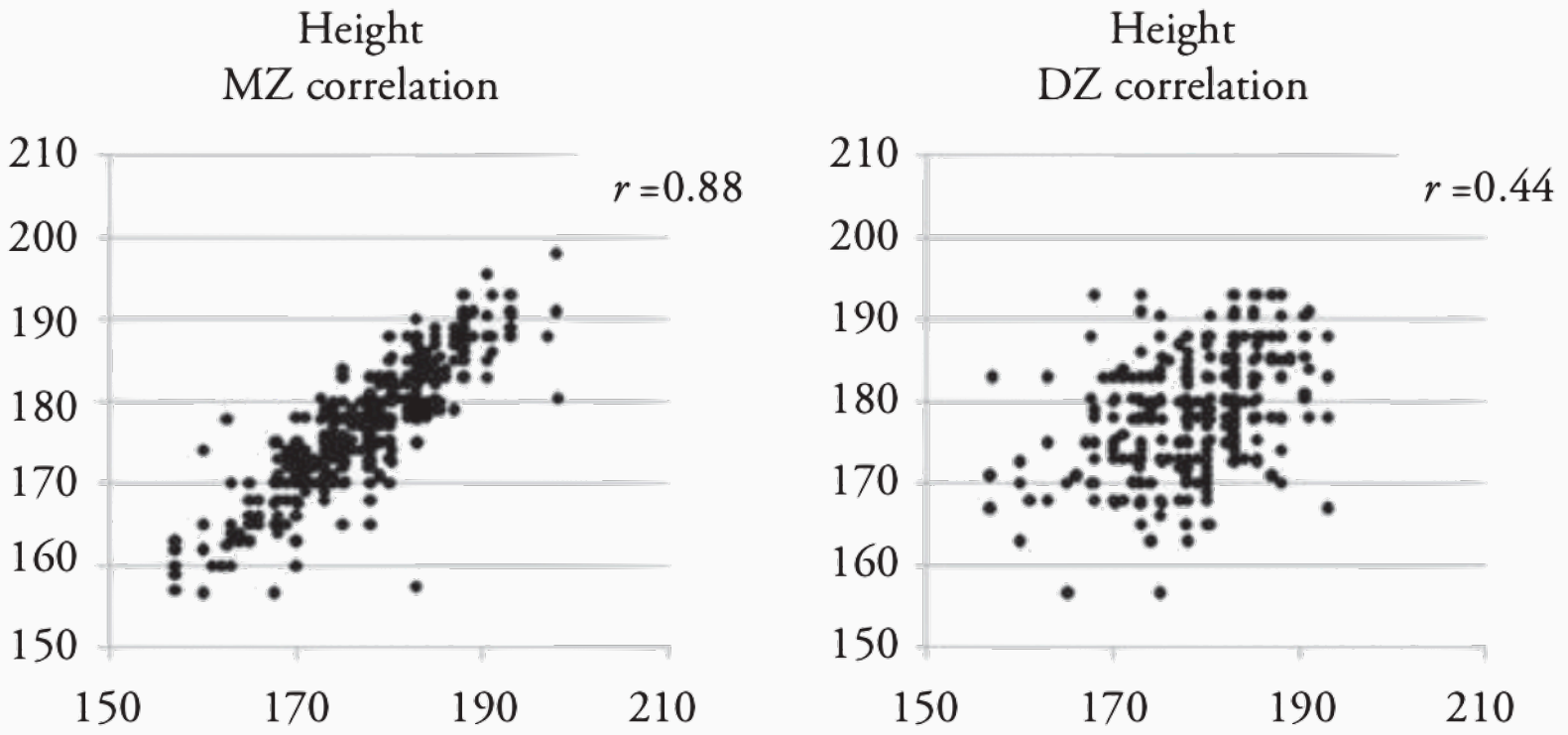


Figure 3: Scatter plot of monozygotic (MZ) and digyzotic (DZ) twin pairfor height (cm) in males. MZ twins share 100% of their parents' genetic material, DZ twins share 50% of genetic material, and unrelated subjects share 0% of the genetic material. MZ and DZ twins also grow up in similar environments.

Methods

Dataset and Minimal Pre-processing

- Human Connectome Project (HCP) 1200 Subjects Release[7]
- HCP functional minimal preprocessing pipeline[4]
  - Artifact removal
  - Motion correction
- 8 cognitive tasks
  - Resting State
  - Working Memory
  - Relational
  - Social
  - Gambling
  - Motor
  - Language
  - Emotion
- Test and retest scans per subject, per task

Task & Twin Subsets of HCP 1200 Subjects Release

Task Identification Dataset

- 424 unrelated subjects
- 8 cognitive tasks
- Total of $424 \times 8 \times 2 =$ **6784 fMRI scans**

Twin Identification Dataset

- 106 pairs of monozygotic (MZ) twins across 8 tasks
- Total of $106 \times 2 \times 8 \times 2 =$ **3392 fMRI scans**
- 58 common dizygotic (DZ) twin pairs across 8 tasks
- Total of $58 \times 2 \times 8 \times 2 =$ **1856 fMRI scans**

Experimental Design

Post-processing Methods

- PCA Reconstruction
- Tangent Space Projection
- Brain Parcellation Granularity

Classifiers

- Convolutional Neural Network
- K-Nearest Neighbors

Adaptation of the Differential Identifiability Framework[3]

- PCA decomposition into orthogonal eigenvectors W sorted by eigenvalues in decreasing explained variance
- Project centered data onto eigenvectors to create PCs Z
- Reconstruct data using subset of *k* PCs and eigenvectors

$$\underset{m\times n}{\mathrm{X_r}} = \underset{m\times k}{\mathrm{W}} \times \underset{k\times n}{\mathrm{Z'}} + \mu$$

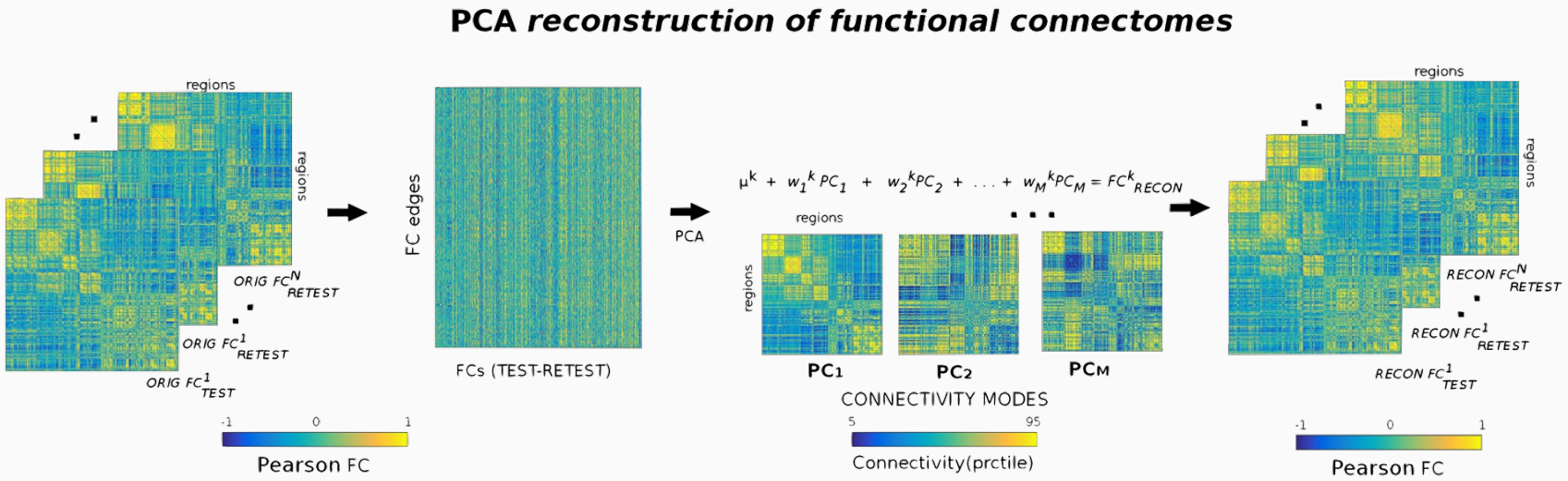


Figure obtained from Amico & Goñi, 2018[3]

Significance of Geodesic Distance

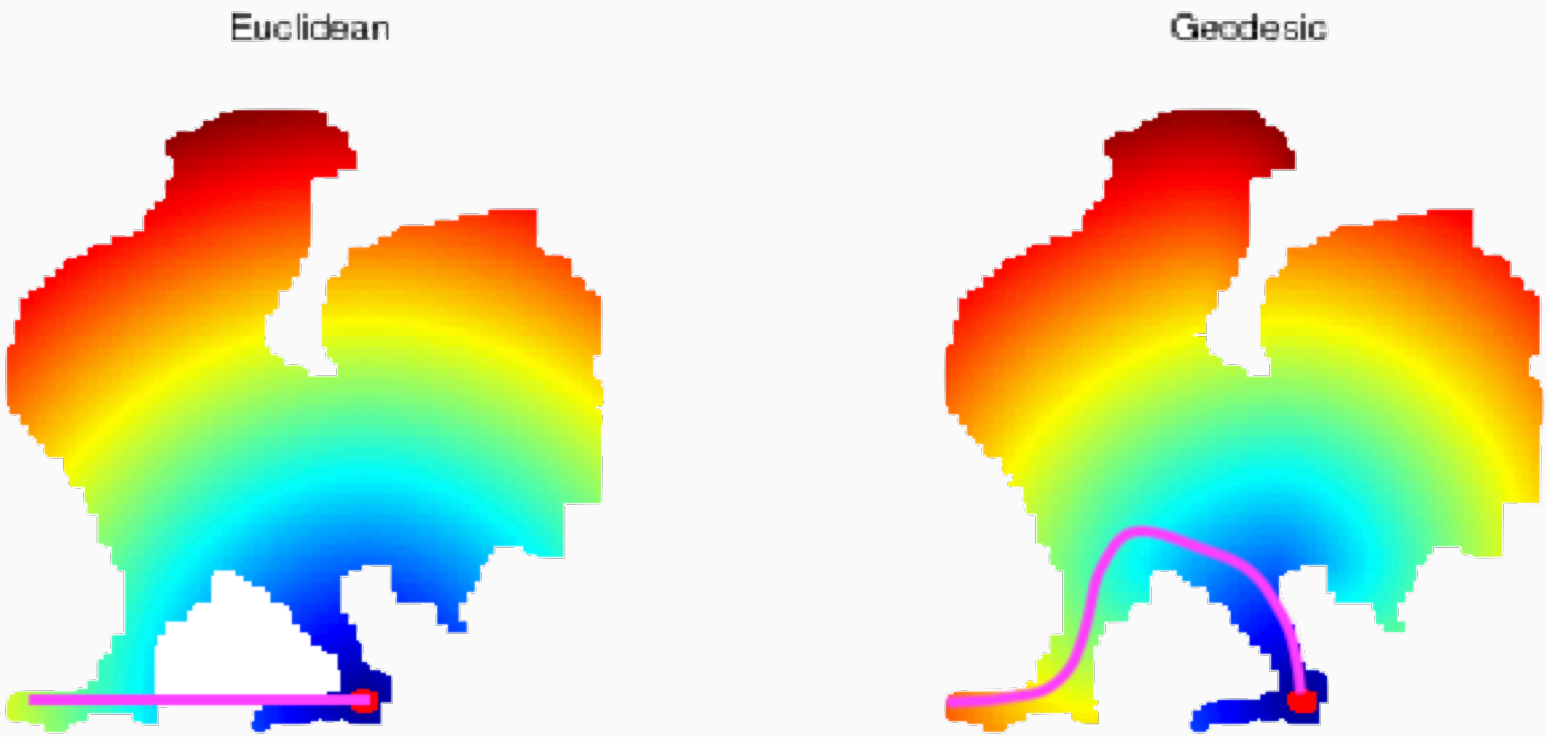


Figure 4: Visualization of Euclidean and geodesic distance between two points on a chicken-shaped surface

Figure obtained from https://dsp.stackexchange.com/

Tangent Space Projection

- FC matrices are positive definite (PD)
- PD matrices do not form a Euclidean space[1]
- Project FC into tangent space to preserve geometry:

$$\hat{\mathrm{C}} = \log_m \left(\mathrm{C}_g^{-\frac{1}{2}} \mathrm{C} \mathrm{C}_g^{-\frac{1}{2}} \right)$$

Table 1: Reference Matrices C_g

Reference	Equation
Euclidean	$\frac{1}{N} \sum_i C_i$
Harmonic	$(\frac{1}{N} \sum_i C_i^{-1})^{-1}$
LogEuclid	$\exp_m(\frac{1}{N} \sum_i \log_m C_i)$
Kullback	$C_e^{\frac{1}{2}} (C_e^{-\frac{1}{2}} C_h C_e^{-\frac{1}{2}})^{\alpha} C_e^{\frac{1}{2}}$
Riemmanian	$\arg\min(\sum_i \delta_R(C_e C_i)^2)$

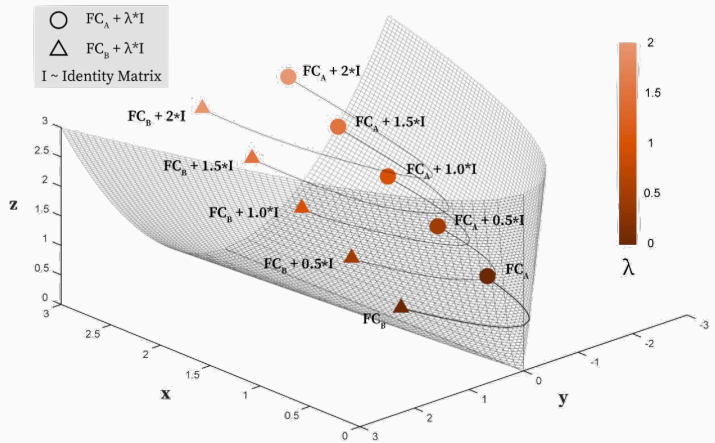


Figure 5: Positive Definite Cone

Figure 4 obtained from Abbas et al. 2020[1]

Mean Reference Matrices for Tangent Space Projection

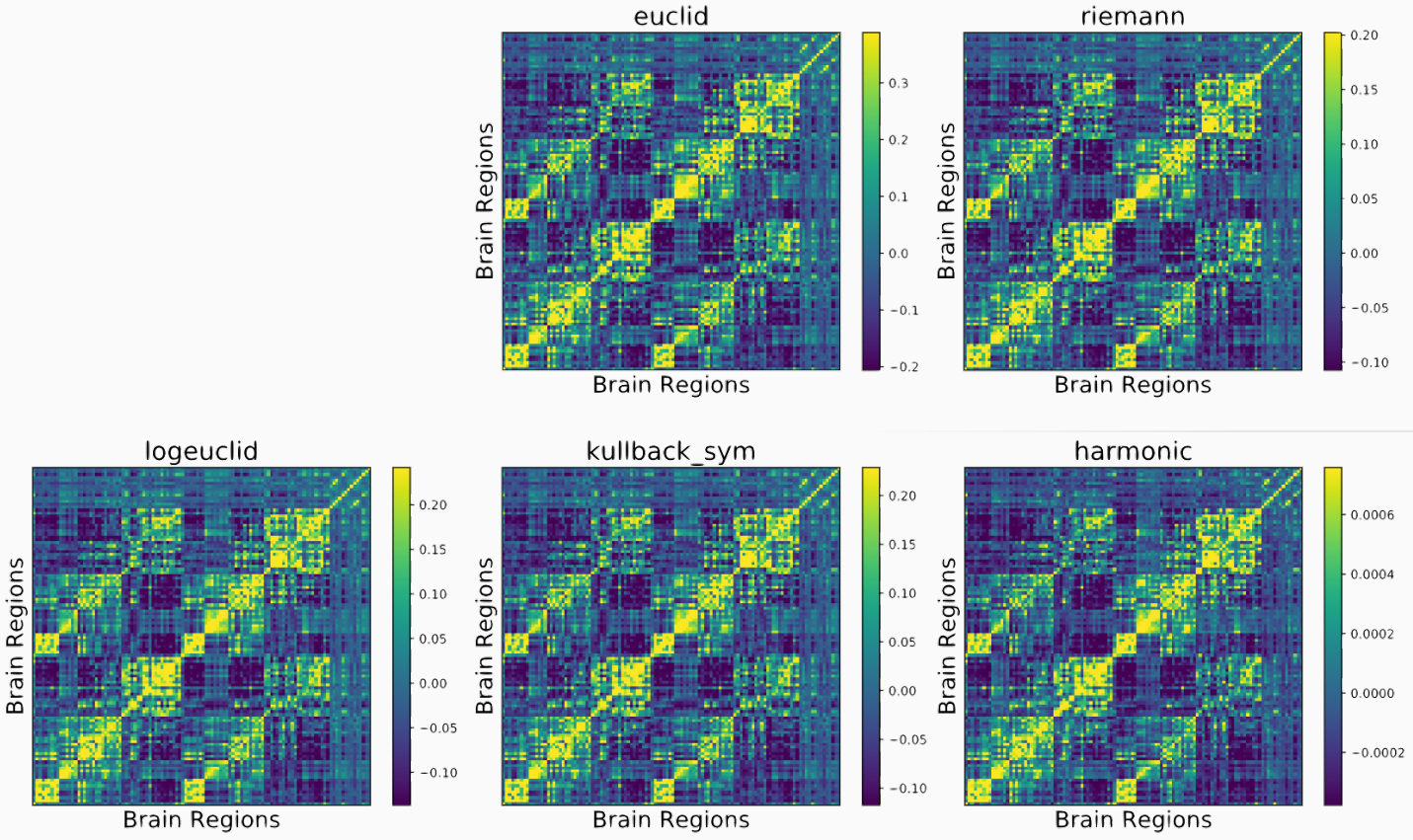


Figure 6: Reference matrices calculated from the Human Connectome Project (n= 424) with Schaefer's 100 brain region parcellation.[9]

Tangent Projected Functional Connectivity Matrices

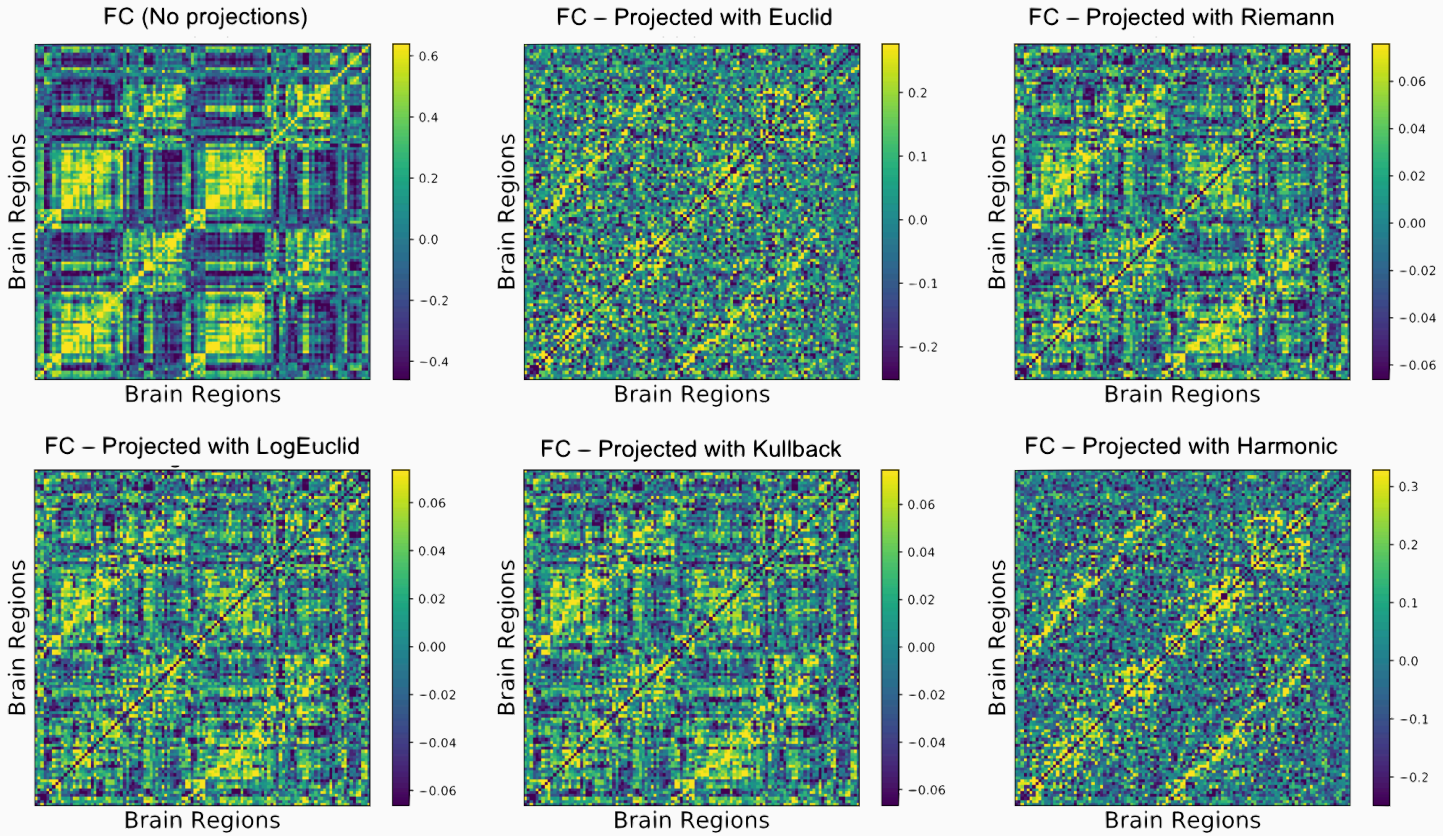


Figure 7: Resting state functional connectomes of Subject 1 after tangent projection with various reference matrices[9]

Brain Parcellation Granularity

Evaluating the effect of parcellation size from 100-500 brain regions

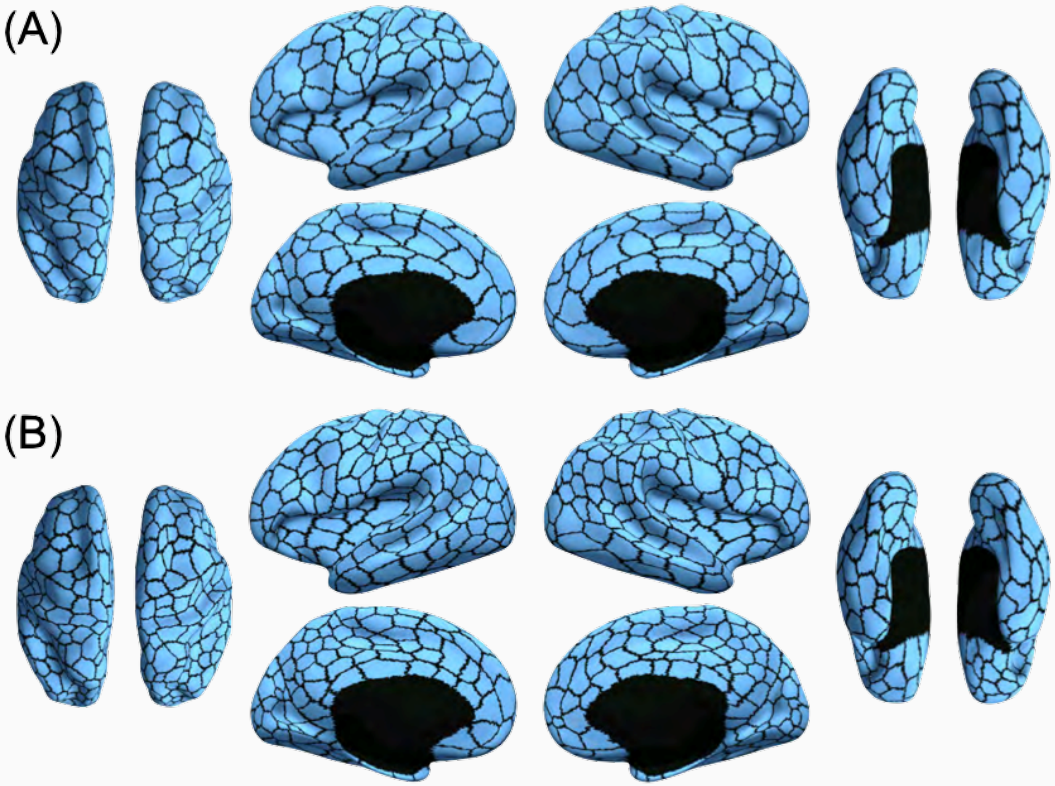


Figure 8: Examples of different Schaefer parcellation granularities[9]

Figure 5 adapted from Schaefer 2018[9]

K-Nearest Neighbors Classifier

1	2	3	4
2	5	6	7
3	6	8	9
4	7	9	10

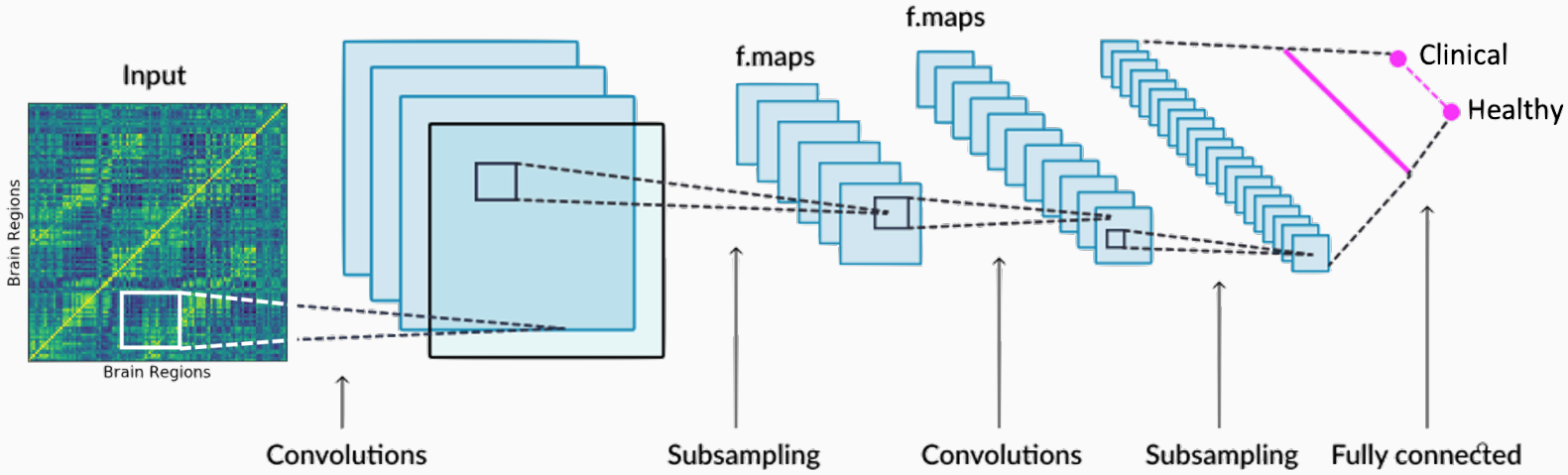
3	1	8	5
1	2	9	10
8	9	8	7
5	10	7	10

2	3	4	6	7	9

1	8	5	9	10	7

Figure 9: Vectorize FCs and predict based on the *k* nearest neighbors

Convolutional Neural Network Classifier



Why Convolutional Neural Networks?

- Preserve spatial information of FC
- Reduces the number of parameters which must be learned
- Does not need feature selection
- Can learn the complex nonlinear relationships of brain functionality
- Recently - enough FC samples to effectively train a model

Example CNN architecture adapted from https://missinglink.ai/guides

Convolutional Neural Network Architecture

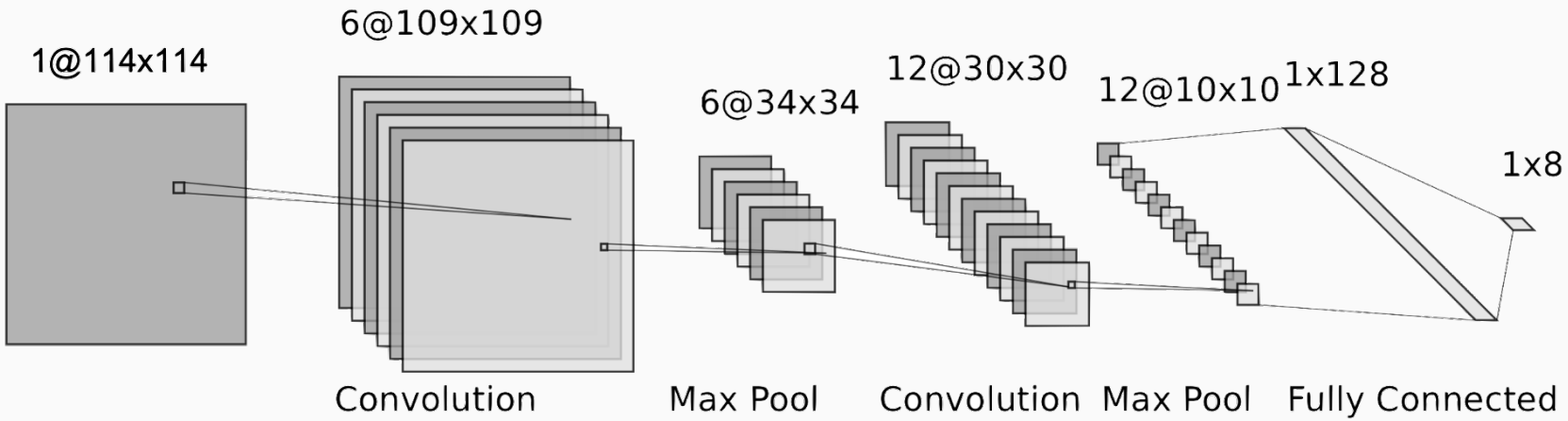


Figure 10: Architecture of Schaefer100 Neural Network

- 80/20 Train/Test split
- Data Normalization
- ReLU activation
- SGD Optimizer
- Cross-entropy Loss
- Learning Rate: $1e-3$
- 200 epochs
- GPU Computing

Results

Task: KNN Classifier Configuration

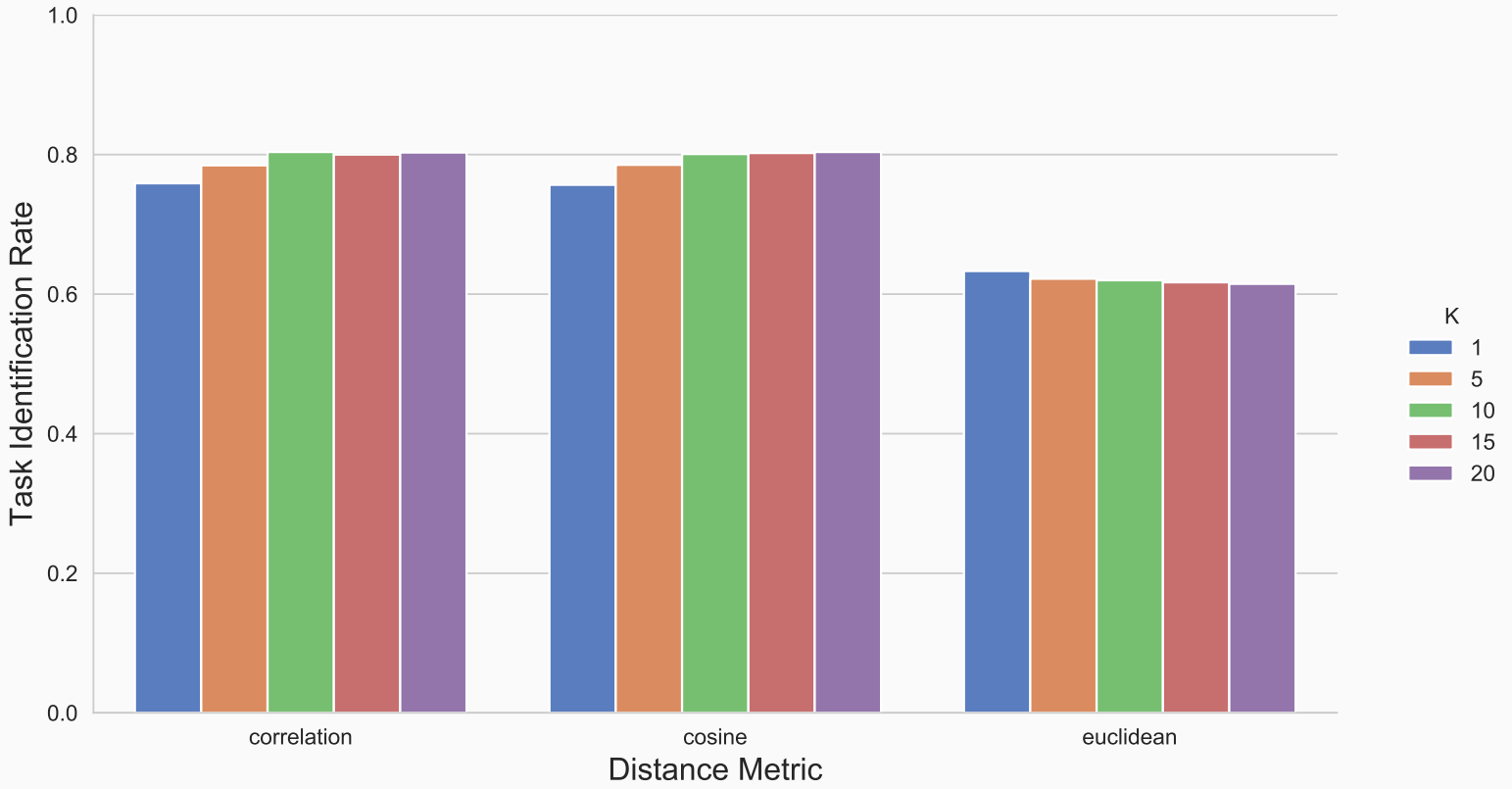


Figure 11: KNN Test Accuracy with various values of *k*

Key Finding

For values of *k* above 10, task identification rate no longer increases significantly. Correlation and cosine perform better than Euclidean.

Task: PCA Reconstruction of Functional Connectomes

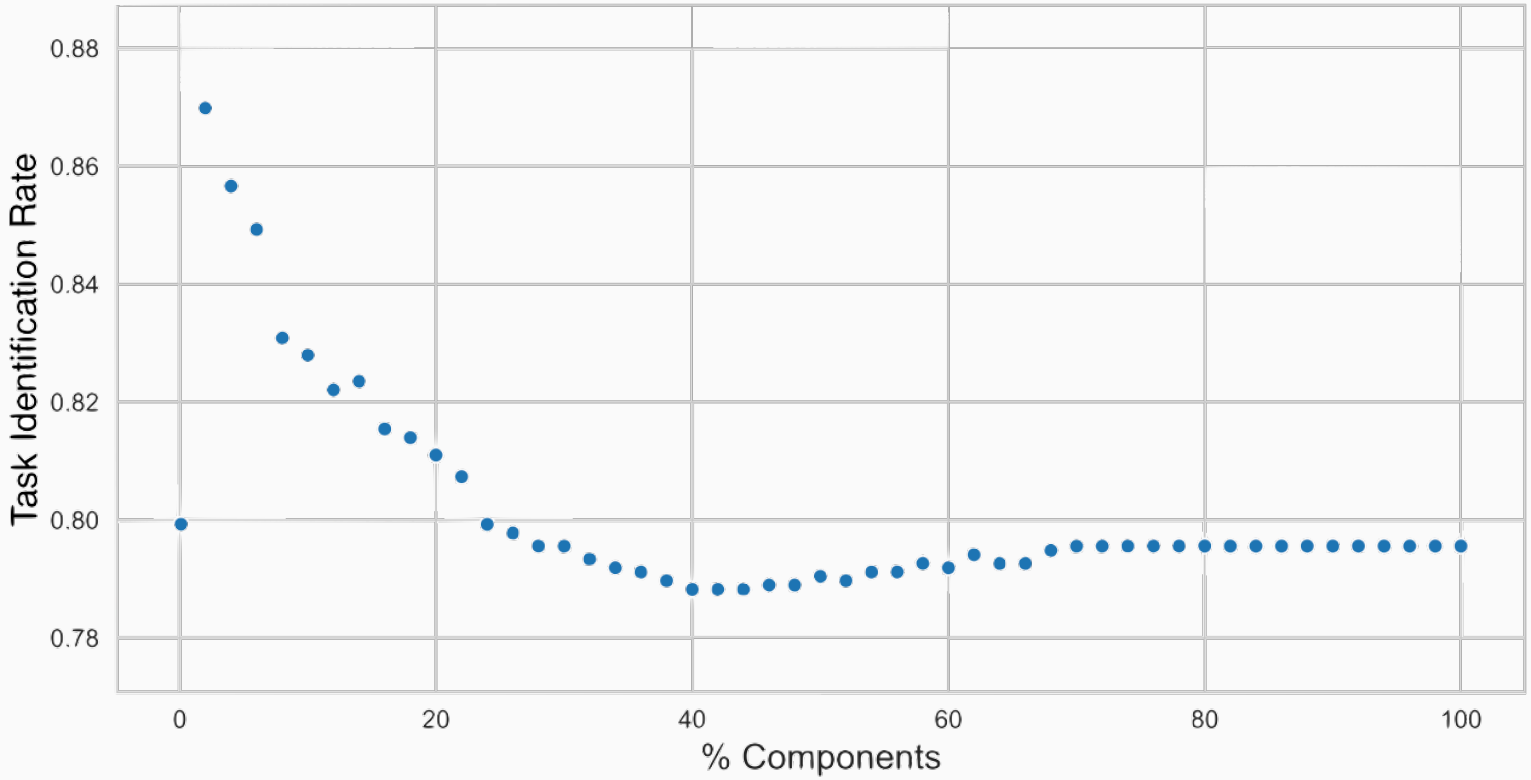


Figure 12: KNN Task Identification Rate with % Principal Components

Key Finding

Optimal PCA reconstruction at roughly **2%** of total PCs

Fine grain search: Optimal reconstruction at **80** of 6,874 PCs

Task: Tangent Space Projection of Functional Connectomes

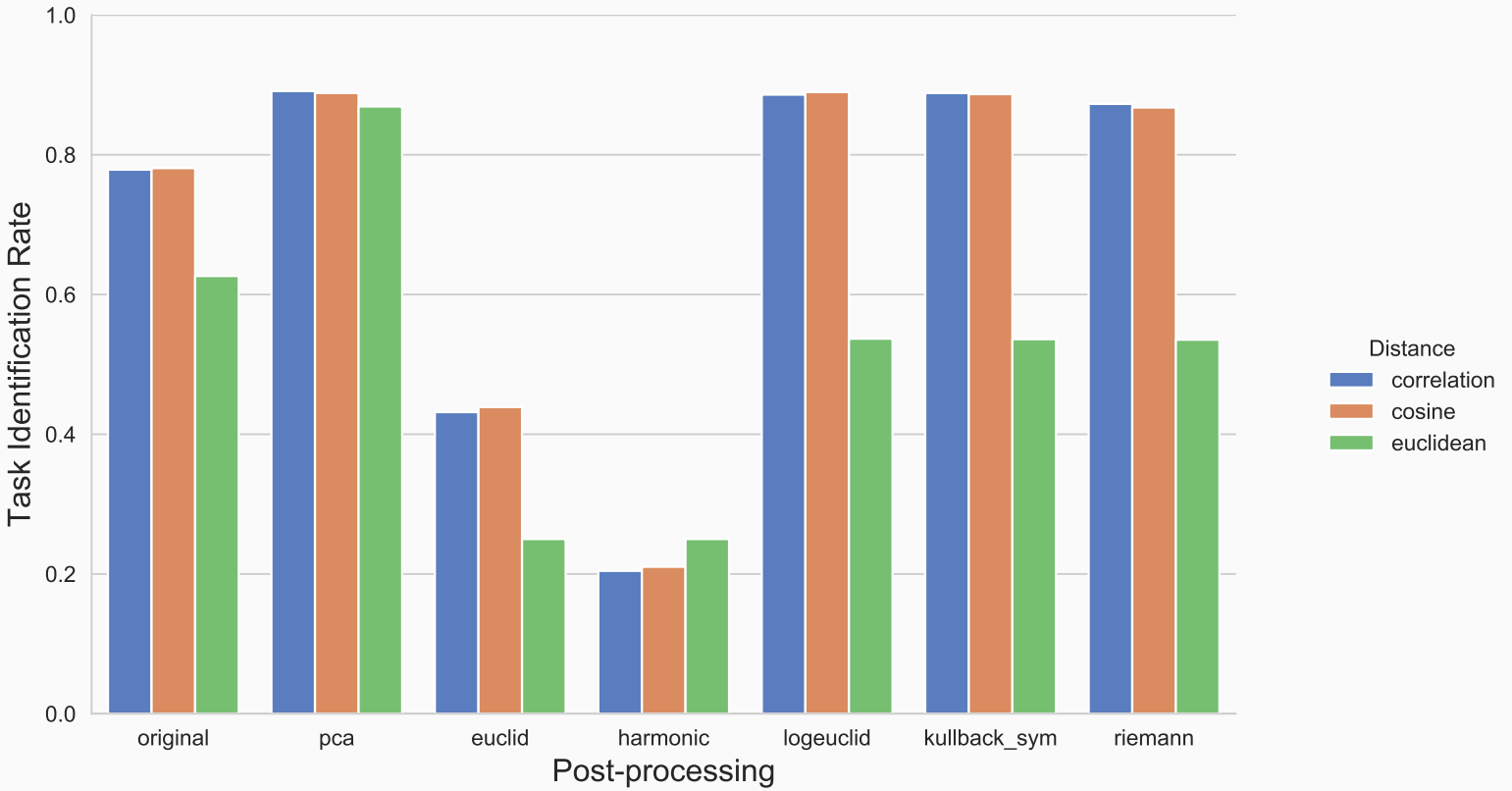


Figure 13: KNN Task Identification Rate with Tangent References

Key Finding

PCA reconstruction and tangent projection with LogEuclid, Kullback, and Riemann reference matrices improve task identification rate

Task: Convolutional Neural Network Training and Validation

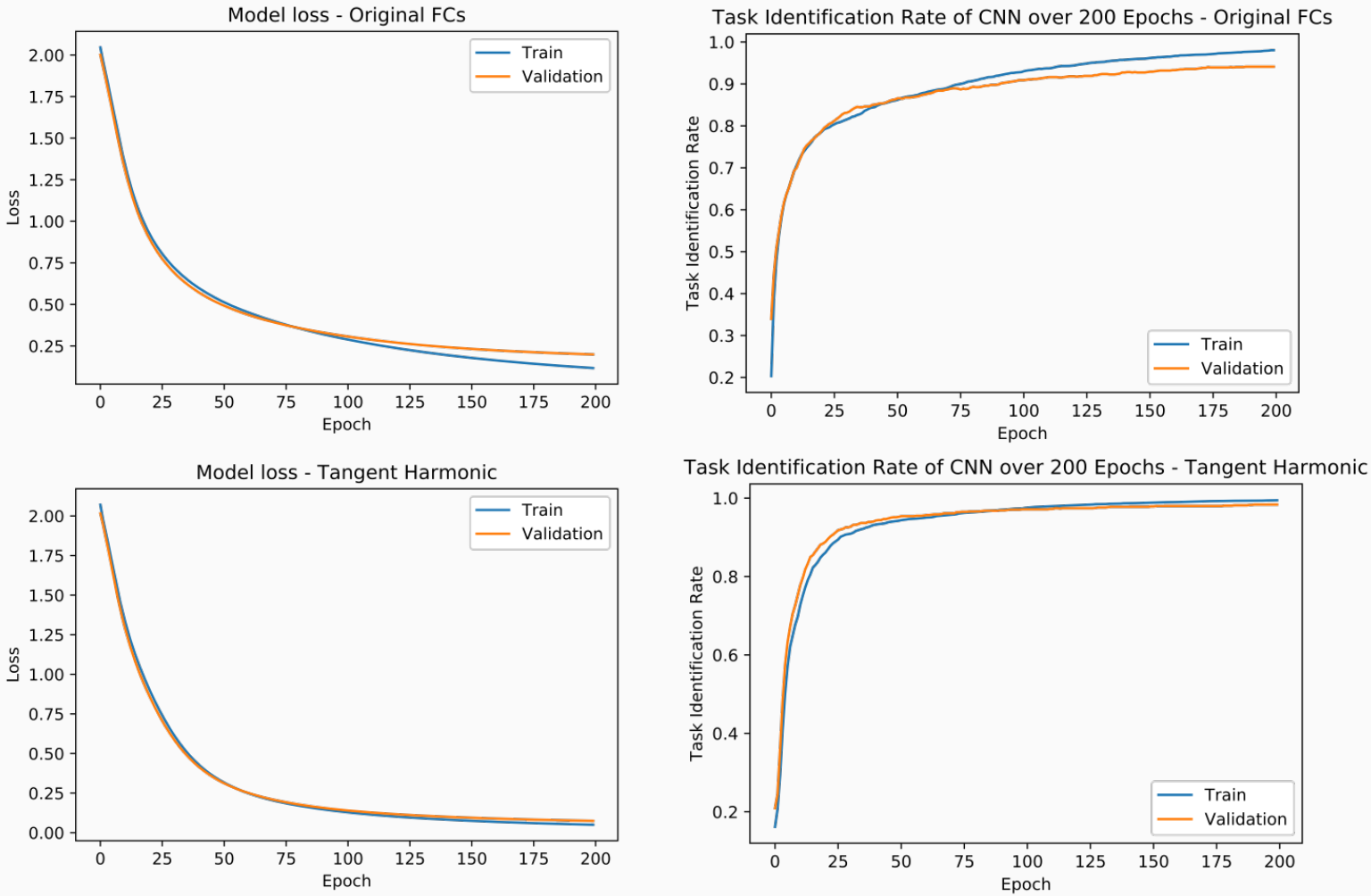


Figure 14: CNN Learning Curves of Original and Tangent Harmonic FCs

Task: Convolutional Neural Network Results

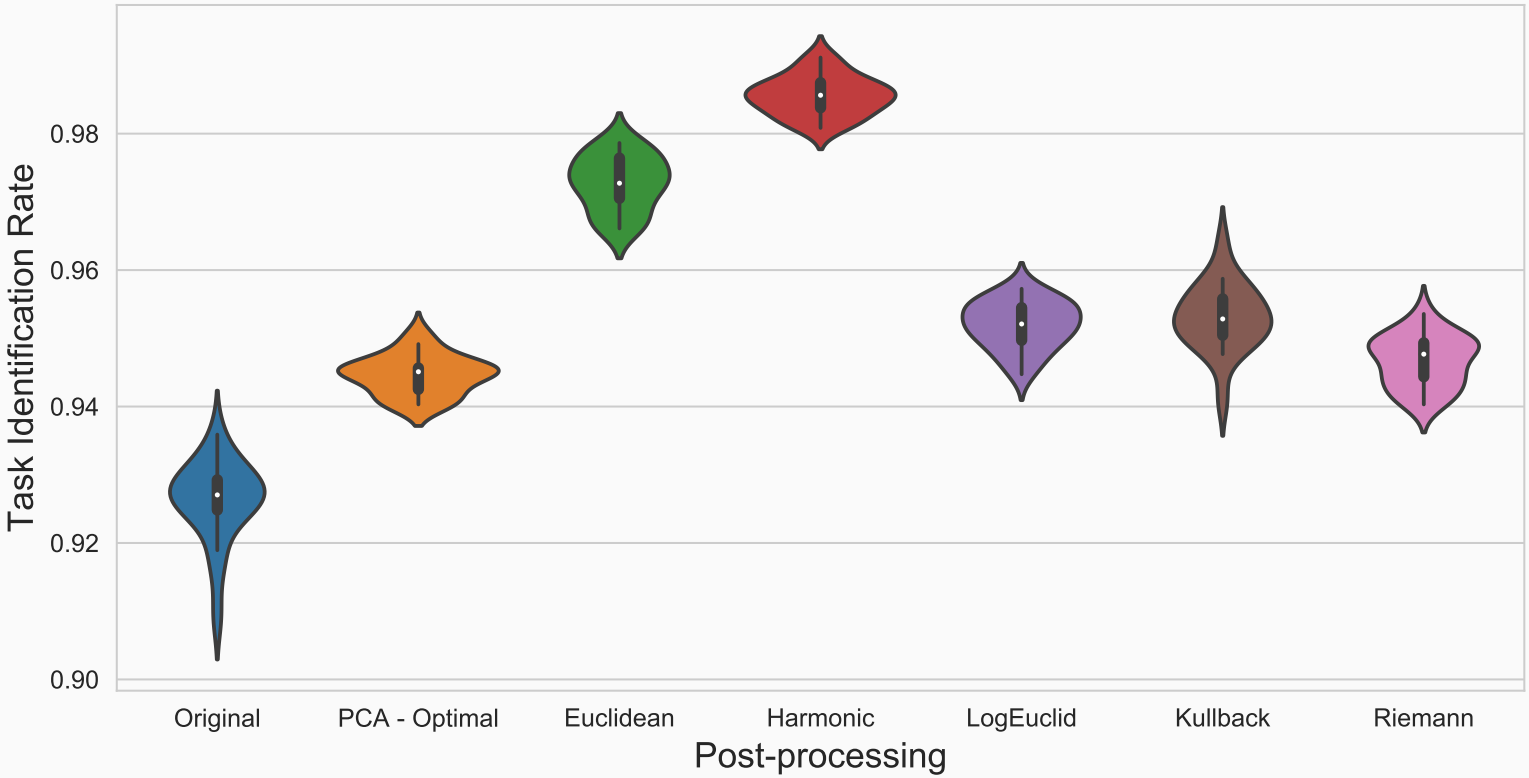


Figure 15: CNN Task Identification Rate with Post-Processing Methods

Key Finding

Tangent projected FCs with harmonic mean reference perform best

Twin: PCA Reconstruction for MZ Twin Identification

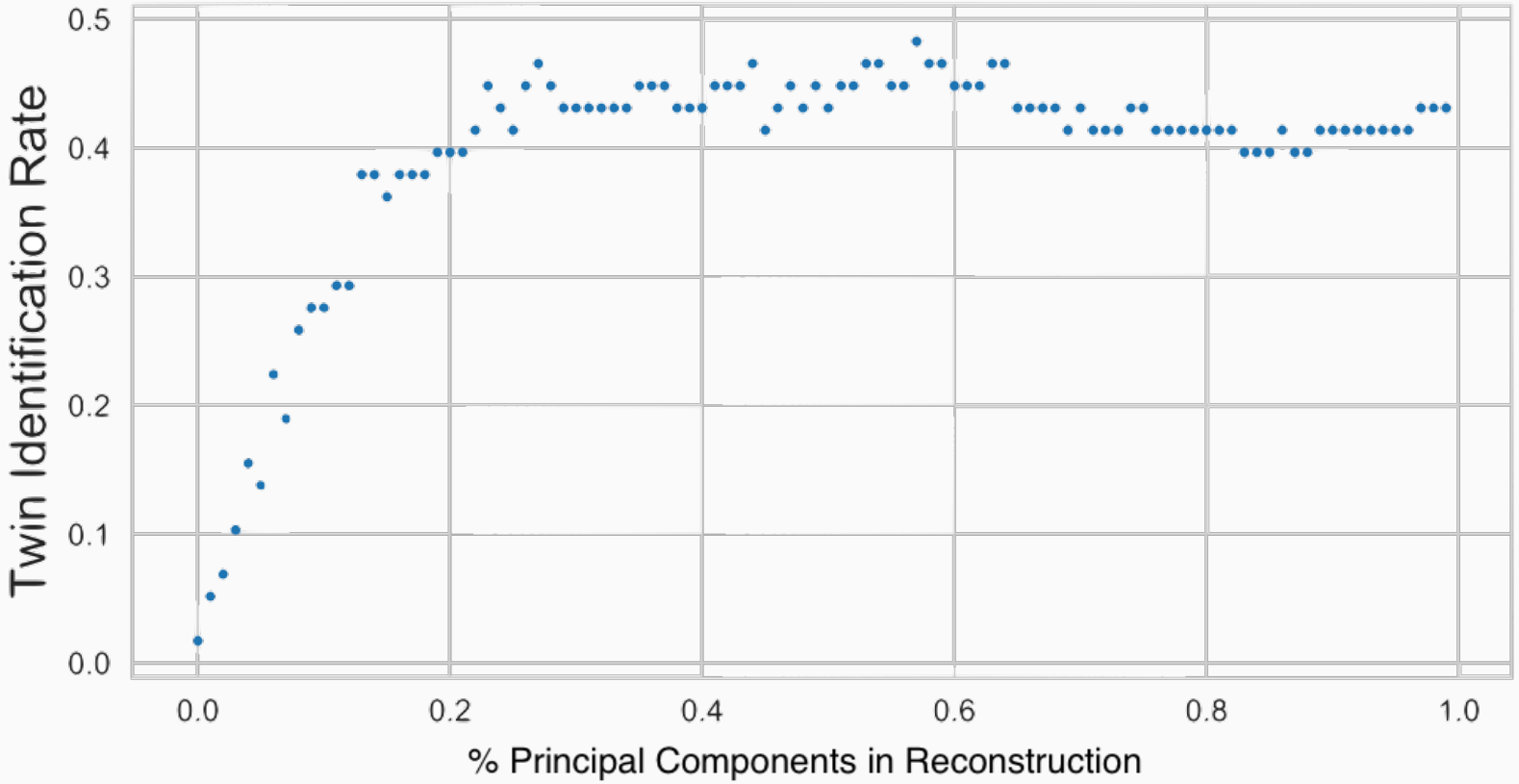


Figure 16: MZ Identification Rate vs. % Components ($n = 106$)

Key Finding

Optimal reconstruction at approximately 50% of total PCs

Twin: MZ Identification with Tangent Reference Matrices

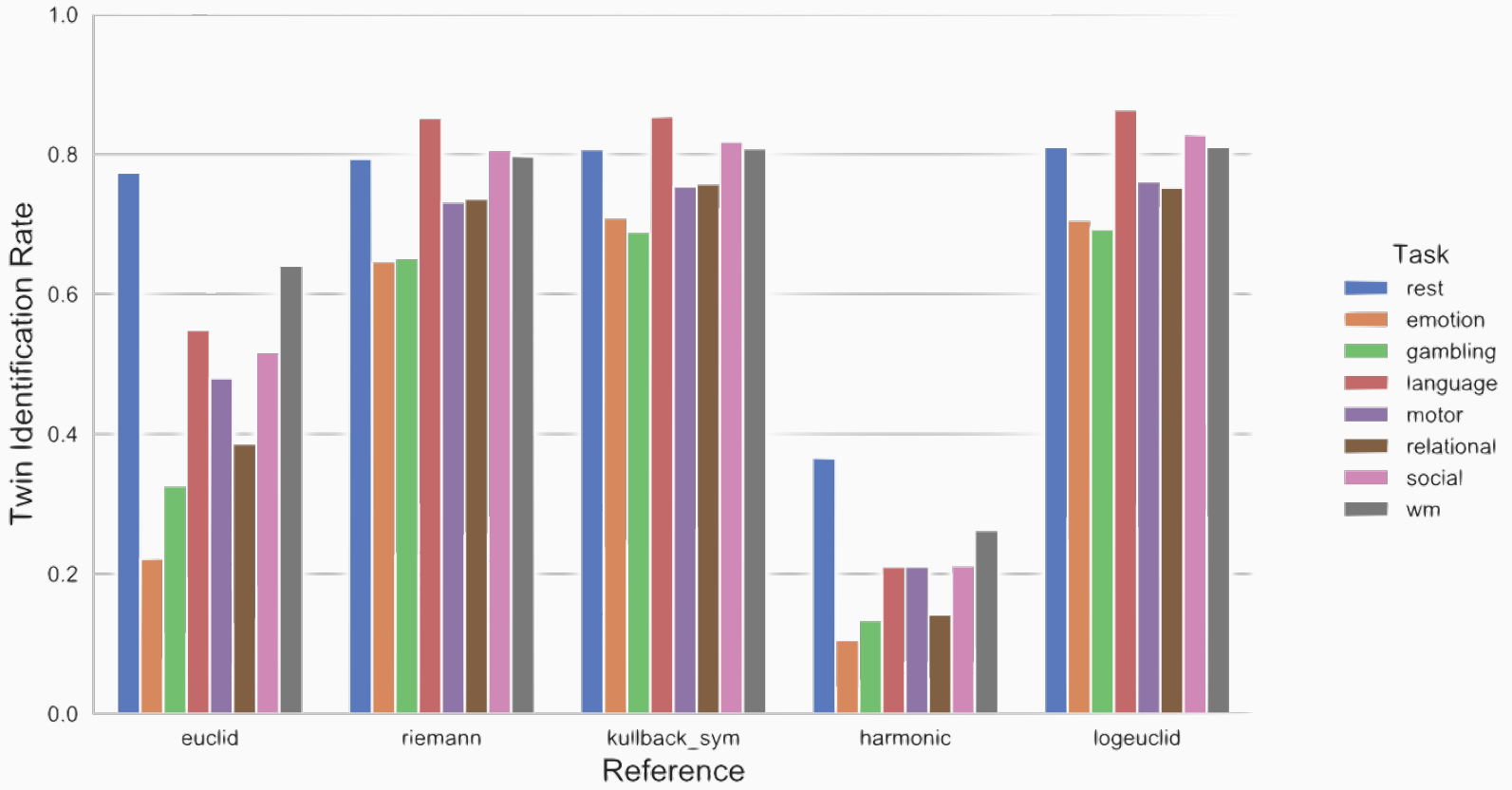


Figure 17: KNN MZ Twin Identification Rate ($n = 106$) with References

Key Finding

LogEuclid, Kullback, and Riemann references perform the best

Twin: MZ Identification across Parcellation Granularities

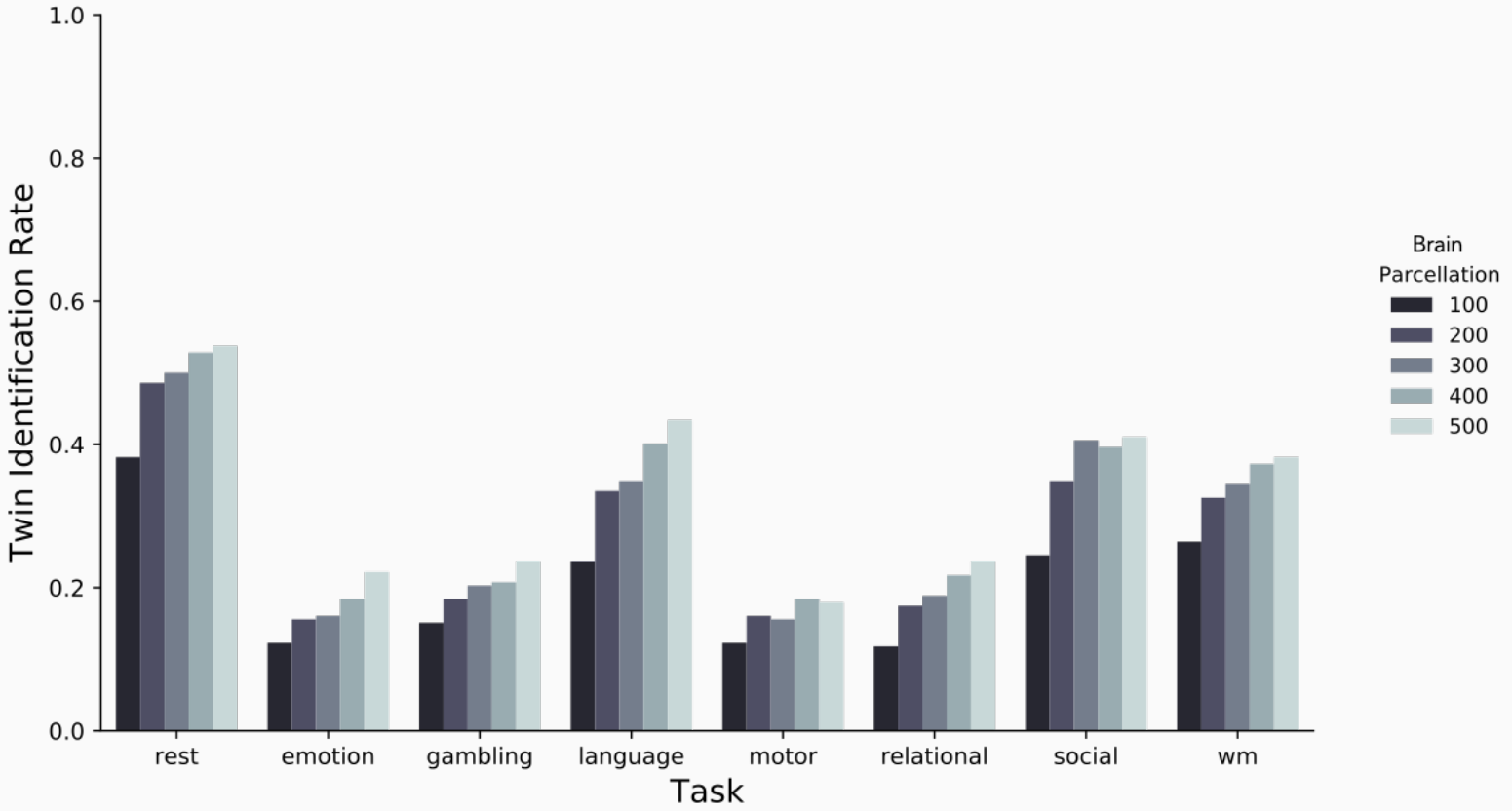


Figure 18: KNN MZ Identification Rates ($n = 106$) with Original FCs

Key Finding

Increasing parcellation granularity increases identification rate

Twin: MZ Identification across Post-processing Methods

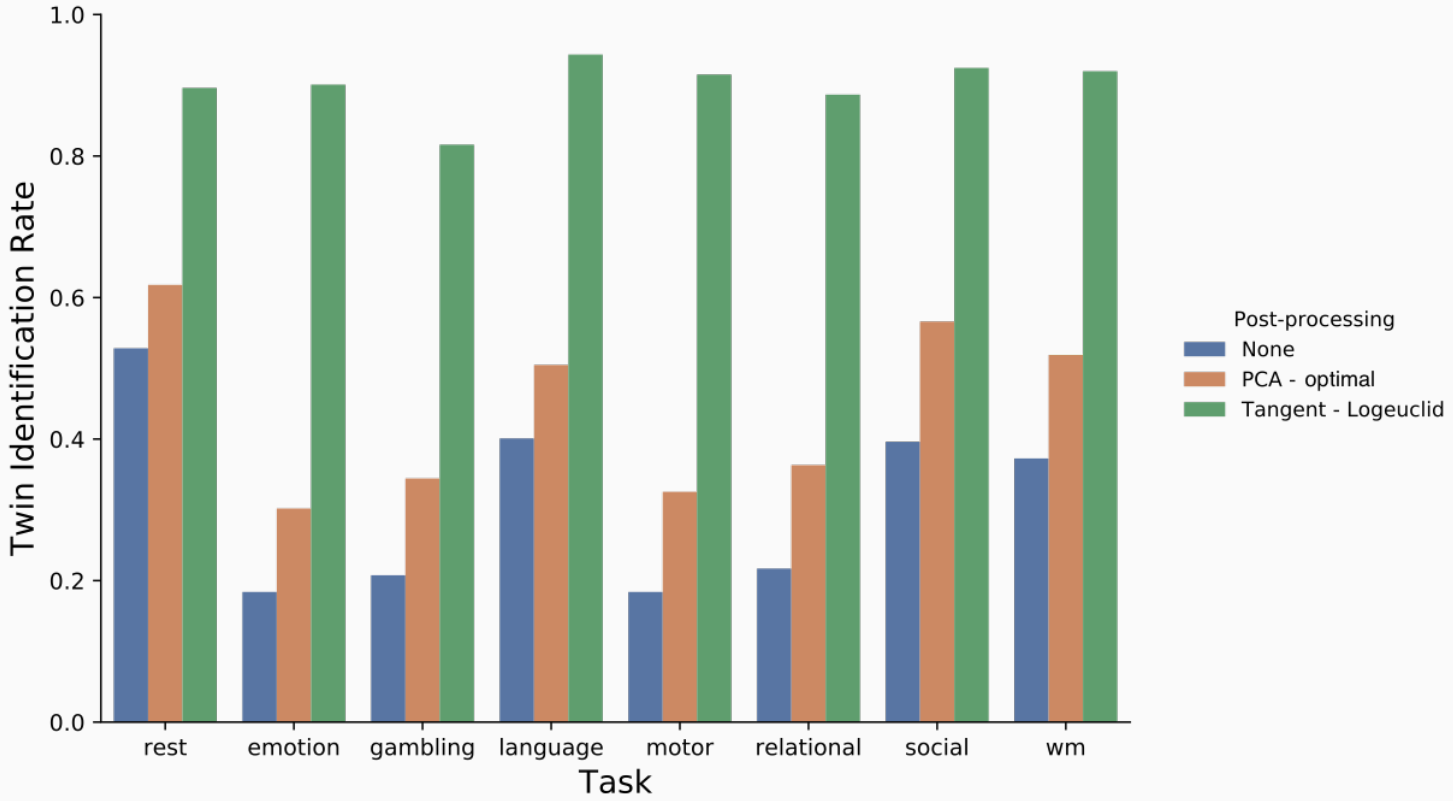


Figure 19: KNN MZ Identification Rates ($n = 106$) with Schaefer400

Key Finding

Tangent projection (LogEuclid) and optimal PCA reconstruction increase KNN MZ twin identification rate compared to original FCs

Twin: PCA Reconstruction for DZ Twin Identification

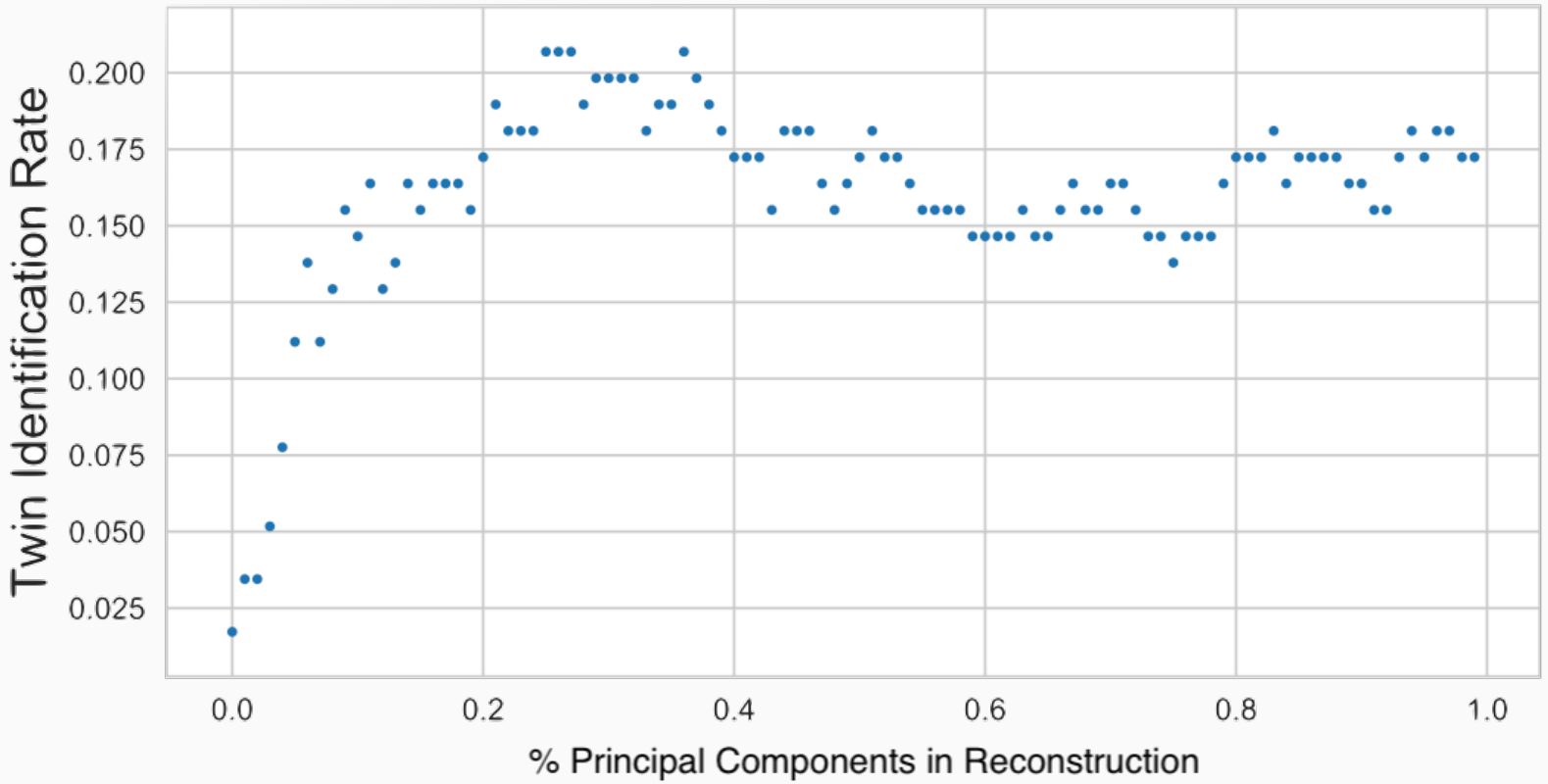


Figure 20: DZ Identification Rate vs. % Components ($n = 58$)

Key Finding

Optimal reconstruction at approximately 30% of total PCs

Twin: DZ Identification with Tangent Reference Matrices

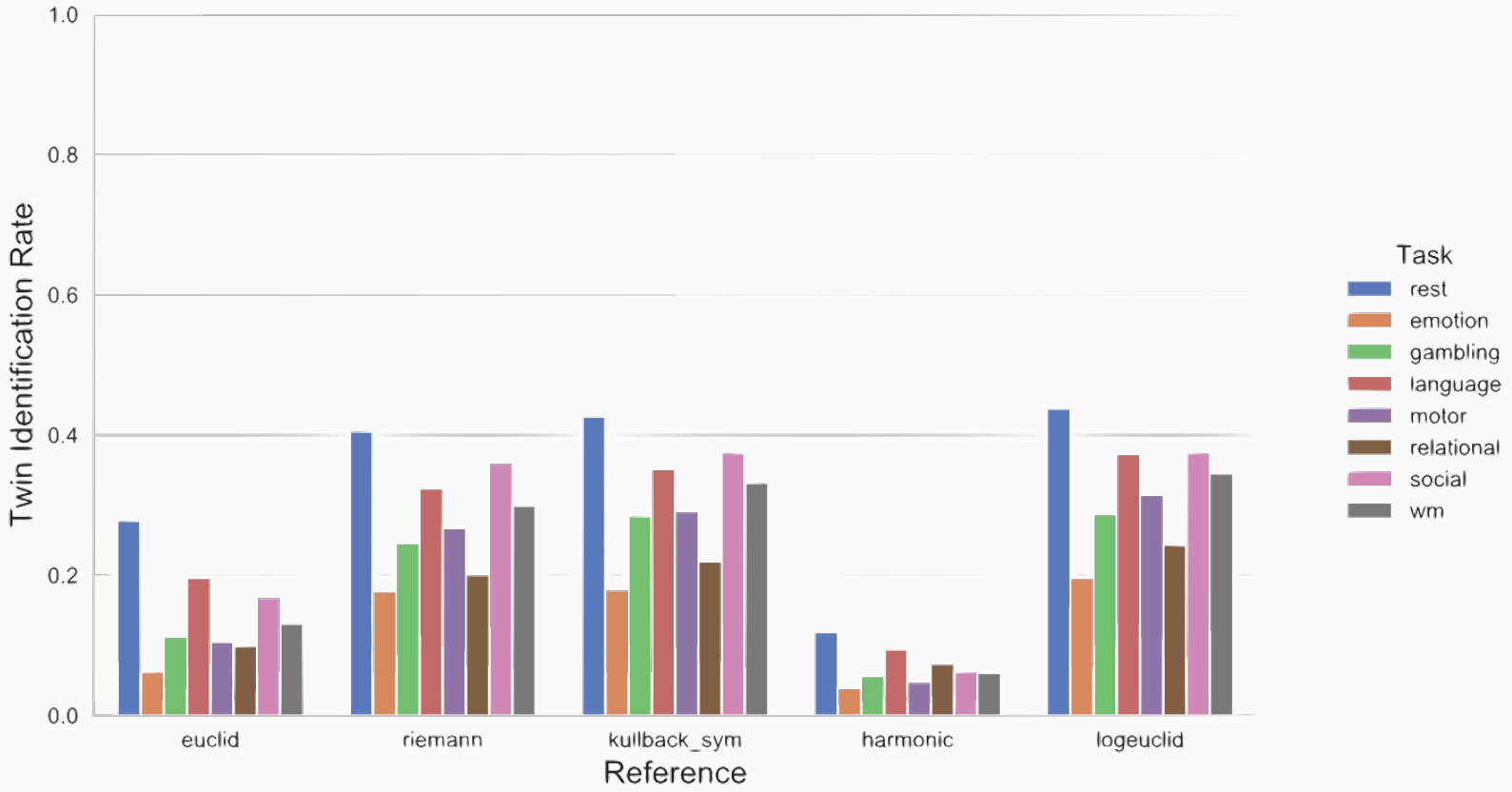


Figure 21: KNN DZ Twin Identification Rate ($n = 58$) with References

Key Finding

LogEuclid, Kullback, and Riemann references perform the best

Twin: MZ vs. DZ Identification Rates

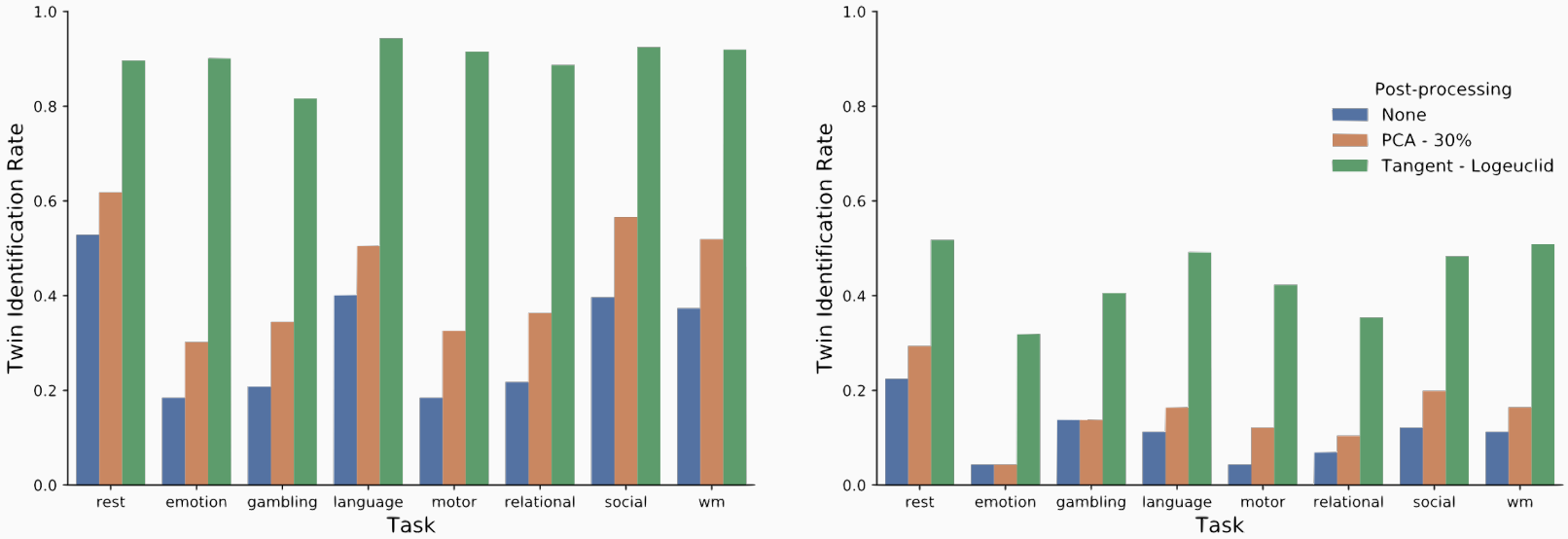


Figure 22: KNN MZ and DZ Twin Identification Rates with Schaefer400

Key Finding

DZ twin identification Rate with Tangent projected (LogEuclid) FCs surpasses MZ twin identification rate with original FCs

Subject: Identification across Parcellation Granularities

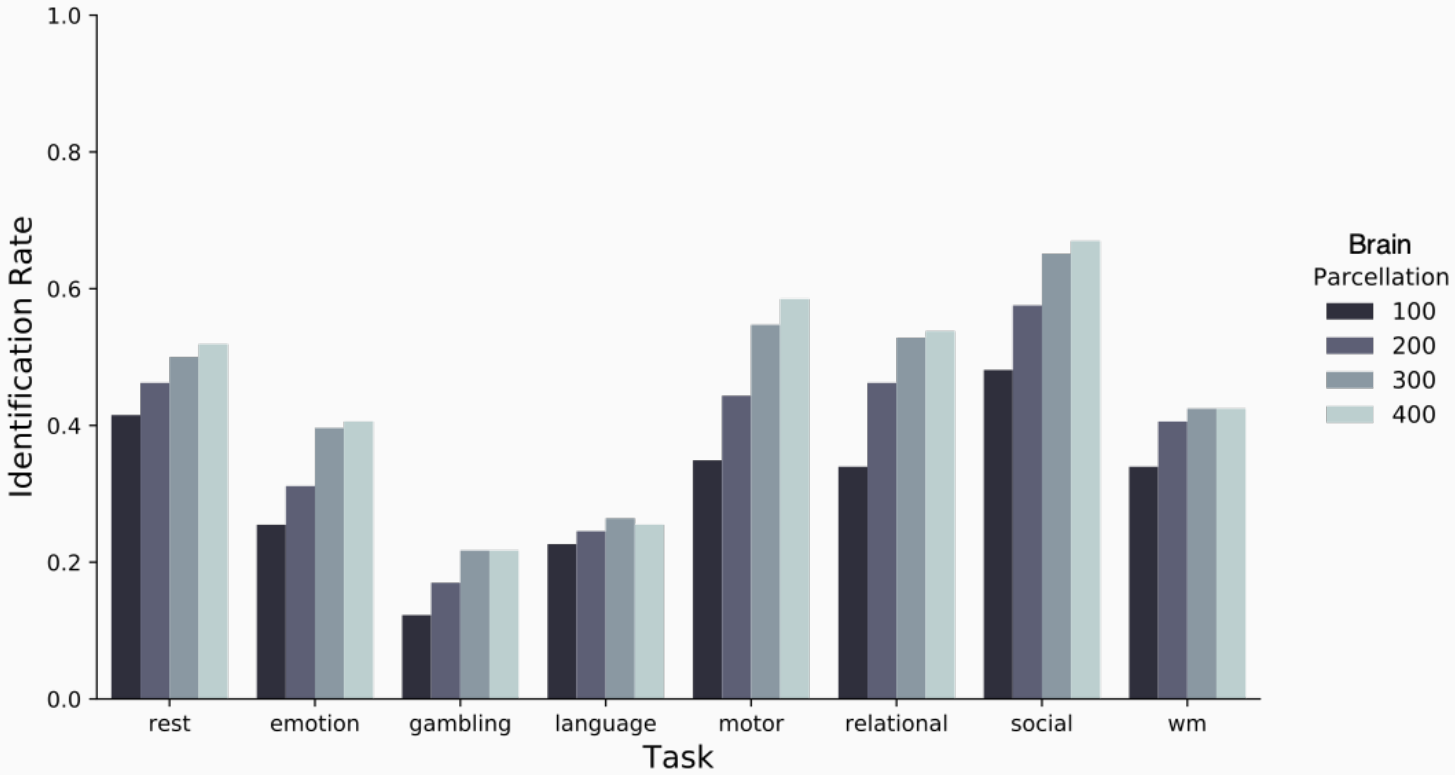


Figure 23: KNN Subject Identification Rate ($n = 106$) with Original FCs

Key Finding

Increasing parcellation granularity increases identification rate

Subject: Identification with Post-processing Methods

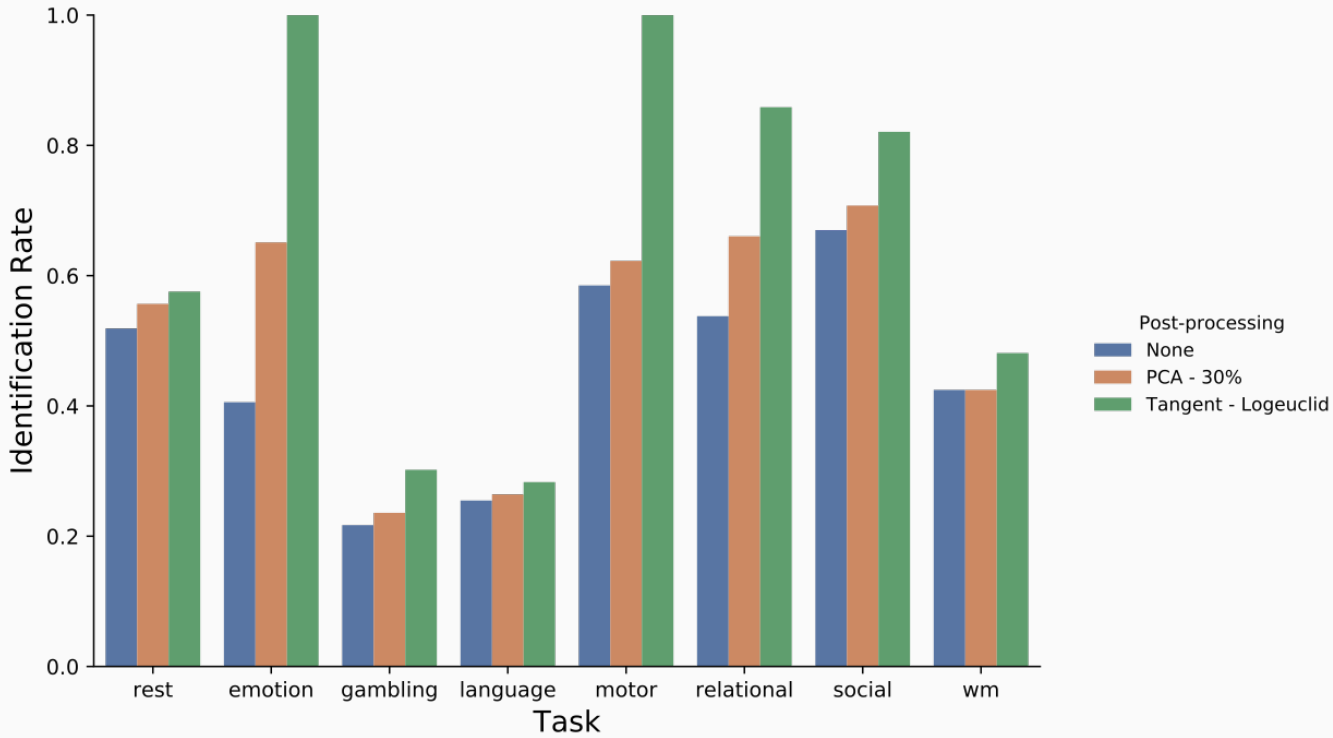


Figure 24: KNN Subject Identification Rate ($n = 106$) with Schaefer400

Note

Similar results to MZ twins but with lower performance in gambling and language FCs. Likely due to fewer FC samples per label.

Discussion

Research Outcomes

- Tangent space projection preserves the geometry of functional connectivity matrices (+0.061 identification rate vs. original FCs).
- Optimal PCA reconstruction depends on the dataset. For task, this is at 80 of 6,784 principal components. For MZ and DZ twins, optimality is at 50% and 30% of total components, respectively. PCA reconstruction increases task and twin identification rates.
- Increasing parcellation granularity from 100 brain regions to 400 brain regions improves both task and twin identification rates with the KNN classifier.
- Tangent projected FCs with the harmonic reference allow CNN classifier to outperform the state-of-the-art task identification rate by 0.049.
- Tangent projected FCs with the logarithmic Euclidean reference allow KNN classifier to outperform state-of-the-art MZ and DZ twin identification rates by 0.303 and 0.297, respectively.

Areas of Improvement and Future Work

- Perform a structured hyperparameter search for the convolutional neural network with open-source packages
- Investigate effect of brain parcellation size on task identification rate with the CNN classifier
- Understand the significance of the reference matrix in tangent projection and its effect on classifier performance (e.g., harmonic reference vs. logarithmic Euclidean)
- Apply the proposed post-processing methods to clinical fMRI cohorts and obtain classifiers for diagnosis and disease progression

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- Dr. Mario Ventresca
- Dr. Juan Wachs
- Purdue School of Industrial Engineering

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Questions?

PCA Reconstruction Visualized

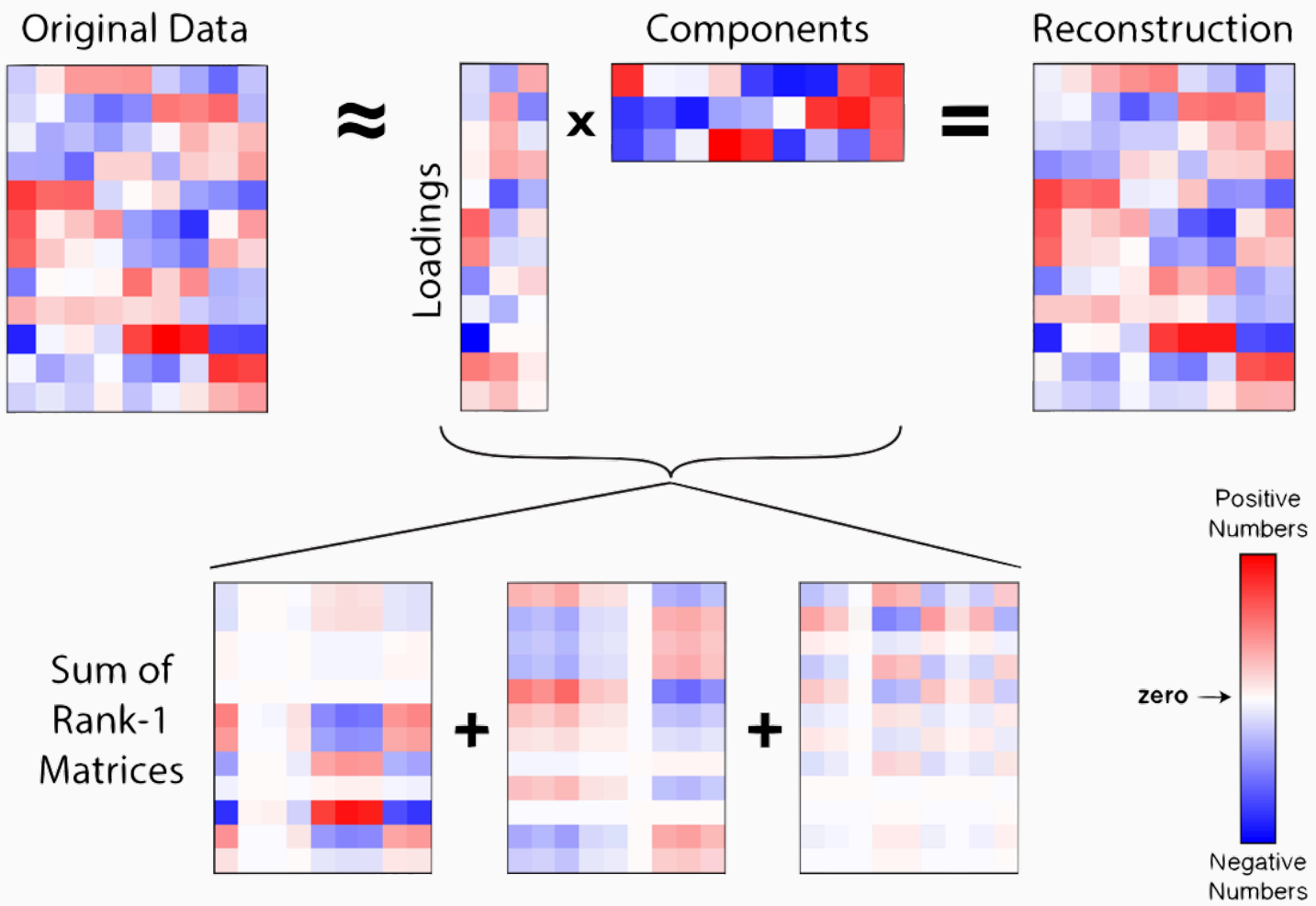

Figure 25: PCA reconstruction with 3 PCs

Figure obtained from http://alexhwilliams.info/itsneuronalblog/2016/03/27/pca/

Twin: DZ Twin Identification across Post-processing Methods

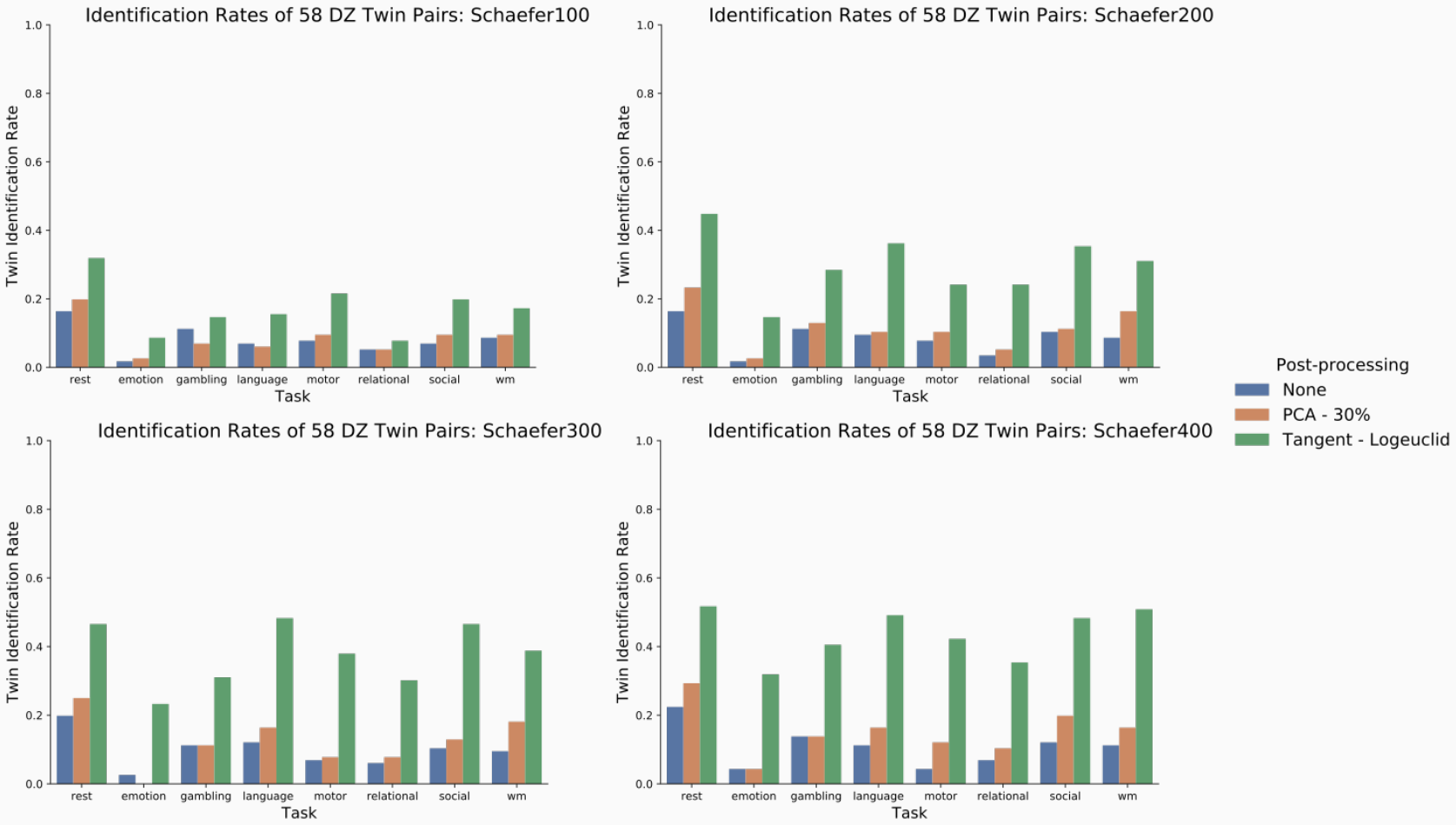

Figure 26: CNN Task Identification Rate with Post-Processing Methods

Twin: DZ Identification across Parcellation Granularities

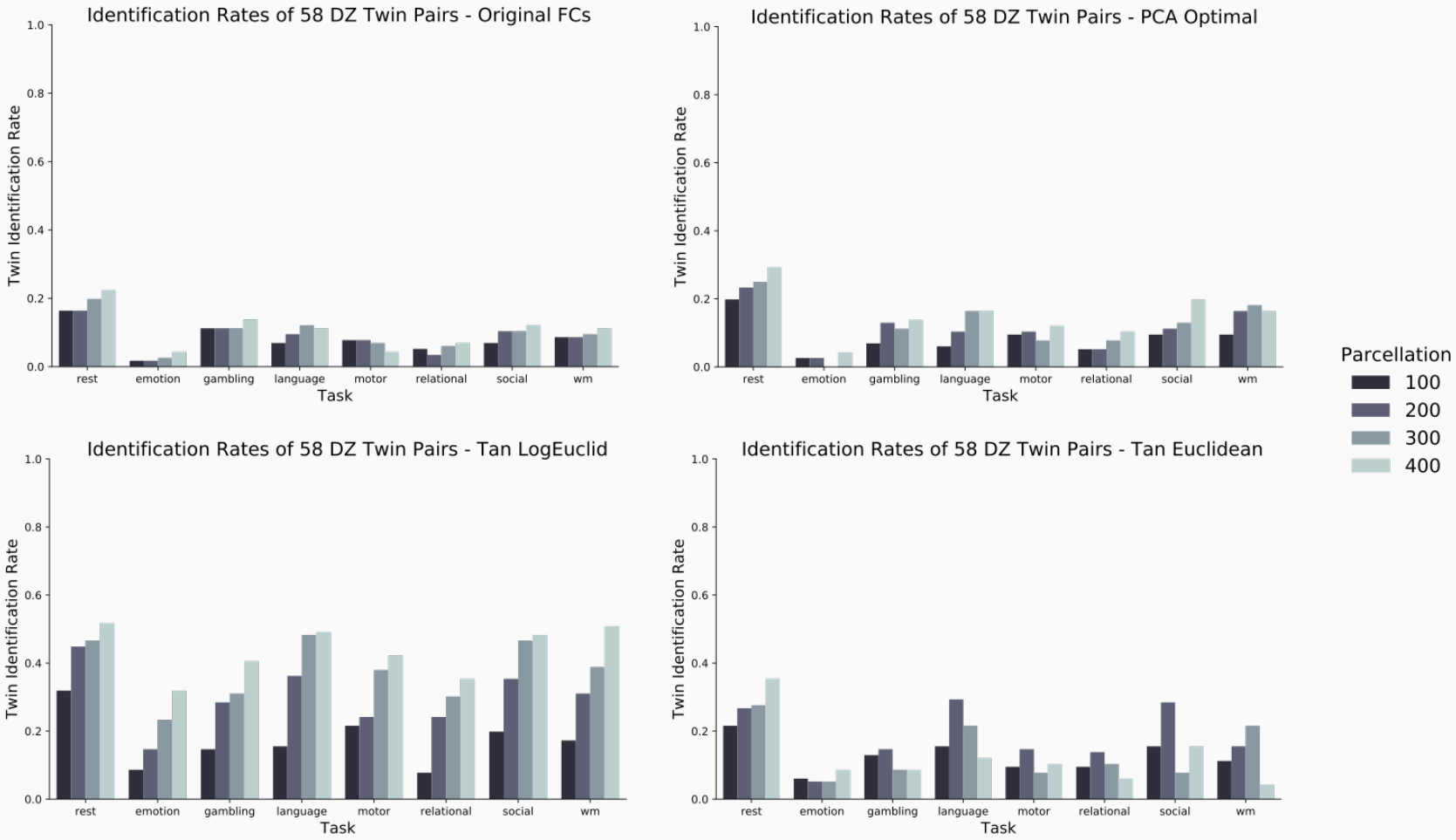

Figure 27: CNN Task Identification Rate with Post-Processing Methods

Twin: MZ Identification across Post-processing Methods

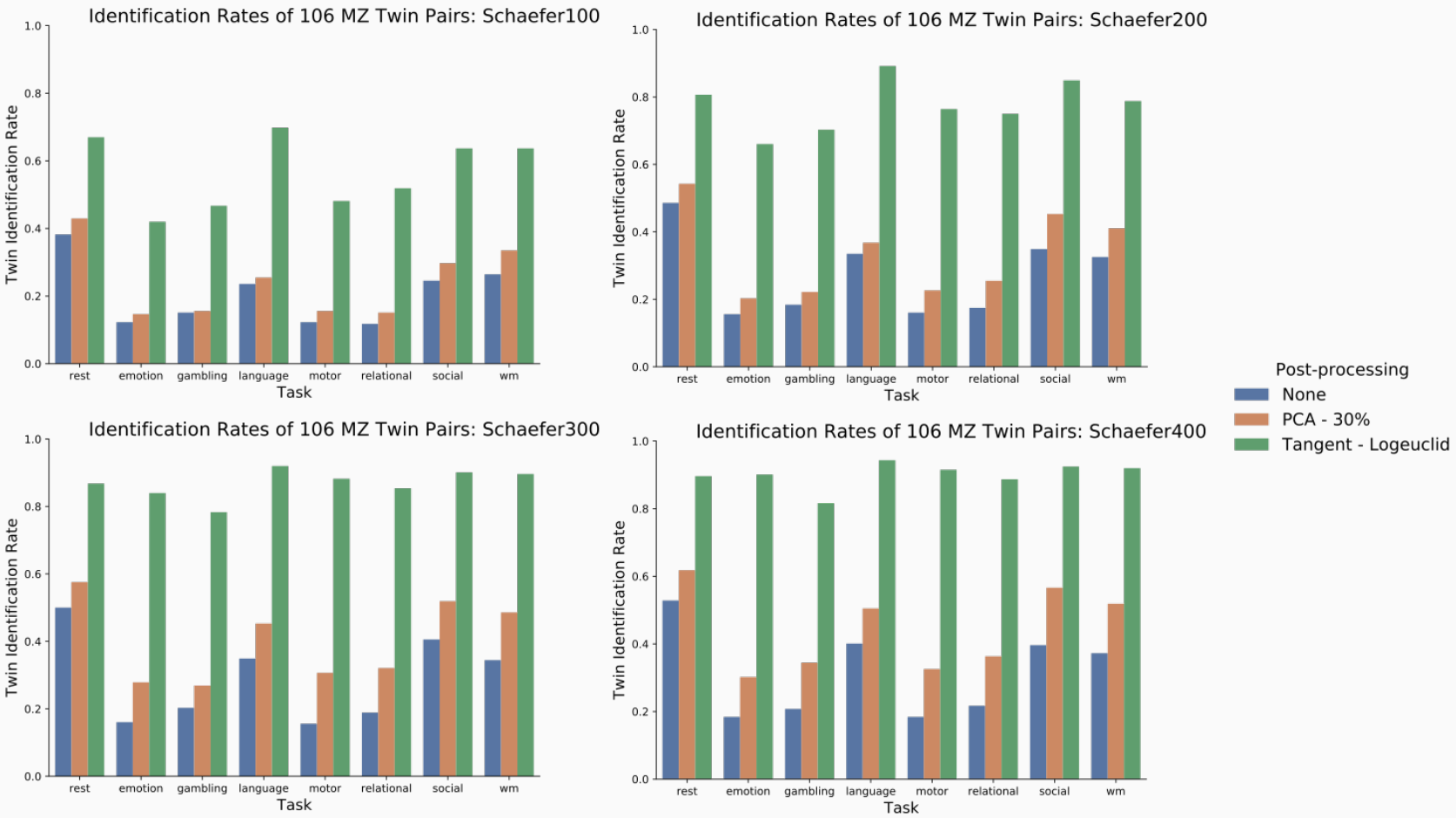

Figure 28: KNN Task Identification Rate with Post-Processing Methods

Twin: MZ Identification across Parcellation Granularities

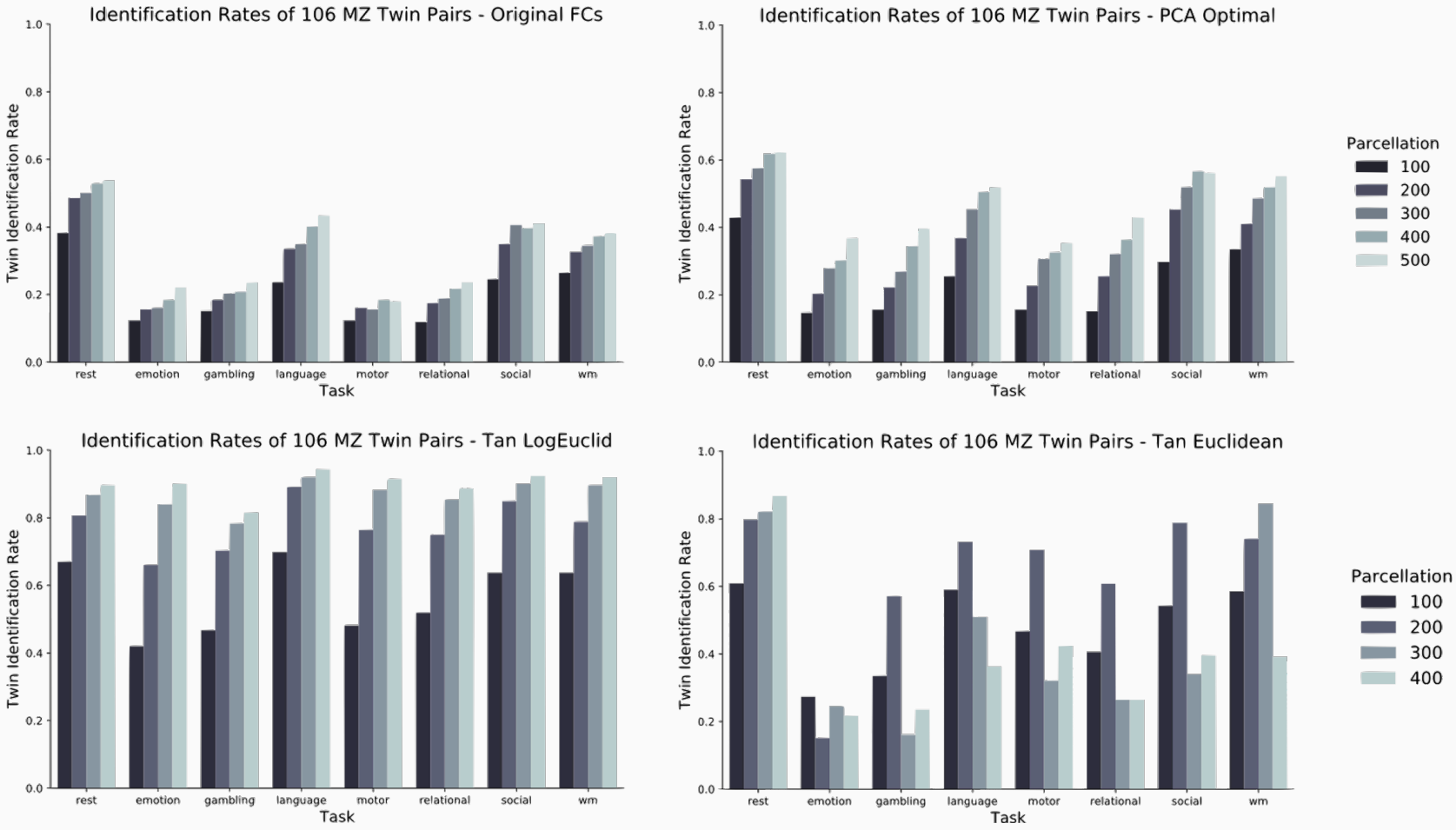

Figure 29: KNN MZ Twin Identification Rate with Post-Processing Methods

Subject: Identification with Post-processing Methods

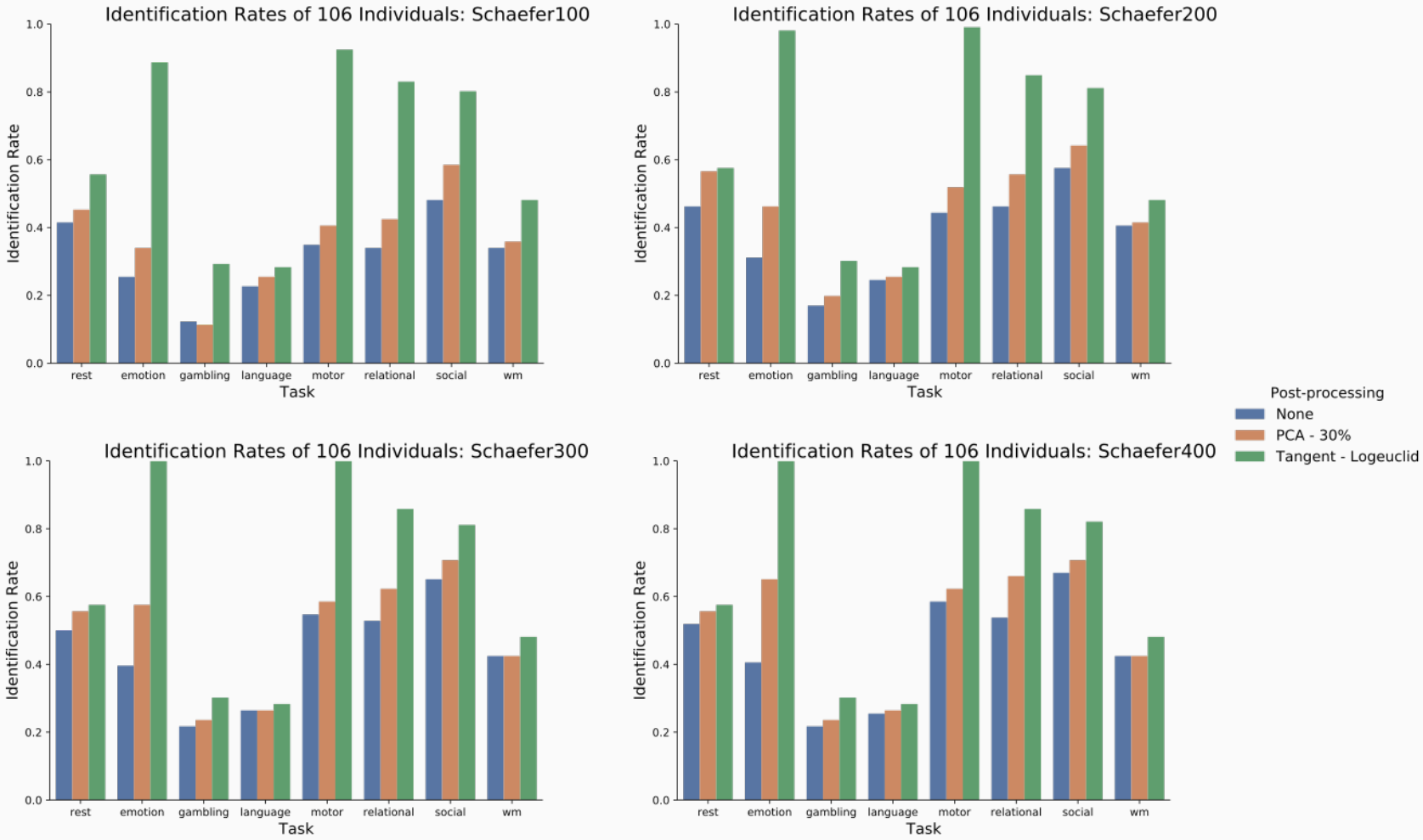

Figure 30: KNN Subject Identification Rate with 106 Individuals

Subject: Identification across Parcellation Granularities

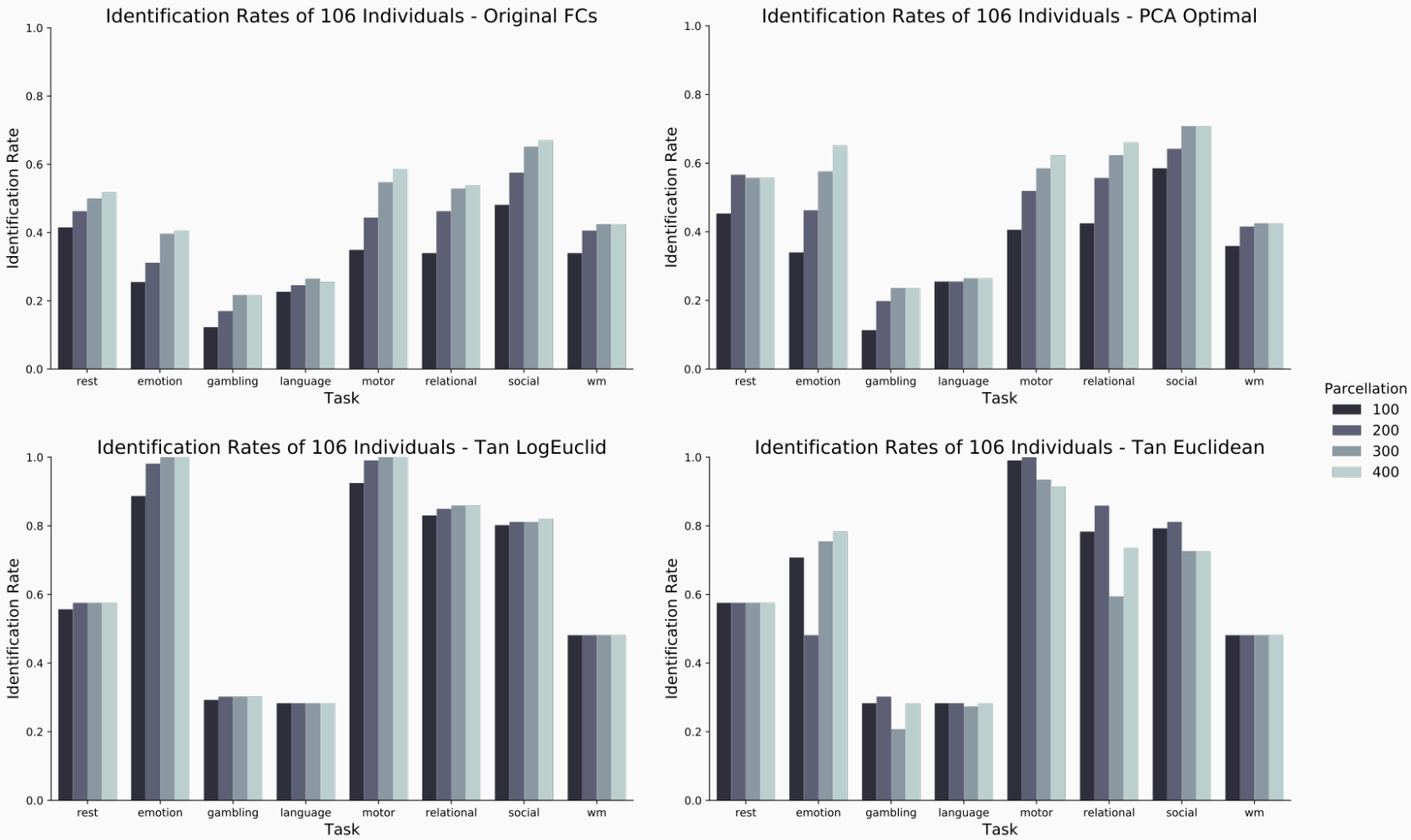

Figure 31: KNN Subject Identification Rate with 106 Individuals

Task: CNN Identification Rates

Post-processing	Task Identification Rate	SD (σ)
Original FCs	0.926	0.006
PCA - Optimal	0.945	0.003
Tan - Euclidean	0.973	0.004
Tan - Harmonic	0.986	0.003
Tan - LogEuclid	0.952	0.003
Tan - Kullback	0.953	0.005
Tan - Riemann	0.947	0.004