White Matter Tract Morphology via Laplace Beltrami Spectra as Classification Features for Neuropsychiatric Disorders

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Introduction

Until recently, it was standard practice in neuroimaging studies to compare brain structures based on their volume. However, it is now evident that volume differences may not be sensitive enough to fully characterize structural differences in the brain. There is increasing evidence that shape analyses of brain structures provide additional information not obtainable by volumetric measurements. Several studies have successfully used the shape of brain structures to predict the presence or degree of neuropsychiatric disorders like Alzheimer's disease, schizophrenia, and autism spectrum disorder. While an improvement on volume only studies, these investigations focus on the grey matter brain structures, overlooking the white matter entirely. Excluding the white matter risks missing potential insights, especially given the range of neuropsychiatric and brain disorders we know are accompanied by changes in the white matter [1].

Here, we present a novel method for the shape analysis of the white matter of the brain. We developed an automated pipeline for computing a global shape descriptor on white matter tracts segmented from diffusion MRI (dMRI) data and tractography. The spectrum of the Laplace Beltrami operator is used to describe the anatomical morphology of twenty major human white matter tracts. We performed machine-learning classification experiments to demonstrate the utility of this approach.

We demonstrate that the shape of white matter tracts allow for distinguishing between (a) male and female brains from the Human Connectome Project [2,3] and (b) between healthy controls and subjects in different neuropsychiatric groups from the UCLA Consortium for Neuropsychiatric Phenomics LA5c Study [4].

Data

Diffusion-weighted and T1-weighted structural MRI data from:

- Human Connectome Project [2,3]
  - 922 Healthy subjects – 492 females, 430 males
- UCLA Consortium for Neuropsychiatric Phenomics LA5c Study [4]
  - 102 Healthy Control (HC) subjects
  - 37 ADHD subjects
  - 43 Bipolar Disorder subjects
  - 38 Schizophrenia subjects

Global Shape Descriptor

The eigenvalues of the Laplace Beltrami Operator (LBO) were used to represent the shape of the surface mesh of each white matter tract. The LBO can be thought of as a Fourier Transform in 3D; it decomposes the shape of an object into eigenvalues and eigenvectors. The eigenvalues of the LBO are isometry invariant, therefore requiring no registration or mapping between the surfaces of different tracts or subjects. The LBO was chosen because it allows for highly discriminative shape comparisons with minimal preprocessing [5, 6].

To achieve scale independence and allow a direct shape comparison between tracts irrespective of size, we normalized the eigenvalues by the surface area of the given tract. We used the first 50 non-zero eigenvalues of the LBO for these analyses.

References

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2. Van Essen, D. C., Smith, S. M., Barch, D. M., Behrens, T. E., Yacoub, E., Ugurbil, K., & Wu-Minn HCP Consortium. (2013). The WU-Minn human connectome project: an overview. Neuroimage, 80, 62-79.
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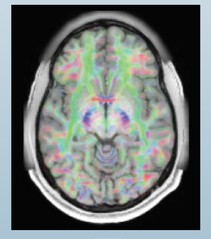
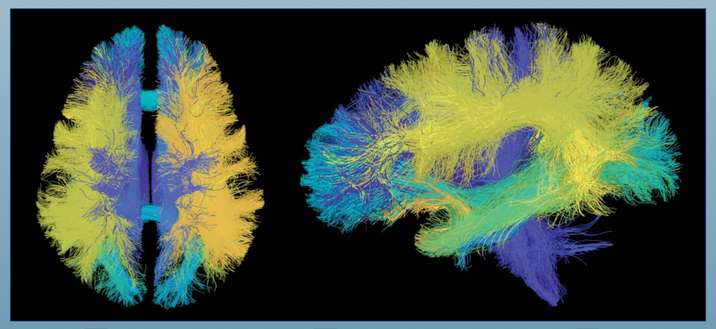
The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage 80: 105-124.
4. Poldrack, R. A. et al. A phenome-wide examination of neural and cognitive function. Sci. Data 3:160110 doi: 10.1038/sdata.2016.110 (2016).
5. Reuter, M., Wolter, F. E., & Peinecke, N. (2006). Laplace–Beltrami spectra as 'Shape-DNA'of surfaces and solids. Computer-Aided Design, 38(4), 342-366.
6. Niethammer, M., Reuter, M., Wolter, F. E., Bouix, S., Peinecke, N., Koo, M. S., & Shenton, M. E. (2007, October). Global medical shape analysis using the Laplace-Beltrami spectrum. International Conference on MICCAI (pp. 850-857). Springer, Berlin, Heidelberg.

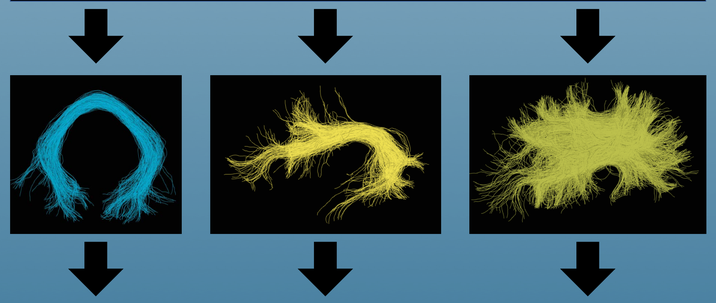
Automated Pipeline for White Matter Shape Analysis

Raw DWI data

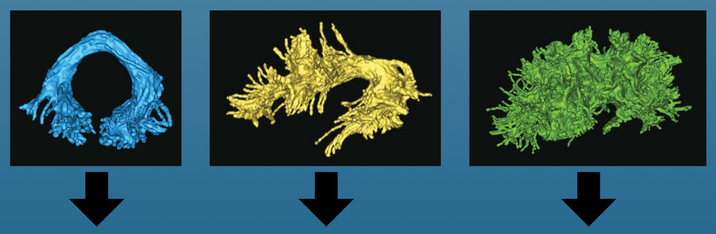


Streamline Tracking and Segmentation

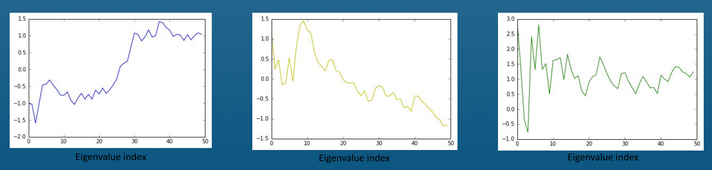




Streamlines to 3D surface



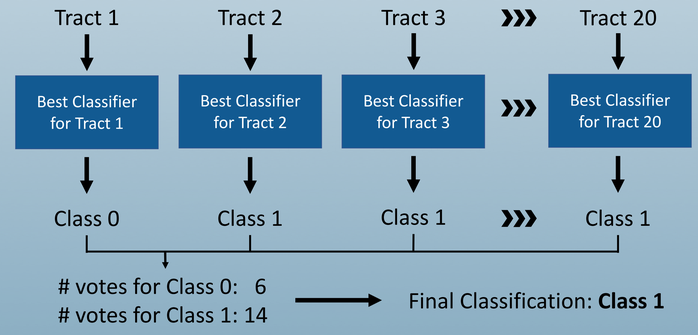
Laplace Beltrami Operator to Eigenvalue Spectrum



Tract 1 Tract 2 Tract 3

Machine Learning: Voting-Based Ensemble Classification

We trained machine learning classifiers individually for each of the 20 tracts and allowed the tracts to vote for the final group classification (mode of votes). We determined the best classifier and hyperparameters for each tract based on an exhaustive grid search with 10-fold cross validation (CV). We performed the overall classification twice: once with all 20 white matter tracts and once using either the top 3 or top 5 best performing tracts.



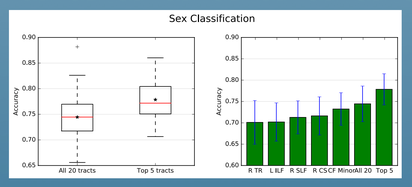
Results

Sensitivity = % accurately classified neuropsychiatric subjects
Specificity = % accurately classified healthy control subjects

Male vs. Female Classification

492 females and 430 males

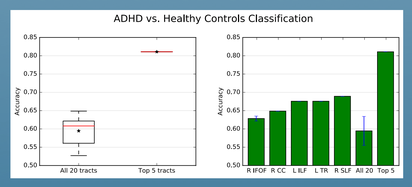
# Tracts	Accuracy
All 20	74.4±4.2%
Top 5	77.8±3.7%



ADHD vs. Healthy Controls Classification

37 ADHD and 37 randomly chosen HC subjects

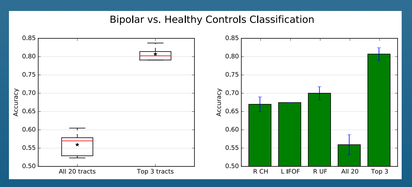
# Tracts	Accuracy	Sensitivity	Specificity
All 20	59.5±3.9%	61.4±5.7%	57.6±6.9%
Top 5	81.1±0.0%	97.3±0.0%	64.9±0.0%



Bipolar Disorder vs. Healthy Controls Classification

43 BD and 43 randomly chosen HC subjects

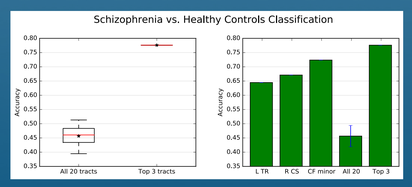
# Tracts	Accuracy	Sensitivity	Specificity
All 20	55.9±2.7%	49.3±4.3%	62.6±6.6%
Top 3	80.7±1.7%	80.9±1.7	80.5±1.9%



Schizophrenia vs. Healthy Controls Classification

38 SZ and 38 randomly chosen HC subjects

# Tracts	Accuracy	Sensitivity	Specificity
All 20	45.7±3.7%	34.2±3.7%	57.1±6.0%
Top 3	77.6±0.0%	76.3±0.0%	78.9±0.0%



Conclusions

These experimental results suggest that the shape of the major white matter tracts of the human brain contains useful information that can be exploited for potential use in diagnosis and classification of the human brain.