Detection of Local Cortical Asymmetry via Discriminant Power Analysis

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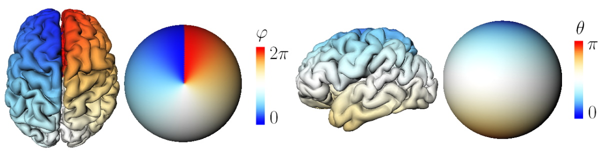
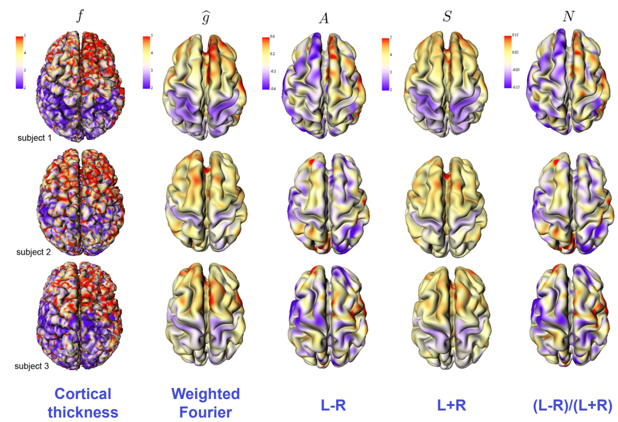
1. Introduction

We present a discriminant power analysis framework for localizing the abnormal cortical thickness asymmetry pattern in a clinical group. The proposed framework is based on the recently developed *weighted Fourier series representation* (Chung et al., 2007).

As an illustration, we show that a group of high functioning autistic subjects has a cortical thickness asymmetry pattern that differs reliably from controls. Unlike previous literature, our approach does not require any preselected feature vectors and performs the classification at each mesh vertex.



Deformable surface algorithm (MacDonald et al., 2001) was used to establish a smooth from a unit sphere to a cortical surface.

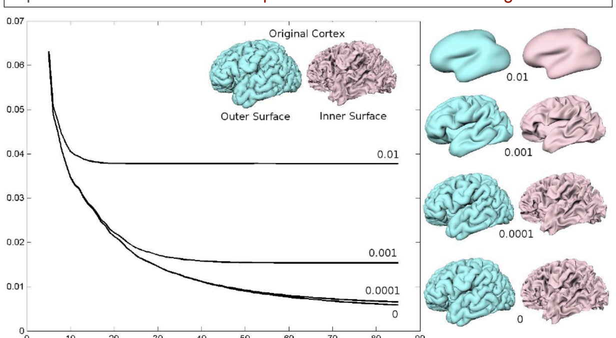


2. Weighted Fourier Series

The Weighted Fourier series representation encodes the surface coordinates using using the series expansion

$$g(\theta,\varphi)=\sum_{l=0}^{k}\sum_{m=-l}^{l} e^{-l(l+1)t}\langle f, Y_{lm}\rangle Y(\theta,\varphi),$$

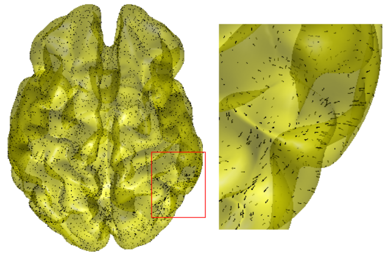
where Y_{lm} are the spherical harmonics. The bandwidth t controls the amount of smoothing. The SPHARM coefficients $\langle f, Y_{lm}\rangle$ are estimated via the iterative residual fitting (IRF) algorithm (Chung et al., 2007). The MATLAB implementation is available at http://www.stat.wisc.edu/~mchung.



Weighted Fourier representation of cortex at different bandwidths (t = 0.0001,0005, 0.001, 0.01). The plot shows the sum of squared residual over the degree of the representation. The weighted Fourier series terminates where the sum of squared residuals flattens out first.

4. Surface Registration and Asymmetry Index

The surface registration between subjects was established in the least squares fashion (Chung et al., 2007). It is shown that the optimal displacement between two weighted Fourier representations is simply obtained by subtracting the two representations. The hemispheric correspondence is established similarly without image flipping. Then the asymmetry index (L-R)/(L+R) is established at each mesh vertex.



Left: The 42 degree weighted Fourier representation with displacement vector fields (small black arrows). The displacement is between the representation and the average template. The vector fields are subsampled coarsely for better visualization.

Right: enlargement of the red rectangle.

References

•Chung, M.K., Dalton, K.M., Shen, L., Evans, A.C., Davidson, R.J. Weighted Fourier Series Representation and Its Application to Quantifying the Amount of Gray Matter, *IEEE Transactions on Medical Imaging* **26**:566-581, 2007.

•Hair, J, Aanderson,R., Tatham, R., Black, W. 1998. *Multivariate Data Analysis*. Prentice Hall, Inc.

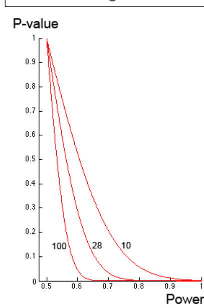
5. Logistic Discriminant Analysis

In almost all two-group comparison settings, the two- sample t-test with the equal variance assumption has been used as a standard test procedure. This hypothesis driven approach inherently introduces a multiple comparison correction issue in the P-value computation. We propose a different approach called the *logistic discriminant analysis* that does not require require a hypothesis on model parameters.

At each mesh vertex, the asymmetry index is feed into the logistic model. Let Y_i be the clinical status of the i-th subject modeled as a Bernoulli random variable, i.e. Y_i = 1 if the subject is autistic and 0 otherwise. Let $\pi_i = P(Y_i = 1)$ be the probability of clinical status. We set up a logistic model that links the probability of clinical status to asymmetry index:

$$\log\frac{\pi_i}{1-\pi_i}=\beta_0+\beta_1\frac{L_i-R_i}{L_i+R_i}$$

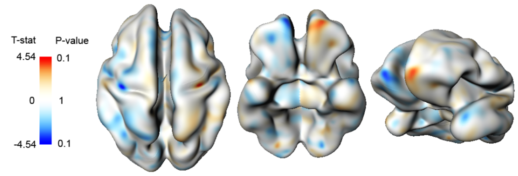
The parameters of the model are estimated by maximizing the likelihood function using the Newton-Raphson method.

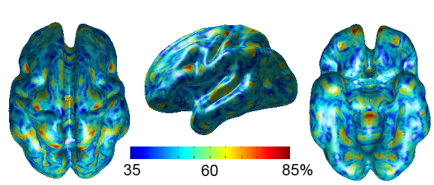


P-value vs. discriminant power plot for various sample size n = 10, 28 and 100.

6. P-value vs. Discriminant Power

Once the parameters are estimated, subjects are classified as autistic if P(Y=1) > P(Y=0) and controls otherwise. The classification error rate r, which is the overall probability of misclassifiction, is estimated by the leave-one-out cross-validation scheme. The discriminant power (DP) is then given as 1-r and it is displayed in the bottom figure localizing the regions of abnormal asymmetry pattern in autistic subjects. In order to show that the DP-map can be used as an alterative to the usual P-value map, we determined the statistical significance of DP using Press's Q-statistic (Hair et al., 1998). The lef figure shows the P-value plot of Press's Q-statistic as a function of DP for various sample sizes. For n=28, DP=0.85 corresponds to the small P-value of 0.0002.





Top: two sample t-test result showing the focalized regions of abnormal asymmetry pattern. The t-statistic is thresholded using the random field theory based multiple comparison correction.

Bottom: logistic discriminant power map. The high discriminant power regions correspond to the high t-statistics regions.