Partial Correlation Mapping of Cognitive Measure and Cortical Thickness in Autism

Moo K. Chung[1,2,3]**, Kim M. Dalton**[3]**, Steven Robbins**[4]**, Alan C. Evans**[4]**, Richard J. Davidson**[3]

[1]Department of Statistics, [2]Department of Biostatistics and Medical Informatics

[3]Waisman Laboratory for Brain Imaging and Behavior

University of Wisconsin, Madison, WI 53706

[4] Montreal Neurological Institute, Montreal, Canada

June 13, 2005

Introduction

We present a basic methodological framework for correlating cognitive measures to anatomical measures and apply it to comparing 14 high functioning autistic (HFA) and 12 normal control (NC) subjects [2]. Subjects were screened to be right-handed males. A *facial emotion discrimination task* was performed for the both groups. The task scores for HFA and NC are 27.14 $\pm$ 15.34 and 39.42 $\pm$ 0.79 respectively.

MRIs were also collected and both the outer and inner cortical surfaces were extracted for each subject via a deformable surface algorithm [1, 2]. The details of image segmentation and normalization techniques can be found in [2]. To increase the signal to noise ratio in the thickness measures, surface based smoothing is applied [1, 2]. Afterwards, we correlate the task scores with the cortical thickness in a group of autistic subject while removing the effect of age and cortical area difference. A permutation test is performed to determine if the correlation is significantly different between HFA and NC.

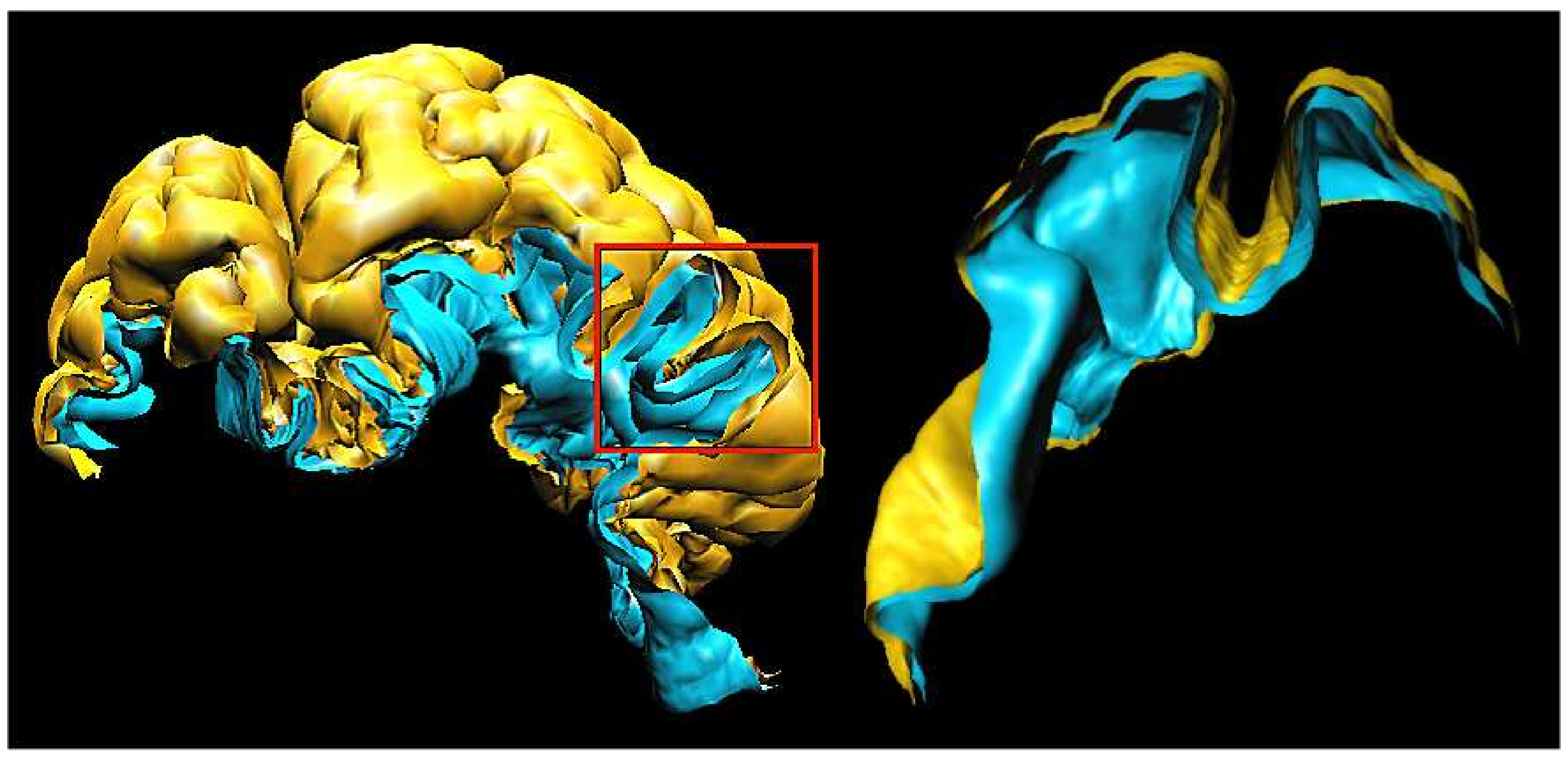

Figure 1: Left: part of the cortex showing the outer and inner surface that bound gray matter. Right: enlargement of the boxed region. The cortical thickness measures the distance between outer and inner surfaces.

Surface-based Smoothing: heat kernel smoothing

The cortical thickness measurements are always contaminated with noise. In order to increase the signal-to-noise ratio, new surface-based smoothing called *heat kernel smoothing* is used [2]. We smooth the cortical thickness measures Y with heat kernel K_σ on the cortical surface $\partial\Omega$: $\int_{\partial\Omega} Y(p)K_\sigma(p,q) \quad \mu(q)$. This is a more efficient technique than previously developed diffusion smoothing [1]. The `MATLAB` code can be found in `http://www.stat.wisc.edu/~mchung/hk/hk.html`.

Partial Correlation

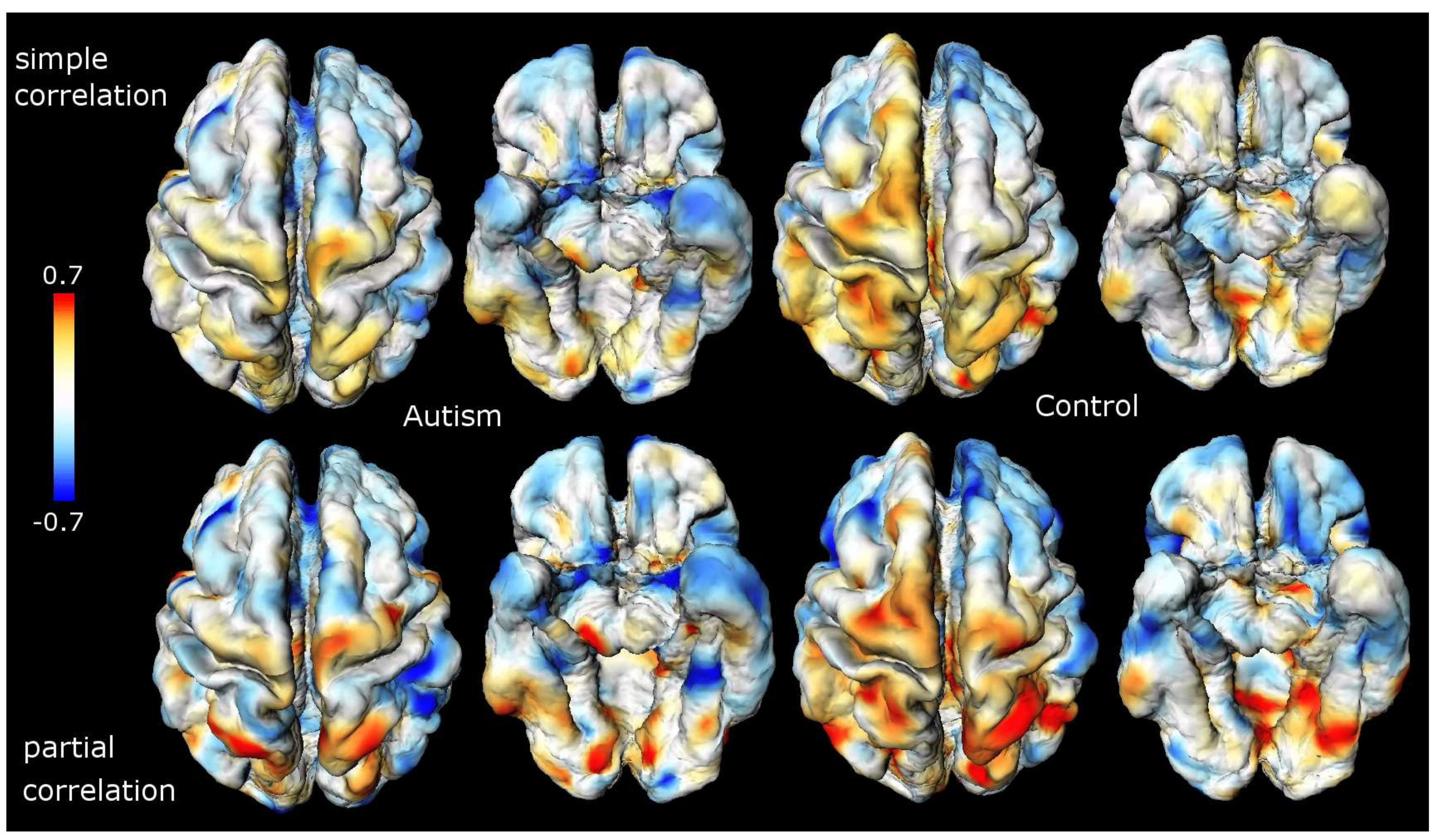

Figure 2: Correlation map of the thickness and the facial emotion discrimination task score. Top: Simple correlation. Bottom: Partial correlation.

Let $Y = (Y_1, Y_2)'$ be two variables of interests to be correlate and $X = (X_1, X_2)'$ be covariates that should be removed. In this study, we have Y_1 = cortical thickness, Y_2 = task score, X_1 = age, and X_2 = total surface area. Let Σ_{YX} be the cross covariance matrix of Y and X and we define Σ_{XX} and Σ_{YY} similarly. Then the partial covariance of Y given X is $\Sigma_{YY} - \Sigma_{YX}\Sigma_{XX}^{-1}\Sigma_{XY} = (\sigma_{ij})$. The *partial correlation* $\rho_{Y_i,Y_j|X}$ is then defined as the correlation between Y_i and Y_j while controlling for other variables X, and given by $\rho_{Y_i,Y_j|X} = \sigma_{ij}/\sqrt{\sigma_{ii}\sigma_{jj}}$.

Permutation Test

Let ρ_1 and ρ_2 be the partial correlation of the autistic and normal subjects (Figure 2). We are interested in testing

$$H_0 : \rho_1(p) = \rho_2(p) \text{ for all } p \in \partial\Omega \text{ vs. } H_1 : \rho_1(p) \neq \rho_2(p) \text{ for some } p \in \partial\Omega.$$

Let r_j be the sample partial correlation for the j-th group. We can use $R(p) = r_1(p) - r_2(p)$ as a test statistic at each point p and $\sup_{p\in\partial\Omega} R(p)$ for correcting multiple comparisons in one sided test. We estimate the distribution of $\sup_{p\in\partial\Omega} R(p)$ under H_0 via random permutations. Each permutation produces two sample correlations denoted by r_1^* and r_2^* and there are $(n_1 + n_2)/!$ possible permutations. Then we estimate the distribution of the $\sup_{p\in\partial\Omega} R(p)$ by

$$P\Big(\sup_{p\in\partial\Omega} R(p) \leq h\Big) = \frac{\#\text{ of } \sup_{p\in\partial\Omega}[r_1^*(p) - r_2^*(p)] \leq h}{(n_1+n_2)!}.$$

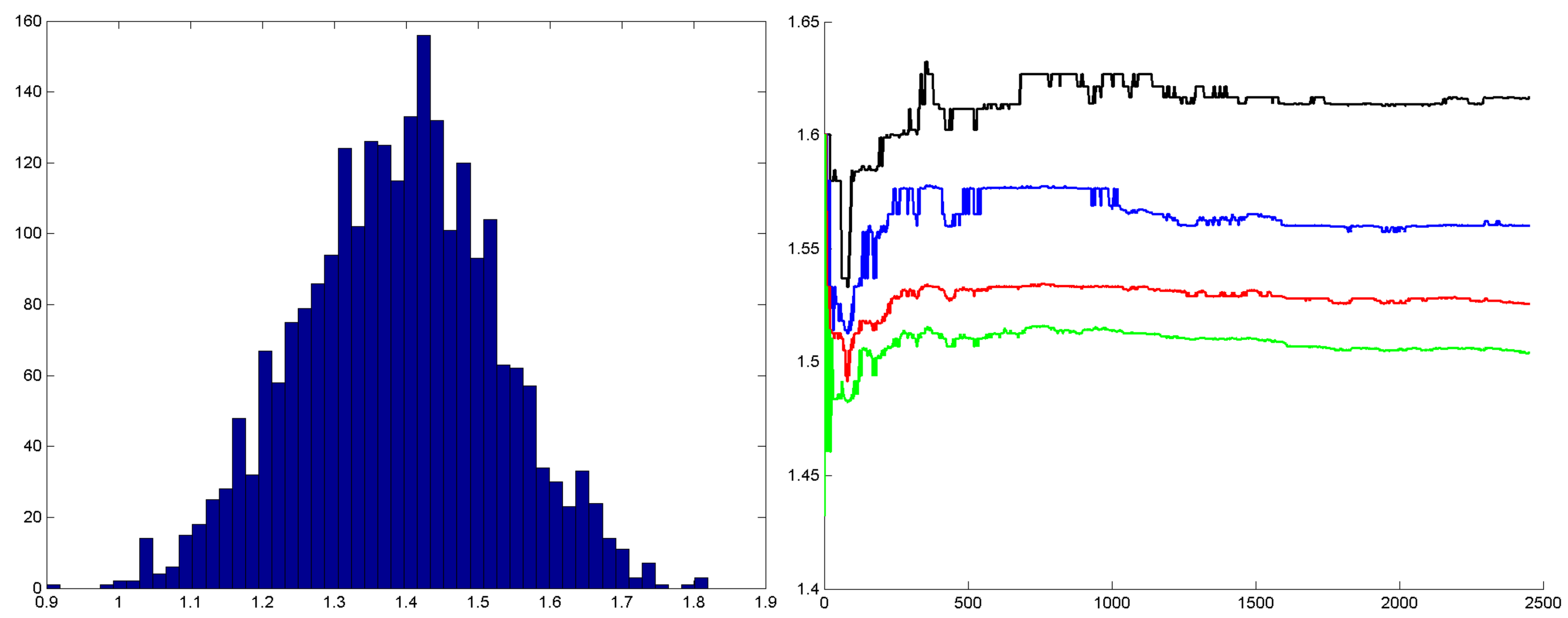

Figure 3: Left: histogram of $\sup_{p\in\partial\Omega} R(p)$ based on 2400 permutations. Right: plots of 95% (black), 90% (blue), 85% (red) and 80% (green) upper percentiles over the number of permutations showing the convergence after approximately 2000 permutations.

Results

Heat kernel smoothing was applied to the cortical thickness measures to increase the signal-to-noise ratio with relatively large FWHM of 30mm [2]. The sample partial correlation between the thickness and the task score were computed for both groups while removing the effect of age and total cortical area difference. Age distributions for HFA and NC are 15.93 ± 4.71 and 17.08 ± 2.78 respectively. The cortical area distributions for HFA and NC are $(283 \pm 3) \times 10^3$ mm and $(273 \pm 6) \times 10^3$ mm respectively.

The distribution of $\sup_{p\in\partial\Omega} R(p)$ is estimated using 2400 random subsamples form $(n_1 + n_2)!$ permutations to save computational time (Figure 3). After 2000 permutations, the percentiles seem to converge. The 95% upper and lower percentiles are ± 1.62 while the maximum and the minimum sample correlations are 1.32 and -1.23 so we do not reject H_0 at $\alpha = 0.05$. We conclude that there is no correlation difference between HFA and NC.

References

1. Chung, M.K., Worsley, K.J., Robbins, S., Paus, P., Taylor, J., Giedd, J.N., Rapoport, J.L., Evans, A.C. 2003. Deformation-Based Surface Morphometry with an Application to Gray Matter Deformation, *NeuroImage*. **18**:198-213.

2. Chung, M.K., Robbins,S., Dalton, K.M., Davidson, R.J., Alexander, A.L., Evans, A.C. 2005. Cortical Thickness Analysis in Autism via Heat Kernel Smoothing. *NeuroImage* **25**:1256-1265.