Shape Changes in Schizophrenic Brains

Neal Birchfield [1] Lizzie Haub [1] Nathan Mills [1] Riley Ott [1]

[1]Purdue University Fort Wayne

Introduction

In this work, we will be utilizing transformation grids and a two sample F-test to determine if there is a statistically significant difference in brain shape of patients diagnosed with schizophrenia compared to patients without schizophrenia. The data was taken from MRI scans of patient's brains and methods were conducted using R. We focused on 13 landmark locations in the brain for both groups of patients. To visualize the 13 landmark locations, refer to Figure 1 below.

Our analysis will use a transformation grid to examine the shape of the cortical surface in the 13 landmark locations of people with schizophrenia as well as control volunteers. Our analysis will also include a Two Sample Test dealing with the Goodall two independent sample F test. This will allow us to test whether the mean shapes of the 13 brain landmarks are different in the two groups: the control subjects and the subjects with schizophrenia.

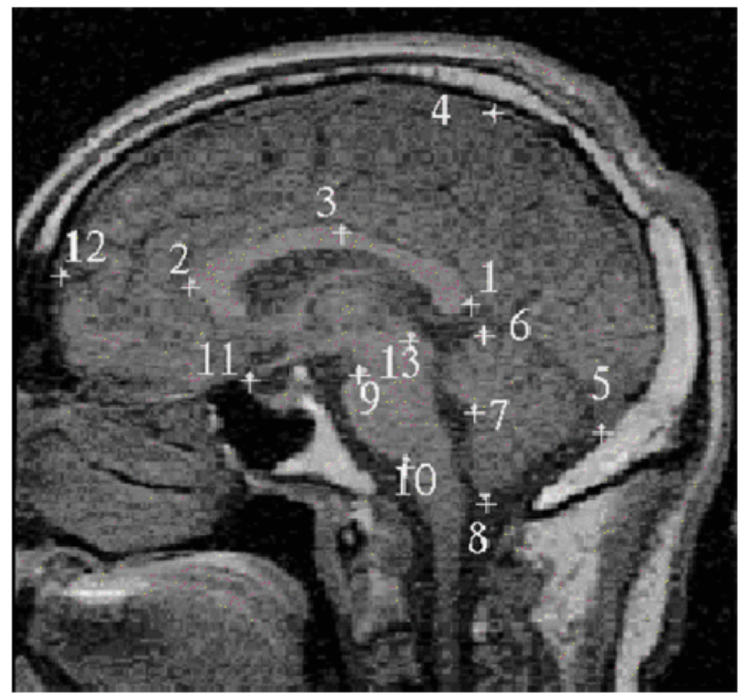

Figure 1. The 13 landmark locations include the splenium (1), the genu (2), the top of the corpus callosum (3), the top of the head (4), the tentorium of the cerebellum at the dura (5), the top of the cerebellum (6), the tip of the fourth ventricle (7), the bottom of the cerebellum (8), the top of the pons (9), the bottom of the pons (10), the optic chiasm (11), the frontal pole (12), and the superior colliculus (13).

Data Set and Software

The schizophrenia data set used for this statistical study can be found in the shapes package in R. The analysis of this data was also conducted in R.

The schizophrenia data set identifies $k = 13$ locations in the brain in $m = 2$ dimensions. The two dimensions are represented by a control group that consists of 14 patients, and a schizophrenic group that also consists of 14 patients.

Conclusion

After creating the transformation grids and conducting a Goodall two-independent sample F-test, we can conclude that there is a statistically significant difference in the brain shape between patients with schizophrenia and patients without schizophrenia. The transformation grids reveal that there are specific points on the brain that have different locations in the brains of patients living with schizophrenia compared to the brains of individuals living without schizophrenia. With the Goodall F-test, we see that there is a significant difference in the average shape of the brains for the control group compared to the schizophrenic group. These differences in location and mean shape prove to be significant enough that it may be useful for doctors to study these differences to find treatments for patients living with schizophrenia.

Method 1: Transformation Grids

Thin plate splines will be used to interpolate the brain scans into two dimensional plots. The natural one dimensional cubic spline is a special interpolant, specified as $g(x)$, minimizes the roughness penalty

$$\int |\ \partial g^2/\partial x^2\ |\ dx$$

which is subject to interpolation as the landmarks. There are differences in this approach using shape analysis. The thin-plate spline is bijective. A bijective thin-plate spline would be synonymous to a monotone cubic spline. Being a natural interpolant in two dimensions, the thin-plate spline minimizes the amount of bends in transforming the two grid. This can also be considered a roughness penalty. Using the two dimensional case $(m = 2)$ we consider the $(2x1)$ landmarks on the first figure t_j, where $j = 1, ..., k$, maps exactly into the second figure, y_i, where $i = 1, ..., k$.

We can produce transformation grids using thin-plate splines for the deformation of two objects. We derive these transformation grid ideals from the cartesian transformation grids of Thompson (1917). In our case, these objects will be the brains of the control group and the brains of the schizophrenic group. To do this, a regular square grid is drawn on one object, the schizophrenic group, and the grid is then deformed to lie on the second object, the control group individuals. Corresponding parts of the brain will then be located in the corresponding grid blocks. At the points where two lines on the grid meet, t_i, the position which corresponds to the second object is then calculated using a pair of thin-plate splines (PTPS) transformation $y_i = \phi(t_i), i = 1, ..., n_g$. n_g is the number of junctions or crossing points on the grid. These junction points are joined with a line in the same order as the first object to create a deformed grid over the second object. A PTPS is produced using the following bi variate function

$$\phi(t) = (\phi_1(t), \phi_2(t))^T = c + At + W^T s(t)$$

The previous PTPS can be used to create a transformation grid from a regular square grid on the first object to a deformed grid on the second object. We think of each square in the deformation as being deformed into the shape of a quadrilateral with four shape parameters. Using the shapes package in R, we will produce these transformation grids for the schizophrenia data set.

Method 2: Goodall's Two Sample F-Test

As noted previously, the schizophrenia data set contains $k = 13$ landmarks in $m = 2$ dimensions: control patients and schizophrenic patients. There are 14 patients in each group. To determine if there is a significant difference between the two groups, we will be using Goodall's two-independent sample F test that uses the statistic:

$$F = \frac{n_1+n_2-2}{n_1^{-1}+n_2^{-1}} \frac{d_F^2(\hat{\mu}_1,\hat{\mu}_2)}{\Sigma_{i=1}^{n_1} d_F^2(X_i,\hat{\mu}_1)+\Sigma_{i=1}^{n_2}(Y_i,\hat{\mu}_1)} \sim F_{q,(n_1+n_2-2)q}$$

This test calculates the mean shape of the brains of the control group, individuals 1 through 14, and the mean shape of the schizophrenic group, individuals 15 through 28. In general, we reject H_0 for large values of this test statistic, which in turn means we reject H_0 for small p-values. For our purposes, we will be testing $H_0: \mu_1 = \mu_2$ against $H_a: \mu_1 \neq \mu_2$, where μ_1 represents the mean shape of the brain of the 14 control patients, and μ_2 represents the mean shape of the brain of the 14 schizophrenic patients. p-values are given based on re-sampling, by either a permutation or a bootstrap test. The permutation test is without replacement, while the bootstrap test involves sampling with replacement.

Analysis and Discussion

Transformation Grids

The output of the grids show shape differences between normal, healthy brains and schizophrenic brains. The grid mapping begins to show the shape differences between the two types of brains. Looking at Figure 2, we can observe different gaps between the red (normal brain) and green (schizophrenic brain) points. The distance between these points can be measured in many ways, including linearly. The further apart the two points are mean there are larger shape differences in that part of the brain. On the contrary, points that are similar and almost touching conclude that those parts of the brain are similar between the two test groups.

We can see a dip in the shape between landmarks 9 and 13. It is also observed that a deformation occurs around landmarks 1, 6, and 7. This appears to be the largest difference in shape between the two groups. Based on these landmark deformations, it leads us to believe that the shape differences occur in the following parts of the brain the splenium, top of the cerebellum, tip of the fourth ventricle, top of pons, and bottom of pons. These locations formed a ringed concave in that part of the brain. Based on these observations, we can conclude that these landmarks are affected by the condition and would likely qualify as an indicator of schizophrenia.

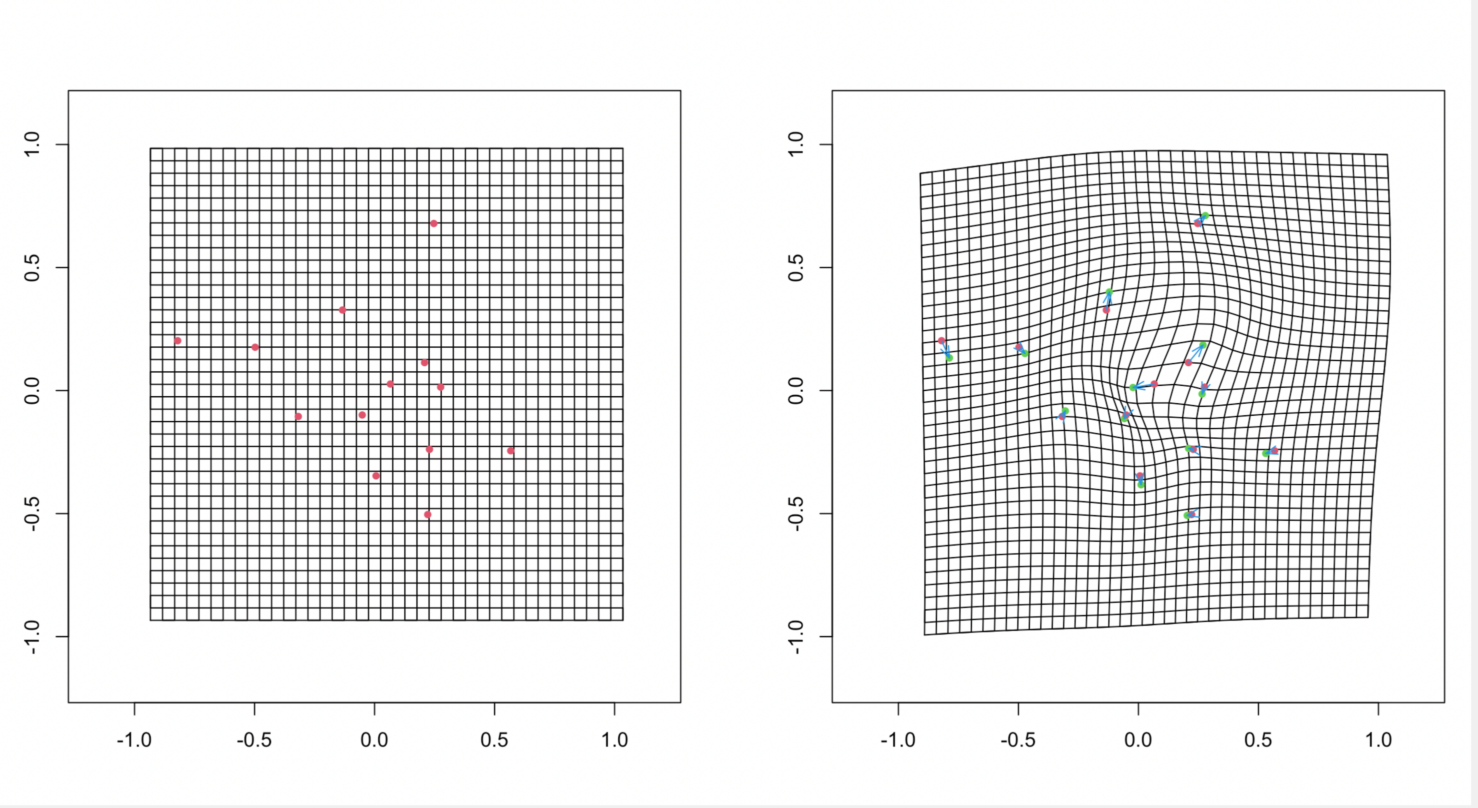

Figure 2. *Left*: a 40x40 grid has been placed over the estimated mean control shape. *Right*: a 40×40 grid has been manipulated to show the differences between the mean shape of the schizophrenic patients and the control patients magnified three times. Arrows are drawn from the control mean to the schizophrenia mean. As reference, Figure 2 mirrors the landmark points in Figure 1.

Goodall's F-test

After conducting the Goodall two-independent sample F-test in R using the function testmeanshapes without replacement, we obtain a tabular p-value of 0.008. When the test is run with replacement, the same p-value is obtained. Based on this, we would reject H_0 in favor of H_a, so we can conclude that $\mu_1 \neq \mu_2$. This means that the mean shape of the control group is significantly different from the mean shape of the schizophrenia group. This leads us to determine that the brain shape of a person living with schizophrenia is different than the brain shape of a individual not living with schizophrenia.