Detecting Anatomical Changes Using Logistic Regression of Structure Masks

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Introduction Neuroscientists are often interested in determining whether external covariates are related to changes in brain shape. There are three main ways currently being used to determine anatomical changes in human brains: 1) deformation fields produced from nonlinear warping techniques [1-3]; 2) surface extraction techniques [4,6,7,10] and 3) voxel analysis of structure masks [9]. Using results from random field theory, we show how logistic regression of structure masks can be used to detect anatomical changes.

Methods The value 1 is assigned to voxels inside the structure mask, and 0 to voxels outside. In order to detect differences between such images from two different populations, the probability maps of the two populations can be compared using the standard two-sample test for comparing binomial proportions. The more general problem of regressing on one or more covariates (e.g. sex, age) is more difficult. One approach to this problem is to first smooth the images and treat the data as if it had a Gaussian distribution as in [9].

A more efficient estimator of the probability is to use logistic regression [5]. Starting with binary images based on the structure masks, we smooth them with a Gaussian kernel as in [9] and then carry out logistic regression at each voxel. This models the probability of being inside the structure at a particular voxel as the inverse logistic transform of a general linear model. The smoothed data are treated as a quasi-binomial random variable with unknown scale parameter, which is estimated from the deviance of the model. The model is fitted by an iterative re-weighted least squares algorithm [9] to obtain smooth t random fields for testing parameters in the linear model, which can then be analyzed (asymptotically) using the results of [8]. Though these t random fields are based on non-stationary Gaussian random fields, the same techniques can be applied to these fields using an estimate of local FWHM of the random field which is robust against non-stationary noise. Although logistic regression takes more time than fitting a linear model by least squares, it is faster than the nonlinear warping and surface extraction techniques used to study anatomical differences. It also allows for more accurate inference than the method of [9] because inference is based on the binomial distribution, and the Gaussian random field approximation is not necessary.

Results Thirty-five automatically segmented grey-matter images from a group of healthy subjects were binarized into 1 for gray matter, 0 otherwise. The images were then smoothed with a 10mm FWHM Gaussian kernel. To test the methodology, logistic regression was carried out, regressing an intercept and the subject's sex as covariates. The resulting t field was searched for local maxima, but no significant regions of activation were found in this preliminary study. Although other researchers have found differences between male and female brains [10], the null result here may be due to small sample size or the heterogeneity of the subjects in this particular sample.

In order to validate the approach, small artificial hemispherical "bumps" of grey matter were added to the edge of the grey matter on 7 of the first 10 subject images. An extra covariate, taking the value 1 for the first 10 subjects and 0 for the remaining 25, was added to the linear model, and logistic regression was repeated to test for this extra covariate. Bumps of diameter 6, 10, and 14 mm were used, and the method detected both the 10 and 14 mm bumps at $p < 0.05$ when the entire brain was searched.

Conclusion Using logistic regression to compare binary images provides a general way of regressing covariates against anatomical changes in different subjects. It provides a more efficient estimator than least squares estimators, as well as better prediction and better statistical accuracy. The disadvantage of the logistic regression method is that it takes more time than least squares, though it is faster than deformation and surface extraction techniques.

References

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