Multivariate SPM: Application to basis function characterisations of event-related fMRI responses

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Most existing statistical methods for analysing neuroimaging data are univariate, testing the significance of, for example, a single parameter estimated from the least mean squares fit between a model and the data. Below we describe one implementation of a multivariate statistical technique, within Statistical Parametric Mapping (SPM), and illustrate its potential application to tests of multiple basis function parameterisations of event-related fMRI responses in a Random Effects analysis across subjects.

Multivariate Tests using Wilks Lambda

Multivariate tests are analyses that consider more than one dependent variable. In simple terms, they identify linear combinations of the variates and apply standard analyses of variance to these linear compounds. More precisely, assume *n* observations of *p* variates. Using the general linear model, the fitted response, **Y**, and residuals, **r**, are:

$$\mathbf{Y}=\mathbf{X}\text{pinv}(\mathbf{X})\mathbf{y} \qquad \mathbf{r}=\mathbf{y}-\mathbf{Y}$$

where ***y*** is a *nxp* data matrix (potentially adjusted for confounds) and **X** is the design matrix (model) comprising one or more regressors. Wilks Λ-statistic is defined through the likelihood ratio:

$$\Lambda=|\mathbf{R}|/(|\mathbf{H}|+|\mathbf{R}|)$$

where **H** is the matrix of squares and products of the fitted response, $\mathbf{Y}^T\mathbf{Y}$, and **R** is the corresponding matrix for the residuals, $\mathbf{r}^T\mathbf{r}$. These determinants can be vewied as a multivariate characterisation of variance, with Λ decreasing as the variance ratio of fitted response to residuals increases. The Λ-statistic can be expressed as a function of the eigenvalues, θ_i, *i=1..p* of the matrix $\mathbf{HR}^{-1}$ (Chatfield & Collins, 1980):

$$\Lambda=\prod_{i=1}^{p} 1/(1+\theta_i)$$

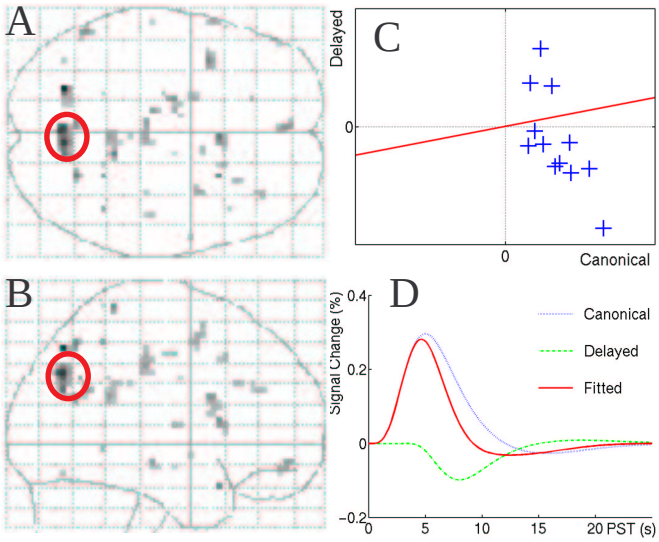
which allows a good approximation to the F-ratio using the transformations described by Rao (1951). For example, with one degree of freedom (df) in the model (i.e., rank(**H**)=1), the transformation is:

$$(1-\Lambda)/\Lambda\ (s-p+1)/p \ \sim\ F(p,\ r-p+1)$$

where s is the residual df, a ratio equivalent to that derived from Hotelling's T^2-test. The generalised eigenvalue decomposition of $\mathbf{HR}^{-1}$ is also equivalent to a canonical variate analysis, where θ_i are the canonical values. The fitted response and residuals can be projected onto the first canonical vector, which can be viewed as the direction (linear compound) that maximises the variance of fitted responses while simultaneously minimising the residual error.

Example Application

12 subjects made old-new decisions to words presented every 5s in an episodic recognition task. Event-related responses to words were modelled with a canonical haemodynamic response function (HRF; Friston et al., 1998) and an HRF delayed by 3 seconds. Differences in parameter estimates between old and new words for both the canonical and the delayed basis function were then entered into a one-sample multivariate analysis to produce SPMs of the F-statistic (see above). Regions evidencing differences significant at p<.001 uncorrected included Precuneus and Posterior Cingulate (Fig 1A/1B, SPM99 MIP). Parameter estimates for each subject from the maximum of the Precuneus region (+6 –69 +36), F(2,10)=43.8, are plotted in Fig 1C, together with the direction of the canonical vector. The fitted differential response derived from the basis functions is plotted in Fig 1D and is consistent with a greater earlier response in this region to old than new words.



Conclusion

Multivariate analyses offer potential advantages, such as eschewing the sphericity assumptions made in univariate repeated measures designs. The example given here is a multiple basis function characterisation of haemodynamic responses; another example is multivariate analysis of the proportions of grey matter, white matter and CSF in Voxel-Based Morphometry (Ashburner & Friston, in press). One disadvantage is that multivariate tests are only powerful when *n>>p* (ideally with ten times as many observations as variates), potentially requiring large subject samples.

References

1. Chatfield, C. & Collins, A. (1980). *Introduction to multivariate analysis*. Chapman & Hall.
2. Rao, C. (1951). *Bull. Int. Stat. Inst., 33*, 177.
3. Friston, K. et al. (1998). *Neuroimage, 7*, 30.