Inference on Individual Differences in Functional Imaging: A test for correlations among tasks

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Objective

Complex experimental designs often yield multiple measurements of interest on each subject. For example, a 2×2 factorial design will yield $q = 4$ contrasts for each of N subjects. When analyzing all $N \times q$ measurements together at the second level, the problem of inter-task dependence or "non-sphericity" must be accounted for. SPM ([1]) treats the inter-task correlations as nuisance parameters, estimating an $q \times q$ inter-task covariance and adjusting the inferences accordingly ([2]).

However, correlations among tasks are of great theoretical interest in psychological studies, because they provide information about how tasks are related to one another. Hence the goal of this work is to analyze inter-task correlations as parameters of interest, not simply as nuisance parameters. Specifically, we wish to detect pairs of effects where a high response in one effect predicts a high (or low) response in the other effect. This kind of information in human performance is the basis of arguments for general factors underlying mental abilities (e.g., Spearman's G) but has seldom been applied to brain imaging data.

Working with a two-level model for fMRI data, we estimate the $q \times q$ matrix of correlations between q at each voxel and create statistic maps that detect the presence of non-zero correlation across different tasks. Then using scatterplots and the individual correlations, we assess and interpret specific patterns of dependence. We demonstrate our method with a fMRI study of attention switching.

Methods

We work with the following two-level model for fMRI data for N subjects:

$$\begin{aligned} Y_k &= X_k \beta_k + \epsilon_k, \\ \epsilon_k &\sim \mathrm{N}_n(0, \sigma^2 I_n),\ k = 1, \ldots, N, \\ \beta_k &= \beta + \delta_k, \\ \delta_k &\sim \mathrm{N}_p(0, \Sigma),\ k = 1, \ldots, N, \\ &\epsilon_1, \ldots, \epsilon_N, \delta_1, \ldots, \delta_N \text{ are independent.} \end{aligned} \tag{1}$$

In (1), Y_k is of length n, the number of scans. The first level models the fMRI data for the k-the individual and the second level models the population mean β (a length-p vector) while allowing for a nondiagonal covariance Σ. We wish to test if the covariance matrix of a set of contrasts of the vectors of activation coefficients is diagonal. We assume that the within-subject variability σ^2 is known, which is reasonable since n is generally large and consequently an accurate estimate of σ can be obtained.

Allowing some possible loss of information, we work with the following modified formulation of this problem. To begin with, we assume that $X_k = X$ for all k. Denote by C, the $q \times p$ matrix whose rows give the q contrast vectors. We pre-multiply both sides of the first equation of (1) above by $D \stackrel{def}{=} C(X^{\mathrm{T}}X)^{-1}X^{\mathrm{T}}$ and both sides of the second equation by C and obtain a transformed two-level model. The observations in the first-level are given by $Z_k \stackrel{def}{=} DY_k$ and the regression parameters corresponding the two levels are given by $\gamma_k \stackrel{def}{=} C\beta_k, \gamma \stackrel{def}{=} C\beta$. The vectors Z_k, γ_k, γ are all $q \times 1$. The covariance matrix in the second-level is given by $\Gamma = C\Sigma C^{\mathrm{T}}$.

It is possible now to formulate our question in terms of Γ. We want to test the following:

$$\mathrm{H}_0 : \Gamma \text{ is diagonal against } \mathrm{H}_1 : \Gamma \text{ is non-diagonal.} \tag{2}$$

In this initial work, we will assume that we have an orthogonal design. That is, we assume that the p contrast estimators are independent, specifically that $U \stackrel{def}{=} C(X^{\mathrm{T}}X)^{-1}C^{\mathrm{T}}$ is diagonal. With this assumption, any correlation observed in Z_k at the second-level is attributable to population-level inter-task correlation. In this case we can use Bartlett's modification ([3]) of the relevant Likelihood Ratio Test (LRT) ([4], pp. 137-138) as an *ad-hoc* solution. However, when the design is not orthogonal, correlation observed in Z_k could be attributable to within-subject design-induced dependence, simply detecting a non-diagonal U (see Future Work for more on this case).

The data consist of $q = 4$ contrasts on each of $N = 39$ subjects. They are computed from fMRI data with $n = 1440$ observations, and where X is $n \times p$ with $p = 48$. The experiment used a 2×2 factorial design, with "Switch Type" (attribute or object) and "Representation" (external or internal) factors.

We estimate each γ_k by the corresponding Z_k, and treat these N *estimates* as independent and identically distributed observations from $\mathrm{N}_q(\gamma, \Gamma)$. Our ad-hoc solution is given by the generalized likelihood ratio test (LRT) for correlation. It is straightforward, and is proportional to the logarithm of determinant of the sample correlation matrix based on Z_k's. Using an asymptotic χ^2 approximation with $q(q-1)/2 = 6$ degrees of freedom, along with Bartlett's correction, we find P-values and thresholds that control the false discovery rate. Significant voxels are interrogated with scatterplots and post-hoc tests (testing for non-zero correlation at each element of Γ).

Results

A 5% FDR threshold ($P < 0.0049$, $\chi^2_6 \geq 18.62$) found 2389 voxels with significant correlation. See Figures 1-4 for the various patterns of correlation were detected. Not shown are various voxels where outliers appeared to induce spurious correlation.

Discussion & Future Work

While inter-task correlation is often ignored, regarded simply as a source of "nuisance nonsphericity", we assert that it is a potentially rich source of information about individual differences. We find that the *ad-hoc* LRT-based correlation test presented can detect interesting correlations, though it is also sensitive to outliers.

In future work we would like to address the following: 1. Deriving tractable expression for the LRT for general models ($X \neq X_k$, $Var(\epsilon_k) \neq \sigma^2 I$) corresponding asymptotic distribution, 2. Robustness, creating a test that is less sensitive to outliers; 3. Greater generality, allowing for non-orthogonal designs, accounting for correlation induced by the first level design matrix; and 4. Small sample performance, using Bayesian methods to regularize estimates with small groups.

Figures

The format of the figures is as follows: **Left:** Thresholded images of Bartlett's statistic showing the regions of significant inter-task correlations. **Middle:** Correlation matrix image showing the correlation values in white, standard deviations in black, and P-values for non-zero correlation in yellow. Bold font numbers indicate 0.05 significance, Bonferroni corrected for searching over the 6 correlations. **Right:** Scatterplot matrix for the 4 tasks showing data for all 39 subjects, with 95% confidence ellipsoids.

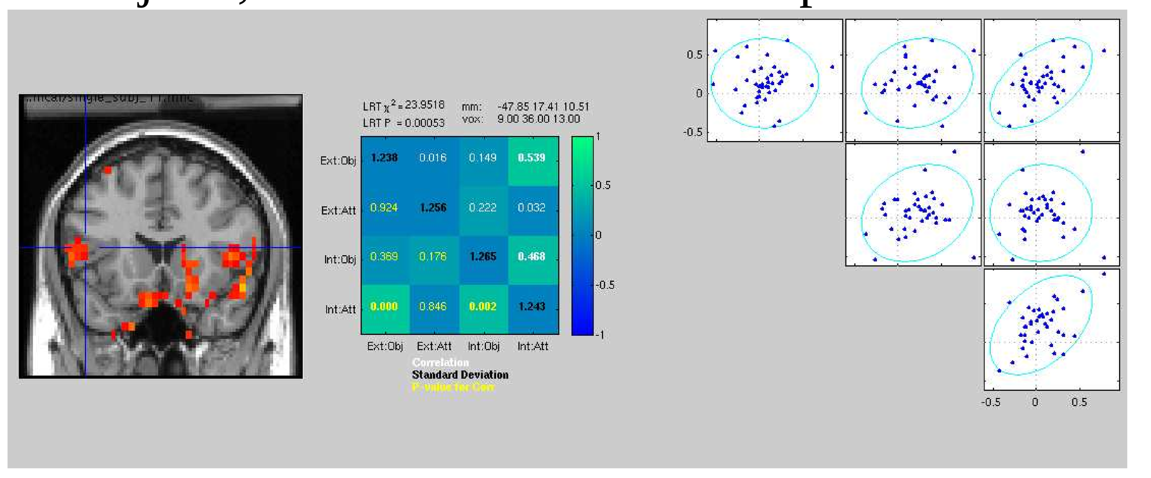

Figure 1: Left inferior frontal gyrus voxel showing positive correlation between attribute and object types of switching, for both external and internal conditions. The functional correlations here are consistent with the idea that switch costs are interrelated, though the heterogeneity of the correlations suggests that this region does not uniformly mediate switching across types.

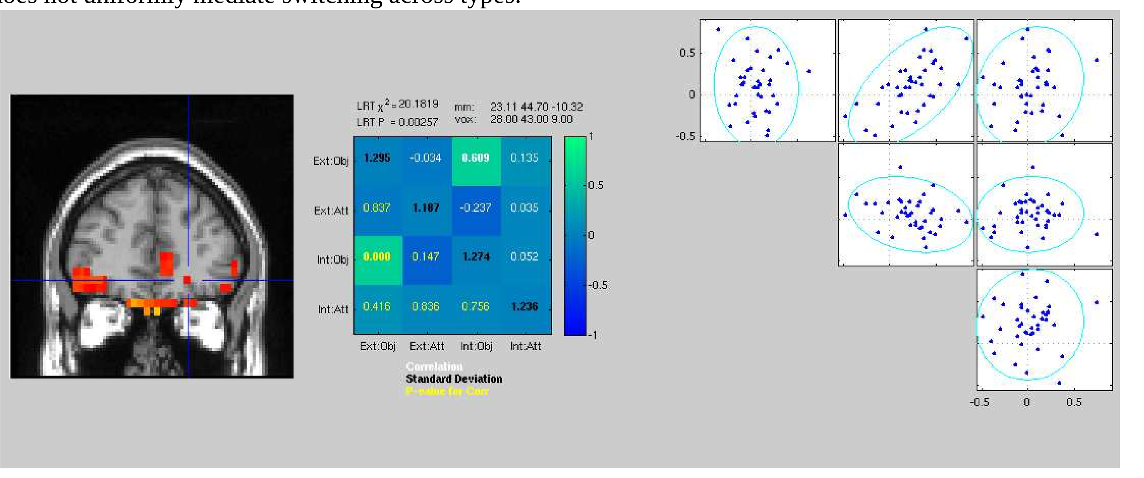

Figure 2: While many regions show a correlation between different switch types, this medial orbitofrontal region shows positive correlation between the two object switching conditions, internal and external, for the same switching type (object). This pattern is consistent with the notion of a general object switching mechanism implemented in part in this region.

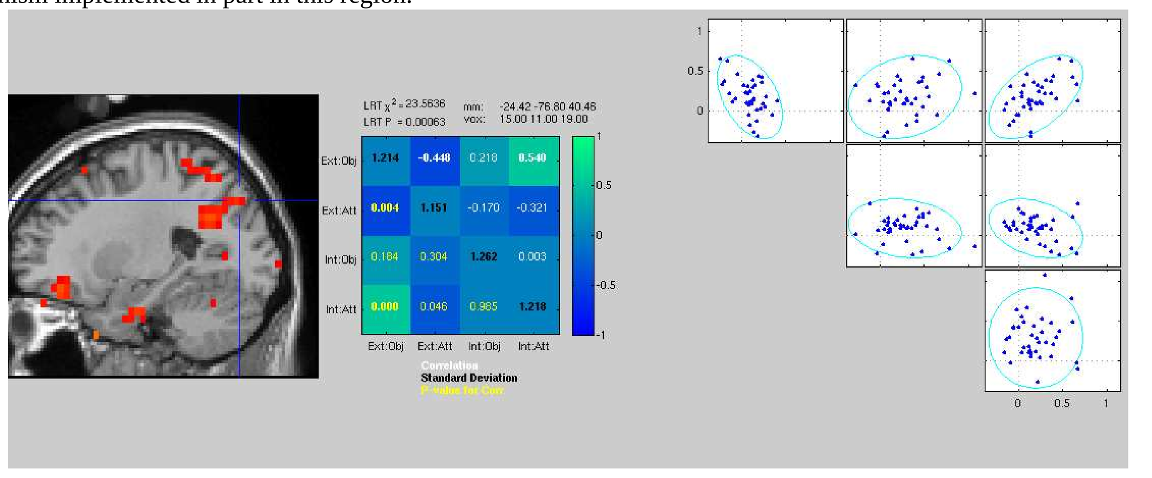

Figure 3: Voxel in the superior parietal cortex showing *negative* correlation between switching types when stimuli are present externally, and *positive* correlation between external presentation of object switching and internal representation of attribute switching. This suggests that different types of switching are heterogeneous in more complex ways that might be inferred from analyzing performance alone.

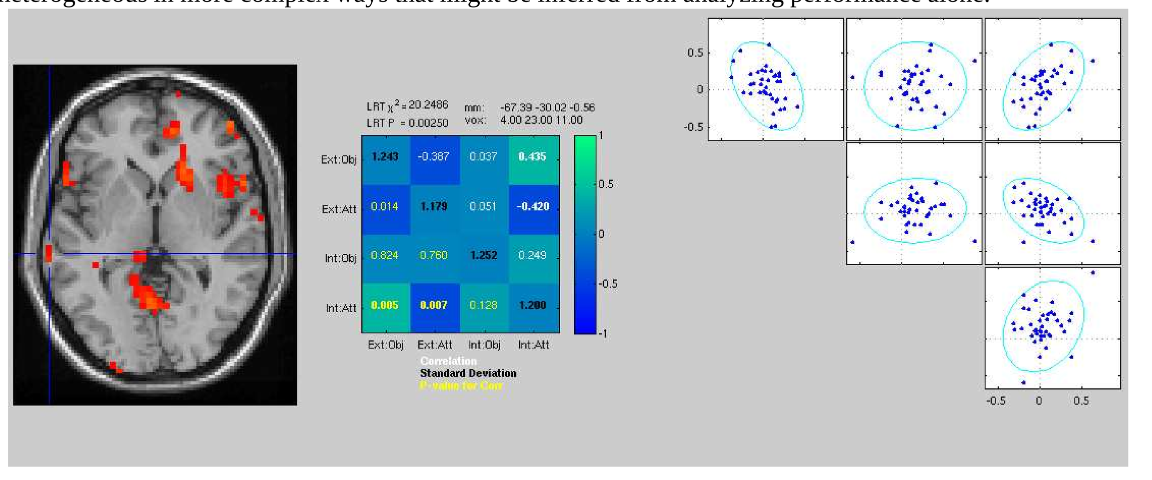

Figure 4: Superficial superior temporal voxel exhibiting positive correlations between External Object and Internal Attribute switching (+0.435) and negative correlations between External Attribute and Internal Attribute switching (-0.420). Note than none of the effects considered shows any mean effect (data are centered near zero), thus this region would never be identified through any analysis based on a t- or F-statistic.

References: [1] SPM, http://www.fil.ion.ucl.ac.uk/spm; [2] Friston, Glaser, Henson & Ashburner, *NeuroImage* 16:484–512, 2002; [3] Bartlett, *Jour. Roy. Statist. Soc., B* 16:296–298; [4] Mardia, Kent, and Bibby (1979), *Multivariate Analysis*, Academic Press, London.