Jackknife Assessment of Individual Subject Effects on a Mixed-Effect Group Level fMRI Analysis

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Background

Data drawn from several subjects in a functional MRI experiment demonstrate variance at two levels. Variance at the intrasubject level manifests itself as the residual in the single-subject General Linear Model (GLM). In addition, the underlying effects themselves show a significant amount of variability across different subjects. Maximizing sensitivity for real activations while minimizing false positives involves properly estimating not just individual effect magnitudes, but also variance at both intrasubject as well as intersubject levels. In this study, we used a jackknife statistical analysis to quantify the impact of intrasubject level effect magnitude and variance on the T-statistic values derived from a mixed effects group analysis.

Methods

Data for this study were drawn from 40 different subjects who performed a rapid event related task, the Go/Nogo task [Garavan et al., 1999; Liddle et al., 2001] (consisting of random ITI between 1.5 and 3.5 sec., 120 Go trials, 30 Nogo trials). Data analysis using the FMRISTAT package [Worsley 2002] in MATLAB was performed voxel-wise, using a GLM-based deconvolution to allow for flexibility in terms of the actual time course of response both within and across subjects. The time courses for 'Go' and 'Nogo' conditions were modeled independently using six contiguous boxcar functions of 3 seconds duration each. Additional regressors were used to account for motion related spikes as well as baseline drift. The start of the response was assumed to coincide with the stimulus and its duration was modeled over 18 seconds, allowing for overlap from consecutive stimuli. Estimates of the effect magnitude and corresponding residual variance from this stage were generated for each subject. Data from each of the 40 subjects were then combined using a mixed effects linear model. Clusters of activated voxels were chosen from the group t-statistic map. Multi-subject analysis was then repeated by dropping one subject at a time, and new T-values were computed for voxels in the chosen clusters. The impact of dropping each subject from the GLM was then compared with intra-subject effect magnitude and variance.

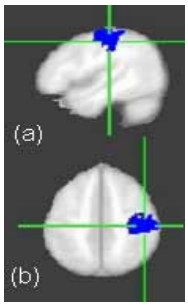

Fig 1 (a) Sagittal and **(b)**axial views of the analyzed cluster

Results and Conclusions

Results displayed here correspond to the largest, most robust cluster, situated in motor cortex (See Fig. 1). Similar results were seen for other clusters as well. Dropping single subjects from the group GLM changed the average T-value of the cluster by as much as 12%. The most significantly activated voxel within this cluster showed a T-value of 5.717. Figure 2(a) shows the individual contrast magnitudes as well as standard deviations for each individual subject at the same voxel. Note that with the large number of subjects in this experiment, a statistically significant group effect was achieved even when individual subjects showed a poor contrast to noise ratio, since the effects are consistent across the group. Fig. 2(b) shows the T-value of the same voxel upon dropping each of the 40 subjects, one at a time. Subjects 6, 11 and 36 in particular cause a sharp drop in the T-value upon being left out of the group analysis. In other words, these three subjects made the single biggest contribution to the group T-statistic. Fig 2(c) shows the average T-statistic value across all voxels in the cluster as each subject is dropped. The strong correlation between plots 2(b) and 2(c) indicates that the T-value at the voxel in consideration in 2(b) is representative of the whole cluster. We quantified the role of individual effect magnitudes and standard deviations in determining the change in group T-value using linear regression. Figure 3(a) shows the measured drop in T-statistic and the predicted change in T-statistic. A linear combination of individual subject effect and variance was able to account for 69% of the variance in the drop in group level T-value. Using only the quotient of individual subject effect and standard deviation (ef/sd) as a regressor accounted for 89% of the variance in the drop in T-value. These results suggest that even with large numbers of subjects, group analysis of fMRI data was highly sensitive to the inclusion or omission of individual subject's data. The impact of single subjects on the significance of group level mixed effects analysis, which was as large as 12% for our group of 40 subjects, may be predicted accurately by the individual effect magnitude to variance ratio.

References 1.FMRISTAT: http://www.math.mcgill.ca/keith/fmristat 2.Garavan, et al. Proc Natl Acad Sci USA 1999; 96:8301-8306 3. Liddle, et al. Hum Brain Map 2001; 12:100-109 4.AFNI: http://afni.nimh.nih.gov/afni

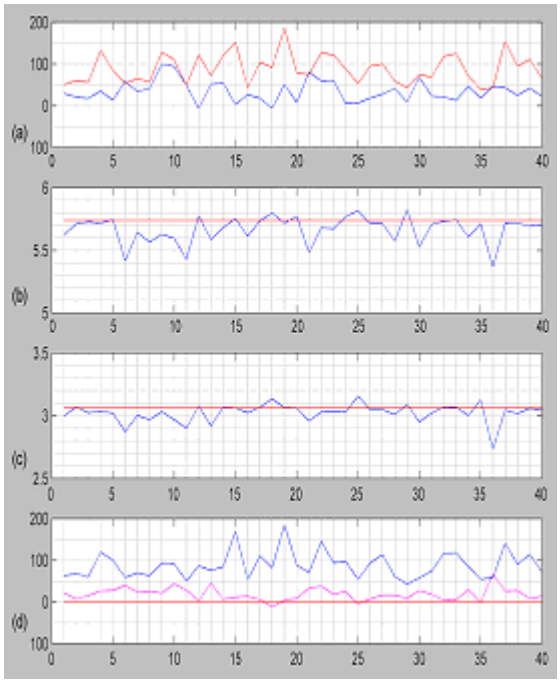

Fig 2. (Left) **(a)** Individual subject effect magnitudes (blue) and standard deviations (red) for Go-Nogo contrast at the voxel with maximum T-value for analysis with all 40 subjects **(b)** T-value (blue) at the same voxel upon dropping the corresponding subject. T-value evaluated with all subjects is shown in blue **(c)** Average T-value (blue) over the cluster shown in Fig 1 upon dropping the corresponding subjects. Note the strong correlation between 2(b) and 2(c). The average T-value for the cluster with all 40 subjects is shown in red **(d)** Mean effect (magenta) and standard deviation (blue) for the Go-Nogo contrast over the same cluster for individual subjects. Zero level (red) is shown for emphasis on the predominantly positive nature of the effect which yields the high T-value in (b) and (c)

Fig 3. (Right) **(a)** Observed change in T-value at the same voxel as Fig. 2(a) upon dropping individual subject (blue) and the predicted value using effect and standard deviation for the same subject (red). The R-squared value observed was 0.69 **(b)** The same change in T-value now overlaid with the linear predictor evaluated using the individual subject T-value at the same voxel. The R-squared is now 0.89