New Thresholding Correction Methods on BOLD fMRI for Interpreting Brain Function

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Synopsis

In order to reduce the type I and II errors and obtain more accurate brain activation map, fMR images were statistically analyzed with uncorrected *t*-test, false discovery rate(FDR) and family-wise error rate(FWE) in the general linear model (GLM) through statistic parameter mapping software(SPM). This study compared and evaluated the power of thresholding correction methods with uncorrected *t*-test, FDR and FWE, and further discussed about new thresholding correction method.

Methods

fMRI data sets, which were obtained with odorant stimulation, was considered for this study and the same was preprocessed using SPM2 with random field approach, smoothing and temporal autocorrelation. In order to exclude affections of degree of freedom and standard deviation, we used data sets of all same size. Quantification of BOLD activation, in terms of number of activated pixels, utilized MRIcro software and home-made program.

Results and Discussions

The activation maps with correction of FDR and FWE, and without correction were different. FWE correction got the least false regions and smallest activated regions with higher p-value threshold (Fig. 1). The *t*-value corresponding to a significance level of p 0.05(α) showed different threshold value as uncorrected *t*-test 1.67, FDR 2.50 and FWE 5.27, and the percentage of activated pixels was uncorrected *t*-test 14.77, FDR 9.43 and FWE 1.13, respectively. Applied to same threshold *t*-value 5.27, FWE has the more power than other methods, and FDR has unsteady results, it is similar to the uncorrected *t*-test. Therefore, FWE correction has the most power. However, FWE correction at the vermis was still observed with false-positive pixels. Figure 2 demonstrated a pixel which was significant with reversed BOLD effect, where coefficient β_1= -5.56, β_2= -1.85 and *t*= 6.36 at x=-2, y=-46 and z=0 of MNI coordination of β. In this study, we suggest a new thresholding method. The GLM formula for given three conditions i.e., rest, task1 and task2, was represented in brief as $y=\beta_1 \cdot Cond_1+\beta_2 \cdot Cond_2+\beta_3 \cdot Cond_3+e$ … (1). Where, y= observed signal intensity or output; β= estimated coefficient of each time series pixel; Cond= condition or input; and e= residual error. Mathematically, the estimated β value might be either positive (+) or negative (-) during all condition. In *t*-test of SPM, these β values as the contrast value were used to obtain the *t*-values at corresponding conditions as follows;

$$T = \frac{C^T\beta}{\delta\sqrt{C^T(X^TX)^{-1}C}} = \frac{\beta_{Contrast1} - \beta_{Contrast2}}{\delta\sqrt{C^T(X^TX)^{-1}C}}$$

This linear model of formula (1) is described as an input-output system. Especially, the coefficients corresponding to all pixels with $\beta_{1\ to\ 3}$ were represented as Δy/ΔCond, respectively. Based on BOLD hypothesis, when the blood flow increases at the activated brain regions, signal of the regions also increases. Therefore, the β values corresponding to those regions would be positive values (+). On the other hand, when it is negative value, the resultant output y also will be negative. In other words, BOLD effect will be reverse (Fig. 2).

Conclusions

In SPM, FWE has the least false region and the much more reliable result than the uncorrected or FDR. However, FWE still observed some false-positive pixels. In order to exclude those false-positive pixels, it is necessary to use thresholding β value for statistical analysis. As well as this thresholding would be very helpful to eliminate those pixels at group analysis such as two sample *t*-test or paired t-test.

Reference

1. Chumbley JR & Friston KJ, NeuroImage 2008.
2. Genovese CR et al, NeuroImage 2002; 15: 870–878.

Acknowledgment

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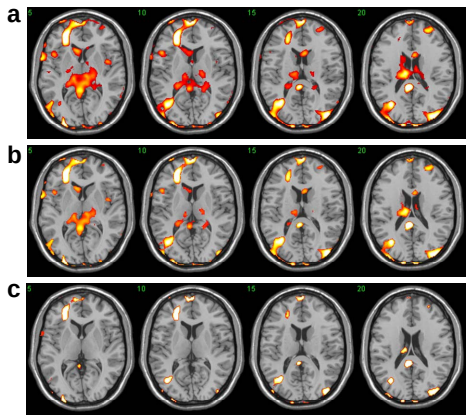

Figure 1. Activation maps obtained using different threshold method with uncorrected *t*-test (a), FDR (b) and FWE (c) corresponding to significance level of p 0.05

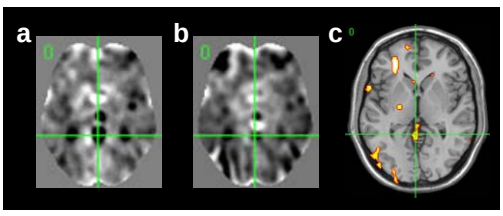

Figure 2. A false-positive pixel with reversed BOLD effect observed at which coefficient β_1= -5.56 (a), β_2= -1.85 (b) and *t*-value= 6.36 (c) at x=-2, y=-46 and z=0 of MNI coordination of β