Variability of Spatial Location of Activation in fMRI and PET CBF Images

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Introduction. Most statistical analysis of fMRI and PET CBF data is concerned with the *detection* of local activation. In this abstract, we propose two theoretical methods for assessing the *variability* of the spatial location of these activations, once they are detected. The methods use random field theory[1] to give approximate standard errors and confidence intervals for the spatial location of the activation.

Overall spatial error can be broken down into three components as follows:

$$\text{Spatial error} = \text{Registration error} + \text{Structure/function error} + \text{Random error}.$$

The first is registration error due to anatomical variability of the underlying structures. This can be reduced by linear brain alignment prior to processing, and it can be eliminated (in principle) by non-linear warping of the brain to an atlas standard. The second is structure/function error due to variability of function within the same structure. For example, function may be located at the fundus, midway up, or on the shoulder of a sulcus. The effect is to blur the response on data averaged across a number of subjects. This source of variability cannot be eliminated by current non-linear warping methods.

The third is random error due to the smoothed random noise added to the true underlying activation signal. This source of error would still remain even if the first two sources of error could be eliminated. Random error is due to the fact that the location of the maximum (signal + noise) is not equal to the location of the maximum signal alone. This source of error can be estimated from random field theory[1]. This opens up the possibility of estimating the structure/function error by eliminating registration error, and subtracting estimated random error from the remaining observed spatial error.

Methods. Activation is detected by local maxima of a smooth Gaussian statistical parametric map (SPM$\{Z\}$) derived from the data. We shall assume that the spatial extent of the signal prior to smoothing has a Gaussian shape that matches the point spread function (psf) of the smoothed data. The first theoretical result is the standard deviation of the spatial location of the peak activation in SPM$\{Z\}$:

$$\text{Standard deviation(peak location)} \approx \frac{\text{FWHM}}{\text{Max } Z\sqrt{4\log_e 2}},$$

where FWHM is the full width at half maximum of the psf, and Max Z is the local maximum of the SPM$\{Z\}$. The second theoretical result is an approximate 3D confidence region for the location of the peak activation:

$$\text{Confidence region(peak location)} \approx \left\{(x,y,z) : Z(x,y,z) \geq \sqrt{(\text{Max } Z)^2 - \chi_3^2(\alpha)}\right\},$$

where (x,y,z) is the coordinates of a voxel in the confidence region, $Z(x,y,z)$ is the value of SPM$\{Z\}$ at that coordinate, $\chi_3^2(\alpha)$ is the upper α point of the χ^2 distribution with 3 degrees of freedom, and $100(1-\alpha)\%$ is the desired confidence. In other words, it is the set of voxels where SPM$\{Z\}$ exceeds the threshold $\sqrt{(\text{Max } Z)^2 - \chi_3^2(\alpha)}$.

Results. The methods were checked by simulation. Gaussian white noise was simulated, a signal was added, and the result was smoothed with a Gaussian psf. A crucial condition is the assumption that the signal shape matches the psf. Under this assumption, both methods performed equally well, but if this assumption was not satisfied, for example if the signal was wider than the psf, then the first method gave a standard error that was too small. However the second method gave a confidence region that was still reasonably accurate, even when the signal had a non-Gaussian shape, for example a 'box' shape. We therefore recommend the second confidence region method. When applied to some typical fMRI and PET CBF data sets, the 95% confidence regions had half-widths of 3–10mm.

Reference

1. Adler R (1981) *The Geometry of Random Fields.* Wiley: New York