Evaluating fMRI Spatial Extent in Groups with Different CNR

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SYNOPSIS
A method to allow comparison of the spatial extent of fMRI activations between two groups with differing CNR was developed. The method was evaluated in two subjects and was found to successfully recover many of the active voxels across a wide range of CNRs. The error in the estimation of the size of the activation was smaller than the uncorrected case for all but the smallest CNRs. The technique increased the number of false positives and consistently overestimated the activation size while the uncorrected data underestimated the size. Further work is necessary to establish the robustness of the technique.

INTRODUCTION
A common objective of functional magnetic resonance imaging (fMRI) is to evaluate the spatial extent of brain activation in one or more groups. These groups may consist of longitudinal studies within the same subject or comparison across differing subject populations. A frequently used approach to evaluating spatial extent is to count the number of voxels that meet specified statistical criteria. However, if the different groups do not have the same contrast-to-noise (CNR), the spatial extent difference will be a function of both the CNR differences and the functional differences between the groups [1]. In order to fairly compare the spatial extent of activations with different CNR, one must account for the CNR differences between the statistical maps. The goal of this research was to develop a method to allow comparison of the spatial extent of activations between two different groups for statistical maps calculated using a t-statistic.

THEORY
The formula for the calculation of the t-statistic is shown in Equation 1 where μ1, σ1, and n1 are the mean, standard deviation, and number of samples from condition x. Assuming that the standard deviation and number of samples from each condition are equal, then Equation 1 can be simplified to a linear relationship between t and CNR as shown in Equation 2. The proposed method to account for the differences in the CNR is then to calculate a corrected “t-statistic” as shown in Equation 3 where the subscripts indicate the appropriate values for groups A and B. 

\[ t = \frac{\bar{x}_1 - \bar{x}_2}{\frac{\sigma_1}{\sqrt{n_1}} + \frac{\sigma_2}{\sqrt{n_2}}} \]  
\[ t = \frac{\bar{x}_1 - \bar{x}_2}{\sigma} \sqrt{\frac{1}{n_1} + \frac{1}{n_2}} = CNR \sqrt{\frac{1}{n_1} + \frac{1}{n_2}} \]  
\[ t_{corrected} = t_B \frac{CNR_A}{CNR_B} \sqrt{\frac{n_1}{n_1^{-1}} + \frac{n_2}{n_2^{-1}}} \]  

METHODS
Two subjects were recruited under a protocol approved by the local Institutional Review Board. Single-shot gradient-echo images were acquired using a 1.5T GE Signa NVi scanner using a quadrature RF volume head coil. Imaging parameters were TR=1s, TE=40ms, flip angle=81°, matrix=64x64, FOV=24cm, and slice thickness=5 mm. The event related stimulus consisted of a black and white radial checkerboard shown for 500 ms every 14 to 18 s interleaved with a fixation cross. A total of 192 (subject 1) or 154 (subject 2) trials were collected in series lasting ~6 min each.

Data were analyzed using MATLAB (Mathworks, Natick, MA). Epochs consisting of 5 pre-stimulus and 13 post-stimulus time points (samples) were extracted from the full image time courses. To allow for a controlled comparison across groups with different CNR, 1 to 192 (subject 1) or 154 (subject 2) epochs were randomly chosen from the individual time courses and averaged. A correlation coefficient between these mean signal time courses and an empirical hemodynamic response function was calculated and converted to a t-score for each possible number of trials included. Using Equation 3 and the relationship that noise (σ1, σ2) decreases as the root of the number of trials, a corrected “t-map” was calculated for each possible number of trials, using the map with the maximum number of trials as a reference. These maps were then analyzed for true positive and false positives using “corrected t”>3.6 as an active threshold. To simplify the analysis and avoid biasing due to slice acquisition timing differences, the counts were restricted to the brain in a single slice of each subject.

RESULTS AND DISCUSSION
As shown in Figure 1, before correction, for the original t-test, the number of true positive voxels (TP) increases as the number of trials increases and the number of false positive voxels (FP) remains consistently low throughout. With the correction, the TP remains near the actual number of positive voxels except at a very low number of trials. However, the FP increases rapidly as the number of trials decreases. Therefore, as expected, the adjustment decreases the number of type-2 errors at the expense of type-1 errors. Since the objective of this technique is to evaluate spatial extent, the difference between the total number of active voxels at each number of trials and the true number of active voxels was computed. The original and corrected t-maps consistently underestimated and overestimated the size of the activation, respectively. Figure 2 shows the magnitude of this difference. One can see that for all but the lowest number of trials, the error in the estimation of the number of active voxels is smaller for the corrected t-maps. Results were similar for both subjects. Further work is necessary to establish the robustness of the technique.

Figure 1 (Left): Number of active voxels for corrected and uncorrected true positive and false positive activations for a subject 1.
Figure 2 (Right): Absolute value of difference between total voxels above threshold and actual number of active voxels.