Simple subject-specific spatial smoothing for BOLD fMRI

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Introduction

Spatial smoothing is a crucial processing step preceding statistical analyses of blood-oxygenation-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) data [1]. The primary benefit of spatial smoothing (SS) is increased BOLD contrast-to-noise ratio (CNR) through local averaging of thermal noise [2,3]. Although group analyses also require smoothing to decrease anatomic and functional heterogeneity between subjects [4], this requirement does not apply when analyzing fMRI data from a single subject. Choosing an appropriate SS kernel size for individual subjects is difficult because the optimal value varies both between subjects [5] and activated foci of different sizes within subjects [6,7]. Over-smoothing data decreases spatial specificity and can completely blur out highly focal regions of activation [6]. Although locally adaptive SS techniques have been proposed [8-10], the use of a single SS kernel size for one or many subjects is virtually ubiquitous in the preprocessing of BOLD fMRI data. Thus, the goal of this work is to present a simple and computationally efficient approach to assist researchers in selecting an appropriate SS kernel size for region of interest (ROI) analyses in individual subjects.

Methods

Experiments were performed on a Philips whole-body 7T scanner. Four volunteers (Sub1, Sub2, Sub3, Sub4) were recruited to take part in fMRI studies under a protocol approved by the institutional review board. The visual paradigm was a block design with alternating 24 sec segments of activation (flashing checkerboard) and baseline (central fixation) acquired using single-shot echo-planar imaging (matrix=192x192, TE=25 ms, TR=2000 ms, FOV=19.2 cm, θ=80°, 9 slices, 96 volumes, 1x1x2 mm^3 voxels). Each subject performed eight runs acquired with increasing SENSE [11] reduction factors (R=1, 2, 3, …, 8). Preprocessing and statistical analyses were performed using AFNI [12]. Each run was spatially smoothed (using `3dmerge`) with 16 full-width-at-half-maximum (FWHM) kernel sizes between 0 and 15 mm (in 1 mm increments). Statistics were calculated using a deconvolution analysis with ARMA(1,1) correction for temporally correlated noise (using `3dREMLfit`). An ROI in the visual cortex was selected for each subject by including voxels with *t*-statistics ≥ 2.0 in data processed with more than half (≥ 9 out of 16) of the smoothing kernels for the majority (≥ 5 out of 8) of the runs. These criteria ensured that only voxels with robust activation were included in the analyses.

Previous works have supported the hypothesis that BOLD CNR is maximized when the FWHM kernel size matches the extent of the underlying activation feature [3,13-15,6,16]. The ideal kernel size is not known *a priori*, but it may be inferred from the point at which further increasing the kernel size either decreases, or does not significantly increase, the *t*-statistics of activation. Let $t(k)$ be the *t*-statistic for a voxel with SS kernel size k, and M be the maximum *t*-statistic for all k. Starting with $k = 0$, let k increase while $\{t(k+1) \geq t(k)\}$ OR $\{(t(k) \geq 0.8M)$ AND $(t(k+2) > t(k))\}$ OR $\{(t(k) < 0.8M)$ AND $(\max(t(k+2),t(k+3)) > t(k))\}$. These conditions permit k to increase until $t(k)$ is at, or very close to, the global maximum. This selection of k is applied to each voxel within the ROI for all runs.

Results

Figure 1 displays a histogram of selected k for all voxels in all runs for each subject. As predicted by the matched filter theory described above, the *t*-statistics increase as k increases until a maximum is reached, and then decrease as k continues to increase past the ideal value. The peak of the histogram reveals the kernel size that results in the highest overall *t*-statistics in the ROI. As shown in Fig. 1, the peak is different for each subject: (a) 2-3 mm for Sub1, (b) 4 mm for Sub2, (c) 5-6 mm for Sub3, and (d) 4-5 mm for Sub4.

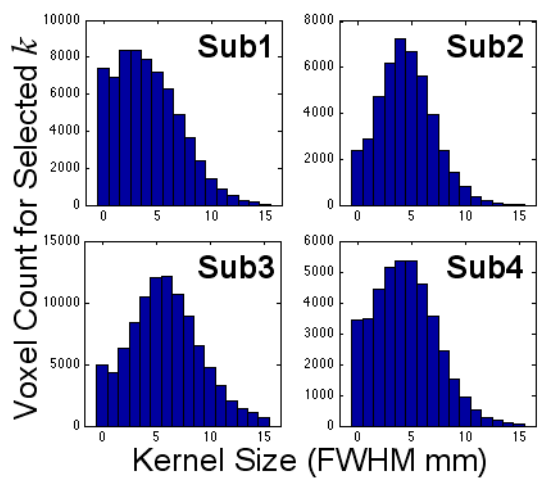

Fig. 1: Histograms of selected k for all voxels within the ROI summed over all eight runs for each subject. The peak of the histogram is unique for each subject, and is used to infer an appropriate SS kernel size.

Discussion

These results confirm previous statements that stress the benefit of even a modest degree of spatial smoothing [1,16] and the importance of considering a range of SS kernel sizes when analyzing and interpreting functional data [17,18,13,14,16,19,5,1,20]. If these data were to be analyzed at both the individual and group levels, then these results strongly suggest that a broad smoothing kernel size (FWHM = 6-9 mm) appropriate for group analyses may be far from optimal for single-subject analyses. Over-smoothing can lead to an increase in Type II errors (false negatives) by lowering *t*-statistics to below the set threshold for statistical significance, as well as an increase in Type I errors (false positives) from activation "bleeding" into adjacent regions where there is no genuine activation.

A recent report used simulations to suggest that the optimal SS kernel size is also dependent on the BOLD CNR – widening in regions of low CNR [21]. BOLD CNR is degraded by physiological noise and geometric distortions when the reduction factor is low (R=1 or 2), and limited signal-to-noise and an unacceptably high SENSE *g*-factor when the reduction factor is high (R=7 or 8), so the kernel size may depend on the SENSE reduction factor. Although a significantly different kernel size is chosen for two of the low-CNR runs (R=8 for Sub1 and R=1 for Sub4), there is good agreement between kernel sizes selected for individual runs (acquired at varying SENSE reduction factors) for each subject. However, more data are required to rigorously prove or disprove the possibility that the optimal kernel size widens in fMRI studies that utilize high SENSE factors.

Finally, the observation that the histograms in Fig. 1 have relatively broad peaks is significant because this highlights the fact that the kernel sizes selected to maximize *t*-statistics vary within the ROI. This re-emphasizes the benefits of locally adaptive SS techniques to reduce statistical errors and optimize BOLD CNR.

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References

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