Detection Power Adjustment Method for Improved Comparisons between Multiple-Session Individual-Subject fMRI Scans

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Introduction

FMRI is an important tool for probing neural mechanisms associated with recovery and re-organization of brain function in cerebral and cerebrovascular pathologies [1]. Often these studies are longitudinal, involving multiple FMRI sessions separated by days or weeks. In order to properly evaluate reorganization of brain function, FMRI activation maps from sessions before and after therapy need to consider and correct for differences in task performance [2] and noise structure between sessions [3], since the detection power of the FMRI experiment is critically dependent on both [4]. In this work, a data-driven method to compensate for these differences is proposed and implemented in studies of brain reorganization with rehabilitation therapy in aphasia patients

Methods

Two non-fluent aphasia patients with left hemisphere stroke were scanned on a 3T GE LX scanner, once before rehabilitation therapy and once after. Written informed consent was obtained for both patients. Whole-brain FMRI scans were obtained with a 1-shot spiral gradient echo sequence. The patients overtly generated single word responses to a series of 45 semantic category stimuli. The inter-stimulus intervals (ISIs) were varied pseudo-randomly in an event-related design. Patient responses were monitored and coded into two categories, "correct" and "other" responses, producing two corresponding analysis vectors. For each voxel, the observed signal time-series was modeled as the sum of convolutions of the "correct" and "other" analysis vectors and their corresponding best-fit fifteen-lag impulse response functions (IRFs) obtained via deconvolution analysis. Signal due to the "other" responses was regressed out, leaving only the signal due to "correct" responses to contribute towards the activation statistic, the co-efficient of determination, R^2. Simulations and analysis were done with *AFNI* and *Matlab*^{TM}.

Results and Discussion

Detection power depends on the distribution of the activation statistic under the alternative hypothesis. The distributions of R^2 for different levels of epochal BOLD signal change, 0.5% to 6% in steps of 0.5%, were simulated for the pre- and post-therapy (Tx) sessions for each patient. The noise test-bed for the distribution was formed by fitting mixed auto-regressive of order 1, AR(1), plus white Gaussian noise models [7] to all the voxel time-series in the dataset of each session. The BOLD signal for a given epochal signal change (as % baseline) was simulated by convolving a generic BOLD hemodynamic response (from *AFNI*) of appropriate amplitude with the "correct response" analysis vector of that session. Figure 1 shows the R^2 distribution obtained by deconvolution analysis of the simulated noise-test beds with 2% BOLD signal from the pre-Tx (dashed) and post-Tx (solid) datasets for patient 1. The patient produced 24 "correct responses" in the pre-Tx session compared to 32 in the post-Tx session. This is reflected in the increased detection power (larger proportion of voxels, which is termed "probability density", above the R^2-threshold, R^2_{th},) in the post-Tx dataset compared to pre-Tx ($p < 0.0001$, KS difference test) in Figure 1. Increased detection power in the post-Tx session was observed for all added BOLD signals, 0.5%-6%. The null R^2-distributions were not significantly different ($p > 0.9$, KS difference test), indicating that change in detection power between sessions is primarily due to task-performance differences.

Figure 2 shows left lateral sagittal activation maps thresholded at $R^2 > 2$ for the pre-Tx (2a) and post-Tx (2b) datasets of patient 1. There seems to be an increase in lateral frontal activation from pre-Tx to post-Tx. However, the post-Tx session had a higher detection power than the pre-TX session (Figure 1), and thus it is uncertain whether the apparent increase in activation from pre- to post-Tx is due to greater recruitment of the cortex or just an artifact of increased post-Tx detection power.

To compensate for detection power differences between sessions, R^2-values of the pre-Tx dataset were adjusted in the following manner. For a given voxel, the epochal % signal change was inferred from the deconvolved IRF, and rounded to the nearest half %. Given the epochal % signal change and the pre-Tx probability density, *PDpre*, corresponding to the voxel R^2-value, the R^2-value was adjusted to the value of R^2_{th} for the same % signal change in the post-Tx simulated R^2-distribution for which the post-Tx probability density was *PDpre* . Figure 2c shows the left lateral sagittal activation map of the pre-Tx dataset after adjustment for detection power differences. Proper assessments about reorganization/lateralization of language function with rehabilitation therapy should be made using Figures 2c and 2b. There is a decrease in left lateral frontal activation from pre- to post-Tx. An increase in right medial frontal activation from pre-Tx (compensated for detection power) to post-Tx datasets was also observed, consistent with the hypothesis of shift in cortical areas of language processing from left to right hemisphere [5]. Patient 2 had similar numbers of "correct responses" in the two sessions (42 and 44) and did not show discernible differences between activation maps before and after compensation for detection power.

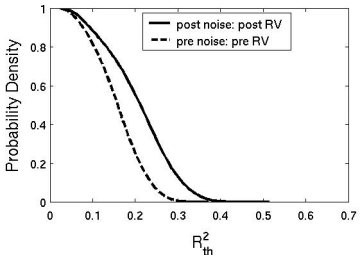
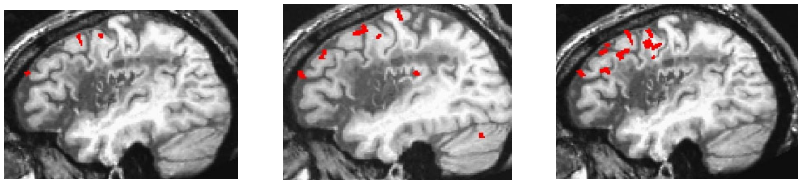


Figure 1. Detection power (probability density) for pre-Tx (dashed) and post-Tx (solid) sessions.



(a) **(b)** **(c)**

Figure 2. Activation in left lateral hemisphere for pre-Tx session (a), post-Tx session (b), and pre-Tx session normalized for detection power (c). Note different conclusions for uncorrected (b-a) and corrected (b-c) comparisons.

References: 1)Thulborn K., et al., Stroke, **30**:749, 1999. 2)Moore A., et al., Proc J Intl Neurophysch Soc, **9**: 192, 2003. 3)Howseman A., et al., Neuroimage, **7**:S599, 2001. 4)Liu TT, et al., Neuroimage, **13**:759, 2001. 5)Crosson B., et al., J Cogn Neuro (in press), 2004.