Evidence of Altered BOLD Hemodynamic Response in Patients with Ischemic Stroke

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Introduction

Blood oxygen level dependent (BOLD) functional magnetic resonance imaging (FMRI) is increasingly being used to monitor recovery of brain function after stroke [1,2]. Most studies in stroke FMRI simply apply the principles of BOLD FMRI of normal subjects to stroke patient populations. Ischemic stroke is associated with impairment of cerebral hemodynamics, which leads to alterations in cerebral blood flow, blood volume and oxygen extraction fraction, as well as vascular enhancement [3], all quantities that influence the BOLD response [4]. Primary auditory cortex can be activated by externally controlled stimulus paradigms. In this study, differences between the hemodynamic responses (HDRs) in the infarcted hemisphere and the intact hemisphere auditory cortex of patients with ischemic stroke were examined, and characteristics of the HDR of normal controls and stroke patients were compared.

Methods

Six normal control subjects, ages 50-70 yrs, and 5 non-fluent aphasia patients, ages 50-70 yrs, with left hemisphere stroke were scanned on a 3T GE LX scanner. Scanning parameters: 1-shot spiral gradient echo sequence [5]; 32 4-4.5 mm sagittal slices covering the whole brain, TR/TE/FA= 1660ms/18ms/70°, 3mm x 3mm in-plane resolution, five 111-image runs for the normal subjects and five 161-image runs for the patients. High-resolution anatomic images were obtained using a *T1*-weighted spoiled GRASS sequence (TR/TE/FA= 23ms/6ms/25°; 124 1.3mm slices; 0.9mm x 0.9mm in-plane resolution). Foam padding was provided to minimize head motion. Written informed consent was obtained for all the subjects. The patients were asked to generate single word responses to a series of semantic category cues. The inter-stimulus interval was varied pseudo-randomly between 24.9, 26.6, 28.2 or 29.8 sec for patients and 16.6, 18.3, 19.9 or 21.6 sec for controls. A total of 45 semantic category cues were presented auditorily.

Data Analysis

The five functional runs were registered, detrended of low-frequency drifts and concatenated to give voxel time-series comprised of 805 images (555 images for controls). For each voxel, the observed voxel FMRI intensity time-series was modeled as the convolution of the experimental auditory cue stimulus vector and the best-fit fifteen-lag impulse response. The co-efficient of determination, R^2 and F-statistic were used to assess brain activation. Images were Talairached and voxel hemodynamic responses (HDRs) above the activation threshold, $R^2 > 0.2$ (p-value < 10^{-7}) for patients and $R^2 > 0.3$ (p-value < 10^{-7}) for controls, within left and right Broadmann area (BA) 42 (primary auditory cortex) were extracted and averaged. The full width at the zero-crossing or return to baseline (FWB) and the full width at half maximum (FWHM) of the responses were calculated after fitting them to regularized generic hemodynamic responses [6] with a non-linear large-scale least-squares optimization method. Analysis was done with *AFNI* and *Matlab^{TM}*.

Results and Discussion

The left auditory cortices (BA 42) of all the stroke patients were perilesional to the infarcts. Fig 1 shows the averaged HDR of the auditory cortex (BA 42) in the infarcted left hemisphere (red) and intact right hemisphere (blue) for an aphasia patient. The stroke region shows a broader response compared to the intact hemisphere. Fig 2 shows the plot of the difference in FWB between stroke (left) and intact (right) hemisphere BA 42 HDRs for 5 ischemic stroke patients (P1-P5, red) and between the left and right BA 42 HDRs of 6 control subjects (C1-C6, blue). The inter-hemispheric difference of the auditory cortex FWBs among the controls was not significant (paired t-test $p > 0.3$), whereas the BA 42 FWBs of the stroke hemisphere responses were significantly higher than the intact hemisphere BA 42 FWBs (paired t-test $p < 0.005$). There was no significant difference between the times-to peak of HDRs in stroke (left) hemisphere BA 42 and the intact (right) hemisphere BA 42 (paired t-test $p > 0.2$). The differences in the breadths between the stroke and intact hemisphere BA 42 HDRs arose mainly from differences in the fall-to-baseline times between the two hemispheres. This indicates that increase in breadth of cortical HDR perilesional to the infarcts may have a basis in altered visco-elastic properties of the tissue in the vicinity of the infarct. The intact hemisphere BA 42 BOLD responses were similar in shape to the control patient HDRs. There was no significant difference in the amplitude of the HDR between the stroke and intact regions or between patients and controls. The results demonstrate significantly broader hemodynamic response to neural stimuli in the vicinity of the stroke. These characteristics should be accounted for when designing and analyzing quantitative FMRI paradigms in stroke patients.

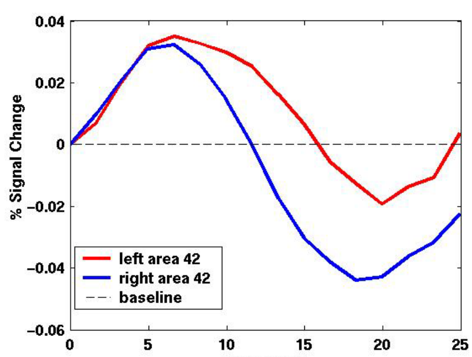

Fig.1 Averaged HDR of activated voxels in area 42 of the stroke hemisphere (red) and intact hemisphere (blue).

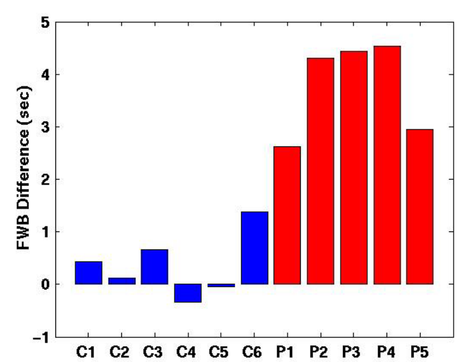

Fig.2 Bar plots of the inter-hemispheric difference of the full width at baseline of averaged HDR of activated voxels in area 42 for controls (C1-C6; blue) and stroke patients (P1-P5; red).

References 1) Cao Y., et al., *Stroke*, **30**:2331, 1999. 2) Thulborn K., et al., *Stroke*, **30**:749, 1999. 3) Derdeyn C., et al., *Neurology*, **53**:103, 1999. 4) Buxton R., et al., MRM, **39**:855, 1998. 5) Noll D., et al., *JMRI* **5**:49, 1995. 6) Cox R., *Comp. Biomed Rsrch*, **29**:162, 1996.