Functional magnetic resonance imaging based on SEEP contrast: Reproducibility, hemodynamic response function, and anatomical specificity

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Introduction

Functional magnetic resonance imaging based on a proton-density change has previously been demonstrated[1-3]. The proton-density change contrast mechanism is theorized to arise in the extravascular space and so we have termed the effect "SEEP" for "Signal Enhancement by Extravascular water Protons". We have proposed that the change in proton-density arises from the usual flux of water from the capillary beds to form extracellular fluid in the CNS. The change in blood flow to sites of neuronal activity that gives rise to the BOLD effect is associated with a local change in cerebral perfusion pressure, thereby altering the fluid balance across the blood-vessel walls resulting in a locally increased proton density. Here we investigate the anatomical location of SEEP signal changes, the reproducibility across repeated experiments, and estimate the SEEP hemodynamic response function (HRF).

Methods

Eight healthy volunteers were studied in a 1.5 T GE Signa Horizon LX clinical MR system. Functional image data was acquired from eight, 4 mm thick slices, using echo-planar imaging with a 128 x 256 matrix. In separate experiments data were acquired with SEEP contrast (spin-echo EPI, TE = 23 msec, TR = 3 sec) and BOLD contrast (gradient-echo EPI, TE = 50 msec, TR = 3 sec). Activity in the motor and sensory areas was elicited by having the subject perform a two-hand finger-touching task. A block design was used with 8 alternated periods of rest and finger-touching, each of 24 seconds duration. FMRI experiments were carried out four times with each subject, twice with SEEP contrast and twice with BOLD contrast.

Data were analyzed by means of correlation to a model paradigm after smoothing in-plane with a 3 x 3 boxcar filter. Correlation T-maps were constructed for each experiment and were combined with a conjunction analysis by taking the minimum T-value at each voxel [4]. Separate conjunction maps were made for BOLD and SEEP contrast. Time course data from active voxels were used to determine the average response to the stimulus, which was used to estimate the HRF. Data with SEEP contrast were then re-analyzed with a modified paradigm based on the observed HRF in order to estimate the optimal model paradigm in an iterative fashion

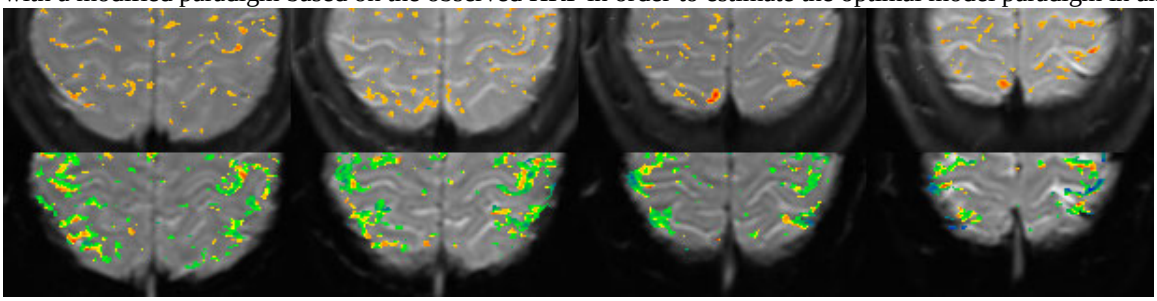

Figure 1: Conjunction maps from duplicate experiments obtained from one subject with SEEP contrast (top) and BOLD contrast (bottom). The posterior half of four slices is shown.

Results and Discussion

Areas of activity in the somatosensory cortex were consistently observed in all studies, with both BOLD and SEEP contrast, and an example from one subject is shown in Figure 1. Reproducibility was also observed in all subjects with duplicated experiments. With SEEP contrast, areas of activity coincided with areas of activity identified with BOLD contrast, but were more localized and tended to follow the gray matter. The signal change observed with SEEP contrast upon neuronal activation averaged approximately 2.5%, consistent with the approximately 2% signal changes observed in previous studies with lower resolution. The average time course response and hemodynamic response function observed with BOLD contrast was consistent with that used in the "Statistical Parametric Mapping" software, SPM2b. The time courses observed with SEEP and BOLD contrast are shown in Figure 2, as well as the estimated model time courses for both contrasts. The results obtained demonstrate good reproducibility with SEEP contrast, and a high degree of localization to gray matter regions in the brain. The observed hemodynamic response function is consistent with the proposed SEEP theory, as it necessarily lags the perfusion changes and BOLD response.

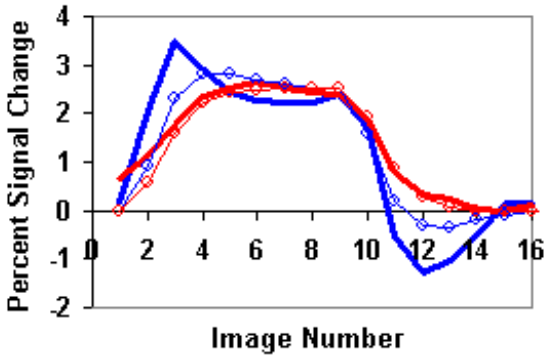

Figure 2 Thick lines show the average response to a stimulus (8 points on, 8 points off) with BOLD (blue) and SEEP (red). Thin lines and circle symbols represent the corresponding best estimated model paradigms.

References

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