Bolus Gd-DTPA washout dynamics predict BOLD dynamics

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Introduction:

Studies have demonstrated significant variations across space and across subjects in the temporal dynamics of the blood oxygenation level dependent (BOLD) fMRI response. These variations are likely to be vascular in origin (1). One approach to increasing the temporal resolution in fMRI is to characterize and to correct for differences in latency due to hemodynamic variability.

In this study, we investigate the vascular contribution to this variability by comparing the temporal dynamics of the BOLD signal change in each voxel to the dynamics of a bolus injection of a contrast agent gadopentetate dimeglumine (Gd-DTPA) (Magnevist, Berlex Lab. Inc). A previous study has found a slight correlation between the onset delay Gadolinium (Gd) bolus and the latency of the BOLD signal. (2) This onset delay, however, is dependent on differences in the vasculature from the site of injection, not purely the differences in local vasculature reflected in the BOLD signal delay. Our hypothesis is that the wash-out time of the Gd bolus is more reflective of the time for blood to travel from the arterioles through veins and is therefore more predictive of BOLD onset time and duration. The goal of the present study is to compare various aspects of the dynamics of the Gd bolus induced signal changes (such as the onset of the signal decrease, the wash-in time, wash-out time, and duration of the bolus) to the dynamics of the BOLD response on a voxel-wise basis to test this hypothesis.

Methods:

Multiple series of T2*-weighted MR images through the visual cortex were acquired on a 3T GE-Signa scanner. (TR=500ms, TE=30ms, FOV=24cm, slice thickness 5mm, matrix size 64x64, 600 images/run). In 4 runs, subjects viewed a contrast reversing checkerboard presented in a blocked (1 run, 20s stimulation, 40s fixation) or event-related (3 runs) design. In 2 runs, subjects viewed no visual stimulus and received a bolus injection of Gd-DTPA after 1 minute of scanning.

Functional areas were identified by correlating the measured response with an ideal reference function (the stimulus timing convolved with a gamma-variate function). Hemodynamic BOLD response functions were determined by deconvolving the event-related time courses. Deconvolved BOLD responses and the signal time course measured during the Gd bolus were fit on a voxel-wise basis to separate gamma-variate functions,

$$S = k\,(t-t0)^{r}\exp(-(t-t0)/b)$$

where k, t0, r, and b are free parameters in the fit describing the amplitude, onset delay, wash-in time, and the wash-out time, respectively. Gadolinium delay, wash-in, and wash-out time constants were also determined by detecting the time of initial deviation from baseline, minimum, and return to baseline of the signal. The latency of both BOLD and Gd responses were also computed by finding the peak of the correlation function of the time course with an ideal response.

Results:

A gamma-variate function provided a good fit to the Gd-induced signal change and to the BOLD response (with different fit parameters) (Fig. 1a and 1b), and these fits were repeatable across runs. Time constants of both Gd bolus and activation induced signal changes varied across the brain and within the activated visual cortex. There is only a slight correlation between the latency of the Gd bolus (as measured by the peak of the correlation function) and the latency of the BOLD response (CC=0.53) (Fig 1c) This correlation disappeared when the onset times determined from the fit were used as a measure of delay. In contrast, the washout time of the Gd, (as determined by the parameter 'b' in the gamma-variate fit) was highly correlated with the latency of the BOLD response (CC=0.80) (Fig. 1d). Other fit parameters showed no significant correlation.

Discussion:

The delay of the BOLD signal change depends in large part on the rate of propagation of oxygenation changes from the arteriolar sphincters to the voxel of interest. The onset of the Gd bolus induced signal decrease is dependent upon variations in vasculature all the way from the injection site, regions with a longer washout of the Gd likely reflect regions with slower venous transport, leading to more delayed BOLD responses. The latter part of the Gd-induced signal curve is therefore more predictive of the BOLD latency. This high degree of correlation further suggests that the time constants determined from a bolus of Gd can be used to calibrate the relative timings of the BOLD signal such that cascaded neuronal activity can be resolved more accurately.

References:

1. Z.S. Saad, *Hum .Brain. Map.*, 13 (2001)
2. B. Biswal, *JCAT*, 27 (2003).

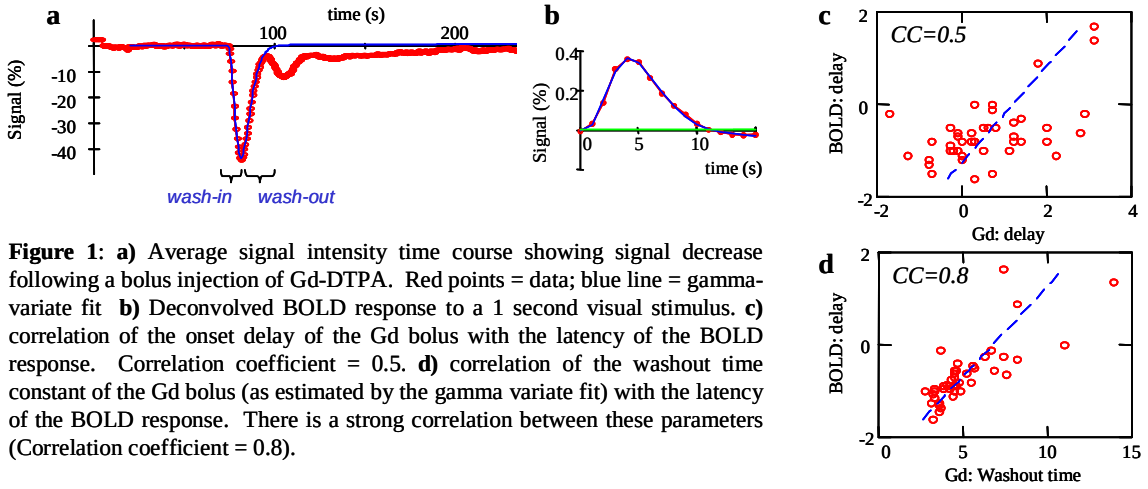

Figure 1: **a)** Average signal intensity time course showing signal decrease following a bolus injection of Gd-DTPA. Red points = data; blue line = gamma-variate fit **b)** Deconvolved BOLD response to a 1 second visual stimulus. **c)** correlation of the onset delay of the Gd bolus with the latency of the BOLD response. Correlation coefficient = 0.5. **d)** correlation of the washout time constant of the Gd bolus (as estimated by the gamma variate fit) with the latency of the BOLD response. There is a strong correlation between these parameters (Correlation coefficient = 0.8).