Investigating the Change in Cerebral Blood Volume to an Event-related Stimulus using an Infusion of Gd-(HP-DO3A)

N. P. Blockley[1], S. T. Francis[1], P. A. Gowland[1]
[1]Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, United Kingdom

Introduction

The aim of this study was to investigate cerebral blood volume (CBV) changes following a short stimulus. This was achieved by measuring changes in R_2^* maps during infusion of a paramagnetic contrast agent (Gd-(HP-DO3A) [1]). Previous work [2] yielded measurements of the fractional change in CBV during a 12s block stimulus paradigm of 2s temporal resolution. To further improve understanding of the BOLD effect we extend this work to an event-related paradigm of 300ms temporal resolution.

Theory

The change in the transverse relaxation rate (R_2^*) in the presence of a contrast agent (CA) can be modelled [2] by equations 1 and 2. The superscripts *act* and *rest* refer to the on and off periods of the stimulus paradigm. Blood volume, *V*, is either arterial (*a*) or venous (*v*) and χ_{agent} is the susceptibility contribution of the CA. The R_2^* change on activation is indicated by Δ and the change due to the presence of a CA by δ. Assuming that vessels in a voxel are uniformly and randomly oriented, the relaxivity constants κ_v and κ_a are equal. If we combine these equations we find that their ratio is equivalent to the fractional change in CBV, equation 3. Therefore the ratio of the gradients of plots of ΔR_2^{*act} and R_2^{*rest} versus CA concentration will yield a measure of blood volume change on activation (ΔCBV).

$$\delta(\Delta R_2^{*act})_{agent} = (\kappa_v \Delta V_v + \kappa_a \Delta V_a)\chi_{agent} \quad (1)$$

$$\delta(R_2^{*rest})_{agent} = (\kappa_v V_v + \kappa_a V_a)\chi_{agent} \quad (2)$$

$$\frac{\delta(\Delta R_2^{*act})_{agent}}{\delta(R_2^{*rest})_{agent}} = \frac{\Delta V_{tot}}{V_{tot}} \quad (3)$$

Method

Two subjects were scanned with a purpose built 3T EPI scanner. Excitation was via a TEM volume coil and reception by means of an occipital surface coil. Two images, with TE = 27ms and 52ms, were acquired after a single excitation, using a multiecho EPI sequence. A matrix size of 64 x 64 was used; in-plane resolution 3mm x 3mm and slice thickness 4mm. Three sagittal slices [3] across the visual cortex were imaged every 300ms. A gradient switching frequency of 1.38kHz was used. The paradigm consisted of 4.8s of visual stimulation (LED goggles flashing at 8Hz) followed by a 55.2s off period; this was repeated for 20 cycles. To maintain alertness subjects were asked to respond with a button press at 34.8s. The triple dose CA infusion began after 4 cycles, and ended 16 minutes later. A T_1 vs. CA concentration calibration curve was produced using blood taken prior to the experiment. In-vivo CA concentration time courses were then created using blood samples taken at 5 time points during the fMRI experiment; 7, 11, 15, 19 and 30 minutes. Image data were realigned in SPM2 [4] and R_2^* maps created. Regions of interest were selected by analysing the first 4 cycles of the paradigm in SPM2, and choosing clusters of the 20 most active pixels. For these pixels R_2^* time-courses were extracted, filtered with a Gaussian of FWHM 0.6s, and ΔCBV calculated using equation 3. Stimulus cycles with motion greater than 1mm were excluded from these calculations.

Results

Figure 1 shows R_2^* values measured at peak and baseline time-points of the haemodynamic response (HR) as a function of CA concentration. The HR was largely suppressed at peak CA concentration, as the effect of an increased volume of CA was balanced by increased blood oxygenation. Figure 2 shows the average ΔCBV, and corresponding BOLD signal change, across a cycle.

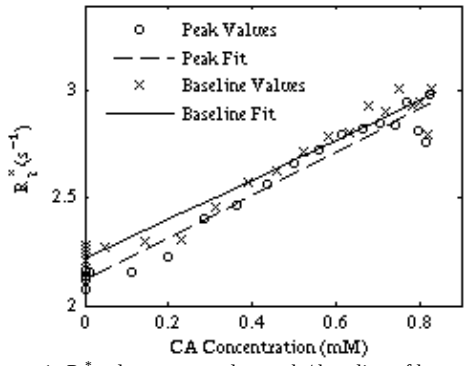

Figure 1- R_2^* values extracted at peak / baseline of haemodynamic response function, for each stimulus cycle. Cycles displaying motion greater than 1mm were excluded. (Subject: 3133)

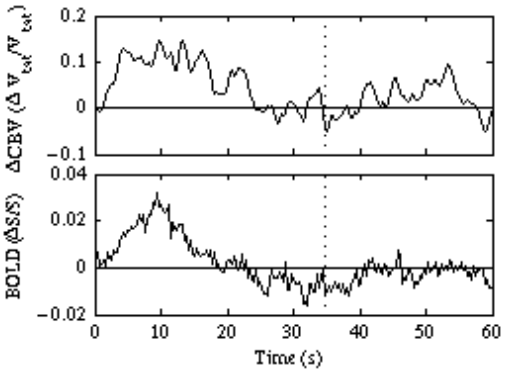

Figure 2 - Average ΔCBV timecourse across a cycle (top) and BOLD response averaged over first 4 cycles. Dotted line represents timing of button press paradigm. (Subject: 3133)

Discussion

We have measured ΔCBV in response to an event-related paradigm with high temporal resolution. This data can be used to validate models of the BOLD effect [5]. ΔCBV of 0.68±0.14 (Subject 3132) and 0.09±0.03 (Subject 3133) were calculated, at the peak of the BOLD signal. ΔCBV has generally been estimated to be ~0.28 [2] for a block paradigm, but a reduced value could reasonably be predicted at shorter stimuli. For subject 3132, M_0 maps reveal large flow effects, implying large blood vessels, within the bounds of the cluster and could be expected to alter the value of ΔCBV. Therefore it is clear that ΔCBV is highly dependent on the local vasculature. In future studies baseline CBV maps will be acquired prior to the fMRI experiment and compared to maps of ΔCBV.

References

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