Estimation of vascular contribution to DfMRI (Diffusion weighted fMRI) signal.

S-I. Urayama[1], K. Aso[1], T. Aso[2], S. Kohno[1], N. Sawamoto[1], H. Fukuyama[1], and D. Le Bihan[2]
[1]Human Brain Research Center, Kyoto Univ., Kyoto, Kyoto, Japan, [2]NeuroSpin, CEA, Saclay, France

Introduction

Upon visual stimulation transient increases in diffusion-weighted MRI (DfMRI) signals at high b-value (b>1000 s/mm²) in activated cortex have been shown to precede hemodynamically relevant BOLD fMRI signals by several seconds. This finding suggests a direct link of the DfMRI signal to early neuronal activation events, such as cell swelling [1]. However, based on data obtained during a hypercapnia challenge it has been suggested that vascular effects might still be the predominant source of DfMRI signals [2], although no mechanism has been proposed to explain how *increases* in CBV or CBF could result in increased diffusion-weighted signals. Interestingly, conditions were blood flow is severely *decreased*, such as acute stroke, also lead to a significant profound increase in diffusion-weighted signals (i.e. reduced ADC). To estimate the contribution from vascular sources to the DfMRI signal, responses to visual stimulation and hypercapnia challenges were monitored during the same session and analyzed on an individual subject basis.

Materials & Methods

Acquisition : Six subjects were scanned with a whole-body 3T scanner (Trio, Siemens, Erlangen, Germany) equipped with a 8-channel phased-array coil using a twice-refocused diffusion spin echo sequence [1]. Axial slices were acquired during 1/visual stimulation (flickering checkerboard, 8 Hz, 7/35sec on/off, 7 iteration/run, 4/2 runs for DfMRI/BOLD) and 2/CO_2 inhalation (5/20/75% CO2/O2/N2, 40/60sec on/off, 3 iteration/run, 4/2 runs for DfMRI/BOLD) stimuli. The other imaging parameters were: image matrix = 64x60x8, FOV = 240x225 mm, TE = 84/30 msec (DfMRI/BOLD), TR = 1 sec, scan-time/run = 310 sec, b value = 2000 s/mm², MPG direction = (1,1,1), partial Fourier = 6/8 or 8/8 (DfMRI/BOLD). In 2 subjects DfMRI data were also obtained with b=250s/mm².

Data processing: SPM5 software was used for the statistical analysis on an individual subject basis. To extract time courses, a sphere VOI with a radius of 30 mm was centered on the early visual area of each subject. All grey matter voxels were taken into account and all signal changes were measured using the same VOI. To decrease noise, moving average smoothing was used as 3 or 5 points for visual stimulation and CO_2 inhalation, respectively.

Results

Figure 1 shows the typical time courses of DfMRI and BOLD responses during the visual stimulation and the hypercapnia challenge. Table 1 shows the amplitude response for DfMRI and BOLD for each subject, as well as the amplitude response ratio between DfMRI and BOLD. Although the amplitude of the signal change is similar during visual stimulation for DfMRI and BOLD (0.89+/-0.12), the response is much larger with BOLD than DfMRI during the hypercapnia challenge (0.44+/-0.12). These results indicate that, if DfMRI signals are contaminated by vascular effects, those effect account for less than half of the total diffusion response. Also the DfMRI signal response during CO_2 inhalation was not significantly different with b=250s/mm² and 1800s/mm² in contrast that the response with the visual stimulus was larger with b=1800s/mm² than 250s/mm², as reported in the previous work [1].

Discussion

In contrast to a previous study [2] in which group analysis was done because of insufficient signal to noise ratio, sufficient number of runs made it possible to analyze data individually. The new results show that at least half of the DfMRI signal response is not explained by vascular sources. For the other half the mechanism underlying the DfMRI signal changes during hypercapnia are not clear, as the physiology of the response to hypercapnia challenges is not well understood. Although hypercapnia globally leads to an increase in CBV/CBF other confounding phenomena take place. Neuronal and cellular mechanisms at the origin of the vascular response [3] may also have impacts on water diffusion measurements. Clearly further studies are necessary to fully appreciate the origin of the DfMRI signal during activation.

References

[1] D. Le Bihan et al. (2006) PNAS 103, 8263-8268; [2]. K. Miller et al., (2007) ISMRM, 24; [3] C.M. Peppiatt CM, et al. 2006, Nature 443:700-704

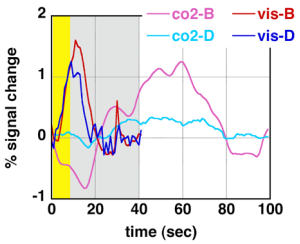

Figure 1 Typical time courses of DfMRI (bluish) and BOLD (reddish) response with visual (dark) and CO2 (light) stimuli (volunteer #1). Yellow and gray rectangles on the background represent the stimulus durations.

Table 1 The amplitude response and the ratio for each subject. The amplitude is the difference between the maximum and minimum response.

vol	vis-D	vis-B	v-D/B	co2-D	co2-B	c-D/B
1	1.42%	1.65%	0.86	0.51%	2.08%	0.24
2	1.46%	1.50%	0.98	1.18%	2.55%	0.46
3	0.95%	1.00%	0.95	0.89%	1.84%	0.48
4	0.90%	1.20%	0.81	1.19%	2.01%	0.59
5	1.38%	1.33%	1.04	1.08%	3.10%	0.35
6	0.95%	1.32%	0.72	0.97%	1.98%	0.49
av	1.19%	1.33%	0.89	0.97%	2.26%	0.44
sd	0.25%	0.23%	0.12	0.25%	0.48%	0.12