Inter-areal and inter-individual variations in diffusion-weighted fMRI signal

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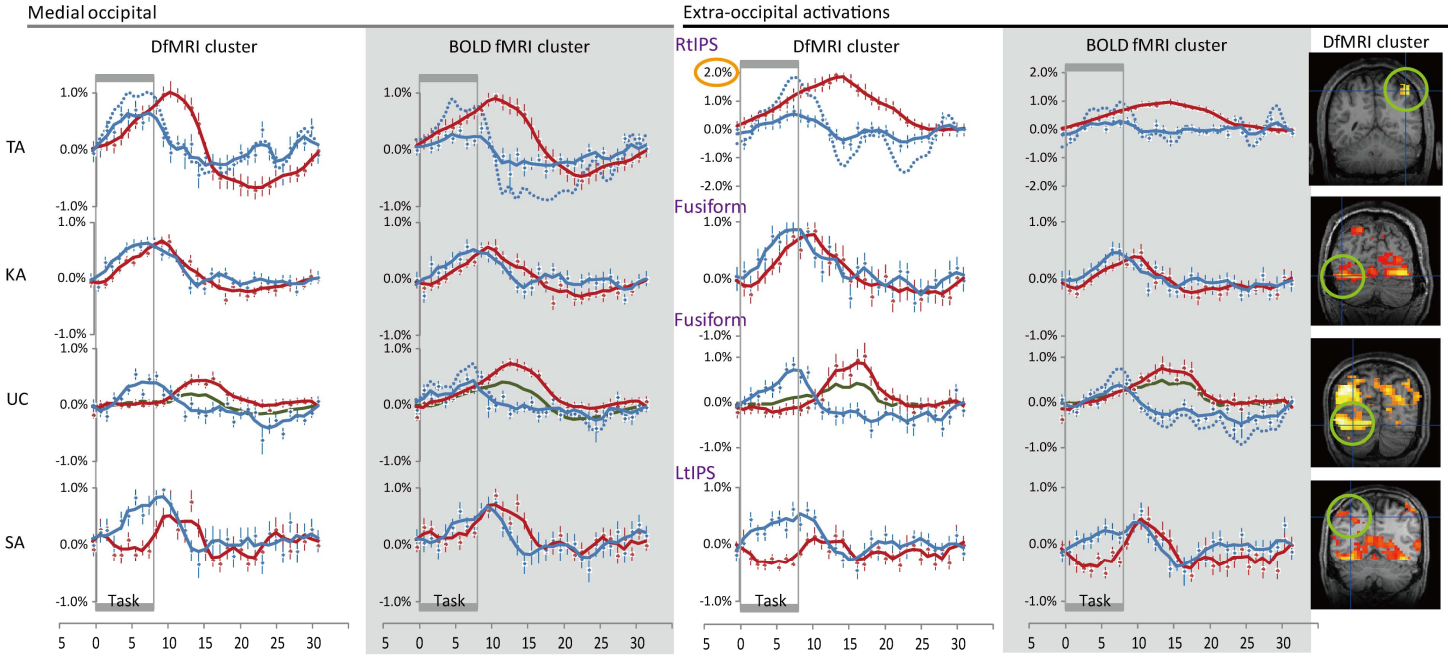
INTRODUCTION: Neuronal activation can be detected with heavily sensitized diffusion-fMRI (DfMRI)[1]. The striking temporal precedence of the diffusion response to BOLD in the visual cortex suggests a non-vascular source, superimposed to a residual tissue BOLD component [2, 3]. The purpose of the present study was to verify that such DfMRI signal features can also be found outside the primary visual areas.

MATERIALS & METHODS: MR images were acquired on 7 healthy subjects using a 3T scanner with an 8-channel head coil. The visual stimulation consisted in the random presentation of single Kanji characters from a small database (20-character subset for each run from 200 Kanjis) projected at 1 sec intervals onto a screen with a DLP projector. In order to recruit activation in the parietal and fusiform areas, we used a two-back working memory task: Subjects had to press a button when the present Kanji was identical to the second previous one. Each task block lasted for 8s (8 characters) separated by a 24s resting period.

Data acquisition: We used a twice refocused, SE EPI sequence sensitized to diffusion by an interleaved pair of bipolar gradient pulses (b=1800s/mm², along X, Y and Z axes). All functional images were acquired in semi-coronal section covering the occipital and parietal lobes. The acquisition parameters were: 64 × 60 pixels, 192mm FOV, 4-mm slice thickness with 50% gap, TR = 1000 ms, TE = 85 ms, interleaved 8 slices. Between the DfMRI runs, GRE-EPI or b=0 (i.e. non diffusion-weighted) SE EPI images were also acquired for comparison (BOLD fMRI).

Data processing: Slice-timing and motion correction was done using SPM5. After spatial smoothing at 8x8x6mm FWHM kernel, standard SPM analysis was performed using the DhRF model [2] instead of the canonical HRF for DfMRI to model the template time course. The model included both time and dispersion derivatives of the response function to compensate for inter-areal/subject variation in signal responses. All the SPM maps were thresholded at .001 uncorrected for multiple comparison. BOLD fMRI data were processed using the canonical HRF.

From the DfMRI and BOLD clusters identified in the SPM maps, we extracted both the diffusion-weighted and the BOLD raw signal time courses averaged over trials (54-72 trials for DfMRI, 27-36 trials for BOLD fMRI). Only significant pixels within the 12mm-radius sphere centered on the local statistical peak were included. Error bars indicate SEM across trials. DfMRI response is shown in blue and BOLD in red. Subject UC had both GRE and SE-BOLD runs (green) and subject SA had only SE-BOLD (red). A 3-point moving average was used to create the lines. Scaled plots are also shown for shape comparison in selected plots (broken line). Four representative subjects are shown.



RESULTS AND DISCUSSION: The DfMRI (b=1800) responses consistently showed a time precedence over BOLD confirming earlier reports [1,2,3], both in DfMRI and BOLD clusters. A major finding is the consistent response patterns between different clusters of a given subject. Diffusion responses occurred not only earlier, but were more uniform across subjects (single positive response peaking at the end of the stimulus period followed by an immediate signal decrease; mean peak latency after task offset = -0.6s for DfMRI and 2.8s for BOLD), while there was significant variation in the BOLD response across subjects. On the other hand, in some clusters such as right IPS of subject TA, a large contamination by the tissue BOLD response overwhelmed a poor DfMRI activation. More interestingly, large initial BOLD undershoots were observed in DfMRI clusters of subjects UC and SA, while the DfMRI response was positive, supporting the assumption that the DfMRI and BOLD responses have different origins. Such uncoupling between the DfMRI and BOLD responses could, for instance, originate from neuronal subpopulations where activation (positive DfMRI response) is accompanied by acute increase in oxygen consumption (negative BOLD response)[4] without a large increase in blood flow. The mechanisms underlying those differences between the DfMRI and BOLD responses obviously need further investigation.

1. Le Bihan, D., et al. (2006) Proc Natl Acad Sci U S A, 103; 2. Aso, T., et al. (2009) Neuroimage, 47; 3. Kohno, S., et al. (2009) J Cereb Blood Flow Metab, 29; 4. Malonek, D., et al. (1996) Science, 272