Mapping Cat Visual Orientation Columns Using CBV-weighted fMRI

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INTRODUCTION

To date, most fMRI studies have been performed using conventional BOLD methodology with a spatial resolution of several millimeters. For further in-depth investigation of cortical information processing, it is crucial to map sub-millimeter functional architecture, such as cortical orientation-selective columns. However, the spatial specificity of hemodynamic responses is controversial (1-3). In this abstract, the spatial specificity and reproducibility of CBV-weighted fMRI signals at columnar resolution was examined in cat visual orientation columns. CBV-weighted fMRI was obtained with intravascular injection of MION (monocrystalline iron oxide nanoparticles) to induce a susceptibility effect and therefore act as a plasma blood volume tracer.

METHODS

Five fMRI studies with two orthogonal stimuli in four ~1.3% isoflurane anesthetized cats were performed on a 9.4T/31cm system (Varian) with a 1.6-cm diameter surface coil. Blood pressure, arterial blood gas, end-tidal CO_2 and rectal temperature were kept within normal ranges (5). A single 1-mm thick imaging slice was selected tangential to the surface the cortex in visual area 18. To obtain CBV contrast (4), 10 mg Fe/kg MION was injected i.v. CBV-weighted images were acquired with TE = 10 ms, TR = 2 s, matrix size = 128x128, and FOV = 2x2 cm^2, using the 4-segmented GE EPI technique. Binocular visual stimulation consisted of moving black/white gratings at a selected orientation. Each fMRI run involved 10 control – 10 stimulation –10 control images. To minimize systematic variations, fMRI runs with two orthogonal orientations (e.g., 0º and 90º) were interleaved for 40-70 repeated runs. At each orientation, "single-condition" maps were obtained: simple subtraction maps were initially determined as the difference between images acquired during stimulation vs. control condition without any threshold applied to data, then single-condition percentage change maps were generated with the statistical threshold set to a t-value of 2. To determine active and inactive domains, a "differential" iso-orientation map (6) was obtained by subtracting single-condition percentage maps induced by one orientation stimulation (e.g., 90°) from those induced by the orthogonal orientation stimulation (e.g., 0°). An average distance between iso-orientation patches within rectangular 3 × 4 mm ROIs along the anterior-posterior direction was determined by auto-correlation analysis of the differential iso-orientation map (3). To estimate the functional contrast of CBV changes between "active" and "inactive" columns, averaged time courses were generated from pixels within the rectangular ROIs assigned to a selected orientation domain (e.g., 0°) during the preferred orientation stimulation (e.g., 0°) and the same pixels were used to obtain the time course during its orthogonal orientation stimulation (e.g., 90°). Then the ratio between the signal changes of a selected orientation domain stimulated by the preferred orientation to that by the orthogonal orientation was calculated. To determine the reproducibility, all fMRI data with the same stimulation paradigm was divided into two sub-groups, even and odd runs. Then, differential iso-orientation maps were determined from the two sub-groups. Cross-correlation methods were used to determine reproducibility of the differential iso-orientation domains within the rectangular ROIs.

RESULTS

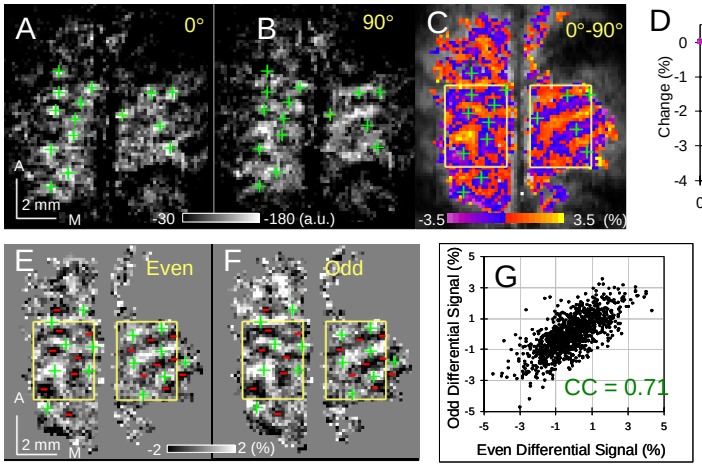

Fig. 1. Results of columnar-resolution CBV-weighted fMRI studies. (A, B) Single-condition maps of 0º and 90º stimulation in one animal. Green '+' signs indicate high response areas induced by 0º stimulation and were overlaid on A, B and C. (C) Differential map of the same animal. Blue/purple indicates 0º domains, while red/yellow indicates 90º domains. Rectangular ROIs were defined for further analyses. (D) Averaged time courses of active domains within the ROIs during preferred and orthogonal stimulation (n = 10 orientations in 5 studies). (E, F) test and re-test maps of differential maps. '+' and '-' signs determined in the even runs were overlaid on even (E) and odd (F) fMRI runs. (G) Cross-correlation analysis within the ROIs between even and odd fMRI runs.

Raw stimulation-induced signal change maps were obtained without any statistical threshold (Fig. 1A and B for 0° and 90° gratings, respectively). Patchy clusters were observed in both single-condition 0° and 90° maps. More importantly, large signal changes induced by orthogonal stimuli are located within complementary territories. According to intrinsic optical imaging studies, differential signal of hemodynamic responses induced by two orthogonal stimuli seems to be correlated with spike firing rates of neurons in the active domain (6). Therefore, "patches" within the differential map (Fig. 1C) were assigned to iso-orientation domains based on whether subtraction yielded positive or negative signals; regions sensitive to 0° orientation ("0° iso-orientation domain") are shown as blue/violet, while pixels with preferential activity for the orthogonal stimulus ("90° iso-orientation domain") are red/yellow. Clearly, patchy clusters preferential to the two orthogonal stimuli are segregated and inter-digitized. The average anterior-posterior distance between iso-orientation domains within ROIs in differential maps (Fig. 1C) is 1.37 ± 0.28 mm in all studies (n = 10 hemispheres), which is consistent with previous measurements (2-3). Fig. 1D shows the averaged time course data from pixels within the ROI of all studies. The averaged ratio between CBV changes induced by preferred orientation vs. orthogonal orientation gratings is 1.69 ± 0.24 (n = 10). Fig. 1E and F show the reproducibility of differential iso-orientation maps from one animal. In both differential iso-orientation maps corresponding to even (Fig. 1E) and odd (Fig. 1F) subsets of fMRI runs, dark patches indicated by red '-' signs are regions which selectively respond to 0° gratings, while patches indicated by green '+' signs are regions selectively responding to 90° gratings. Signal changes of the odd differential map (Fig. 1F) within rectangular ROIs were plotted against those of corresponding even differential map (Fig.1E) in Fig. 1G, where each data point represents one pixel. An averaged cross correlation coefficient between the differential maps within the ROIs for all studies is 0.58 ± 0.14 (n = 5, $p<0.001$). This demonstrates that differential iso-orientation maps obtained by CBV-weighted fMRI are highly reproducible and that CBV regulates at a sub-millimeter columnar level.

Reference (1) Menon RS, et al. MRM 1999;41:230-235. (2) Kim D-S, et al. Nature Neurosci 2000;3:164-169. (3) Duong TQ, et al. PNAS 2001;98:10904-10909. (4) Kennan RP, et al. MRM 1998;40:840-846. (5) Duong TQ, et al. MRM 2000;44:231-242. (6) Shmuel A, et al. J Neurosci 1996;16:6945-6964.

Supported by NIH (EB003375, NS44589, EB003324, EB002013, RR17239) and McKnight Foundation.