Visualization of Stripe of Gennari-like Structure in the Primary Visual Cortex by High-resolution MRI: Correlation of Structure vs. Function

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Introduction

The visual cortex consists of six cellular layers between the pial surface and the underlying white matter, all of which are aligned parallel to the pial surface. Each layer is involved in different cortical information processing. The middle of the cortex (notably layer IV in the primary visual cortex, which contains the myelin-rich stripe of Gennari) is known to have the highest capillary density and the highest metabolic responses. In humans and primates, layer IV can be identified by its prominent anatomical and functional MRI contrast (1-3). The cat visual system is an excellent cortical layer model for examination of the spatial distribution of fMRI signals (4-6). However brain topography varies among individual cats. Therefore it is extremely advantageous to know the *in-vivo* correlation between the structural and functional contrast of cortical layers by MRI, which has not yet been reported in this model. In this study, we compared *in-vivo* high-resolution T_1-weighted images with total CBV fMRI responses to examine whether there is a correlation between structural and functional contrast on an individual basis. To determine whether blood contributed to the *in-vivo* contrast, we also performed T_1-weighted imaging in the paraformaldehyde-fixed brain and in a contrast agent injected brain.

Methods

Two female adolescent cats were studied on a 9.4-T MRI (Varian) system under ~1.5% isoflurane anesthesia with air supplemented with O_2 to attain a total O_2 level of ~30% throughout the experiments. Animals were maintained within a normal physiological range. Coronal images were acquired with FOV = 2.0×2.0 cm^2. T_1-weighted structural images were acquired with a four-shot turbo-FLASH sequence with TE = 5 ms, TR = 10 ms, intersegment duration = 4 s, pixel resolution = 78 μm × 78 μm × 2 mm and flip angle = 10°. For CBV fMRI studies, GE-EPI images (TE = 10 ms) were obtained after the injection of ~10 mg/kg monocrystalline iron oxide nanoparticles (MION); image parameters were TE = 10 ms, TR = 1 s, pixel resolution = 312 μm × 312 μm × 2 mm and flip angle ≈ 20°. Stimulation-induced percentage CBV changes were calculated as previously described (7); BOLD signal contributions were removed by acquiring baseline images with TE = 20 ms before MION, and R_2^* change induced by MION was measured with TE = 20 ms. Binocular full-field visual stimuli were presented with square-wave high-contrast moving gratings (2 cycles/sec) with 0.15 cycles/degree of spatial frequency during 40-s stimulation. After MR experiments, the cat brain was fixed with 4% paraformaldehyde in 0.1 M PBS. Then, this fixed brain was placed in a container with agarose gel for MR imaging. Since the fixation changes T_1 values of the brain, the TI value was adjusted to replicate the cortical contrast of *in-vivo* images.

Results and Discussion

T_1-weighted images appear in Fig. A with TI = 1.4 s and in Fig. B with TI = 1.25 s. In Fig. A, hyperintense layers are clearly observed in middle cortical regions (outlined by black dashed lines). These layers are likely due to the myelin-rich stripe of Gennari, which is a prominent feature in layer IV. Similar observations were observed in primate and human visual cortex (1,6). With a different TI value, these layers become hypointense, as can be seen in Fig. B, where the outline of Fig. A is superimposed as a white dashed line for better visualization. This inversion of contrast confirms that the signal source is related to longitudinal relaxation properties. Fig. C shows a T_1-weighted image of the same brain after MION injection. The penetrating vessels are clearly observed as dark lines due to increased susceptibility effects from MION injection (see arrows), but the hyperintense layers were still remained, showing blood signal was not contributed for hyperintense layers. Fig. D shows a T_1-weighted image of the same brain after paraformaldehyde fixation. Although the brain was slightly distorted by the fixation process, a hyperintense layer is still clearly observed in the middle of the cortex (see arrows). Since all blood is replaced by the perfusion solution, the hyperintense layer observed in the fixed brain must arise from the structural features. Fig. E shows that highest functional CBV responses (yellow pixels) are well correlated with the same overlaid contour lines (black dashed lines) from the structurally-defined contrast. Since this contrast appears to arise from the stripe of Gennari, the region of highest CBV fMRI response likely correlates with the sites of neural activation. Histology comparisons are required for definitive assignment of regions of T_1-weighted contrast to anatomical features, such as myelin-stain.

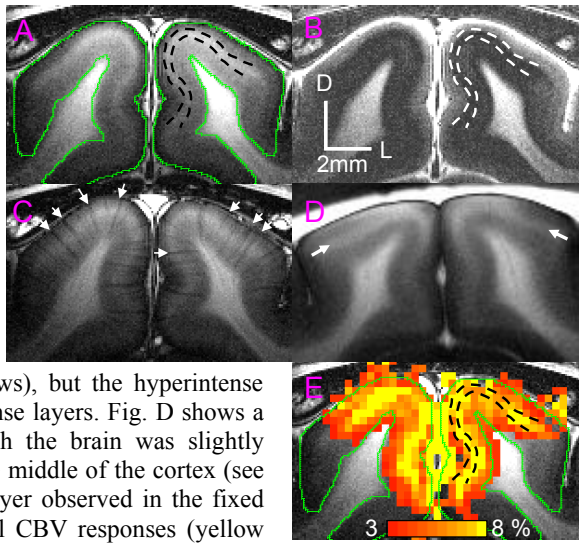

Fig. In-vivo T_1-weighted images with (A) TI = 1.4 s and (B) TI = 1.2 s. (C) In-vivo T_1-weighted images with TI = 1.4 s after MON injection. (D) T_1-weighted image of the paraformaldehyde-fixed brain with TI = 0.7 s. The presence of agarose above the brain appears uniformly white. (E) Visual stimulus-induced CBV fMRI percentage-change map generated with the aid of a susceptibility contrast agent. Dashed lines outline the contours of T_1-weighted hyperintense layer within the cortex (A), while green contours outline gray matter.

References
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Acknowledgments: NIH grants (EB003324, EB003375, NS44589, RR17239)