Determination of Intracortical Venous Vessel Density Using Venography at 9.4T

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Introduction

BOLD fMRI has been routinely used to map human and animal brain function. The source of the BOLD signal is a change of T_2* in and around capillaries and draining veins. Thus, the visualization of detailed venous architecture and the quantification of intracortical veins in the brain are crucial to understand the physiological basis of BOLD fMRI and to determine the spatial resolution of BOLD signals. In humans, the distance between intracortical veins of intermediate size is 0.7-1.0 mm [5]. If the BOLD signal is sensitive to these intracortical veins, their density will dictate the limit of spatial resolution of BOLD fMRI [1]. To determine the spatial resolution limit of BOLD fMRI in animals, we classified the intracortical veins according to their penetration depth and present the quantitative analysis of venous vessel density in and around somatosensory cortex in rats and the visual cortex in cats utilizing 3D high resolution BOLD venography acquired at 9.4T.

Materials and Methods

Subjects were (i) 3 male Sprague-Dawley rats weighing 300-400 g and (ii) 3 female American shorthair cats weighing 600-1200 g. During MRI scan, they were mechanically ventilated under 1.5% isoflurane anesthesia in a N_2O/O_2 mixture of 70:30. Body temperature was maintained at 37.0~37.5 °C for rats and at 38.0~38.5 °C for cats by a warm water pad and end-tidal CO_2 was monitored throughout the experiment.

A Varian 9.4T/31 cm Varian MRI system was used with a 12-cm I.D. Magnex gradient coil. The RF coil was a custom-made quadrature type surface coil composed of two coils (1.6 cm i.d. for rat and 2.2 cm for cat). Voxel-localized shimming (PRESS) was performed. Venogram were acquired by a flow compensation, low-bandwidth (32~50Hz), 3-D gradient recalled echo pulse sequence. To reduce scan time along both 1st and 2nd phase-encoding directions, 75% of partial Fourier acquisition was used. Imaging parameters were as follows: TR = 50 ms, TE = 20 – 25 ms, FOV = 3.0 x 1.5 x 1.5 cm^3 for rats and 4.0 x 2.0 x 2.0 cm^3 for cats, matrix = 384 x 192 x 192, flip angle = ~15°, and scan time = 34 min 38 sec. Then, the 3-D dataset was zero-padded to a matrix size of 512 x 256 x 256. Nominal resolution is 58 µm in rat studies and 78 µm in cat studies. To visualize a 2-D format from the 3-D dataset, a 16-plane (~ 1 mm thick) slab was selected. Then, minimum intensity projection (mIP) and non-uniformity correction algorithm [4] were applied for better visualization of the veins as suggested previously [3], and for correction of non-uniform B_1 field of surface coil, respectively.

To measure the venous vessel density, the number of veins were counted between the surface of cortex and white matter / cortex interface continuously. To avoid ambiguity in identification, continuous patterns were regarded as veins if they occurred within more than 4 continuous planes (≈234µm) for rats or 3 planes (≈234µm) for cats.

Results and Discussion

The intracortical vessels were classified into 5 groups according to their penetration depth in human brain by Duvernoy [5]. The class 1 vein penetrates up to external granular layer (layer II), class 2 to pyramidal layer (layer III), class 3 to ganglionic layer (layer V), class 4 to multiform layer (layer VI), and class 5 vascularizes white matter. Examples of vessel classification are shown at Fig. 1(c) and (d). In both rat and cat images, the white matter area is depicted with green contours. Clearly, intracortical veins can be visualized as dark lines along the cortex. Classes 1-3 can not be easily separated, but these types of vessels were seen most commonly. Usually, class 5 veins were found more frequently in cats than in rats, as shown in Fig. 1 (c) and (d).

Cortical regions were selected, mostly perpendicular to the intracortical veins and their side views are shown in Fig. 1(a) and (b) for rat and cat, respectively. Their in-plane views are shown in Fig. 1(e) and (f), with dark spots indicating veins. Corresponding results of density counting as a function of cortical depth are shown in Fig. 1(g) and (h); Venous vessel density was measured within square 2.8 x 2.8 mm^2 ROIs as depicted in Fig. 1(e) and (f). The vessel density was the highest at the surface of the cortex, and decreased with cortical depth. The intracortical venous density of the two species was similar, and ranged ~6/mm^2 to 1/ mm^2 depending on cortical depth (Fig. 1(g) and (h)). Average distance between neighboring veins is 0.4 mm - 1.0 mm. Because our venographic image can not detect all sizes of intracortical veins, especially class 1, the vessel density at the superficial cortical area may be under-estimated. However, since small vessel contributions to the BOLD fMRI signal would be negligible, our quantitative results still present the reasonable information about the limit of spatial resolution of BOLD fMRI. At the middle of the cortex, an average inter-vein distance is ~0.5 mm in both species. Thus, functional microarchitectures with > 1 mm size can be reasonably mapped by the conventional BOLD technique.

Intracortical veins can be counted utilizing 3D high resolution BOLD venography at high fields. Based on the intracortical venous vessel density, the spatial limit of BOLD fMRI in a specific region can be investigated.

References

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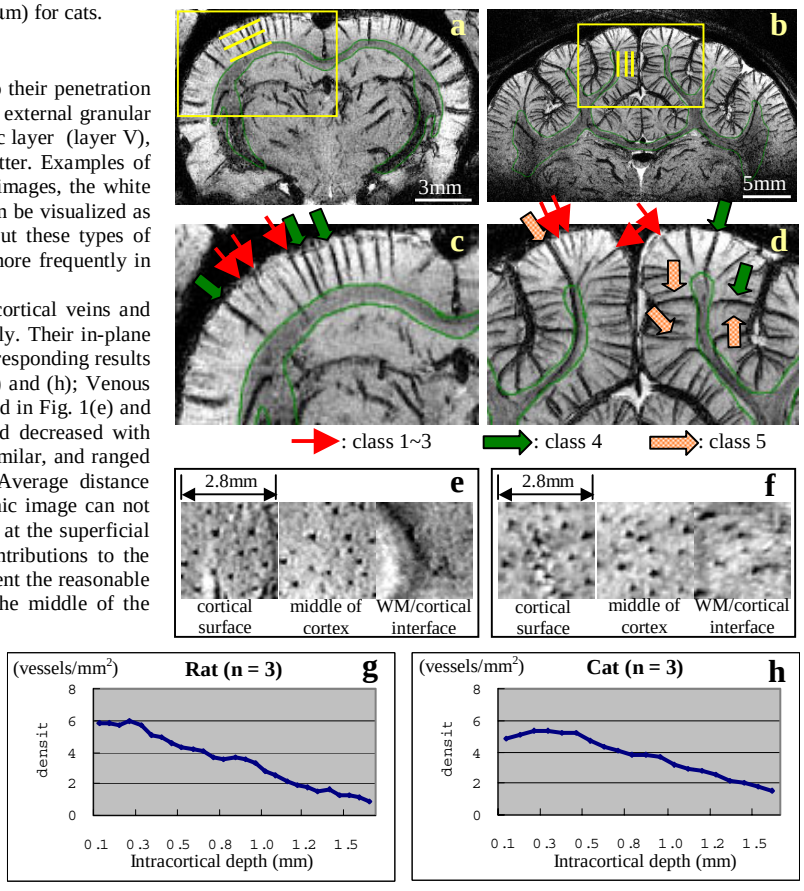

Figure 1. Venous vessel classification and density in rat and cat brain. The mIPped images are shown for rat (a,c) and cat (b,d). Top of the images (a-d) is dorsal. The enlarged images of the yellow box and in-plane images of the 3 corresponding yellow lines for (a) and (b) are shown in (c), (d), (e), and (f), respectively. Depth-dependent intracortical venous densities are shown for rat (g) and cat (h). Green contours: white matter area, red arrows in (c) and (d): class 1-3 veins, green arrow: class 4 veins (penetrating into layer 6), and orange arrows: class 5 veins (vascularizing white matter).