Cerebral Blood Flow MRI and CBF fMRI of Rat Brain up to 50x38x1000µm

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TARGET AUDIENCE Researchers in high resolution imaging, perfusion imaging, and functional imaging.

PUPROSE We previously reported high spatial resolution basal CBF maps of the rat brain at 75x56x1000µm.[1] In this study, we further pushed the spatial resolution to 50x38x1000µm for basal CBF imaging. Moreover, we also investigated lamina-specific CBF fMRI responses in a rat forepaw stimulation model. Comparisons were made with lamina-specific BOLD fMRI responses.

METHODS For basal CBF measure, four male adult Sprague-Dawley (SD) rats (250~300g) were anesthetized with ~1.2% isoflurane in air. For forepaw stimulation, two male SD rats were anesthetized with α-chloralose (60 mg/kg first dose, followed by 30 mg/kg per hour, intravenous infusion). Body temperature, respiration rate, heart rate and blood oxygen saturation level were continuously monitored and maintained within normal ranges. MRI experiments were performed on a on a Bruker 11.7-Tesla/16-cm scanner. Surface coils (0.9-cm ID) with active decoupling were used for brain imaging and a neck coil for perfusion labeling.

Quantitative CBF was measured using the continuous arterial spin-labeling technique[3] with four-shot, gradient-echo EPI. MRI parameters were: FOV=12.8mm x 9.6 mm, matrix=192x144 and reconstructed to 256x256, TR=3s, TE=9ms, labeling duration= 2.65s and post-labeling duration=250ms. fMRI of the cortex at 100x75x1000 µm was acquired using single shot gradient-echo EPI cASL, FOV = 12.8 x 9.6 mm, matrix size = 96x72, reconstructed to 128x128.

CBF of the cortex were flattened[4] and layer I to VI were assigned according to thickness reported in literature[5]. CBF profiles across the cortical depth were obtained by averaging along the length of the cortex. For fMRI analysis, cross correlation was performed to obtain percent change maps associated with the forepaw primary somatosensory cortices. CBF percent changes profiles across the cortical depth were also derived.

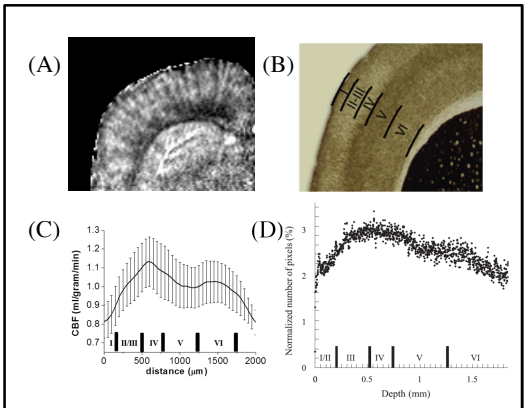

Figure 1. (A) CBF map (50µm x 38µm x 1mm), (B) AChE staining, (C) Group-averaged (n=4) successive depth profile of cortical CBF (from surface to deep brain), (D) Successive depth profile of microvascular distribution [7].

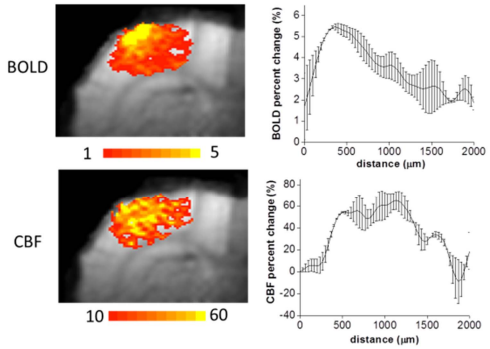

Figure 2. BOLD and CBF responses of forepaw stimulation and their group-averaged depth profiles

RESULTS Figure 1A showed the CBF maps of a representative rat at 50x38x1000µm spatial resolution. Distinct CBF contrast can be seen among the cortical gray matter, caudate putamen gray matter and corpus callosum white matter. Radially oriented columnar structures (bright and dark stripes) are consistent with the descending arterioles. The laminar structures are consistent with the vascular distribution in the cerebral cortex. For comparison, a corresponding brain slice stained with acetylcholinesterase from a rat brain atlas[6] shows the laminar structures with overlaid cortical layer assignments (**Fig. 1B**). Group-averaged (N=4) CBF profile across the cortical thickness exhibited a blood flow peak in layer IV and VI (**Fig. 1C**). Cortical layer I to VI assignments were made based on cortical thicknesses.[5] For comparison, **Figure 1D** shows the microvasular density distribution obtained using confocal laser scanning microscopy.[7]

The BOLD and CBF responses of forepaw stimulation and their group-averaged fMRI profiles as a function of cortical depth are depicted in **Figure 2.** The CBF fMRI responses peaked in layer IV-V, whereas the BOLD fMRI responses peaked in the superficial layers.

DISCUSSIONS High resolution CBF map showed remarkable columnar and layer specific characteristics in cortex. Previous basal CBF and CBV images showed a peak in the middle of the cortex, typically only in layer IV. The difference in spatial resolution could have contributed to the discrepancy.

Previous fMRI studies of visual stimulation in monkeys[8] and cats[9] showed that the CBF and CBV responses peaked in the middle of the cortical layer thought to be layer IV, whereas BOLD responses peaked in the superficial layers. We found that the CBF responses at considerably high spatial resolution was broad, covering layer IV and V, with a hint of a double peaks. Our finding is consistent with Goense et al. who reported a double-peak CBV fMRI response in the excitatory regions in monkeys[8]. The discrepancy of the location of peaks between basal CBF and functional CBF response may result from the relative lower spatial resolution of fMRI and/or distortion of single shot EPI used in fMRI.

CONCLUSION This study presents very high spatial resolution CBF imaging of the rat brain, revealing detailed columnar and laminar perfusion information. Perfusion signals peaked at layer IV and VI in the cortex, consistent with vascular density profiles previously reported. In contrast to BOLD fMRI response which peaked at the superficial layer, CBF fMRI showed a broad peak in layer IV and V. This study sets the stage for investigating CBF dysfunction in neurological disorders at very high spatial resolution.

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