Perfusion-based high-resolution fMRI in the primate brain using a novel vertical large-bore 7 Tesla setup

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INTRODUCTION

Functional MR imaging in monkeys promises a bridge between brain research in humans and the large body of systems neuroscience work in animals. Prerequisite for successful interspecies-comparisons, however, is a profound understanding of the neural events underlying the hemodynamic responses. Combined physiology and neuroimaging experiments made the first step in this direction by examining directly the relationship of cell activity to the BOLD signal [1]. The tight coupling between regional neural activity and blood flow, however, suggests that perfusion-based MRI may improve even further the electrophysiological investigations of the neurovascular coupling, as perfusion imaging measures cerebral blood flow (CBF) directly at the capillary level. Moreover, CBF changes and interleaved-acquired BOLD data can be combined to compute changes in oxygen consumption rate.

Obtaining functional CBF maps with high spatial resolution is challenging, because the CBF signal is intrinsically low and the signal-to-noise ratio is critical. Here we report the first high-resolution CBF maps that were obtained with voxel sizes as small as 0.5 x 0.5 x 3 mm^3 in the *Macaca mulatta*. High sensitivity was achieved by using a high magnetic field scanner and custom-made RF combination-coil designs. CBF maps and functional CBF data were acquired and compared with BOLD data in the macaque primary visual cortex.

METHODS

A novel vertical Bruker MR system (7 Tesla / 60 cm) was set up, in which MR imaging, MR spectroscopy, and simultaneous electrophysiology can be performed in the anaesthetized or the awake, behaving monkey (Fig. 1) [2]. The system is quality shielded for low and high-frequencies to ensure noise-free recording of both local field and action potentials inside or outside the magnet bore. The 38-cm gradient insert (33-cm inner diameter with noise insulation) achieves 82 mT/m in 130 µs. An actively-decoupled RF saddle coil was used for transmission and a 30-mm Bruker surface coil for reception. A full-field visual stimulus (8 Hz flickering LED array) was used in a block design with 4 repetitions of on- and off- (48 s, 8/8 images) stimulation-periods.

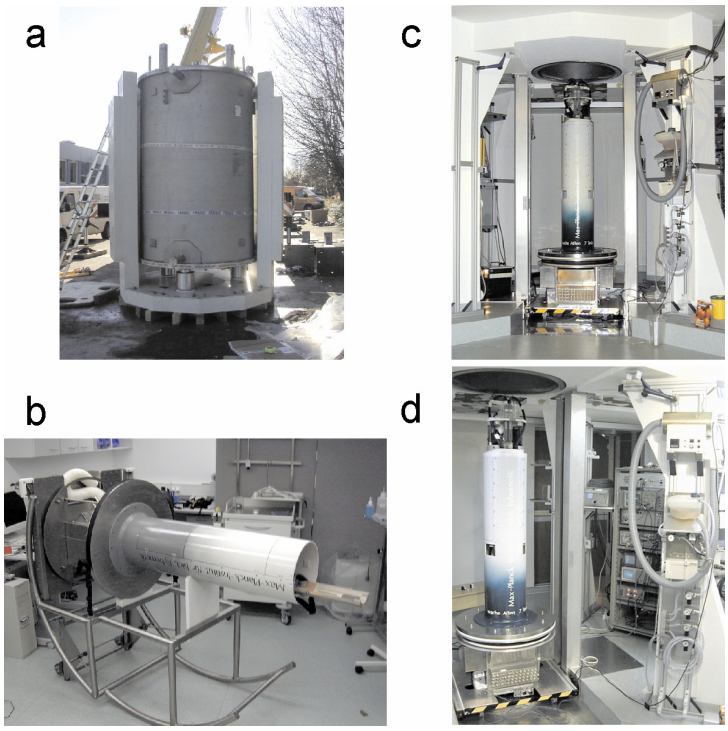

Figure 1: Vertical 7 Tesla / 60 cm MR system.
(a) magnet with iron shielding; (b) chair for anaesthetized monkey preparation; (c,d) chair and electrophysiology setup below the magnet bore.

Single-shot GE-EPI was acquired at two resolutions of 0.75 x 0.75 x 3 mm^3 (128 x 48, FOV 9.6 x 3.6 cm^2) and 0.5 x 0.5 x 3 mm^3 (128 x 48, FOV 6.4 x 2.4 cm^2) using outer-volume suppression [3].

The FAIR module used adiabatic slice-selective / non-slice-selective inversion (TR = 3 s x 2, TIR = 700 – 1500 s, inversion slice thickness 8 mm). Functional CBF and BOLD scans (FAIR off) were acquired interleaved with TE = 12 and 20 ms, respectively. For semi-quantitative analysis, a M_0 image was measured at TR = 10 s and CBF was calculated according $CBF = (S_{SS} - S_{NS}) / M_0 \cdot \lambda / (TI \cdot (2 \cdot \exp(-TI/T_1) - \exp(-TR/T_1)))$, $\lambda = 0.9$ mL/g. T_1 was assumed to be 1.9 s as determined in a separate study for gray matter in monkey primary visual cortex V1.

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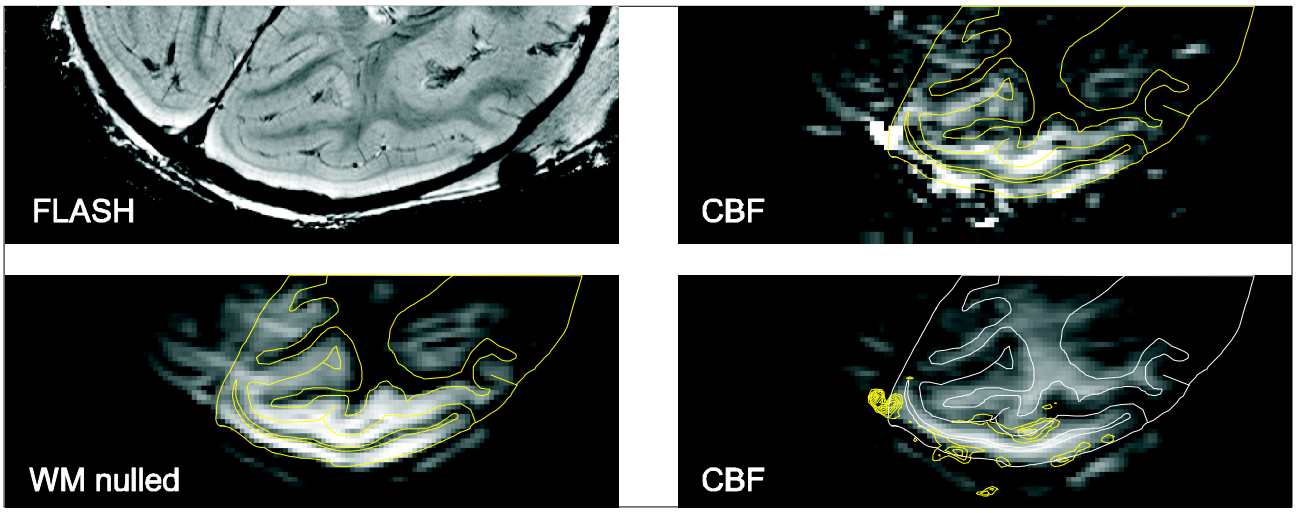

Figure 2: Axial CBF map acquired with FAIR GE-EPI at 0.5 x 0.5 x 3 mm^3 resolution - CBF contours.

RESULTS AND DISCUSSION

Anatomical FLASH, inversion-prepared EPI, and CBF maps at 500 μm in-plane resolution are shown in Fig. 2. Excellent single-shot EPI image quality was achieved by the use of OVS-aided FOV reduction in PE (48 lines). T2* blurring was still negligible at a readout duration of 31 ms, which is similar to T2* of 25 ± 10 ms at 7 Tesla. A high-resolution CBF map with 500 μm in-plane resolution is shown with anatomical boundaries overlaid. The CBF map (average of 6 series) has high intensities in the gray matter as well as in the blood vessels – white matter is clearly delineated.

Upon visual stimulation, CBF increased in average by 33% from 64.8 (0.6 *se*) mL/100g/min at rest to 86.1 (1.2) mL/100g/min during activation (Fig. 3). A *t*-test ($p < 0.05$) revealed activated voxels along the whole visual cortex V1 (*t*-values from 2 to 8, red…yellow). Robust and consistent functional CBF changes were observed, which were excellently localized to gray matter only. In contrast, the BOLD signal was spatially more spread (not shown). This observation is consistent with the fact that functional CBF maps are very well localized to gray matter (capillaries), while BOLD maps are less localized due to contributions of proximal draining veins.

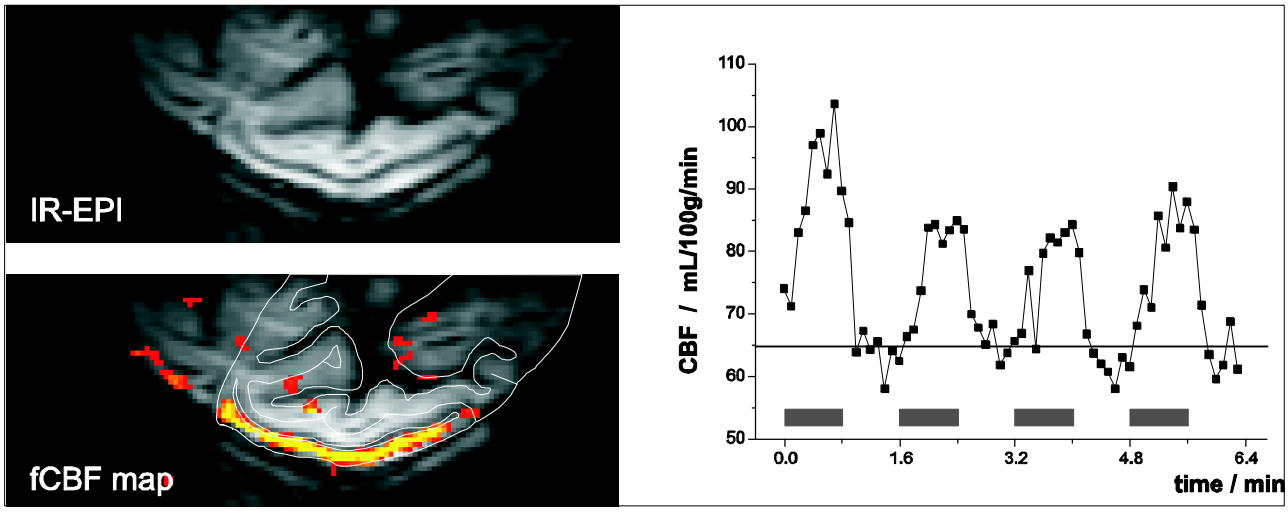

Figure 3: Functional CBF map and time course, in-plane resolution 500 μm.

In conclusion, the increased sensitivity in high magnetic fields together with the optimization of the resonators yield highly spatially resolved perfusion images in the monkey brain. The functional CBF signal is entirely localized within cortex, providing unequivocal evidence for its high spatial specificity. This specificity is of paramount importance for studies seeking to understand the physiological basis of functional neuroimaging.

[1] Logothetis, NK et al. *Phil. Trans. R. Soc. Lond. B* 357:1003 (2002); *Nature Neurosci* 2(6):555-62 (1999); *Nature* 412:150-57 (2001); *Neuron* 35:227-42 (2002). [2] Pfeuffer, J et al. *Proc. ISMRM Toronto* 1877, 2089 (2003). [3] Pfeuffer, J et al. *Magn. Reson. Med.* 47:903-11 (2002).