A Comparison of Whole Brain Functional MR Images Obtained with BOLD and CBV Contrast during Somatosensory Stimulation in the Rat

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Introduction

Whole-brain functional MR images allow the visualization of active neural networks. While whole-brain fMRI is routine in humans, few studies have been done in small animals, though the well-characterized rodent nervous system is extremely important in neuroscience research (1-3). In this study, BOLD and CBV functional images were obtained from the same rats to compare the sensitivity of the two methods to activation in secondary regions of the brain during somatosensory stimulation.

Methods

Seventeen rats were studied. Each rat was anesthetized with halothane, orally intubated and given venous and arterial lines. Two needle electrodes were inserted into each forepaw. The animal was placed on a warm water pad to maintain body temperature, and a bite bar and ear pieces were used to prevent head movement. Expired CO_2, rectal temperature, and blood pressure were continuously monitored, while blood gases were measured and maintained at normal levels. Anesthesia was switched to an α-chloralose infusion for imaging (4). Imaging was performed on an 11.7 T/31 cm magnet (Magnex) interfaced to a Bruker AVANCE console. A home-built rectangular surface coil (2x3 cm) was used as a receive coil. A spin-echo EPI sequence with the following parameters was used for all functional studies: FOV 1.92 cm, matrix size 64 x 64, nominal in-plane resolution 300 µm, effective TE 30 ms (BOLD) or 20 ms (CBV), BW 200-250 kHz, TR 1.5 s. Ten to eleven 2 mm thick interleaved slices that covered the brain from olfactory bulb to cerebellum were imaged during each TR. The stimulation paradigm was 60 images during rest, 30 during stimulation (3 Hz, 2 mA), and 60 during rest. A correlation map was calculated using STIMULATE (Univ. of Minn.) After BOLD functional studies were performed, ten rats were injected with 20 mg/kg iron oxide intravenously, and CBV activation maps were obtained in the same slices as the BOLD maps. To investigate the relationship between the contrast dose and the incidence of activation in secondary areas, four rats were given 30 mg/kg iron oxide and three rats were given 10 mg/kg. A digitized rat atlas was warped to each image so that activation maps could be compared in a common space.

Results

Activation was observed in SI (BOLD, 10/10 rats; CBV, 10/10), SII (BOLD, 7/10; CBV, 5/10), thalamus (BOLD, 2/10; CBV, 2/10), and cerebellum (BOLD, 8/10; CBV, 7/10). Time courses from BOLD and CBV studies were comparable, with both methods giving a peak signal change in SI of about 8%. Incidence maps from the BOLD and CBV studies showed similar incidence of activation in SI, SII, and the thalamus, but the BOLD incidence maps show more activation along veins draining into the sagittal sinus (Figure 1). Incidence maps of the cerebellum were less similar. BOLD maps show activation along the superior surface of the cerebellum, while CBV maps show patchier activation below the surface.

The incidence of activation was greater in all areas with the 30 mg/kg dose of iron oxide than with the 20 mg/kg or 10 mg/kg dose, while activation in the accompanying BOLD studies remained the same. At the 30 mg/kg dose, the amount of activation below the surface of the cerebellum increased (Figure 2). The average percent decrease in signal from SI during stimulation was 14% with the highest iron oxide dose.

Discussion

Overall patterns of activation were very similar with BOLD and CBV-weighted fMRI. Draining veins which are consistently detected with spin echo BOLD at 11.7T are absent from CBV maps, indicating the activation there is due to drainage rather than a volume change. There are several possible explanations for the difference in the location of cerebellar activation seen in BOLD and CBV studies. The BOLD maps may include increased contributions from surface draining veins. Also, the increased susceptibility differences associated with the iron oxide contrast agent cause greater distortion in areas of the brain near large blood vessels, so the activation may appear shifted.

With a 20 ms echo time, the BOLD effect contributes to the image signal (~6-8%) even when iron oxide contrast is used, working against the negative change during activation seen in CBV images. Increasing the dose of contrast enhances the CBV weighting and improves sensitivity to activation in secondary regions.

References: 1. Dijkhuizen RM, et al. PNAS 2001;98(22):12766-71. 2. Morton DW, et al. Radiology 2001; 218(2): 598-601. 3. Keilholz SD, et al., submitted. 4. Silva AC, et al. J Cereb Blood Metab 1999;19:871-9.

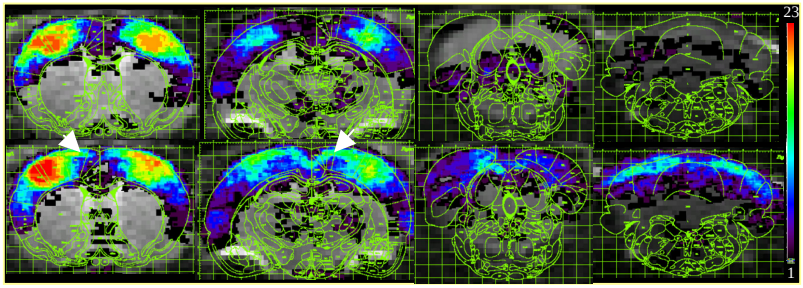

Figure 1. Incidence maps of CBV (top) and BOLD (bottom) activation. Arrows indicate draining vessels in the BOLD maps.

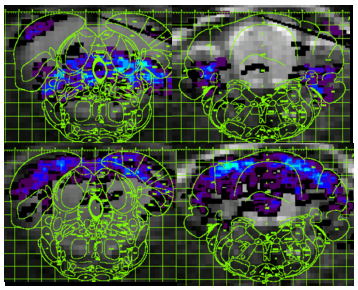

Figure 2. Incidence maps of CBV activation at 30 mg/kg (top) and BOLD activation (bottom). A large shift in cerebellar activation is evident.