Functional Imaging of Cat Spinal Cord by CBV-weighted fMRI

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INTRODUCTION

Since 1990 functional MR imaging has been widely used to study brain functions [1]. Although the volume of literatures published in brain functional MR imaging has been grown dramatically over the past decade, the number of published studies of functional MR imaging of the spinal cord is limited. This is mainly due to that significant technical challenges are associated with detecting the blood oxygenation level–dependent (BOLD) effect in the spinal cord [2-4]. Most of the difficulties are caused by the technical limitations, such as motion artifacts, chemical shift, and susceptibility artifacts; or by the low sensitivity of BOLD signal. The CBV-weighted fMRI with injection of monocrystalline iron oxide nanoparticles (MION) as an intravascular contrast agent improved the sensitivity of brain fMRI [5, 6]. Therefore, whether a reliable functional MR imaging signal can be detected from the spinal cord by CBV-weighted fMRI was investigated in this study. Functional MR imaging of spinal cord will be of great value in both basic research and clinical applications.

METHODS

Cats were under α-chloralose anesthesia (65 mg/kg, i.v.) during the fMRI scanning. Blood pressure, arterial blood gases, end-tidal CO_2 and rectal temperature were maintained within normal ranges. After intubation and surgery, animal was restrained in a supine position with its back laying on a butterfly shaped surface coil. The butterfly coil is composed of two loops, and each loop has a diameter of 3 cm. The supine position significantly reduced movement artifacts due to animal's breathing. NMR measurements were performed on a 9.4T/31cm system (Varian). A single 2-mm thick transverse imaging slice or sagittal imaging slice was selected at the lumbosacral segments of spinal cord. Matrix size was 128x128 for functional imaging, but 256x256 for anatomical imaging. The field of view (FOV) is 5×5 cm^2. Magnetic field homogeneity was optimized by manual shimming. TurboFLASH sequence was used for functional imaging with TR of 9 ms and TE of 5 ms. Functional data of CBV-weighted fMRI was obtained after the intravenous injection of 10 mg Fe/kg of MION. Electrical pulses of intensity 2.5-5 mA, pulsewidth 0.3 ms, and frequency 40 Hz were used to stimulate the left sciatic nerve via a pair of wire electrodes (0.5 mm stainless steel) placed around the nerve. Each run consisted of 60 control - 60 stimulation - 60 control images acquired with imaging TR of 1.25s. To improve the signal-to-noise ratio, the same fMRI paradigm was repeated 10 times. Signals from all fMRI scans under the same conditions were averaged. Cross-correlation method was used to detect the neuronal activations. Cross-correlation value maps were computed by comparing the experimental fMRI time course with the stimulation paradigm on a pixel-by-pixel basis. The cross-correlation value of 0.3 with active cluster size ≥ 4 (with $p<0.05$) was chosen as the threshold to determine the "active" pixels. Then, relative signal change was calculated on the activated pixels. The time courses were generated by averaging the signals from the activated maps.

RESULTS

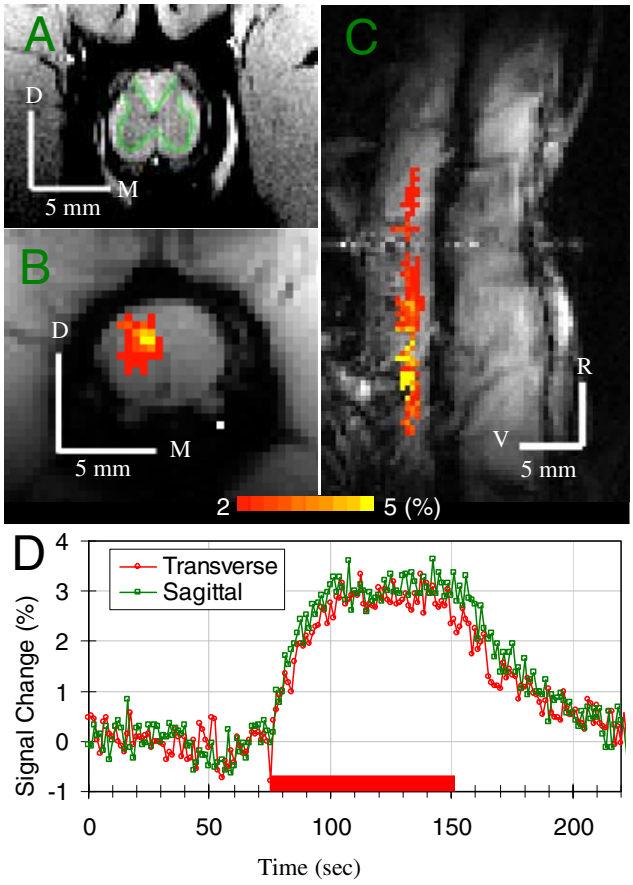

Figure 1 shows a representative T1-weighted anatomical image (**A**) from one cat and a functional data set from another cat, consisting of percent signal changes from a transverse slice (**B**) and a sagittal slice (**C**) of CBV-weighted fMRI during stimulation. The gray matter of spinal cord (which is delineated by green lines) can be clearly identified by T1-weighted image (**A**). The increases of CBV-weighted fMRI signals in both transverse and sagittal slices could be detected during electrical stimulation of the sciatic nerve. The largest CBV changes (yellow pixels) were observed in the gray matter of the spinal cord (**B**). And the spinal activation could be seen in several segments of the lumbosacral spinal cord (see Fig.1 **C**) on both dorsal and ventral horns (see Fig.1 **B**). The spinal activation induced by sciatic nerve stimulation was only observed in the spinal cord on the same side of the stimulation (left side, see Fig.1 **B**). Fig.1 **D** shows the time courses of spinal activation calculated from Fig.1 **B** or **C**. The fMRI signal change in spinal cord induced by sciatic nerve stimulation reached its maximum of 3% within about 20 seconds, and kept constant during the stimulation. After the cessation of the stimulation, the fMRI signals took relatively long time (>75 sec) to return to the baseline.

CONCLUSION

Our results validate that the neuronal activation in spinal cord can be detected by the techniques that can improve fMRI sensitivity, such as CBV-weighted fMRI. Similar to the CBV response in the brain [7], the largest CBV response in spinal cord is also located in the gray matter. The cat model with CBV-weighted fMRI provides a feasible method to investigate the spinal cord functions in both normal and pathological conditions.

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Figure 1. Anatomical image (A); functional CBV change in a transverse slice (B) and in a sagittal slice (C); (D) shows the time courses of functional CBV changes calculated from (B) and (C). The red bar in (D) indicates the electrical stimulation period. Gray matter of the spinal cord was outlined by green lines in (A). D: dorsal; M: medial; V: ventral; R: Rostral.