FUNCTIONAL MRI OF THE SPINAL CORD IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Introduction:

Functional magnetic resonance imaging (fMRI) of the spinal cord has proven to be useful in investigating sensory and motor activity in the cervical and lumbar spinal cord in healthy subjects (1) and in patients with spinal cord trauma (2, 3). To date, spinal fMRI has been applied in a preliminary study of multiple sclerosis (MS) showing, in patients with the progressive phenotypes of the disease, patterns of cord activity resembling those of subjects with cord trauma (4). Aims of this study were to determine the feasibility of spinal fMRI using a 1.5 Tesla clinical MR system and to evaluate the pattern and extent of the cervical cord activations in patients with relapsing-remitting multiple sclerosis (RRMS) compared with controls, during passive motor and sensory tasks.

Methods:

Twenty-three right-handed patients with RRMS (14 women, 9 men; mean age=38.9; mean disease duration=11.2 years; median EDSS=2.0) and 13 sex- and age-matched right-handed healthy controls were included.

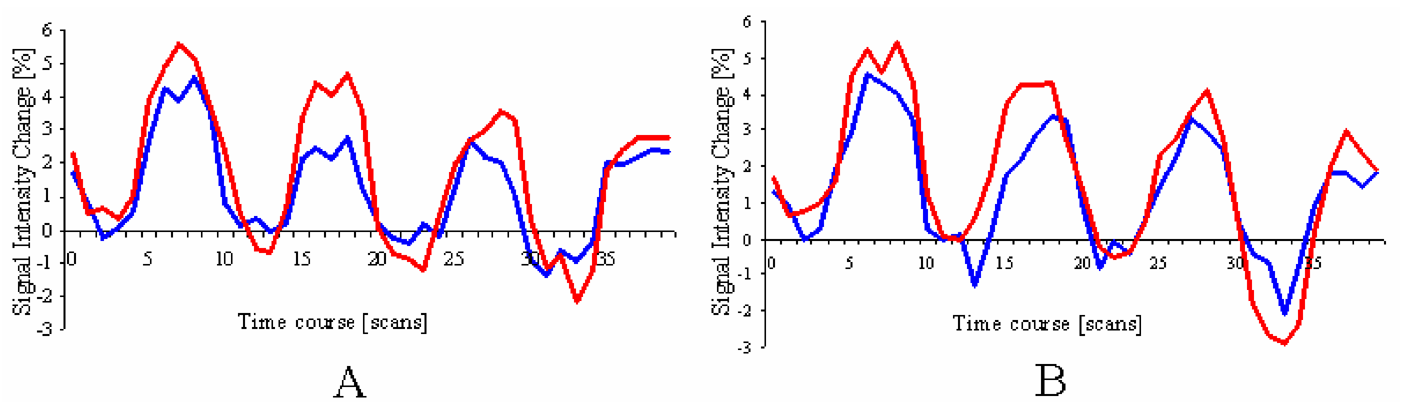
Using a 1.5 Tesla scanner (Magnetom Avanto, Siemens, Erlangen, Germany), we obtained a cervical cord conventional dual-echo turbo spin-echo (TSE) and cord fMRI. Cord fMRI consisted of a proton density-weighted TSE sequence (TR=2850 ms, TE=11 ms, FA=120°, FOV=100 mm^2, matrix=256x256). Nine, 7 mm-thick slices were obtained in the transverse plane, covering cord segments from C5 to C8. Spacing between slices was adjusted to align slices either with the vertebral body centers or with the intevertebral disks (5). The in-plane spatial resolution was kept to 0.39x0.39 mm. Spatial saturation pulses anterior and posterior to the spine were used to avoid aliasing and to reduce motion artifacts from breathing and swallowing. Flow compensation was applied to reduce artifacts from CSF flow. The time for acquiring one functional volume was 13 s. Cord FMRI was carried out in a block design (ABAB), where four periods of rest were alternated with four periods of activation (each period of rest and activation consisting of five measurements). The subjects were scanned when performing a passive motor task (flexion-extension of the right wrist), and a sensory task (tactile stimulation of palm of the right hand). Both stimuli were paced by a metronome at 1 Hz frequency and were administered to the subjects by an observer inside the scanner room.

FMRI data were analyzed using a custom-made software written in MatLab (The MathWorks, Natick, MA) (6). Images were first registered to reduce the effects of motion by means of rigid-body translation and rotation. Then, only a small region of interest (spinal cord white and grey matter), manually drawn for each slice, was used for the registration process, to avoid the effects of changes in the tone or position of the surrounding muscle (2). FMRI data were finally analyzed using a General Linear Model with basis sets composed of a box-car modelling the stimulus paradigm and of a linear ramp to account for baseline trends (6). Statistical maps were generated for all the subjects ($p<0.02$). The mean signal intensity change induced by the proton density increase during both tasks was computed for all activated voxels within the spinal cord.

Results:

Cervical cord hyperintense lesions were found in six RRMS patients. During both tasks, RRMS patients experienced a higher cord mean intensity change than controls (RRMS patients *vs.* controls: 3.48±1.08% *vs.* 2.64±1.36% during passive motor task; 3.38±0.86% *vs.* 2.89±1.15% during sensory task) (Figure). Compared with controls, RRMS patients showed a bilateral increase of the number of clusters of activation during passive motor task, while, during sensory task, they had a more prevalent activity of the cord side contralateral to the stimulus.

Figure Average signal intensity change of healthy controls (blue line) and RRMS patients (red line) for all activated pixels inside the cervical cord during the passive motor (A) and sensory task (B).



Conclusions:

Spinal fMRI is able to detect neuronal activity in the appropriate spinal cord segments in healthy volunteers and MS patients. RRMS patients showed an abnormal functional recruitment of the cervical cord compared to controls, during passive motor and sensory tasks. The absence of clinical involvement related to the investigated tasks rules out possible gross fMRI biases and suggests functional reorganization of the cervical cord to occur in RRMS patients. Cord fMRI holds significant promise to improve our insight into the role of cord damage/dysfunction in causing MS disability.

References:

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