Detection of Spinal Activation of Rat Using Generalized Likelihood Ratio Tests

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Introduction

Functional MR imaging of the spinal cord (spinal fMRI) could be used as a research tool for assessing spinal cord function. Since the spinal cord is contained within the vertebral column, differences in the magnetic susceptibilities between the bone, cartilage and tissues result in subtly different magnetic fields within these materials, and could cause distortion and loss of signal. To reduce the impact of these inhomogeneities, spin-echo (SE) instead of gradient-echo (GE) sequences are generally used in spinal fMRI with a concomitant drawback, the decreased changes in fMRI signal with SE data [1]. The small physical dimension of the spinal cord, the distribution of white and gray matter, and the surrounding cerebrospinal fluid (CSF) create a requirement for high resolution to avoid partial volume effects due to tissue heterogeneity. The higher resolution results in lower signal-to-noise ratio (SNR) in spinal fMRI data than that in conventional brain functional MRI (fMRI) data.

Both brain fMRI and spinal fMRI studies intend to determine those regions in the brain or spinal cord where the signal changes upon stimulus presentation by statistically analyzing a set of acquired images. The Student-t test is the widely used statistical method and based on the assumption of Gaussian distribution of fMRI data. Since the magnitude data of fMRI are in Rician distribution that tends to a Gaussian distribution only at high levels of SNR, the Gaussian distribution of spinal fMRI data may be invalid due to the low SNR. The decreased changes in spinal fMRI signal would also reduce the detection of active regions by the popular analysis methods. In the present study, the generalized likelihood ratio tests (GLRT) method based on the general linear model (GLM) was tested. The GLRT method with a modified hemodynamic response function (HRF) was applied to magnitude spinal fMRI data on Gaussian distribution and Rician distribution respectively [2]. The test results were compared with that of Student-t test.

Materials and Methods

Animal preparation: Wistar rats were anesthetized with 2.5% isoflurane and the rats were secured in an MR-compatible stereotaxic headset. The femoral artery was cannulated for blood gas measurements and blood pressure monitoring. Core temperature was monitored and maintained at 37±0.5°C using a temperature-controlled water pad inside the magnet.

Hind paw stimulation: Electrical stimulation (6mA, 0.3ms pulse length, 3Hz) was used. One of two small needle electrodes was placed subcutaneously and taped between 3rd and 4th toes on plantar surface of the left hind paw, and the other electrode was placed between 3rd and 2nd toes on the dorsal surface of the same paw. The stimulation paradigm consisted of 42 time points with a series of rest and stimulation periods: off (rest1 - 10), on (stim1 - 8), off (rest2 - 6), on (stim2 - 9), off (rest3 - 7). Five stimulation experiments were performed with a rest of 10 min between experiments.

MR imaging acquisition: A 9.4T horizontal bore magnet (Magnex, UK) equipped with an Advance console (Bruker, Germany) and a 5cm birdcage volume coil were used. Five axial slices were positioned within the spinal cord at the center of the vertebrae covering predominantly the vertebral discs as follows: First slice located at the vertebrae L3, second slice positioned at L2 vertebrae while the third, fourth and fifth slices covered L1, T13 and T12 neuronal inputs respectively [3]. Anatomical T2-weighted Fast Spin Echo (FSE) images of the spinal cord were acquired (TR/TE= 5s/12ms, FOV = 2×2cm, matrix size 128×128). At the same slice positions, a multislice, single-shot FSE sequence was used to acquire the fMRI data (TE = 3ms, effective echo time TEeff = 43.7ms, FOV = 2×2cm, matrix size 64×64, slice thickness 2mm, 0.5mm gap). Each slice shot was gated with the respiratory cycle, therefore, the effective repetition time (TR) was about 7s and not constant.

Data analysis: The spinal fMRI data were pre-processed by SPM5 software (Institute of Neurology, Queen Square, UK) in realignment and smoothed to reduce the effect of motion and increase the SNR. The processed data were further processed using a Matlab program developed in house to determine the voxels showing activation. Our custom software was written for Student-t test and the GLRT methods based on GLM in activation detection, and included the assumptions of Gaussian distributed data and Rician distributed data. A modified hemodynamic response function, a gamma-variate function with the modified parameters: 4s time to peak and 2.95s full width at half maximum [4], was used in GLRT methods. The results of GLRT methods were compared with that of Student-t test.

Results and Discussion

The MR images were obtained from Wistar rats (n=4). The data were processed by the custom program and the activation areas were detected by Student-t test (Figure 1a) and GLRT with HRF (Figure 1b) on the Gaussian distributed data, the false positive rate was 0.005. The stimulation paradigm and corresponding intensity in the activation area are shown in Figure 1c. The results show that the proposed method, GLRT with HRF could detect the activation regions with higher detection rate than Student-t test in the Gaussian case.

Results from real spinal fMRI data show that the proposed method, GLRT with HRF on Gaussian distributed data, provides a much better performance than the conventional Student-t test method and enhances the ability of spinal activity detection. The results of GLRT method on the Rician distributed data were negative. No activation was detected in this study using this method, though it is theoretically possible that this method could improve the detection rate by 3-5% in low SNR conditions [2]. The main problem is that, to the GLRT method used on the Rician distributed data, the maximization of the likelihood functions are nonlinear optimization problem and the solution would be obtained by iterative numerical optimization method, in which the correct maximum likelihood estimator is hard to be determined due to the noise impact. The GLRT with the modified HRF and the assumption of Gaussian distribution appears to be a powerful tool for exploratory analysis of spinal fMRI data.

References

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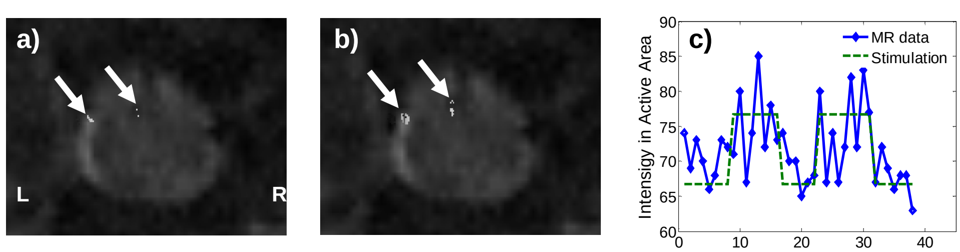

Figure 1, results of the experiment.
a) Active areas detected using Student-t test; b) Active areas detected by GLRT method with HRF on Gaussian distributed data. Active areas indicated by white arrow. (p=0.005); c) Stimulation paradigm and corresponding intensity in active areas.