Test-retest reliability of spinal cord fMRI in healthy participants

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Background

Functional imaging studies of the human spinal cord (spinal fMRI) have demonstrated the value and potential future uses of this technique for characterizing the effects of traumatic spinal cord injury, and diseases such as multiple-sclerosis, or for monitoring changes over time or effects of therapy [1,2]. The current spinal fMRI acquisition techniques have also been shown to be practical and feasible in standard hospital MRI facilities. However, one reason that spinal fMRI is not yet in clinical use is that the studies to date have reported predominantly group results to characterize consistent features of spinal cord function across populations, whereas individual assessments are needed. Here, we characterize the reliability of spinal fMRI results in individual healthy participants for mapping spinal cord function involved with thermal sensations. The reliability is determined by means of the consistency of activity detected across three scanning sessions in individuals, in a "test-retest" study. The purpose of this study is to verify the reliability of spinal cord fMRI for future studies of the effects of traumatic injury on spinal cord function. We hypothesize that individual results will be consistent across studies, in terms of locations and magnitudes of signal change, within the limits of the expected dependence on attention, and emotional factors, both which can influence descending modulation of neural activity in the spinal cord, as has been demonstrated previously.[3,4]

Methods

Eleven healthy participants with no prior history of neurological injury or disease (age 25 ± 6 years, range 20 to 44 years, 9 females and 2 males) were studied with a 3 tesla MRI system (Siemens Magnetom Trio). Each participant underwent three MRI sessions, with at least 1 week between repeated sessions. Spinal fMRI data were acquired using our established method based on SEEP contrast ("Signal Enhancement by Extravascular water Protons").[3,4] For each fMRI time-series, a 3D volume from caudal to the T1 vertebra to superior to the thalamus, was imaged 48 times in 7 min 12 seconds, in 9 contiguous sagittal slices, each 2 mm thick, by means of a half-fourier single shot fast spin-echo (HASTE) imaging sequence. The imaging parameters were as follows: sagittal slices, 28 x 21 cm FOV, 1.5 x 1.5 x 2 mm^3 resolution, TE = 38 msec, TR = 9 sec (1 sec/slice), spatial suppression pulses anterior to the spine, and motion compensating gradients in the head-foot direction. The peripheral pulse was recorded throughout each fMRI acquisition for subsequent modeling of physiological noise.

During the initial positioning for each MR imaging session, 4 thermodes connected to a custom-made thermal stimulation device were positioned symmetrically right and left, on the little finger side of the palm of the hand (the 8th cervical dermatome, C8), and on the upper arm near the shoulder (the 5th cervical dermatome, C5). Thermal stimuli were applied in a block paradigm with 3 periods of warm sensations at 44 °C for 45 seconds each, interleaved with periods at skin temperature or passive cooling toward skin temperature. Four different paradigms were applied by varying the rest period durations, and these form a linearly-independent set, enabling the response to each thermode to be detected. During each study participants watched a movie via a mirror and rear-projection screen outside of the MRI system in an attempt to maintain a constant attention focus across studies.

Spinal fMRI data were analyzed by means of a general linear model (GLM) implemented in custom-made software written in MATLAB® (The Mathworks Inc., Natick MA), as described previously.[5] The analysis consisted of 1) smoothing the data with a 3-pixel-wide boxcar function in the direction parallel to the long axis of the spinal cord (accounting for the curvature of the cord), 2) co-registration of the data to correct for subtle movement of the body, 3) defining the GLM basis functions for each slice, accounting for slice timing differences, 4) calculating the GLM fit parameters (i.e. β-values) and significance for each voxel, and 5) spatially normalizing the results for display and group analyses. A predefined region-of-interest mask was used to identify the estimated spinal cord segmental levels or brainstem regions for each area of activity that was detected.

Consistency of results across repeated studies in each individual was characterized by first identifying clusters of active voxels (abs(T) > 2.5) in each study, and then determining the locations of the nearest matching clusters with the same sign of T-values (i.e. positive or negative), and within the same quadrant and segment of the spinal cord, in the other studies. Comparisons were made both within, and across, individuals.

Results and Discussion

Across all subjects, comparisons between all pairs of studies within each participant show that 57% of the active clusters matched, with a mean separation of 2-3 voxels (4.7 mm). Comparisons of all combinations of studies across individuals showed that 57% ± 15% of active clusters matched, with the same sign of signal change, in the same quadrant and segment of the spinal cord. Importantly, we noted two patterns of responses which were consistent with those observed previously in a study of the effects of varying attention.[3] As a result, not all variability can be attributed to errors, but rather reflects sensitivity to neural activity.

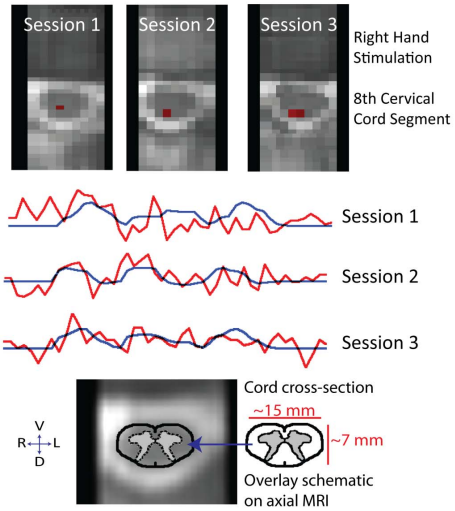

Figure 1: Sample results from one participant across 3 sessions, each 1 week apart, showing a cluster of activity in the C8 right dorsal horn in response to right-hand stimulation

Conclusion

In spite of the known causes of variation in neural activity in the spinal cord due to attention and emotional factors, we have observed a high degree of consistency across repeated studies occurring 1 week apart. Individual spinal fMRI results are therefore judged to be reliable, particularly if causes of normal variations due to attention and emotional factors can be identified.

References

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