# Combined fMRI of the human brain and the cervical spinal cord to investigate pain processing

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## Introduction

Blood-oxygenation level-dependent (BOLD) functional MRI (fMRI) is a well-established method to investigate the central nervous system in vivo, e.g. to study the central representation and modulation of pain. Many fMRI studies on the brain's role in pain processing have been performed and recently interest in the spinal cord's involvement has increased [1–3]. However, to study the functional interplay between the brain and the spinal cord in pain processing, both regions must be covered in a single measurement. Here, first results of a combined fMRI study to investigate the processing of painful thermal stimuli in the brain and the spinal cord are presented.

## Methods

Measurements were performed on a Siemens TIM Trio 3T system with a 12-channel head and 4-channel neck coil (both receive-only) using an approach for combined acquisitions of the brain and spinal cord in the same measurement that has been proposed recently [4]. Two subvolumes, one covering 32 slices in the brain, the other covering 8 slices in the spinal cord centred at segment C6, were acquired within a TR of 3.27 s. Different acquisition parameters were chosen for the two subvolumes to match settings typically used for each of the regions. For the brain, a field-of-view of 224×256 mm$^2$, an in-plane resolution of 2×2 mm$^2$, a slice thickness of 2 mm (1mm gap), and a bandwidth 1502 Hz per pixel were used. For the spinal cord, the field-of-view was 112×128 mm$^2$, the in-plane resolution 1×1 mm$^2$, the slice thickness 5 mm (no gap), and the bandwidth 1086 Hz per pixel. Parallel imaging (GRAPPA, acceleration factor 2, 48 reference lines) was applied to minimize echo times and geometric distortions yielding echo times of 30ms and 38ms for the brain and spinal cord subvolumes, respectively. To improve the signal-to-noise ratio a dynamic receive coil element selection was chosen, considering only the signal from the head coil elements for the brain slices and only the signal from the neck coil elements for the spinal slices. A dynamic update of the resonance frequency and the linear shims was performed in order to provide an optimized shim adjustment for both regions. Furthermore, a slice-specific gradient moment in the slice direction was applied for the spinal cord slices to minimize intensity variations along the spinal cord [5].
20 healthy volunteers participated in a pain experiment consisting of 3 sessions. During each session 8 low (46.0°C) and 8 high intensity (47.0°C) thermal stimuli were applied with a 30×30 mm$^2$ Peltier thermode to the left arm at the dermatome C6 in a pseudo-randomized order. The analysis of the brain subvolume followed a standard SPM8 preprocessing and inference procedure. For the analysis of the spinal cord subvolume, the cost function of the realignment procedure was restricted to the spinal cord and directly adjacent tissues and images were normalized to a group's mean T1-weighted image created form two previous studies [6,7]. Finally, a physiological noise modeling approach [6] was employed to account for the influence of cardiac and respiratory related effects in the spinal cord. Data of 3 volunteers were discarded from the analysis due to incomplete physiological data acquisition.

## Results

In the brain, a typical pattern of pain-related BOLD responses to both thermal intensities was observed, e.g., in SI, SII, insula, and ACC (Fig. 1), which were significantly stronger during high-intensity stimulation in the ACC ($t_{(16)}$=10.80, p<0.001), insula ($t_{(16)}$=8.50, p<0.001) and SII ($t_{(16)}$=5.57, p<0.001). In the spinal cord, the strongest BOLD ($t_{(16)}$=4.95, p<0.001) responses to high-intensity stimulation were found ipsilateral to the side of stimulation in the dorsal horn of segment C6 (Fig. 2). At the same site, the strongest responses ($t_{(16)}$=2.37, p=0.015) to the low-intensity condition were observed (Fig. 2). BOLD responses in the spinal cord to the high-intensity condition correlated positively with responses in the insula ($t_{(16)}$=4.86, p<0.005) and SII ($t_{(16)}$=3.89, p<0.005) as shown in Fig. 3. A psychophysical interaction analysis revealed a higher coupling between the spinal cord and the ACC during high thermal intensity compared to low intensity ($t_{(16)}$=3.82, p=0.001).

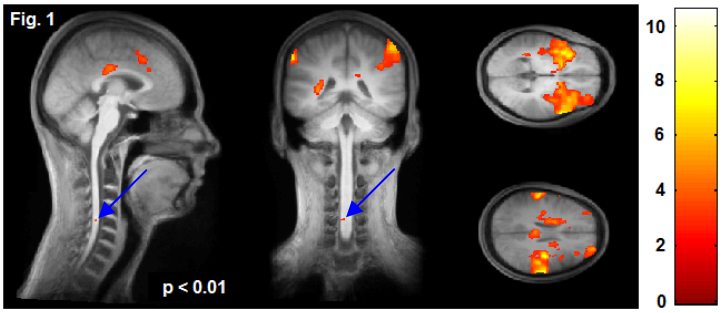


**Fig. 1:** Brain and spinal cord (arrow) activation pattern of painful thermal stimuli. See text for details.

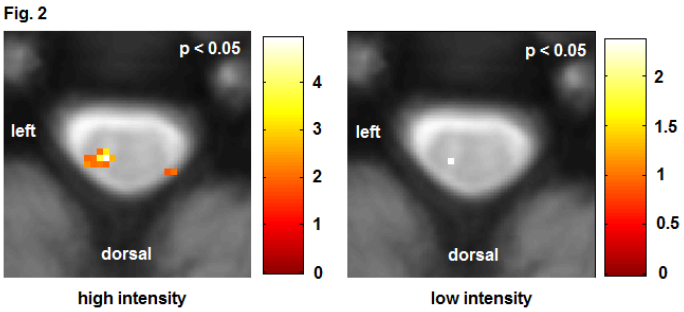


**Fig. 2:** Spinal cord for the high (left) and low intensity stimuli (right). See text for details.

## Discussion and Conclusion

The data confirm findings from previous pain perception studies investigating the brain [8] or the spinal cord [3,6,9]. Furthermore, because combined acquisitions of the brain and the spinal cord were performed, a correlation of the BOLD responses in the spinal cord and in the contralateral thalamus, contralateral S I and ipsilateral insula could be observed. Thus, with such combined spinal and brain fMRI experiments, the interaction of pain processing areas in the full central nervous system could be studied.

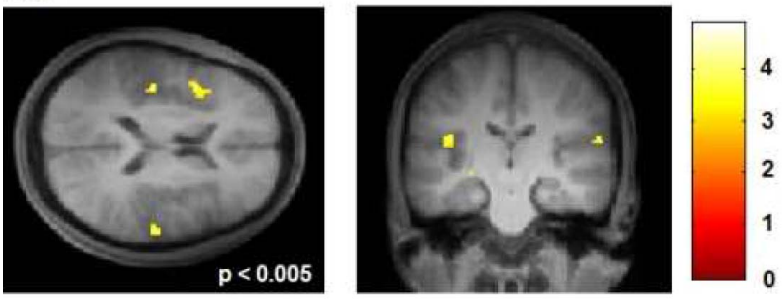


**Fig. 3:** Voxels in the brain in which the signal time course correlates significantly with that observed in the voxels activated spinal in the spinal cord for the high intensity stimuli (see Fig. 2). See text for details

## References

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