

Central pain augmentation in fibromyalgia during subjectively-matched mechanical stimulation.



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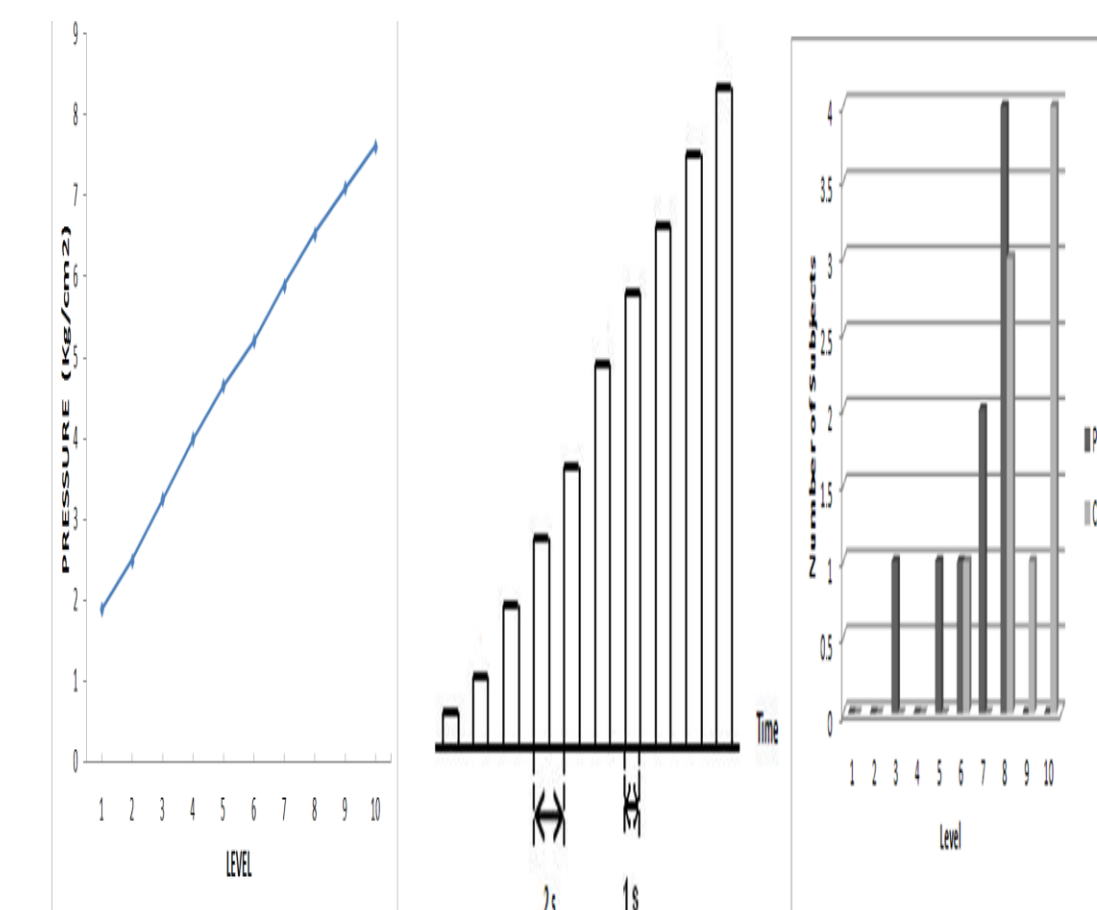


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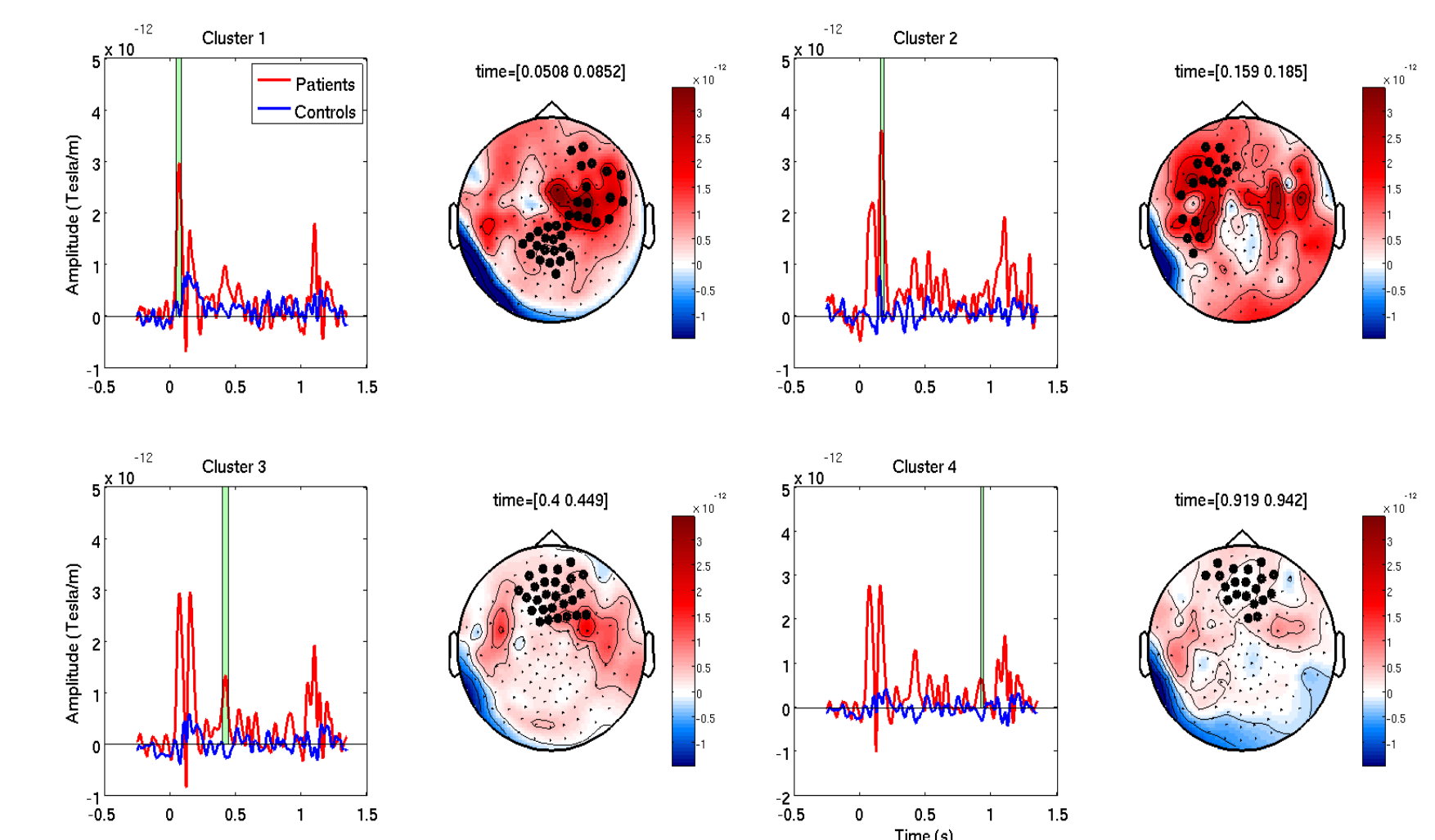
Objective: The precise pathophysiology of fibromyalgia, a syndrome characterized by, among other symptoms, chronic widespread pain, remains to be elucidated (Abeles et al., 2007). The fact that, when subjected to the same amount of stimulation, patients show enhanced brain responses as compared to controls provides evidence of central pain augmentation in this syndrome. We aimed to characterize brain response differences when stimulation is adjusted to elicit similar subjective levels of pain in both groups.

Methods: Magnetoencephalography (MEG) was used to investigate the brain responses to pressure stimulation both above and below the pain threshold in 9 patients and 9 control subjects. A device was developed to deliver pressure pulses in a quantifiable and precise manner. The amount of pressure was adjusted to produce similar subjective levels of pain in both groups. Trains of pulses of one second duration, and one second interstimulus interval were delivered to the trigger point locate at the left lateral epicondyle near the elbow.

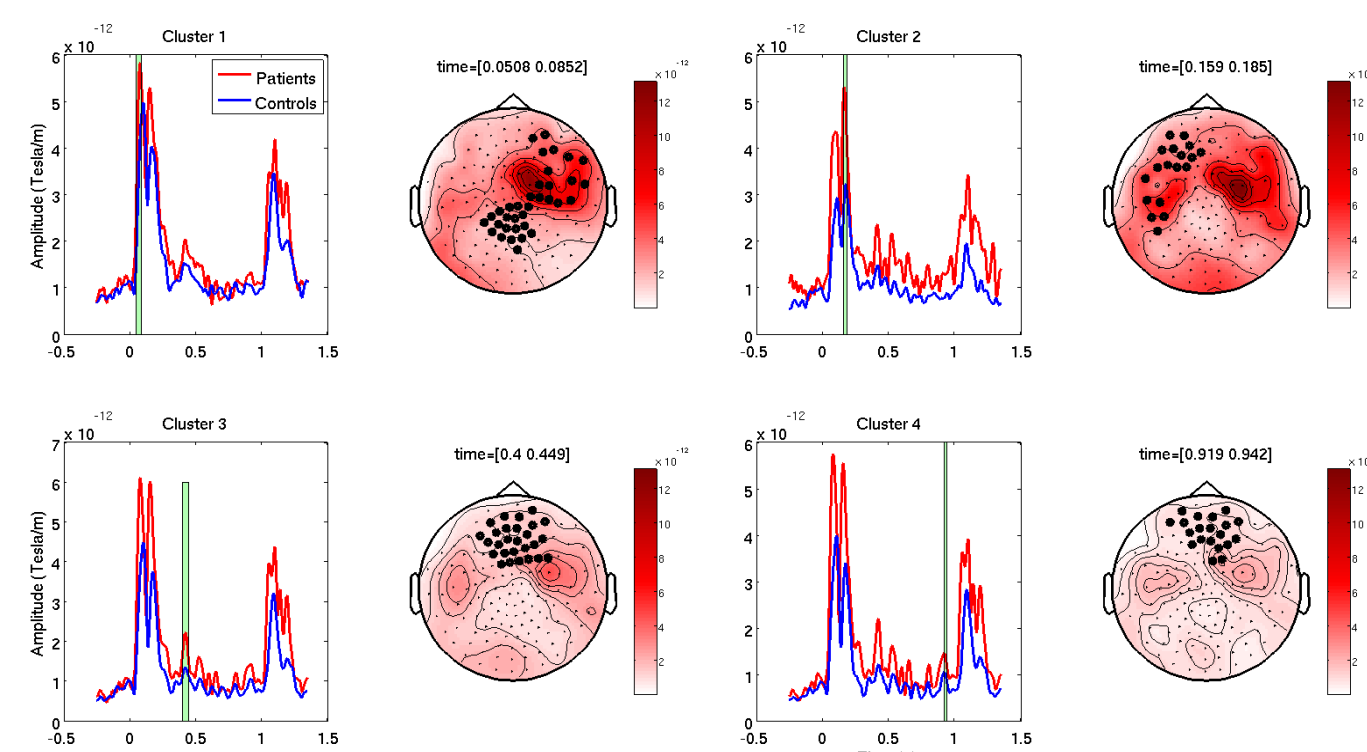
Behaviourally, fibromyalgia patients present with increased sensitivity to pressure stimulation as reflected in reduced pain thresholds (Harris et al., 2006). The figure shows the distribution of pain thresholds for the patient and control group in the present study:



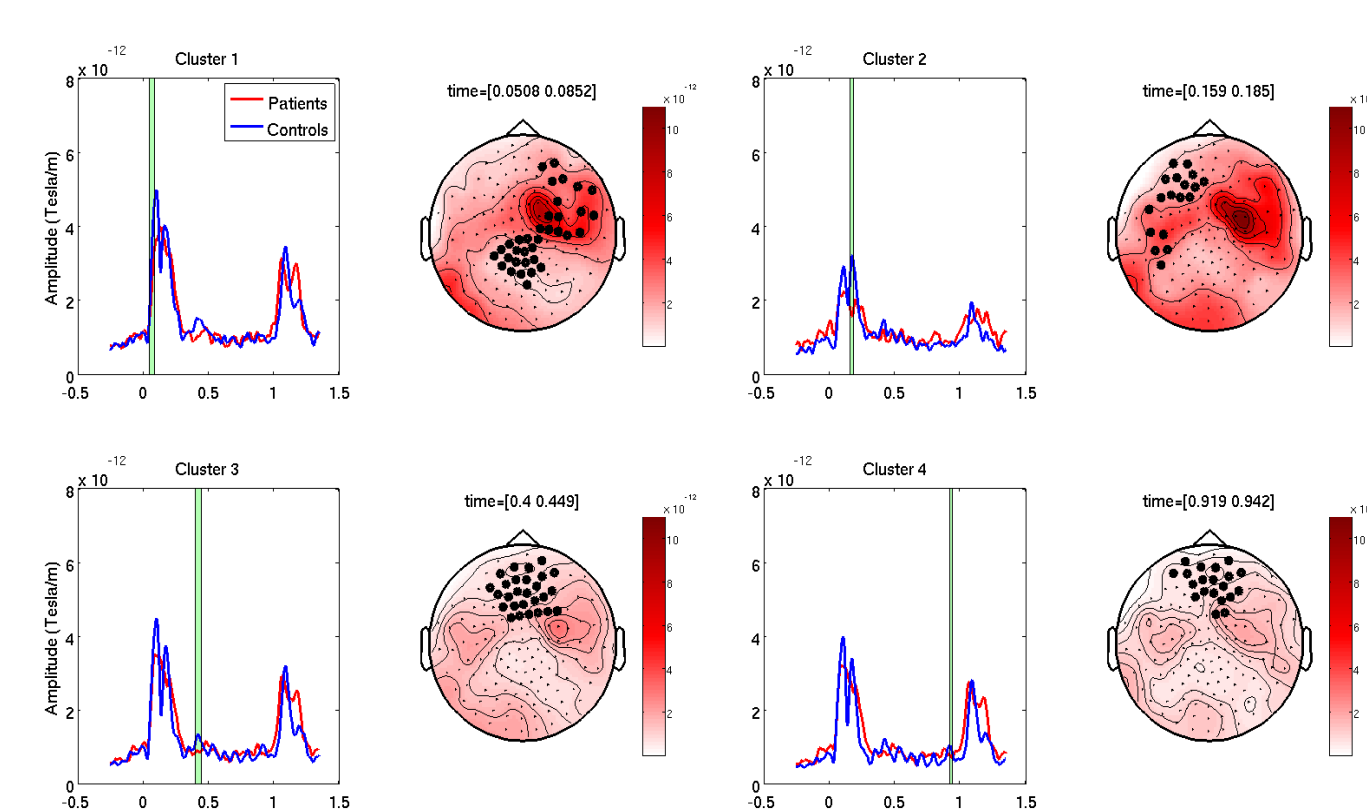
Results in Sensor Space: Spatiotemporal clusters of significant ($p < 0.01$, corrected) signal (suprathreshold-subthreshold) differences between patients and controls after cluster-based permutation testing. Left panel shows the signal profile (suprathreshold-subthreshold) averaged across the sensors comprising the cluster and the group individuals (red=patients, blue=controls). The green line denotes the cluster time window. Right panel: Highlighted are the sensors comprising the cluster. The underlying topographic map shows the cluster signal averaged across the signal time window and all patients and participants. ($p_{\text{cluster}} < 0.005$). Signal change was larger for patients in all 4 locations and latencies.



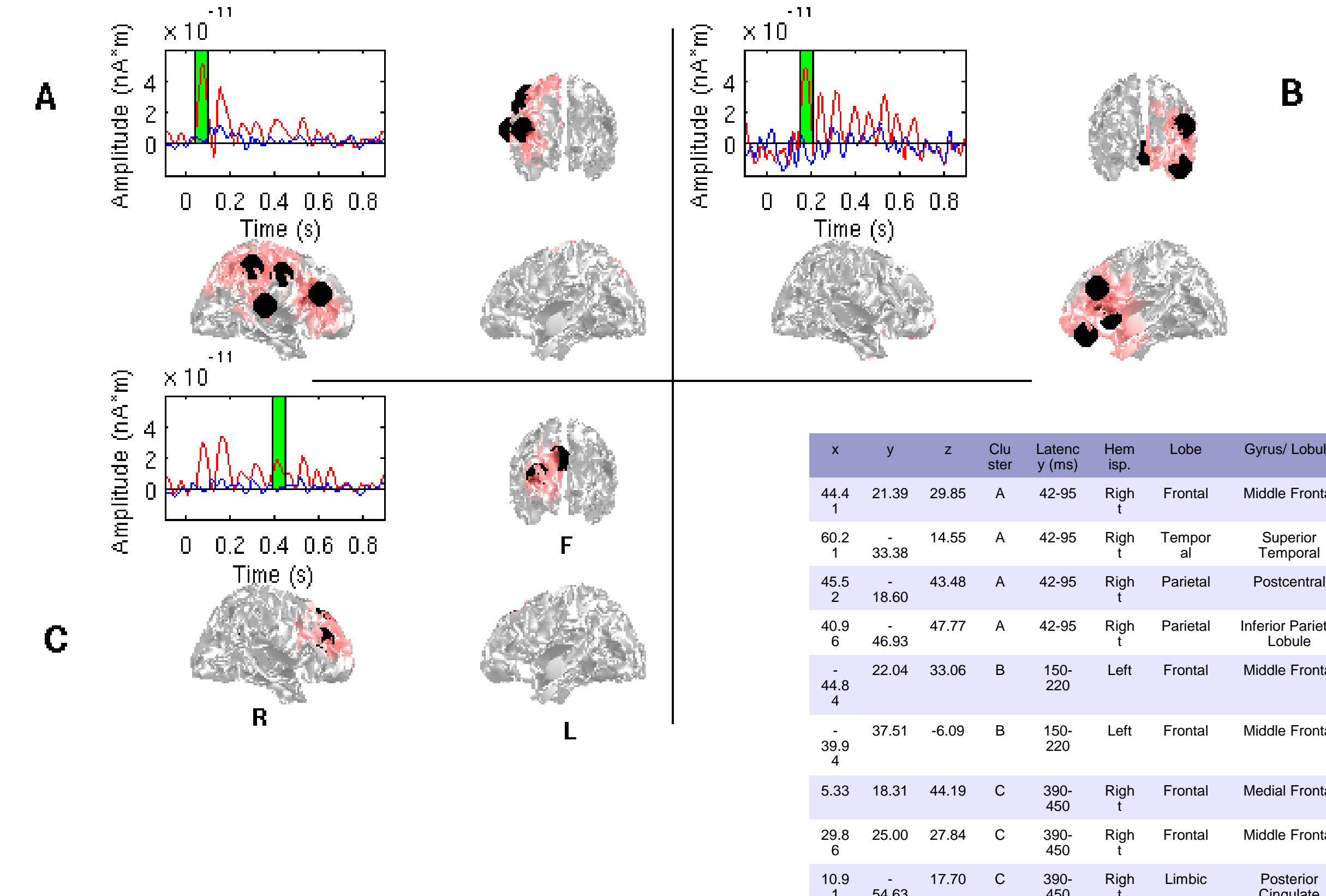
Time-course for the subthreshold condition for the clusters defined in the previous Figure.



Time-course for the suprathreshold condition for the clusters defined in the previous Figure



Results in Source Space: A between-group comparison of differences between responses evoked by stimulation above and below the pain threshold using cluster-based permutation testing. In good agreement with sensor space results, increases in signal amplitude in somatosensory, temporal, parietal and prefrontal areas at short latencies and in prefrontal areas at long latencies were found to be larger for patients than for control subjects.



Conclusion: Fibromyalgia patients show enhanced brain responses after reducing the amount of pressure to produce similar subjective levels of pain than to control subjects. A previous study (Gracely et al. 2002) reported that stimulation adjusted to cause a similar level of pain in both FMS patients and controls activated overlapping groups of brain areas. This has been interpreted as evidence that the hypersensitivity to stimulation experienced by FMS patients could be the result of central pain augmentation. The present analysis, while consistent with the notion of central pain augmentation, reveals that the following areas are more activated in FMS than in controls: somatosensory, temporal, parietal and prefrontal areas at early latencies and prefrontal areas at late latencies. Therefore, brain responses to nociceptive stimuli are not uniquely determined by subjective sensation, but further differences exist between healthy subjects and fibromyalgia patients in both sensory and nociceptive components.

Significance: The present results suggest that central pain augmentation is present in fibromyalgia not only when the objective level of stimulation is kept the same as for control subjects, but also when stimulation is adjusted to produce similar levels of pain in patients and controls.

References: Abeles AM, Pillinger MH, Solitar BM, Abeles M. Narrative review: the pathophysiology of fibromyalgia. *Ann Intern Med* 2007;146:726–734.
Gracely RH, Petzke F, Wolf JM, Clauw DJ. Functional magnetic resonance imaging evidence of augmented pain processing in fibromyalgia. *Arthritis Rheum.*2002; 46:1333-1343.
Harris RE, Gracely RH, McLean SA, Williams DA, Giesecke T, Petzke F, et al. Comparison of clinical and evoked pain measures in fibromyalgia. *J Pain* 2006;7:521-527.