

Working memory impairment in Fibromyalgia patients : fMRI study

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Introduction

Chronic widespread musculoskeletal pain and multiple tender points are characteristic of fibromyalgia (FM) [1]. Patients with FM commonly report cognitive complaints, including memory and attention problems. Recent neuroimaging studies have provided growing evidence to support the view that FM patients have various kinds of abnormalities in the frontoparietal networks. [2]. However, no investigations have directly examined neural processing during performance of working memory in FM patients, except for a brief report [3]. Therefore, the aim of this study is to elucidate the differences in neural activation related to working memory between FM patients and healthy subjects. In addition, we investigate possible differences in the deactivated brain network between FM patients and control subjects during performance of the n-back memory task, to elucidate the coordinated modulation of neural activity for successful memory functioning.

Subjects and methods

A total of 41 female subjects (19 FM patients and 22 healthy controls) were enrolled in this study. FM patients were recruited consecutively from outpatient rheumatic clinics at four university-based hospitals and from one general hospital. All participants agreed to participate in our fMRI study and provided written informed consent. The protocol used for this study was approved by the Institutional Review Board of university hospital. Demographic, clinical, and psychological data, including age, education, disease duration, and tender point count, were obtained from reviews of medical records and an interview with each participant at the time of study enrollment. The severity of depression was evaluated using the Beck depression inventory (BDI).

Functional magnetic resonance imaging was employed to assess cortical activities during the performance of 0-back and 2-back working memory paradigm using Korean alphabet as mnemonic content. In the 0-back condition, participants were asked to remember a target letter that was presented at the beginning of each trial block. In the 2-back condition, they were asked to respond when a letter matched one that had been presented two letters before the present letter. BOLD functional images were acquired using a 3.0T GE HD scanner (EPI, TR=3000ms, TE=40ms, matrix=64x64, Thickness=4.0mm, FOV=220mm, no gap). Anatomical images were acquired using 3D-FSPGR sequence (TR=7.8ms, TE=3ms, matrix=256x256, no gap). Image processing and statistical analyses were carried out using MATLAB v. 7.7 and SPM5. In fMRI data within-group analysis, contrast images from the analysis of individual subjects were analyzed by one-sample *t*-test, thereby generating a random-effects model, allowing inference to the general population. To avoid the possible compounding effect of depression, group analysis was performed with BDI as a covariate. The SPM t 's were thresholded at $P < 0.05$, false discovery rate (FDR) corrected for multiple comparisons across the whole brain. To make direct comparisons of brain activations between control and welder group during 2-back memory task, contrast images for the main effects were assessed using a two-sample *t*-test. SPM t 's were thresholded at $P < 0.005$ uncorrected, and small-volume corrections with FDR in a 5-mm sphere were applied to the ventrolateral prefrontal cortex, superior frontal cortex, anterior cingulate cortex, thalamus, middle temporal cortex, and inferior parietal cortex. We also performed within- and between-group analysis with the opposite contrast (0-back > 2-back) to investigate whether the 2-back memory task was associated with differential patterns of deactivation.

Results and Discussion

We found that healthy subjects showed better performance in terms of accuracy and reaction times during the task (Fig. 1). Differences in task accuracy and response time between the two groups were statistically significant ($p < 0.05$, Student's *t*-test) except for 0-back accuracy ($p = 0.6$, Student's *t*-test). In between-group analyses, FM patients showed reduced activation in the dorsolateral and ventrolateral prefrontal cortex, dorsal cingulate cortex, and inferior parietal cortex (Fig. 2). Our findings suggest that functional abnormalities in the frontoparietal working memory network might contribute to impairments in maintenance and manipulation of working memory in FM patients. After controlling for depression level, our data indicate that the working memory deficit found in FM patients results from pain itself, although depression associated with pain also affects impairment in working memory. With regard to brain deactivation associated with working memory, both healthy subjects and FM patients showed a similarly distributed deactivation cortical network, prominently including the medial prefrontal cortex, anterior cingulate cortex, posterior cingulate cortex, amygdala, and parahippocampal gyrus. Direct comparison of the deactivation networks showed no statistically significant differences in neural deactivation between FM patients and healthy subjects during performance of the n-back test. Taken together, working memory impairments in FM patients may be attributable to differences in neural activation of the frontoparietal network rather than deactivation in the default network.

References

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Results Data

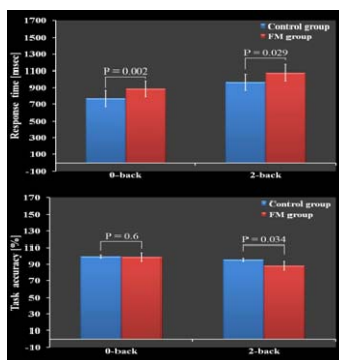


Fig 1. Mean n-back working memory task performance in the control group (blue) and in the FM group (red).

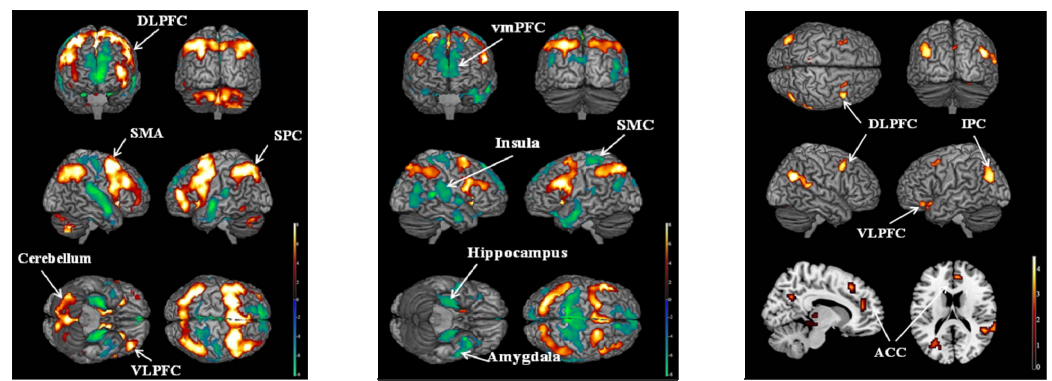


Fig 2. Brain activations during the 2-back memory task in healthy subjects (a) and FM patients (b). Statistical parametric maps of brain regions of (a) and (b) (one-sample *t*-test for each group) showing significant activation at a statistical threshold of $P < 0.05$ (corrected). Statistical parametric maps of brain regions of (c) (two-sample *t*-test) showing significantly reduced activation in FM patients compared to healthy subjects ($P < 0.05$, FDR small volume corrected).