Slow fluctuation BOLD signal component analysis during active press pain stimulation in fibromyalgia patients

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Introduction

Fibromyalgia (FM) is considered to be the central chronic pain syndrome and is associated with widespread pain spontaneously [1]. Fibromyalgia syndrome is not restricted to pain and often leads to other symptoms including debilitating fatigue, sleep disturbance, and depression and anxiety. Currently no investigation is available for identifying low frequency fluctuation components during active press pain stimulation paradigm while recent study evaluated low frequency fluctuation during resting-state. The objective of this study was therefore to (1) evaluate low frequency BOLD fluctuation components during active pain stimulation paradigm using independent components analysis (ICA) and (2) investigate the differences in low frequency BOLD fluctuation components between FM patients and healthy controls.

Subjects and methods

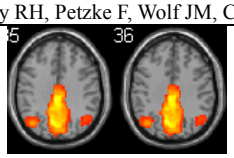
Active press pain paradigm consists of 2 blocks: the "active pain stimulus" block, during which subjects received a pressure at 2.48 kg/cm^2, and the "rest control" blocks, during which the intensity of pressure pain sensations not evoked by stimuli [2]. Data were collected from 45 female subjects in 2 different groups, comprising 20 patients with FM (mean ± SD age 37.4 ± 1.7 years) and 25 age matched healthy controls (mean ± SD age 37.4 ± 8.0 years; p = 0.148 versus patients with FM). Slow fluctuation components between 0.01 Hz and 0.1 Hz in individual subjects were analyzed using ICA . All participants gave their written informed consent. Functional magnetic resonance imaging was employed to assess brain activities during the performance of a painful pressure using a pain stimulation device. BOLD functional images were acquired using a 3.0T GE HD scanner (EPI, TR=5000ms, TE=40ms, matrix=64x64, Thickness=3.0mm, FOV=19.2mm, 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 v7.6 and SPM5. We used this group ICA approach, which has been implemented in the group ICA of fMRI toolbox (GIFT). 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. The SPM{t}s were thresholded at P<0.05, family wise error (FWE) corrected for multiple comparisons across the whole brain. To make direct comparisons of brain activations between healthy controls and patients with FM, contrast images for the main effects were assessed using a two-sample t-test. SPM{t}s were thresholded at uncorrected P<0.005.

Results and Discussion

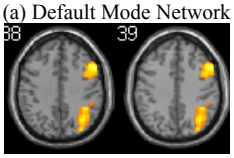
Among 27 independent components (ICs) in pain stimulus blocks and 28 ICs in rest control blocks, the default mode network (DMN) and executive attention network (EAN), which were previously well defined, were identified (Fig1). In case of EAN, left and right EAN were separated (Fig1 b and c). In press pain stimulus blocks, brain regions of precuneus showed a greater correlation with the DMN in healthy controls as compared with patients with FM (Fig2 a). Patients with FM demonstrated greater intrinsic DMN connectivity to brain regions, namely, the right insular, inferior frontal gyrus, left middle cingulum, and postcentral gyrus (Fig2 b). Bran regions of superior and middle fontal gyrus showed a greater connectivity within the right EAN in patients with FM (Fig2 c). No brain regions showed a greater correlation within the right EAN in healthy controls as compared with patients with FM. No difference between patients with FM and healthy controls were found in the left EAN. In rest control blocks, brain regions of the right posterior cingulate cortex showed a greater correlation within the DMN in healthy controls as compared with patients with FM (Fig3 a). Patients with FM demonstrated greater intrinsic DMN connectivity to brain regions, namely, limbic lobe, superior temporal gyrus, caudate and the left putamen (Fig3 b). Connectivity difference between patients with FM and healthy controls were also noted in the left EAN. Patients with FM demonstrated greater intrinsic left EAN connectivity within the left posterior cingulate cortex and the right fusiform (Fig3 c). Brain regions of the right precentral cortex, the left putamen, the left insula and inferior frontal gyrus showed a greater correlation within the left EAN in healthy controls as compared with patients with FM (Fig3 d). No difference between patients with FM and healthy controls were found in the right EAN. Our results therefore demonstrated (1) the existence of intrinsic slow fluctuation BOLD signal components during active pain stimulation paradigm and (2) the possible differences in intrinsic brain connectivity between FM patients and healthy controls.

References

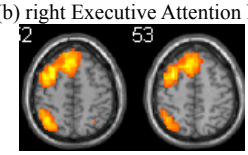
1. Vitaly N., Lauren LC., Park K., Sawsan AS, Clauw DJ., Harris RE., ACR., 62, 2545-2555(2010)
2. Gracely RH, Petzke F, Wolf JM, Clauw DJ., ACR., 46, 1333-1343(2002)



(a) Default Mode Network

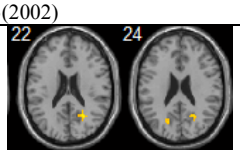


(b) right Executive Attention Network

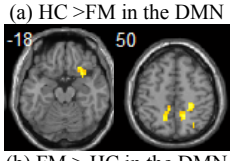


(c) left Executive Attention Network

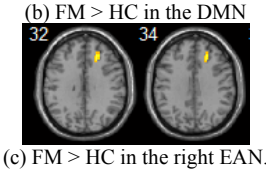
Fig 1. Connectivity within brain networks (a) default mode network (DMN) (a), right executive attention network (rEAN) (b) and left executive attention network (lEAN) (c). Independent component analysis of brain regions (a), (b) and (c) (one-sample t-test for healthy control (HC) subects of 25 subjects during neutral blocks) showing significant activation at a statistical threshold of P<0.05 (FEW corrected)



(a) HC >FM in the DMN

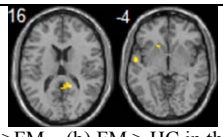


(b) FM > HC in the DMN

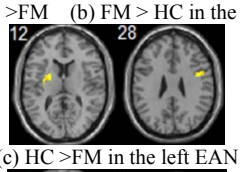


(c) FM > HC in the right EAN.

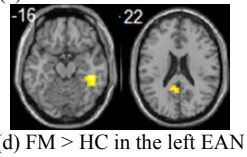
Fig 2. Intrinsic connectivity within brain networks the DMN (a) and (b) and the right EAN (c) during press pain stimulus blocks. Intrinsic connectivity within brain networks of (two-sample t-test) showing significantly differences in patients with FM compared to healthy controls (P<0.005, uncorrected)



(a) HC >FM (b) FM > HC in the DMN



(c) HC >FM in the left EAN



(d) FM > HC in the left EAN

Fig 3. Intrinsic connectivity within brain networks the DMN (a) and (b) and the left EAN (c) and (d) during neutral blocks. Intrinsic connectivity within brain networks of (two-sample t-test) showing significantly differences in patients with FM compared to healthy controls (P<0.005, uncorrected)