**Title:** Brain activity and functional connectivity during emotion processing and regulation in fibromyalgia

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## Objective

Fibromyalgia (FM) is a chronic condition characterized by the presence of widespread pain accompanied by a conglomerate of physical and psychological symptoms. Depression and anxiety are common comorbidities in FM, and disturbances in the emotion processing and regulation have been found as well. The neural underpinning of these disturbances could help to understand the high comorbidity of depression and anxiety in this condition. Here we aimed to characterize the brain activity and functional connectivity during emotion processing and regulation in fibromyalgia using fMRI.

## Methods

In this study, we included 20 women with FM and 31 healthy controls (HC). The two groups were matched with respect to age and years of education. Standard psychometric questionnaires were applied to both groups to measure psychological variables such as alexithymia, positive and negative affect, affective pain, tendency to use emotion regulation strategies, depression and anxiety. Next, participants performed an emotion processing and regulation task during fMRI (Philips Ingenia 3T, 32 channel head coil, TR = 2 s, voxel size =  $3 \times 3 \times 3$  mm). The emotion processing and regulation task presented pictures with positive and negative valence from the International Affective Picture System. The participants had to observe, reappraise or suppress the emotion generated by the pictures which were presented in blocks. Preprocessing of the fMRI data included slice time correction, realignment, co-registration of the functional images to the anatomical images, normalization MNI space and smoothing with a full-width at half-maximum Gaussian kernel of 6 mm. For the first-level analysis, a general linear model was applied to the time series of each participant. For the second level, we performed a whole-brain analysis modeled with a 2 x 2 ANCOVA with valence (positive and negative) as the within-subject factor, and groups (FM and HC) as the between-subject factor and covariates. Then, we used the generalized psychophysiological interaction (gPPI) analysis to assess functional connectivity of hippocampus, amygdala, anterior insula, and anterior cingulate cortex (ACC). We also correlated clinical variables to whole-brain activation and functional connectivity terms.

## Results

In the main analysis we found a significant cluster for the group main effect in the left superior lateral occipital cortex (F =26.53, p = 0.028,  $\eta^2_p$  = 0.18). The post-hoc t-test for the contrast FM > HC was significative for that cluster (t(116) = 5.15, p =0.23, k = 77). In the gPPI analysis, we found an interaction effect (valence x group) for the functional connectivity between the left ACC and the

precentral and postcentral cortex, the frontal operculum, the central operculum and the premotor cortex. The tendency to use suppression as an emotion regulation strategy in FM was negatively correlated with the activity of the left lingual gyrus (r(28) = -.68, p = .003) and the right inferior lateral occipital cortex (r(28) = -.71, p = .003) –during positive valence. Finally, The Toronto Alexithymia subscale "difficulty to identify feelings" was positively correlated to the functional connectivity between right anterior insula and the right superior frontal gyrus, the supplementary motor area and the dorsal anterior cingulate cortex.

## Conclusions

The ACC, an important area for process salient stimuli, emotion, pain and affected in depression and anxiety. In our study we found that ACC functional connectivity was disrupted according to the valence of the emotional stimuli presented, indicating difficulties to process and regulate the emotions on a neural level. We also found a higher functional activity in the left lateral occipital cortex in FM, an area involved in visuospatial processing and object recognition. Furthermore, we found its activity and lingual gyrus activity to be negatively correlated to the tendency to use suppression as a daily life regulation strategy in the FM group. Our results suggest that in order to regulate their emotions, patients with FM need to rely more on visual stimuli. This support the hypothesis of disturbed brain activity related to the emotion processing and regulation in fibromyalgia, which could explain the high comorbidity with depression and anxiety.

Presentation preference: any (oral or poster)