

# Altered insula-default mode network connectivity in fibromyalgia: a resting-state magnetoencephalographic study.

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## Abstract

### BACKGROUND:

Fibromyalgia (FM) is a disabling chronic pain syndrome with unknown pathophysiology. Functional magnetic resonance imaging studies on FM have suggested altered brain connectivity between the insula and the default mode network (DMN). However, this connectivity change has not been characterized through direct neural signals for exploring the embedded spectrotemporal features and the pertinent clinical relevance.

### METHODS:

We recorded the resting-state magnetoencephalographic activities of 28 patients with FM and 28 age- and sex-matched controls, and analyzed the source-based functional connectivity between the insula and the DMN at 1-40 Hz by using the minimum norm estimates and imaginary coherence methods. We also measured the connectivity between the DMN and the primary visual (V1) and somatosensory (S1) cortices as inpatient negative controls. Connectivity measurement was further correlated with the clinical parameters of FM.

### RESULTS:

Compared with the controls, patients with FM reported more tender points ( $15.2 \pm 2.0$  vs.  $5.9 \pm 3.7$ ) and higher total tenderness score (TTS;  $29.1 \pm 7.0$  vs.  $7.7 \pm 5.5$ ; both  $p < 0.001$ ); they also had decreased insula-DMN connectivity at the theta band (4-8 Hz; left,  $p = 0.007$ ; right,  $p = 0.035$ ), but displayed unchanged V1-DMN and S1-DMN connectivity ( $p > 0.05$ ). When patients with FM and the controls were combined together, the insula-DMN theta connectivity was negatively correlated with the number of tender points (left insula,  $r = -0.428$ ,  $p = 0.001$ ; right insula,  $r = -0.4$ ,  $p = 0.002$ ) and TTS score (left insula,  $r = -0.429$ ,  $p = 0.001$ ; right insula,  $r = -0.389$ ,  $p = 0.003$ ). Furthermore, in patients with FM, the right insula-DMN connectivity at the beta band (13-25 Hz) was negatively correlated with the number of tender points ( $r = -0.532$ ,  $p = 0.004$ ) and TTS ( $r = -0.428$ ,  $p = 0.023$ ), and the bilateral insula-DMN connectivity at the delta band (1-4 Hz) was negatively correlated with FM Symptom Severity (left:  $r = -0.423$ ,  $p = 0.025$ ; right:  $r = -0.437$ ,  $p = 0.020$ ) and functional disability (Fibromyalgia Impact Questionnaire; left:  $r = -0.415$ ,  $p = 0.028$ ; right:  $r = -0.374$ ,  $p = 0.050$ ).

### CONCLUSIONS:

We confirmed the frequency-specific reorganization of the insula-DMN connectivity in FM. The clinical relevance of this connectivity change may warrant future studies to elucidate its causal relationship and potential as a neurological signature for FM.