Pain stimulation increases functional connectivity in patients with chronic widespread pain

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Introduction

Chronic widespread pain (CWP) disorders such as fibromyalgia are a major health problem characterized by altered neural connectivity[1]. Pain also causes connectivity plasticity; acute pain shows to enhance default mode network (DMN) connectivity in healthy people[2], and pain sensation increases connectivity in DMN and in the fronto-parietal executive control network (ECN) in CWP[1]. In this study, we have investigated the direct effects of pain both in healthy controls and CWP using 'resting state' fMRI.

We hypothesized that the effect of pain stimulation on functional connectivity in DMN and ECN is more pronounced in CWP than in healthy controls.

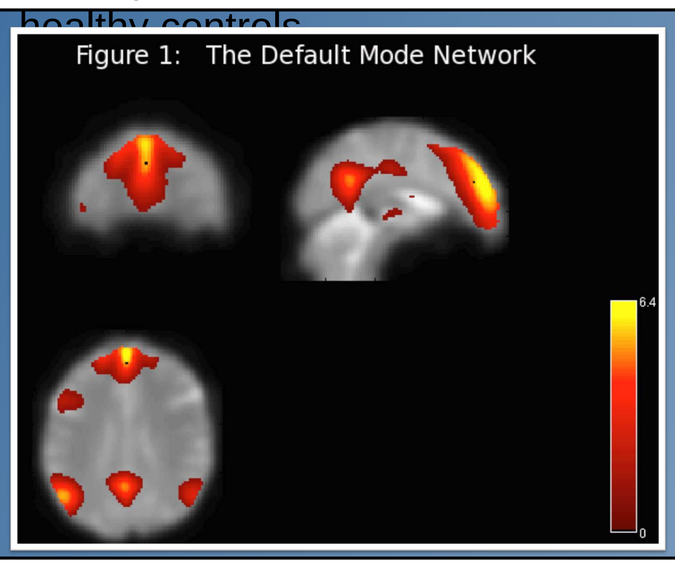

Figure 1: The Default Mode Network

Materials and methods

The participants (all female) were 36 healthy controls (HC) (mean age: 50.7, SD 11.0, range 22-65) and 38 CWP (predominantly fibromyalgia) (mean age: 46.4, SD 11.5, range 21-66). They underwent two 10 min. resting state fMRI sessions, one before and one after a pain fMRI task.

We utilized a group independent component analysis[4] in order to identify the DMN (Fig 1) and left and right ECN (Fig 2). These networks were then tested for connectivity differences within-group related to pain stimulation, and between-group (HC or CWP).

Results & Discussion

Before pain stimulation

Differences were found only in the right ECN. CWP showed less connectivity in the right thalamus, and more in the right parahippocampal gyrus than HC. These two regions are not primary related to the ECN, however the thalamus is part of the pain matrix and modulates pain information. This region might be hypoactive in patients due to their chronic pain experiences disrupting thalamic connectivity.

After pain stimulation

Observed differences were in the DMN ad the left ECN. The left parahippocampal gyrus in the DMN showed increased connectivity for CWP compared to HC, which supports our hypothesis[1] (Fig 3). The increase of parahippocampal connectivity has been linked to CWP before, and hypothesized to be in relation to factors that may follow and/or enhance pain experiences such as accelerated aging and/or stress[3]. Furthermore the data suggested that pain stimulation disrupted connectivity in the left ECN for both groups of subjects in the midcingulate cortex (CC), bordering the supplementary motor area and the anterior CC (Fig 4). This might be related to the participants trying to suppress motor responses during the pain task between the resting state sessions. On the other hand, anterior and midCC are involved in registering unpleasant feelings, and the unpleasantness of the task might have an aftereffect of disrupted connectivity.

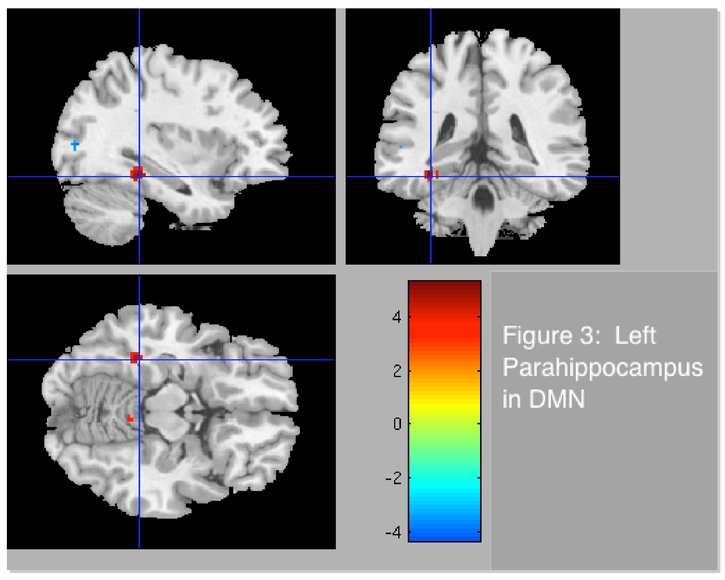

Figure 3: Left Parahippocampus in DMN

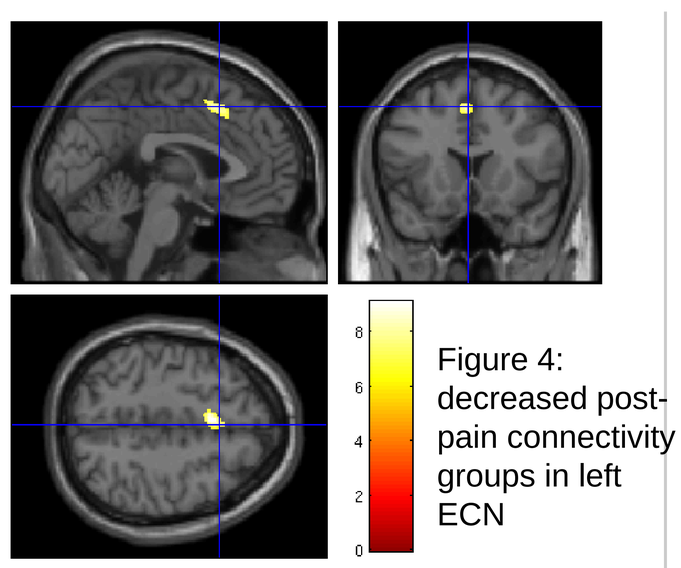

Figure 4: decreased post-pain connectivity groups in left ECN

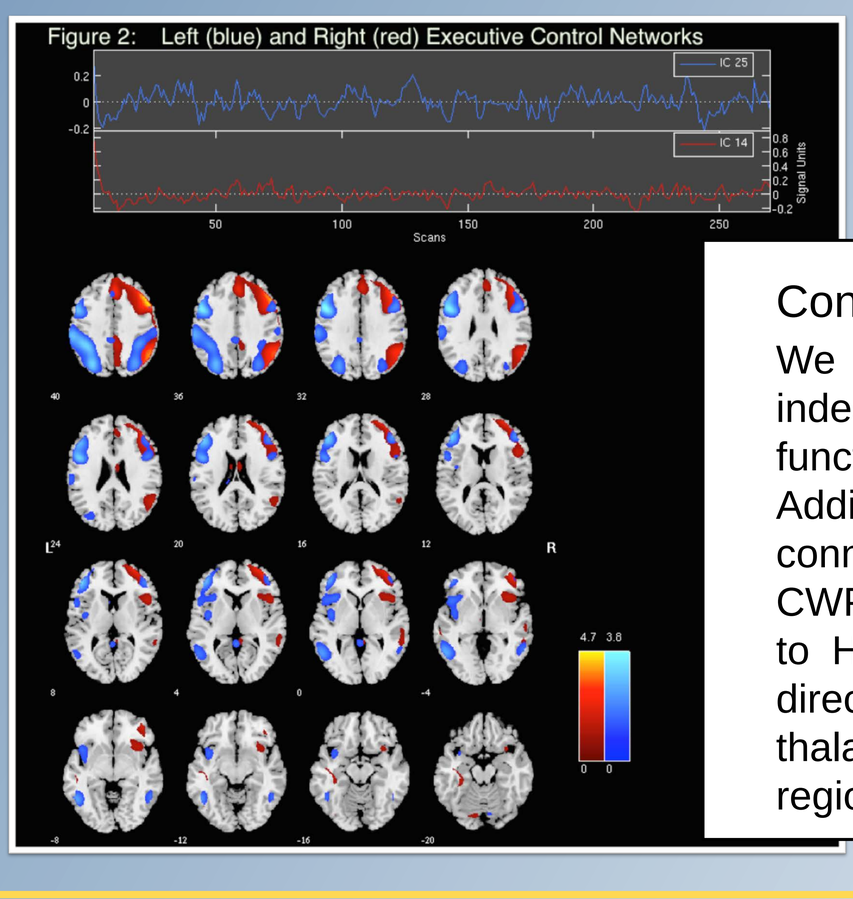

Figure 2: Left (blue) and Right (red) Executive Control Networks

Conclusions

We conclude that pain stimulation indeed significantly alters DMN functional connectivity in CWP. Additionally, decreased functional connectivity in left ECN occurs in CWP after pain stimulation, similar to HC. Future investigations target direct functional connectivity of the thalamus and the anterior CC, regions affected by chronic pain.[6]

More Methods

Of the CWP participants, 10 were free of any indication of depression, the others were diagnosed with mild to more severe depression, and/or anxiety problems. The effect of depression or anxiety on pain perception is a future aim of this study. The control group was free of indications of depression or anxiety.

fMRI parameters: single-shot EPI sequence, TR = 2.2s, TE = 35ms, FA = 77° , voxel size = 3x3x3 mm3 (no gap), 35 slices, FOV = 240 x 240 x 105 mm^3, 270 dynamics.

The pain stimulation task consisted of two sessions where a cuff placed around the lower leg was inflated according to a fixed threshold (session 1) or the individuals pain threshold (session 2).

The images were preprocessed with SPM85. Then, the group ICA results were tested within-group with a paired t-test and between-group with a two-sample t-test, also in SPM8.

Literature

1 Napadow V, LaCount L, Park K, As-Sanie S, Clauw DJ, Harris RE (2010). Intrinsic brain connectivity in fibromyalgia is associated with chronic pain intensity. Arthr Rheum 62(8)

2 Seminowicz DA, Davis KD (2007). Pain enhances functional connectivity of a brain network evoked by performance of a cognitive task. J Neurophys 97(5)

3 Kuchinad A, Schweinhardt P, Seminowicz DA, Wood PB, Chizh BA, Bushnell MC (2007). J Neurosci 27(15)

4 GIFT package: http://mialab.mrn.org/software/gift/

5 SPM software: http://www.fil.ion.ucl.ac.uk/spm/

6 Zhuo M (2013). Long-term potentiation in the anterior cingulate cortex and chronic pain. Phil Trans R Soc B 369 20130146

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