Beyond feeling: chronic pain hurts the brain disrupting the default-mode network dynamics

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INTRODUCTION

- Compared with normal individuals, the brain of chronic pain patients is never truly at rest, due to the continuous pain percept.
- The rest (or default) brain state, acording to recent fMRI studies, corresponds to an antagonistic/agonistic equilibrium quantified by an even distribution of negative and positive functional correlations. We hypothesized that chronic pain corresponds to a disruption of this dynamic balance.
- We used fMRI to study chronic back pain (CBP) patients and matched healthy controls during the execution of a minimally demanding visual attention task.
- We discovered that CBP patients, despite performing the task as well as the controls, exhibit reduced de-activation in medial prefrontal (mPFC) and posterior cingulate/precuneus (PCC) cortices. These areas are primary components of the default mode network (DMN) – a network that is more active at rest and implicated in processing self-referential information.

METHODS

- 15 CBP patients and 15 healthy controls participated in this study
- In the scanner, subjects used the finger-span device to track the changes in the height of a bar projected on a screen (Panel 1).
- GLM model (FSL software; fmrib, Smith et al. 2001) was used to identify brain areas that were activated and de-activated during the task (Panel 2).
- Percent BOLD change was extracted by computing deviation from the mean for voxels within the ROI and averaging the 9 stimulus repetitions for each trial (Panel 3).
- Functional networks were produced by extracting the BOLD time series from a seed region and then computing the correlation coefficient with all other brain voxels (Panel 4).

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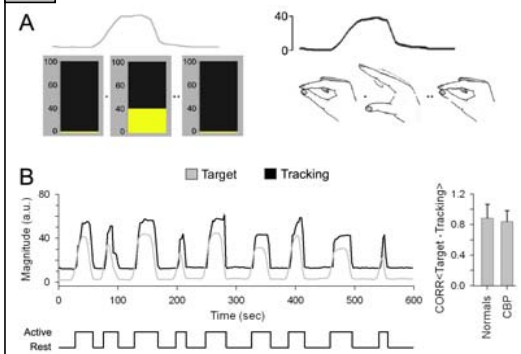
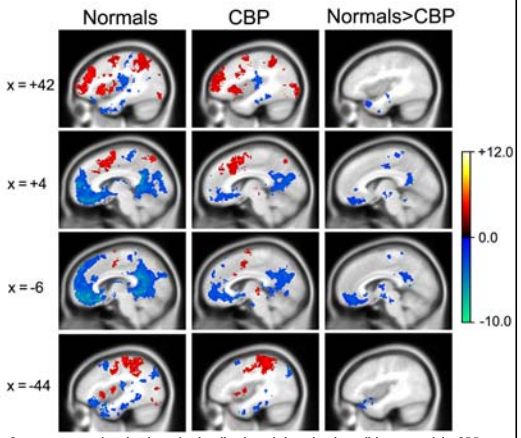
1 Visual attention task and performance



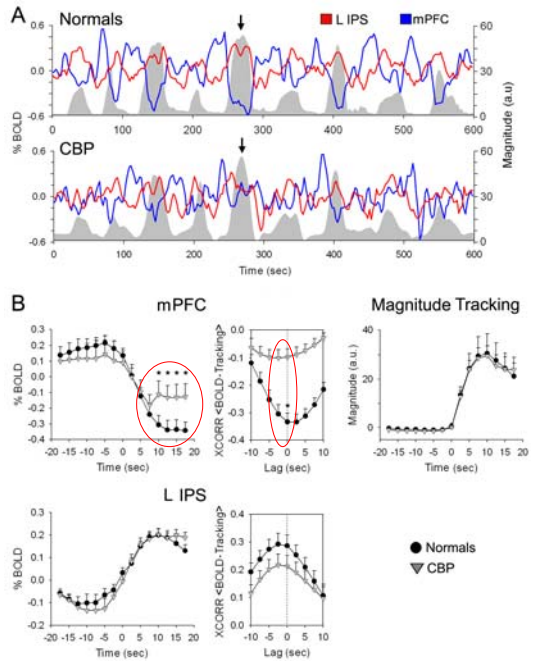
A: Illustration of the task in which subjects continuously tracked the changing vertical height of the target (grey trace) with the modified finger-spanning joystick (black trace)
B: An example from a subject performing the visual attention tracking task. The active/rest time plot shown below represents the vector used to identify brain regions that are activated or deactivated during the task. **Right inset,** Comparison of the group averaged correlation coefficients between the target and its tracking (± SD) demonstrates that the two groups performed the task similarly.

2 Brain activity differences between CBP and healthy controls



Group averaged activations (red-yellow) and deactivations (blue-green) in CBP and healthy controls. Activations were comparable between the two groups, while CBP patients exhibit less deactivation than normal subjects mainly in mPFC, amygdala, and PCC, all of which are considered part of the DMN

3 Differences in time course of BOLD signal between CBP patients and healthy controls

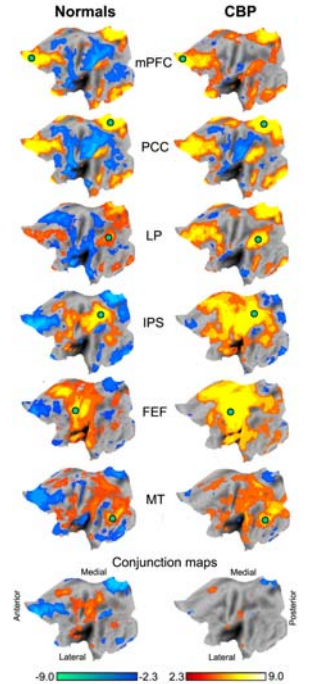


A: Group-averaged BOLD signals from mPFC (blue) and LIPS (red) for controls (top) and CBP patients (bottom) are shown superimposed on the respective group-averaged tracking time courses (grey). The mPFC BOLD signal is more deactivated in normal subjects than in CBP patients each time the subject engages in tracking (see arrow, for example).
B: Triggered average of BOLD responses for mPFC (top) and LIPS (bottom) relative to transition from rest to tracking. The mPFC BOLD signal is anti-correlated to the task time-course in normal subjects but not in CBP patients. Meanwhile LIPS signal was positively correlated to task execution and did not differ between the groups.

CONCLUSION

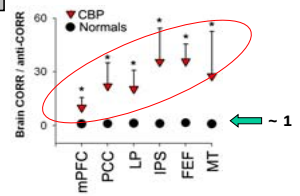
- CBP patients exhibit decreased de-activation of key elements (e.g., mPFC) of the default mode network (DMN).
- CBP patients exhibit a dramatic alteration on the default antagonistic/agonistic balance, as a result of a decrease in the total area of functional anticorrelations together with an increase of the functioal positive correlations.
- This is the first demostration of brain function disrupted by chronic pain. The brain of a chronic pain patient is not simply a healthy brain processing pain information, but rather it is altered by the persistent pain.

4 Disrupted correlation maps in CBP patients.



Group-averaged z-score maps showing regions with significant (p<0.01) correlations (red-yellow) and anticorrelations (blue-green) with three task-negative seed regions: mPFC, PCC, and LP and three task-positive seed regions: IPS, FEF, and MT. The conjunction map in the bottom represents the average of the nodes significantly correlated with five of the six seed regions.

5 Unbalanced default state



Correlated/Anticorrelated ratio is normally around one but it is significantly larger in CBP