PAIN HURTS THE BRAIN: RELATIONSHIP BETWEEN BRAIN ATROPHY AND BRAIN ACTIVITY IN CHRONIC BACK PAIN

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INTRODUCTION

•In an earlier study we used fMRI to identify brain regions involved in spontaneous fluctuations of ongoing pain in chronic back pain patients (CBP) and contrasted this activity to thermal pain in normals and CBP. In a separate study, using voxel-based morphometry (VBM), we demonstrated that CBP is associated with brain atrophy localized to the dorsolateral prefrontal cortices (DLPFC) and right thalamus (Thal). Here we examine the interrelationship between activity and atrophy.

• We also examine connectivity properties of these networks using correlation and partial directed coherence (PDC) analysis.

METHODS

• Gray matter densities in CBP were determined VBM analysis using the SPM 99 package. A nonparametric comparison was performed between a 17 CBP and matched controls (panel 1)

•fMRI activity for spontaneous pain in CBP (n=13) •and thermal induced pain in CBP (n=10) and normals (n=14) were determined using the FSL software package . Events that delineates high-low pain in all pain conditions were derived from the ongoing pain ratings of subjects and convolved with a gamma function to search for brain activity using a GLM model. group average activity was done using the random effect analysis and all appropriate controls were subtracted. The activity maps were transformed into talairach space and loaded on the 152-standard brain(panel 2).

•Brain areas showing significant activity in the 3 pain conditions or areas showing brain atrophy(shown in red) were selected to examine their interrelationships.
For each region, z-scores and activity time-courses were extracted from all subjects.

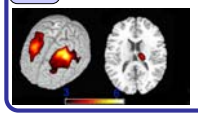
•Z-scores correlations were thresholded at >|0.60|. All correlations presented have a P value < 0.05 (panel 4)

•Time series correlations were threshold at >|0.25|.
All correlations shown have a P value < 0.05 (panel 5)

•PDC is a measure causality. Causality is defined as ability to better predict the current state of a time series when the past states of another time series are incorporated. PDC tests for such causality taking into consideration the influence of all other channels, in frequency space. Significant PDC causality is defined by 10% strength in relation to all other influences. (panel 6)

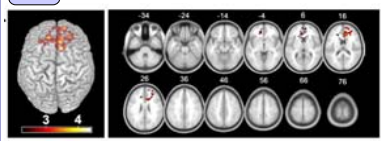
RESULTS

1 VBM Analysis

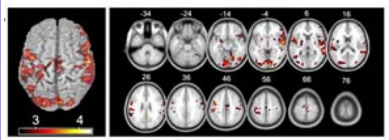


Nonparametric comparison of VBM between CBP and control subjects.Gray matter density is reduced in bilateral DLPFC and right thalamus

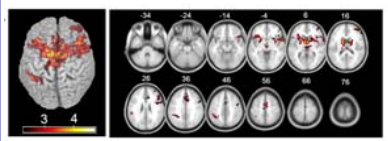
2 fMRI Analysis



Average group brain activity for time periods where spontaneous CBP is high. Activity is limited to the medial prefrontal cortex and rostral anterior cingulate cortex.

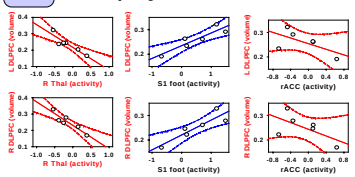


Average group brain activity for painful thermal stimulation in CBP. Multiple primary and secondary somatosensory, insular and cerebellar regions are activated.



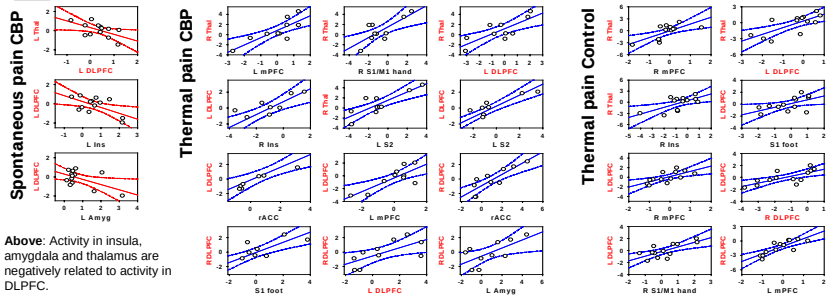
Average group brain activity for painful thermal stimulation in normal controls. Activity is mainly bilateral and seen in insula, basal ganglia, thalamus, cingulate cortex, as well as the right dorsolateral prefrontal cortex.

3 Atrophy v.s. Brain Activity



For spontaneous pain in CBP: the DLPFC volume is negatively correlated to thalamic and cingulate activity and positively correlated with s1 activity.

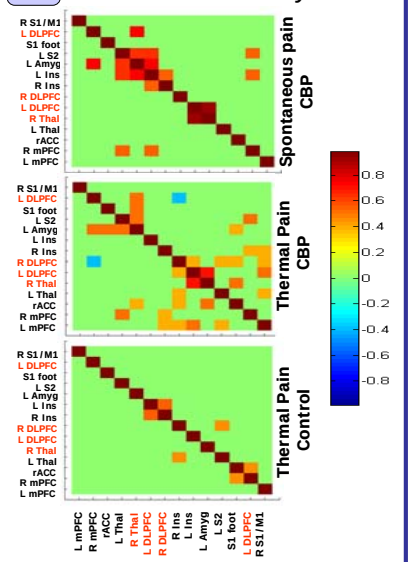
4 Z Scores Correlation Analysis



Above: Activity in insula, amygdala and thalamus are negatively related to activity in DLPFC.

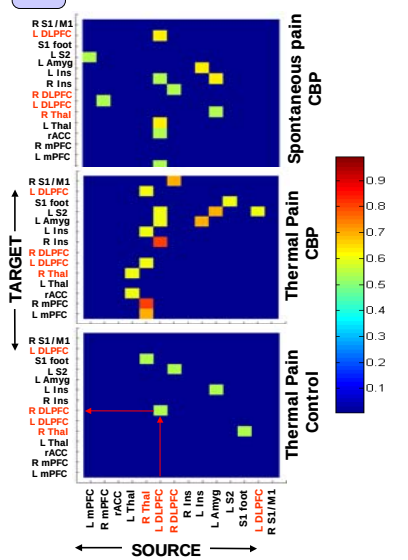
For CBP and control thermal pain: Activity across all areas are positively correlated; implying a change in connectivity between spontaneous and thermal pain.

5 Correlation Analysis



Time series correlation for spontaneous pain in CBP and thermal pain in CBP and controls show results similar to the Z-score analysis in panel 4. *Color codes for the proportion of subjects that exhibit a given correlation.*

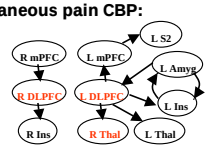
6 PDC Analysis



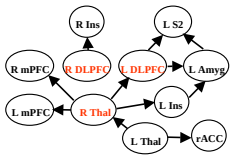
PDC clarifies the causal relationship across examined areas (direction of the arrow). **For spontaneous pain in CBP**: The DLPFC appears to be the main driver of the network. **For thermal pain:** the thalamus is the main driver. *Color codes for the percentage of subjects that exhibit a given correlation.*

7 PDC Maps

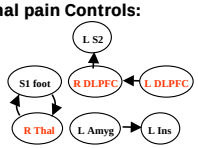
Spontaneous pain CBP:



Thermal pain CBP :



Thermal pain Controls:



CONCLUSIONS

• Given the relationships between brain activity and changes in regional gray matter volumes, the simplest explanation is that local inhibitory interneurons in the DLPFC and thalamus are the main elements undergoing atrophy.

• Spontaneous pain and stimulus induced pain have distinct neural networks.

• here we use a new measure of connectivity, PDC, which reveals causal information flow within the network.

•PDC results show a top-down information flow for spontaneous CBP, namely DLPFC driving other regions. In contrast, stimulus pain exhibit a bottom-up information flow, where the thalamus is the main driver of the network.

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