Brain dynamics for perception of tactile allodynia (touch-induced pain) in postherpetic neuralgia

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INTRODUCTION

Postherpetic neuralgia (PHN) is a debilitating chronic pain condition often accompanied by a sensation of pain when the affected region is touched (tactile allodynia). Here we identify brain regions involved in touch-evoked pain, and delineate regions that specifically code the magnitude of perceived tactile allodynia. Given our recent findings (Baliki et al. 2006; Geha et al. 2007). Our main hypothesis is that tactile allodynia and spontaneous pain should be represented in similar brain regions, involving sub-cortical regions rather than cortical areas involved in the sensory representation of acute pain.

METHODS

• Eleven patients with PHN (10 females) of at least 3 months duration participated in this study; they all rated spontaneous pain > 3/10, and allodynia > 1/10 on VAS.

• Patients were scanned at three different sessions before, 6 hours and 2 weeks after treatment with Lidocaine patches.

• During scanning patients received intermittently non-painful touch stimuli to the affected area to elicit allodynia (**allodynia task**), and to the opposite unaffected side (**touch task**).

• Patients rated their total pain (spontaneous + allodynia) while receiving the non-painful stimuli using a finger-span logging device; they also rated the length of a bar moving at a rate taken from their own pain rating (**visual task**) in a separate scan.

• Average brain maps were generated using the stimulus time course, or the rating time course using FSL 3.3.

BOLD signal was extracted from ROIs taken from the map activation clusters in panel 2 and processed in Matlab.

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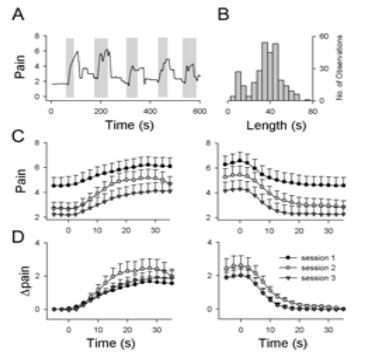
1 Task design and Pain rating



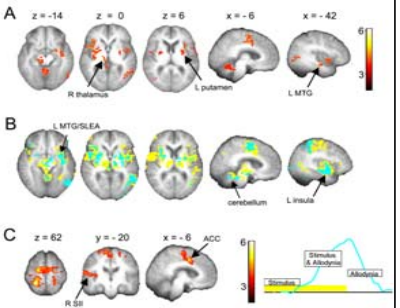
A example of allodynia pain rating from one subject superimposed on the time windows of the touch stimulation.

B shows the distribution of the frequency of each touch stimulus time window used.

C average time course of total pain rating during the allodynia task at time windows of pain increases and decreases.

D same as **C** after discounting spontaneous pain. Note that although total pain decreased with treatment allodynia intensity did not.

2 Brain components of PHN allodynia

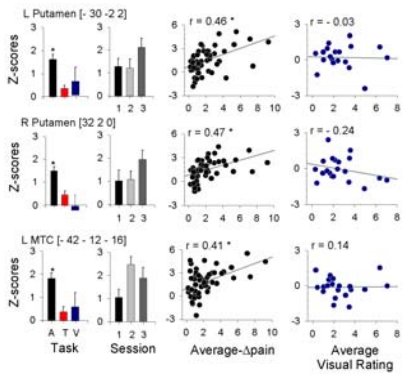


A Average brain activity for allodynia derived using the stimulus time course as the variable of interest.

B Average brain activity for allodynia derived using the stimulus time course (yellow) and for pain rating time course (light-blue).

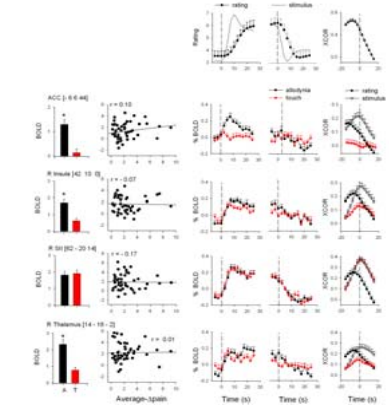
C Paired t-test results (fixed effects, $p < 0.05$), between the two maps shown in (**B**). The components of stimulus derived allodynia show significantly more activity than those for pain rating derived allodynia in SII, bilateral MI/SI, SMA, and ACC.

3 Allodynia intensity encoding



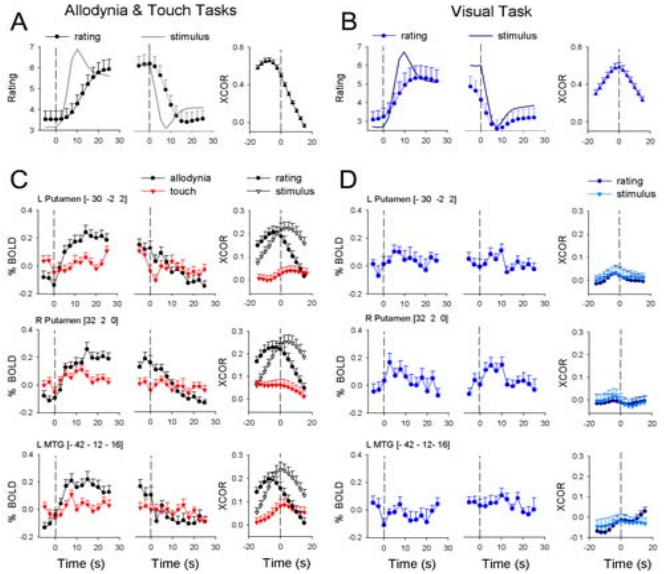
PHN allodynia intensity is encoded in the putamen and medial temporal cortex (MTC). The first panel shows significant increase in brain activity in bilateral putamen and left MTC (including the amygdala/extended amygdala) during the allodynia task (black histogram) compared to the touch task (red histogram) and the visual task (blue histogram). The second panel shows that there is no treatment effect of Lidocaine on brain activity. Scatter plots shows the correlation between the putamen and MTC brain activity and allodynia intensity (left) and change in bar length (right).

5 The "acute pain matrix" does not encode allodynia intensity



Same analysis as in panel **4** **A** and **C** for areas commonly described as part of the acute pain matrix. We show in addition the histogram plot of average brain activity in Z-scores for both the allodynia task and the non-painful touch task.

4 Temporal properties of areas encoding allodynia intensity



A shows stimulus (continuous line) and averaged ratings for tactile allodynia, relative to start and end of the stimulus (first and second panels, respectively).

B shows stimulus (continuous line) and averaged ratings for visual task (all convolved with hemodynamic response function). For both tasks, average cross-correlation (XCOR) between stimuli and ratings is also shown.

C The three rows show regional BOLD time courses relative to start and end of stimuli, as well as cross-correlations (XCOR) with stimuli and ratings, for tactile allodynia and non-painful touch.

D BOLD time courses and cross-correlations are shown for the visual task for the same brain regions as in (**C**).

CONCLUSION

• This is the first demonstration of tactile allodynia pain-related brain activity in PHN and the interrelationship between tactile allodynia and spontaneous pain in chronic pain.

• Tactile allodynia, in contrast to non-painful touch, preferentially activated: 1) cortical areas thought to be involved in sensory (SII, insula), motor (MI, SMA, cerebellum), cognitive/working memory (PFC), and affective/attentional (ACC) processes; and 2) sub-cortical areas involved in sensory (thalamus), sensorimotor behavior (basal ganglia), and hedonics (MTC) processes.

• Most of these areas are seen to be activated by acute pain in normal subjects (Apkarian et al. 2005) and are also observed to be participating in tactile allodynia.

• No area showed a better correlation to ratings of tactile allodynia in contrast to the stimulus provoking tactile allodynia.