An fMRI-pharmacological study of modulation of chronic PHN pain by topical lidocaine

A. Apkarian[1], Y. Sosa[1], M. Baliki[1], T. Parrish[2], R. Harden[3], J. Paice[4], D. Chialvo[1];

1.Department of Physiology, 2. Department of Radiology, 3. Rehab Institute, 4. Department of Oncology and Hematology; Northwestern University Medical School, Chicago, IL 60611

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INTRODUCTION

Chronic neuropathic pain conditions are usually resistant to pharmaco-therapy. LidoDerm patch has been shown to be effective in reducing the pain of post herpetic neuropathy (PHN). Here we present preliminary data where we examine brain activity related to ongoing spontaneous pain and to stimulus evoked (touch allodynia) pain in PHN, and compare the effects of acute to that of longer-term use of LidoDerm.

METHODS

• One patient suffering from PHN was studied with fMRI for pain. He refrained from analgesic medications for 24 hours prior to the study.

•The patient was scanned prior, 6 hours, and 2 weeks post continuous use of LidoDerm.

•Prior to scanning the patient was trained to use the finger-span device to rate magnitudes (fig. 1).

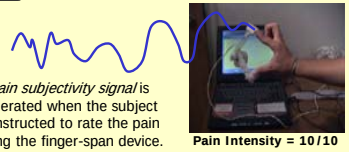
•In the scanner the patient rated 1) the spontaneous fluctuations of the ongoing pain in the absence of any external stimulation (baseline pain rating) using the finger-span device, 2) rated his fluctuations in pain upon the application of a random series of external mechanical stimuli (stimulus pain rating) either to the body area having PHN or to a control area (fig.2) and 3) the length of the bar that fluctuates in time in a pattern derived from their own ratings of pain (visual control signal).

• The signals for pain and visual control are used to calculate the vectors used to search for the BOLD signal and to control for various contaminants (fig. 3).

•BOLD responses is determined using FSL software (fmrib, Smith et al. 2001).

RESULTS

1 On-line signal for pain subjectivity and visual control.



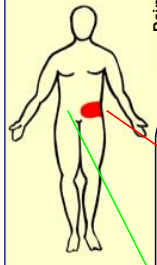
• *Pain subjectivity signal* is generated when the subject is instructed to rate the pain using the finger-span device.

Pain Intensity = 10/10

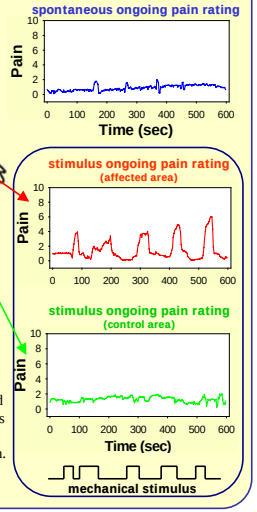
• *Visual control signal* is generated when the subject is instructed to follow a recorded pain rating projected on a screen using the finger-span device.

Pain Intensity = 0/10

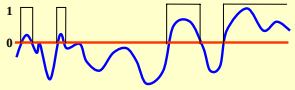
2 Spontaneous and stimulus ongoing pain ratings



Mechanical stimuli were applied using a brush in a pseudo-random fashion to the affected (red) and control areas during different scans within a given session.



3 Vectors and covariance matrices.



• *A binary vector (P_b)* for high – low spontaneous ongoing pain is generated.The mean value of pain subjectivity signal is calculated. Pain ratings having a value larger and smaller than the mean are designated by 1 and 0, respectively.

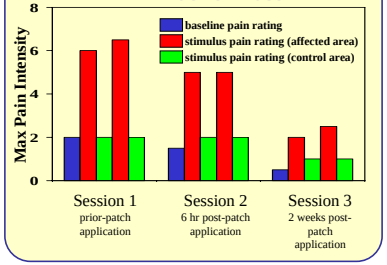
• *A binary vector (P_s)* for high - low ongoing pain upon external stimulation to the affected area is generated.The mean value of stimulus pain rating signal is calculated. Pain ratings having a value larger and smaller than the mean are designated by 1 and 0, respectively.

•*A binary vector (P_c)* for high - low ongoing pain upon external stimulation to the control area is generated.The mean value of stimulus pain rating signal is calculated. Pain ratings having a value larger and smaller than the mean are designated by 1 and 0, respectively

•*A binary vector (**V**)* for visual control is generated from the visual control signal in a similar fashion to P_s. BOLD responses to ***V*** control for motor component.

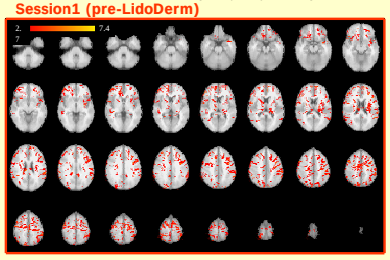
•*A second control vector (S_s)* is generated by inverting in time the original stimulus pain rating. This vector has the same statistical properties as P_s but does not correlate with the pain experience. S_s is used to subtract non-specific activations.

4 Pain intensity ratings were significantly reduced after LidoDerm use



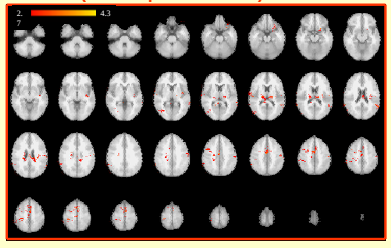
5 Brain activity was significantly reduced after LidoDerm use

Activity map for the group average of stimulus pain ratings- controls (P_s - P_b - P_c - V-S_s) for Session1 (pre-LidoDerm)



•Multiple prefrontal cortical areas are activated. Left SI/MI regions are also activated, which correspond to the right hand used for ratings since this comparison also identifies the times where the rate of hand movement rate is maximal. In addition, multiple anterior cingulate areas are activated as well as, bilateral SII, anterior insula and thalamus.

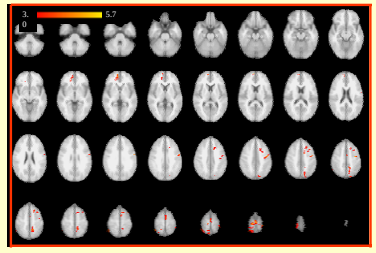
Activity map for the group average of stimulus pain ratings- controls (P_s - P_b - P_c - V-S_s) for Session2 (6-hours post-LidoDerm)



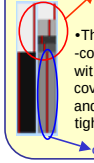
•Note the significant attenuation in brain activity as compared to those in session1. Active brain areas encompass anterior cingulate, posterior insula and some SI and SII areas.

•NOTE: The group average for sessions 3 (2-weeks post-LidoDerm) did not yield any significant brain activity.

6 Activity map for the group Average of all stimulus pain ratings (affected area) –controls for all 3 sessions with their respective mean pain intensities as covariates



Design matrix



•The group average of all stimulus pain ratings -controls for all 3 sessions (P_s -P_c -P_b - V -S_s) with their respective mean pain intensities as covariates exhibit activity in prefrontal cortex and anterior cingulate. These activities are tightly correlated with the pain intensity.

CONCLUSIONS

•Initial analyses indicate that stimulus related PHN pain activates brain regions identified in neuropathic pain conditions, such as in neuropathic chronic back pain and sympathetically maintained pain.

• A single patch used for 6 hours was able to reduce the ongoing pain ratings as well as the stimulus-evoked allodynia pain by 50%. This attenuation in pain perception was maintained with continuous use of the patch for 2 weeks; and decreased brain activity in all areas identified initially.

•Contrasting these activations to other chronic pain conditions, should reveal pathway differences between inflammatory and neuropathic chronic pain conditions.

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