From acute to chronic pain state: Long-term telemetric recording of cortical activity in chronic constriction injury (cci) rats.

A. Apkarian[1], M. Baliki[1], H. Berra[1], O. Calvo[2], D. Chialvo[1], S. Lavarello[1].

[1]Dept. of Physiology, Northwestern University Medical School, Chicago, IL, 60611, [2] Physics Dept., Universidad de las Islas Baleares, Palma de Mallorca, Spain.

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Introduction

Despite many advances, the long-term central nervous system reorganization associated with neuropathic pain is poorly understood.

In this project we monitor the immediate effects of chronic constriction nerve injury over pain behavior and brain cortical electrophysiology in freely moving rats.

Hypotheses:

Our human brain imaging studies suggest that chronic neuropathic conditions, consistent with the behavioral changes, should re-organize cortical electrical dynamics. Thus, we expect to see:

- In the *transition* from acute to chronic:
  i) increased oscillations in resting EEG, at specific frequencies, and perhaps at specific phases of the diurnal cycle.
  ii) more generalized cortical responses to noxious stimuli, with activity switching from contralateral to bilateral thermal-evoked potentials.
  iii) increased synchronization in resting EEG and in thermal-evoked potentials, especially between parietal leads.

- Once neuropathic behavior is established:
  i) increased oscillatory activity in resting EEG localized to the prefrontal electrode.
  ii) cortical responses to noxious stimuli spreading to prefrontal cortex.
  iii) increased synchronization in resting EEG and in thermal-evoked potentials, especially between parietal and prefrontal leads.

- When neuropathic behavior subsides brain EEG and evoked activity revert back to the pre-injury patterns.

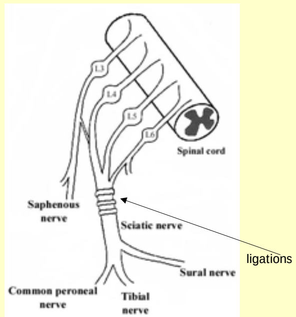
Methods

- **Animals & surgery**: Adults Sprague-Dawley rats are used. One group receives the chronic CCI protocols (Bennet & Xie 1988, see Figure) the other sham surgery.

- **Pain behavioral testing:** Animals are studied behaviorally from 2 weeks prior to 4 weeks post surgery. Sensitivity to mechanical and cold stimuli as well as thermal responses are examined (using AlgoTrack, Hot Plate, and Plantar tests).

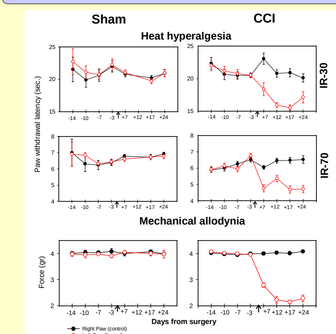
- **EEG telemetry**: Long term EEG radio-telemetry recordings are made using implanted transmitters (Data-Science Instruments) (3 leads, right frontal, right parietal and left parietal cortex).

Chronic Constrictive Injury Model



Bennett and Xie (Pain 33: 87, 1988)

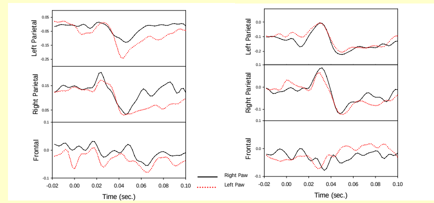
Mechanical & Thermal Responses



Paw withdrawal latencies for Infra Red (IR) intensities 30 and 70 *decreased in the treated paw of CCI rats 7 days post ligation.* Mechanical sensitivity of the treated paw *was significantly increased* after ligation (arrow).

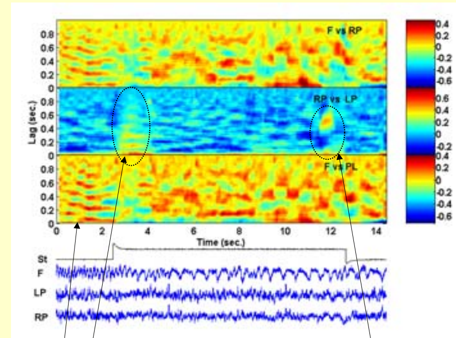
Cortical Dynamics in Response to Painful Thermal Stimuli

Evoked Potentials



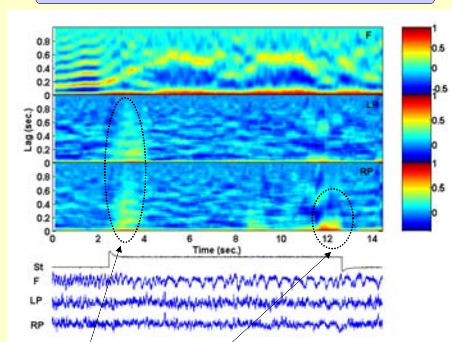
Evoked potentials in response to painful thermal stimuli (starting at time = 0). Plotted are group averages for Sham (n = 3) and CCI (n = 3) rats, from 7 to 40 days post-surgery (102 stimulus-responses per group). Black corresponds to cortical responses to stimuli delivered to the right paw; and red broken to the left (operated) paw. Even though this is a small sample, there is apparent enhanced bilateral potentials in CCI animals, suggesting increased excitability and synchronization across the parietal electrodes.

... and Coherence



Crosscorrelation (top color graphs) of the EEG channels F,LP,RP in response to thermal stimuli (St). Notice that the initial frontal-to-parietal synchrony is destroyed and replaced by the brief parieto-parietal synchrony. Just preceding paw withdrawal this brief parietal synchrony reappears.

Stimulus-triggered Oscillations



Autocorrelation (top color graphs) of EEG (channels F,LP,RP) in response to thermal stimuli (St). Notice somatosensory oscillations at stimulus start and just preceding paw withdrawal. The slowing-down of frontal oscillations is often seen.

Future directions

Cortical states during the transition from acute to chronic pain in animal model can be identified by the analysis of stimulus evoked potentials.

Future studies will investigate the time evolution of the baseline EEG oscillations, as well as the behaviorally triggered EEG oscillations and synchronizations.

It will be essential to clarify those aspects related to pain from others confounders (attention, arousal etc).

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