From acute to chronic pain state: telemetric electrophysiology mapping plasticity of somatosensory cortex in chronic constriction injury rats

H.H. Berra, S. Lavarello, M. Baliki, D.R. Chialvo, A.V. Apkarian
Department of Physiology, Feinberg Medical School, Northwestern University, Chicago, IL, 60611, USA.

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INTRODUCTION

Peripheral injury can give rise to cortical reorganization. Partial peripheral nerve injuries are used as animal models for human chronic pain states, because such animals exhibit pain-like behavior. In this study we examine the relationship between behavioral changes following chronic constriction injury (CCI) and the concurrent cortical reorganization, by monitoring the temporal evolution of these parameters in animals equipped with telemetric recordings.

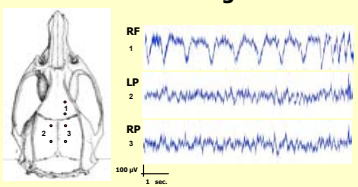
METHODS

In freely moving Sprague-Dawley rats with implanted transmitters (Data-Science Instruments) we monitor the effects of chronic constriction nerve injury (CCI, Bennett & Xie, 1988), to relate pain behavior and brain cortical electrophysiology. Animals are implanted with bilateral parietal (RP, LP) and unilateral right prefrontal (RF) electrodes (n = 23 animals monitored over 5 weeks).

Pain behavioral testing: Animals are studied behaviorally from 1 week prior to 4 weeks post surgery. Sensitivity to mechanical as well as thermal responses are examined. Mechanical responses are quantified using Von Frey hairs induced response threshold forces. Thermal responses are quantified by withdrawal latencies to different intensity infra-red stimuli, on the Plantar Test.

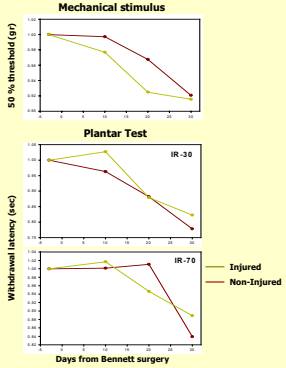
Evoked potentials: Thermal stimulus related evoked potentials (EPt) are collected at different time-points relative to the peripheral induction of CCI. Also large fiber mediated electrical evoked potentials (EPe) are recorded, under anesthesia.

1 EEG radiotelemetry recordings



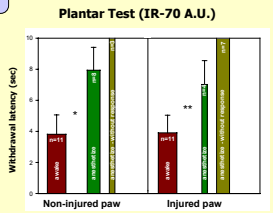
RESULTS

2 Mechanical & Thermal responses



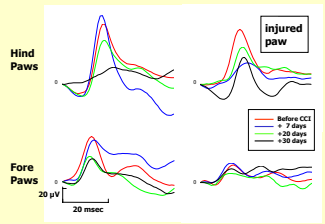
Mechanical thresholds are constant up to 10 days, and decrease bilaterally by day 30 after unilateral CCI injury. Thermal paw withdrawal latencies, for infrared (IR) intensities (30 & 70), show the same temporal evolution as the mechanical responses ($p<0.05$ at 30 days; n=23 animals for all measures).

3 Anesthesia effects



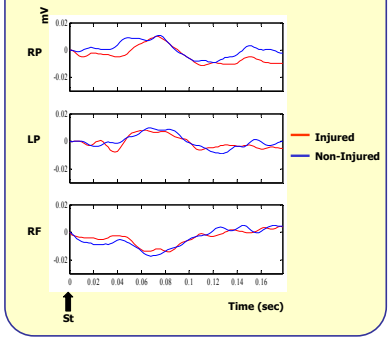
One month after CCI, under anesthesia withdrawal latencies were longer, and the non-injured side shows more responses. Therefore, spinal excitability seems higher on uninjured side, after one month (n = # of animals).

4 Large fiber mediated evoked potentials



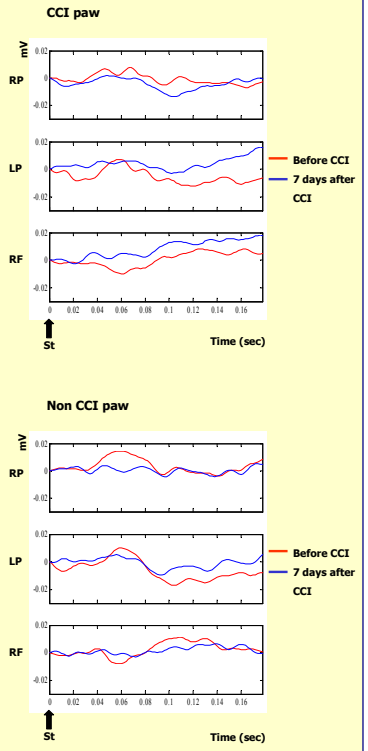
Group averaged (n=11) electrical stimulation contralateral evoked potentials (cEP) show a peak around 15 msec for forepaw and 20 msec for hind paw stimulation (corresponds to ~ 10 m/s conduction velocity). The cEP amplitude for CCI paw decreases in 4 days, and recovers in 20 days; while for the non-injured hind paw cEP decreased only after 30 days ($p<0.05$). No significant changes are seen for forepaw cEPs.

5 Thermal stimulus related evoked potentials



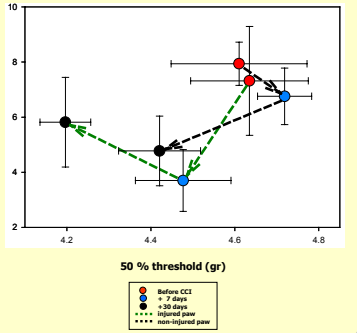
Thermal IR stimuli (70 A.U.) give rise to a well defined EPt peaking around 65 msecs. The EPt is seen in both parietal cortices (RP & LP), and peak in the frontal cortex (RF) as a negative peak. Responses are similar for stimulating either hind paw.

6 Changes in EPt after CCI injury



Comparing EPt amplitudes before injury to 7 days after CCI, we observe preserved EPt in contralateral parietal cortex from the CCI hind paw, and its disappearance everywhere else including from stimulation of non-injured hind paw ($p<0.05$). EPt is average for ~ 40 trials in 23 animals.

7 Mechanical thresholds vs. electrical evoked potentials



For the injured paw, initially (7 days) EPe decrease in amplitude with no change in mechanical thresholds, later (30 days) EPe partially recover while mechanical thresholds are decreased. For the non-injured paw, threshold decreases late after injury (30 days) together with decreases in EPe.

SUMMARY & CONCLUSIONS

1. We observe distinct evoked potentials for mechanical and thermal stimuli.
2. The evoked potentials change in time following unilateral CCI.
3. The changes in evoked potentials are not causally related to the observed mechanical and thermal threshold changes.
4. Anesthesia independent component of the tested behavior is spinally mediated.
5. Therefore, the cortical reorganization does not reflect the tested behavior. This suggests that spinal reflexive behaviors measured in CCI are not related to the induced cortical plasticity.

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