BEYOND PAIN: FUNCTIONAL ALTERATIONS IN THE REWARD-AVERSION BRAIN SYSTEM INDUCED BY CHRONIC PAIN

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Objectives: This research project aims at understanding the alterations that occur following the onset of prolonged and stressful pain conditions, in the connectivity of brain areas that process rewarding and aversive stimuli and in areas critical for learning and memory.

Methods: For achieving our goal we use a combination of novel decision-making and working-memory operant tasks together with state-of-the-art multielectrode neurophysiology recordings in awake freely moving animals. In a typical experiment we chronically implant 16-32 tungsten microwires in up to 4 brain areas.

Final results: We obtained results on five distinct topics:

a) using multielectrodes implanted in the orbitofrontal cortex of adult rats performing the Rodent Gambling Task, we have shown that the neuronal firing rate was correlated with the probability of choosing a low versus high-risk food reward in each trial.

b) using multielectrodes implanted in the hippocampus of rats performing a food-reinforced alternation task, we showed that neuropathic pain induces an increase of the number of place fields encoded in the hippocampal networks.

c) using continuous 24-hour recordings in the thalamocortical loop, we showed that chronic pain disrupts sleep patterns, and causes a large decrease in the functional connectivity in the thalamocortical axis.

d) using in vivo recordings, patch clamp in brain slices, and various behavioral assays, we showed that pain increased neuronal activity in the amygdala that triggered a decrease in prefrontal activation and impaired decision-making.

e) using multielectrodes implanted in the hippocampus and in the prefrontal cortex we showed that pain induces a clear impairment of working memory performance that is temporally correlated with a decrease in single neuron activity in the mPFC.

f) we demonstrated that the lack of pain in the KO mice Prrx1+/− of congenital hypoalgesia causes a behavioural and neurophysiological pattern of brain activity that is the inverse of what we observe in animals with chronic pain.

Conclusions: Our studies demonstrated that chronic pain causes a wide alteration in the functional connectivity of limbic and somatosensory brain circuits, and raises the hypothesis that therapeutic strategies aimed at reversing these alterations may be a valid tool for prolonged pain relief.
Publications: 1 book chapter, 11 published papers, and 3 papers in revision in international peer-reviewed journals of neuroscience (average impact factor of published papers: 5.34).

Book chapters:

Full papers:
Cardoso-Cruz H, Lima D, Galhardo V (2011) Instability of spatial encoding by CA1 hippocampal place cells after peripheral nerve injury. European Journal of Neuroscience, 33:2255-2264

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