Experience of Pain: functional changes induced by chronic pain in the neuronal circuits of reward and aversion

Results:

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.

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.

The results of this project showed that:

a) the neuronal firing rate in the orbitofrontal cortex was correlated with the probability of choosing a low versus high-risk food reward in each trial, and that chronic pain reduced the fraction of risk-aversive neurons;

b) neuropathic pain induces an increase in the number of place fields encoded by hippocampal neurons;

c) chronic pain changes the circadian behavioral state leading to a disruption of sleep patterns, and that there was a large decrease in the functional connectivity between the somatosensory cortex and somatosensory lateral thalamus;

d) pain increases neuronal activity in the amygdala triggering a decrease in prefrontal activation and impairing decision-making;

e) pain induces an impairment of working memory performance, decrease in single neuron activity in the mPFC, and reduction in the frontohippocampal connectivity correlated with correct performance.

f) congenital lack of pain in Prrx11 KO mice causes a behavioural and neurophysiological pattern of brain activity that is the inverse of what we observed in animals with either neuropathic or inflammatory chronic pain.

Published work:

BOOK CHAPTERS:

1. Galhardo, V. (2013) Dynamics of thalamic responses to noxious stimuli. In: Encyclopedic Reference of Pain, 2nd ed, Willis WD, Schmidt RF (eds), Springer-Verlag, ISBN 978-3-642-28752-7.

FULL PAPERS IN ISI PEER-REVIEWED INTERNATIONAL JOURNALS

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2. Monteiro C, Cardoso-Cruz H, Dourado M, Matos M, Lima D, Galhardo V (2013). No Pain, Big Gain: decreased anxiety and enhanced learning in the Prrxl1 knockout mice model of congenital hypoalgesia. Nature Neuroscience, second revision.

3. Cardoso-Cruz H, Dourado M, Monteiro C, Matos M, Lima D, Galhardo V (2013). Modulation of hippocampal dorsoventral field connectivity by dopamine D2/3 receptor activation during spatial working-memory performance in a rat model of neuropathic pain. Submitted to Proceedings of the National Academy of Sciences USA.

4. Cardoso-Cruz H, Sousa M, Vieira JB, Lima D, Galhardo V (2013) Prefrontal cortex and mediodorsal thalamus reduced connectivity is associated with spatial working memory impairment in rats with inflammatory pain. Pain, 154:2397-2406.

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6. Pais-Vieira M, Aguiar P, Lima D, Galhardo V (2012) Inflammatory pain disrupts the orbitofrontal neuronal activity and risk-assessment performance in a rodent decision-making task. Pain, 153:1625-1635.

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9. Cardoso-Cruz H, Sameshima K, Lima D, Galhardo V (2011) Dynamics of Circadian Thalamocortical Flow of Information during a Peripheral Neuropathic Pain Condition. Frontiers in Integrative Neuroscience, 5:43

10. 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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12. Monteiro C, Rebelo S, Galhardo V, Reguenga C, Lima D (2011) Postnatal expression of the homeobox gene Prrxl1 (Drg11) is increased in inflammatory but not neuropathic pain. European Journal of Pain, 15:477-481.

13. Ji G, Sun H, Fu Y, Li Z, Pais-Vieira M, Galhardo V, Neugebauer V (2010) Cognitive impairment in pain through amygdala-driven prefrontal cortical deactivation. Journal of Neuroscience, 30:5451-5464.

14. Silva A, Cardoso-Cruz H, Silva F, Galhardo V, Antunes L (2010) Comparison of anesthetic depth indexes based on thalamocortical local field potentials in rats. Anesthesiology, 112:355-363.

Area(s) of interest:

Brain physiology; Aversive neuronal encoding; Pain

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