

Pain control from the Brain. Novel approaches of chronic pain treatment through manipulation of supraspinal areas

Results:

The project was designed to evaluate the possibility of using gene therapy at the central nervous system as an analgesic tool.

Pain suppression through central electrical stimulation, although effective as an analgesic tool, is impracticable since serious secondary effects occur due to stimulation of neurons involved in other brain functions. Viral vector transduction stands nowadays as a way of overcoming this problem by directing manipulation specifically to pain-control neurons. We focused on the possibility of concomitantly inhibit a pain facilitatory center (DRt) and stimulate a pain inhibitory center (VLM) by the use of multiple transduction from each site with the replication-defective herpes simplex virus (HSV-1).

The migration pattern following injection of HSV-1 in the DRt and VLM was studied. In parallel, information on the membrane receptors present in the neurons to be targeted (DRt and VLM pain processing neurons) and on the neurotransmitters used by the neurons to be transduced was collected.

The results collected allowed us to conclude that HSV-1 is particularly well suited for the purpose of the project since it transduces just a few brain areas projecting to the VLM and DRt, allowing a limited but still amplified action upon each one, and areas other than the DRt and VLM that receive axonal terminations of transduced neurons are few. The neurochemical data point to the use of vectors coding for the GABA_B receptor, GAD and noradrenalin at the DRt, and of vectors coding for GABA_B and α_2 receptor antisense molecules at the VLM. Behavior and pharmacological studies aimed at elucidating the effect of appropriate drugs upon injection in the sites of termination of the transduced neurons are however still needed.

Published Work:

Full papers

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Galhardo, V., Apkarian, A. V., & Lima, D. (2002). Peripheral inflammation increases the functional coherency of spinal responses to tactile but not nociceptive stimulation. *J. Neurophysiol.*, 88(4), 2096-2103. doi: 10.1152/jn.00720.2001

Abstracts

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Opinion Papers

Tavares I. Viruses as new soldiers in the fight against pain. *IBMC News*, year 7, n° viii, (2003)

Theses

Pinto M. "Expressão de receptores GABA_B, ópioides tipo μ e NK1 em neurónios nociceptivos do encéfalo. Um estudo pelo *c-fos* no Rato". Master Thesis, Faculty of Medicine of Lisbon (2001)

Martins I. « *Étude de la migration d'une forme recombinante de HSV-1 dans le cerveau depuis le bulbe: implications pour la thérapie génique de la douleur* ». Master Thesis, Conservatoire National des Arts et Métiers, Paris (2003)

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