

TITLE: Intrathecal Capsaicin in Chronic Pain in the Cat

AUTHORS: James M. Sloan, M.D., Radan Capek, M.D., Richard F.H. Catchlove, M.D.

AFFILIATIONS: Departments of Anaesthesia and Pharmacology, Royal Victoria Hospital and McGill University, Montreal, Quebec, Canada.

**INTRODUCTION:** Administration of capsaicin, a homovanillylamide derivative, into the spinal perfusate produces the release of substance P. Substance P has been located in axon terminals in the dorsal horn and there has been considerable speculation that this putative neurotransmitter is concerned with the transmission of nociception via A-delta and especially fine unmyelinated C-fibres. Subcutaneous capsaicin treatment of neonatal rats has produced similar long-term delayed withdrawal of noxious thermal stimuli, and intrathecal injection in adult rats produced similar long-term thermal analgesia. Capsaicin has been used primarily as a selective neurotoxin for the elucidation of the spinal mechanism of pain in the lab animal. In this study we simulated chronic pain in the cat and assessed whether intrathecal capsaicin modulated the pain response.

**METHODS:** Six adult cats, each caged individually, were assessed for pain response using the Formalin Test.<sup>2</sup> 0.1 cc sterile 5% formalin was injected intradermally in the anterior portion of the main pad of the hind paw and a pain rating was obtained using the formula: Pain Rating =  $T_1 + 2T_2 + 3T_3$

180

where  $T_1$ ,  $T_2$  and  $T_3$  are the times in seconds spent in Category 1, 2 or 3 respectively during each 180 sec. block over a period of 30 minutes. Category 1—the injected paw is favored and the animal limps. Category 2—the injected paw is elevated and not in contact with any surface. Category 3—the animal licks, bites or shakes the affected paw. To assess the validity of the formalin test 2 mgms morphine sulfate was injected epidurally at L6-7 space and the animals were retested 1 hour later.

250 ug capsaicin dissolved in glycerin (.15 cc) was injected intrathecally at L6-7 space through a NO.22 spinal needle with the animal anesthetised. The pain rating was reassessed in 24 hours and 7 days post i.t. capsaicin.

**RESULTS:** Composite pain rating curves are shown below for control, epidural morphine and post intrathecal capsaicin. Although epidural morphine did produce a consistent decrease in pain score without sedation, there was no observed difference from control after intrathecal capsaicin. The animals behaviour and motor function were normal and unchanged the day following intrathecal capsaicin.

**DISCUSSION:** This work does not support other studies that show sensory changes after intrathecal capsaicin. Evidence of C.S.F. flow prior to injecting capsaicin, and the marked contracture of the hind limbs after injection, also reported by others, indicate accurate placement of the drug intrathecally. The intradermal formalin consistently produced blanching and subsequent inflammatory changes. Differences in vehicle (glycerol vs DMSO, the solvent used in most studies) seem unimportant as DMSO has been shown to produce no ultrastructural changes when

applied to the spinal cord.

These results lend support to evidence that depletion of spinal cord substance P may not by itself be sufficient to explain the observed changes in noxious thresholds which may be related instead to non-specific damage to the spinal cord.<sup>5</sup> Electron microscopic immunocytochemistry has demonstrated that Substance P is only associated with large vesicles of primary axon terminals.<sup>4</sup> The presence of numerous unlabelled small vesicles in axon terminals containing substance P suggests that these terminals may contain another neurotransmitter which may have been released with our chronic inflammatory stimulus. It is also possible that the production of substance P in the mature animal is not interfered with as it seems to be in the treated neonate,<sup>5</sup> and that, once released the nerve fibre proceeds to replenish its source. The objective of this study was to assess the possible clinical application of intrathecal capsaicin and these results do not support a clinical use at present.

**REFERENCES:** 1. Yaksh, T.L., Farb, D.H., Leeman, S., Jessell, T.M.: Intrathecal capsaicin depletes Substance P in the rat spinal cord and produces prolonged thermal analgesia. *Science* 206: 481-483, 1979. 2. Dubmisson, D., Dennis, S.G.: The Formalin Test. *Pain* 4: 161-174, 1977. 3. Nagg, J., Emson, P.C., Iverson, L.L.: A Reevaluation of the neurochemical and antinociceptive effects of intrathecal capsaicin in the rat. *Brain Research* 211: 497-502, 1981. 4. Pickel, V.M., Reis, D.J., Leeman, S.E.: Ultrastructural localization of substance P in neurons of rat spinal cord. *Brain Research* 122: 534-540, 1977. 5. Ganse, R., Holzer, P., Lembeck, F.: Decrease of Substance P in Primary afferent neurones by capsaicin. *Br. J. Pharmacology* 68: 207-213, 1980.

