

Sensory Innervation and Development of a Model of Connective Tissue Inflammation in the Low Back of the Rat: Implications for the Future Study of Low Back Pain Pathophysiology.

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BACKGROUND: The role of connective tissue in low back pain is not well understood but could involve localized inflammation and sensory neuroplasticity. Progress in this area has been limited by a lack of data describing the sensory innervation of these tissue layers and the lack of an animal model of connective tissue inflammation. The goals of this study are: 1) to characterize the innervation of a subcutaneous connective tissue compartment located in the lumbar region of the rat between the paraspinal and deep back muscles, spanning superficial and deep fasciae (containing loose and dense connective tissue layers), and 2) to develop a model of connective tissue inflammation specific to this compartment.

METHODS: Sensory innervation: Five adult Wistar rats were euthanized and the tissue was fixed by perfusion. Tissue was excised from the low back from the dermis to the deep spinal muscles. Standard immunofluorescent techniques were used to label all nerve fibers (protein gene product 9.5; PGP9.5), sensory nerve fibers (calcitonin gene related peptide; CGRP), motor end plates (alpha-bungarotoxin) and collagen fibers (collagen-1) and imaged with a confocal microscope. Three-dimensional images were created by collecting a series of optical sections through the Z plane of the tissue. Inflammatory model: Six adult male rats were anesthetized and 3% carrageenan was injected subcutaneously. Animals were evaluated at 24 hours, 1 week and 2 weeks. After euthanasia, tissue was collected from the lumbar region from the dermis to the deep spinal muscles for histological analysis.

RESULTS: 1) Sensory innervation: We observed an extensive network of nerve fibers labeled by PGP9.5 in the connective tissue surrounding the muscles in the low back region. A subset of these fibers stained positively for CGRP and terminated within the connective tissue matrix in the layers surrounding the low back muscles. Many of these CGRP immunoreactive fibers were of small diameter < 2µms, and may be Aδ or C fibers. 2) Inflammation model: Carrageenan was well tolerated by the animals, it did not cause any open wounds in the skin or noticeable irritation. Preliminary analysis of data at one week after injection showed an inflammatory infiltrate localized to the subcutaneous connective tissue compartment without spreading into either the skin or into the deep back muscles.

CONCLUSION: These preliminary results show 1) the presence of sensory nerve fibers terminating within the subcutaneous connective tissue compartment in the rat and 2) the feasibility of inducing a localized inflammation within this compartment. Our next step will involve combining these two studies to examine changes in innervation, proliferation and nervous plasticity induced by inflammation in the back. The ultimate goal of this work is to use this model to analyze how inflamed connective tissue responds to the application of manual therapies.