

Nerve Ingrowth Into Diseased Intervertebral Disc in Chronic Back Pain

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FROM ABSTRACT:

BACKGROUND:

In the healthy back only the outer third of the annulus fibrosus of the intervertebral disc is innervated.

Nerve ingrowth deeper into diseased intervertebral disc has been reported, but how common this feature is and whether it is associated with chronic pain are unknown. We examined nerve growth into the intervertebral disc in the pathogenesis of chronic low back pain.

METHODS:

We collected 46 samples of intervertebral discs from 38 patients during spinal fusion for chronic back pain. 30 samples were from pain levels clinically established by discography and 16 samples were from adjacent vertebral levels with no pain. We obtained 34 control samples of intervertebral disc from previously healthy individuals with normal histology within 8 h of recorded death. We used standard immunohistochemical techniques to test for a general nerve marker, a nociceptive neurotransmitter (substance P), and a protein expressed during axonogenesis (growth-associated protein 43 [GAP43]).

FINDINGS:

We identified nerve fibres in the outer third of the annulus fibrosus in 48 (60%) of the 80 samples of intervertebral discs.

Nerves were restricted to the outer or middle third of the annulus fibrosus in the 34 control samples. Among the patients with chronic low back pain, nerves extended into the inner third of the annulus fibrosus in 46% and into the nucleus pulposus in 22% of samples.

Deep nerve ingrowth into the inner third of the annulus fibrosus, the nucleus pulposus, or both was seen in four (25%) of 16 biopsy samples from non-pain levels and in 17 (57%) samples from pain levels.

Of the 16 paired samples from both pain and non-pain levels, five pain-level samples and one non-pain-level sample showed deep nerve ingrowth.

INTERPRETATION:

Our finding of isolated nerve fibres that express substance P deep within diseased intervertebral discs and their association with pain suggests an important role for nerve growth into the intervertebral disc in the pathogenesis of chronic low back pain.

THESE AUTHORS ALSO NOTE:

“Chronic back pain is one of the leading causes of morbidity and loss of work.”

The pathogenesis of chronic back pain is poorly understood.

Chronic low back pain is not caused by nerve root compression.

Leg pain / sciatica can be caused by mechanisms other than nerve root compression.

These authors cite 5 studies that indicate the intervertebral disc is often the source of back pain.

Immunohistochemical staining techniques show that in healthy human intervertebral discs nerves extend no deeper than the outer third of the annulus fibrosis.

Two studies have shown the nerves extend deeper into the annulus fibrosis and into the nucleus pulposus in diseased intervertebral discs.

In this study, these authors “measured nerve ingrowth in terms of how deep within the annulus nerve fibers were seen and whether nerves had penetrated the nucleus pulposus.”

Deep nerve ingrowth was defined as growth into the inner third of the annulus or into the nucleus.

In this study, the overall disruption of the normal architecture of the disc was greatest in the samples taken from painful discs.

DISCUSSION

Substance P is a nociceptive neurotransmitter and pain mediator.

This study shows that there is an association between substance P and disc degeneration, and the “extent of neoneuralisation is greatest at intervertebral disc levels at which the patient experiences pain.”

Most of the nerves identified in this study accompanied blood vessels, indicating both a nociceptive and vasoregulatory role for these nerves.

“Substance P is a nociceptive pain mediator and it is noteworthy that these neural elements did not occur in any of the control discs but were found commonly in intervertebral discs from pain levels.”

“The presence of these neural elements within the nucleus pulposus was a feature only of intervertebral discs from the pain level.”

“Our findings strongly implicate these fibrils in the pathogenesis of chronic low back pain.”

“Why such nerve fibrils should also be present within a small proportion of the anatomically deranged non-pain level intervertebral discs [12% into the inner third of the annulus; 3% into the nucleus] is open to conjecture. One possible explanation is that pain perception requires a nociceptive trigger as well as innervation.” **[Very Important]**

In this study, no control discs showed nerve ingrowth into the nucleus pulposus. Every time nerve ingrowth was found in the nucleus, it was a painful disc.

In this study, not all painful discs had nerve ingrowth into the nucleus pulposus; 30 – 38% did.

In this study, not all painful discs had nerve ingrowth into the inner third of the annulus; about 60% did.

Studies have shown that discal chondrocytes are capable of producing nociceptive triggers including prostaglandins [PGE2]. **[Important]**

“So what is the biological purpose of nerve ingrowth into intervertebral discs? By analogy with other connective tissues, nerve ingrowth into damaged intervertebral discs could mediate various tissue events, notably healing. Initially, an immobilizing might be beneficial, but because the healing process is thought to be poor in this tissue, unproductive nerve ingrowth and pain may result.”

“We have shown an association between the frequency and site of back pain and nerve ingrowth into the intervertebral disc, or more specifically the nucleus pulposus.”

“Nerve ingrowth may be part of the process of disturbed repair, and is therefore of little value.”

KEY POINTS FROM DAN MURPHY

- 1) "Chronic back pain is one of the leading causes of morbidity and loss of work."
- 2) Chronic low back pain is not caused by nerve root compression.
- 3) Leg pain / sciatica can be caused by mechanisms other than nerve root compression.
- 4) The intervertebral disc is often the source of back pain.
- 5) The best method for staining the neurofilaments in the disc is "immunohistochemistry."
- 6) The normal healthy human disc has nerves into the outer third of the annulus.
- 7) Painful discs have the greatest amount of histological degeneration.
- 8) Substance P is a nociceptive neurotransmitter and pain mediator. There is an association between substance P and disc degeneration.
- 9) The "extent of neoneuralisation is greatest at intervertebral disc levels at which the patient experiences pain."
- 10) "Substance P is a nociceptive pain mediator and it is noteworthy that these neural elements did not occur in any of the control discs but were found commonly in intervertebral discs from pain levels."
- 11) "The presence of these neural elements within the nucleus pulposus was a feature only of intervertebral discs from the pain level."
- 12) "Our findings strongly implicate these fibrils in the pathogenesis of chronic low back pain."
- 13) "Why such nerve fibrils should also be present within a small proportion of the anatomically deranged non-pain level intervertebral discs [12% into the inner third of the annulus; 3% into the nucleus] is open to conjecture. One possible explanation is that pain perception requires a nociceptive trigger as well as innervation." **[Very Important]**
- 14) In this study, no control discs showed nerve ingrowth into the nucleus pulposus. Every time nerve ingrowth was found in the nucleus, it was a painful disc.
- 15) In this study, not all painful discs had nerve ingrowth into the nucleus pulposus; 30 – 38% did.

- 16) In this study, not all painful discs had nerve ingrowth into the inner third of the annulus; about 60% did.
- 17) Discal chondrocytes are capable of producing nociceptive triggers including prostaglandins [PGE2]. **[Important]**
- 18) Nerve ingrowth into damaged intervertebral discs mediates tissue healing, which might be beneficial because of initial immobilization, but because the disc is poor in healing “unproductive nerve ingrowth and pain may result.”
- 19) These authors “have shown an association between the frequency and site of back pain and nerve ingrowth into the intervertebral disc, or more specifically the nucleus pulposus.”