■■■ Focused Review

Innervation of the Anterior Spinal Canal: An Update

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Understanding the innervation of the lumbar spine can be a daunting task. Until recently, only macroscopic visualization and crude histological techniques were available to document the presence of nerve fibers in the anterior spinal canal. Using newer immunohistochemical techniques, studies have been able to more thoroughly investigate the innervation of the anterior spinal canal. The presence of sensory nerve fibers has been definitively identified in all anterior spinal structures. These sensory fibers enable any of the spinal structures the capability of being a pain generator. These sensory nerve fibers tend to form dense interwoven plexuses on the posterior longitudinal ligament and ventral surface of the dura mater. The plexuses allow for anastamoses to take place between nerve fibers from multiple segmental levels. This polysegmental formation causes the expression of low back pain to be diffuse, rather than focal. It is these diffuse pain symptoms that create great difficulty in diagnosing and treating spinal canal structures.

Key words: Back pain, innervation, immunohistochemistry, posterior longitudinal ligament, intervertebral disc.

There has been a plethora of research dedicated to establishing the presence of nociceptive nerve fibers within the annulus fibrosus and posterior longitudinal ligament. Absence of these fibers would negate the disc from being responsible as a pain generating structure within the lumbar spine. Luschka was the first to describe the presence of a nerve re-entering the intervertebral foramen and terminating in the substance of the posterior longitudinal ligament and annulus fibrosus of the intervertebral disc (1). This nerve became known as the recurrent nerve of Luschka, and today we refer to it, as the sinuvertebral nerve. Later studies by numerous authors in the early 20th century confirmed Luschka's findings and established that this nerve provided primary innervation to all structures within the spinal canal (2-6).

In an elegant and meticulous anatomic study, Bogduk et al (7) also demonstrated the course of the sinuvertebral nerve using microscopic analysis, it was revealed the sinuvertebral nerve entered the spinal canal through the intervertebral foramen by passing just inferior to the pedicle. Once in the canal, the nerve traveled superiorly along the edge of the posterior longitudinal ligament (7). During this course, multiple branches are given to the posterior longitudinal ligament. A multitude of smaller branches from the sinuvertebral nerve were identified descending from the intervertebral foramen to terminate at the intervertebral disc level of the parent ventral rami (7). Other authors have reported noting the sinuvertebral nerve existing as a number of small filaments outside the intervertebral foramen (8-10). Up to six filaments have been noted by Edgar et al (10). These filaments were not found to merge as they entered the intervertebral foramen, and the largest filament was noted to follow the typical course described above by Bogduk.

The ascending and descending branches of the sinuvertebral nerve combine to form a plexus on the posterior longitudinal ligament (12, 13). This plexus is most likely formed by anastamoses with branches from the sinuvertebral nerve on the opposite side and with those from superior and inferior adjacent levels (14). There is still controversy in the literature regarding regarding how far these ascending and descending branches may travel prior to anastamoses with neighboring branches. Spurling and Bradford et al (3) noted the descending branches passing two segments below their level of entry into the canal. One early study theorized that ascending branches ran along the whole length of the spinal column, thereby forming anastamoses at all levels (15). Other earlier studies were unable to find any evidence of anastamoses between branches of the sinuvertebral nerve (9, 16). They theorized that each sinuvertebral nerve was purely segmental in its innervation. Bogduk et al and others have demonstrated

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anastamoses of ascending branches one level cephalad of their entry point (7,17). It is generally agreed that anastamoses do exist between ascending and descending branches of the sinuvertebral verve. The level of anastamoses still is in question, but prevailing data would suggest that it occurs one to two adjacent levels above and below its level of entry into the spinal canal (7,17).

Thick meningeal branches from the sinuvertebral nerve, thin branches from the nerve plexus of the dorsal posterior ligament, and small branches of perivascular nerve plexuses of the radicular rami of segmental arteries all coalesce to form an anterior nerve plexus on the ventral aspect of the dura mater (10, 18, 19). Stilwell et al (20) was one of the first studies to demonstrate evidence of meningeal branches penetrating the ventral spinal dura in monkeys (20). Three years later, Bridge et al (21) discovered epidural nerves terminating on the dural surface of the cat, dog, and man. In 1961, Kimmel et al (18) documented the presence of meningeal branches from the sinuvertebral nerve penetrating the spinal dura. Using the process of acetylcholinesterase histochemistry, Groen et al (22) was able to demonstrate the presence of a dense plexus of nerve fibers on the ventral dura of the human fetus. A majority of these ventral fibers were thought to be autonomic in origin. Ahmed et al (23) corroborated Groen's findings of autonomic fibers on the ventral dural surface. More recent immunohistochemical studies have also demonstrated the presence of sensory afferent fibers lining the ventral dural plexus (19, 23).

The nerve branches of the posterior ligament plexus also form the primary innervation of the posterior longitudinal ligament and postero-lateral aspect of the intervertebral disc. The first studies to report the presence of nerve endings on the intervertebral disc and adjacent posterior longitudinal ligament were published in the early 1930's (24 - 26). They noted nerve fibers in the posterior longitudinal ligament and on the superficial aspect of the identified nerve fibers within the outer annulus in the early 1940's.

In 1959, Malinsky et al (27) demonstrated the presence of non-encapsulated nerve endings in the outer third of the annulus fibrosus, and encapsulated fibers on the surface of the disc. The greatest number of fibers was noted to occur in the lateral region of the disc, with the anterior and posterior regions demonstrating few nerve fibers (27). These findings were later confirmed by Rabischong et al (28) in 1978 and Yoshizawa et al (29) in 1980. In Yoshizawa's study, they demonstrated the presence of an abundant axonal network in the posterior ligament and outer half of the annulus fibrosus, with abundant free-lying terminals,

often arranged in complex, branched-spray formations. These free-lying nerve fibers were primarily found in the lateral aspect of the disc, and had similar morphology to pain receptors reported elsewhere (30). Histological studies by Bogduk also supported Malinsky's findings, where he noted nerve fibers up to a depth of one-third the total thickness of the annulus fibrosus (7). Bogduk has also reported additional nervous innervation of the disc through pathways other than direct branches from the sinuvertebral nerve. These included direct branches from the ventral rami, and two types of branches from the rami communicantes. All of these branches enter the posterolateral aspect of the intervertebral disc. Branches from the rami communicantes were also noted to travel caudally and overly the subjacent disc (7).

The advent of immunohistochemical techniques has led to reassessment of spinal neural elements. This reevaluation has offered the added advantage of an enhanced precision in delineating neural structures while simultaneously characterizing neural chemical constituents (31). In other words, this technique will not only identify nerve fibers, but can differentiate these fibers from one another based upon the neural peptides used by each specific nerve type. For instance, a number of neuropeptides are known to occur in afferent nerve fibers. These neuropeptides include substance P, somatostatin, cholecystokinin-like substance, vasoactive intestinal polypeptide(VIP), calcitonin gene-related peptide(CGRP), gastrin-releasing peptide, dynorphin, enkaphalin, and galanin (31- 33). Substance P, vasoactive intestinal peptide, and calcitonin gene related peptide are believed to be specific sensory transmitters (33, 34) and may also be involved in nociceptive transmission (35 - 37), neurogenic inflammation (38, 39), and skeletal metabolism. By using specific antibodies to these peptides an afferent sensory fiber may be identified in spinal tissues, whereas primary motor fibers are not.

One of the first reported studies documenting the presence of sensory nerve fibers within the annulus fibrosus was by McCarthy et al (40) in 1991. In their study calcitonin gene related peptide was used as the specific marker for sensory nerve fibers. Using immunohistochemical techniques, they were able to identify immunoreactive sensory fibers within the outer layers of the annulus fibrosus of all discs sampled. These nerve fibers were concentrated at the interfaces of the posterior longitudinal ligament and disc. No immunoreactive fibers were noted in the inner portion of the annulus fibrosis or nucleus pulposus (40).

More recent immunohistochemical studies in human discs have also demonstrated the presence of sensory nerve fibers in the annulus fibrosus (41, 42). Palmgren et al (41) performed histochemical analysis using substance P and C-flanking peptide of neuropeptide Y (CPON) as nerve markers for sensory and autonomic nerve fibers, respectively. Synaptophysin(SYN) served as a general neuronal marker for the study. Nine normal nondegenerated lumbar intervertebral disc tissue specimens were stained and underwent microscopic analysis. Substance P immunoreactivity was seen in 50% of the posterior annulus specimens. CPON reactive fibers were seen in 75% of the posterior annulus specimens, and SYN fibers were seen in 75% of posterior annular specimens. Interestingly, all anterior annulus specimens demonstrated the presence of substance P and CPON fibers. The depth of penetration of immunoreactive fibers was also recorded using a morphometric scale attached to the microscope. A maximum depth of .50mm was seen for substance P, .45mm for CPON, and 3.5mm for SYN.

In 1994, Ashton et al (43) performed immunohistochemical analysis of 12 human intervertebral discs. These discs were obtained from patients undergoing anterior lumbar fusion secondary to intractable low back pain. Protein gene product (PGP 9.5) served as a general nerve marker, and CPON as a marker for autonomic fibers. CGRP, VIP, and substance P acted as primary sensory markers. Immunoreactivity to CGRP, substance P, CPON, and VIP were seen throughout the outer 3mm of the annulus fibrosus. No immunoreactive fibers were noted penetrating the deep fibers of the annulus or in the nucleus pulposus. Substance P fibers were the sparsest fibers seen on microscopic analysis. Only a small number of these fibers were detected in the periphery of the disc. CPON fibers were exclusively noted traveling in association with blood vessels (43).

Only two studies to date have been able to document, via immunohistochemical techniques, the presence of nerve fibers penetrating the inner half of the annulus fibrosus and into the nucleus pulposus (44, 45). In both studies disc specimens were taken from patients with chronic low back pain undergoing anterior spinal fusion. All biopsy specimens were taken from the anterior portion of lumbar intervertebral discs. Freemont et al (45) examined 46 intervertebral discs from 38 subjects. Substance P immunoreactive fibers were identified in the inner third of the annulus fibrosus in 46% of non-control discs in this study (45). Freemont noted an association with blood vessels and nerve fibers penetrating the inner portions of the annulus

fibrosus. Coppes et al (44) examined 10 degenerated lumbar discs and two normal (control) discs. He was able to identify only "occasional single immunoreactive nerve fibers" for substance P into the inner third of the annulus. In contrast to Freemont's observations,Coppes study did not note any correlation between ingrowth of blood vessels and nerve tissue into the annulus.

A multitude of animal studies have also documented the presence of nerve fibers in the posterior longitudinal ligament and annulus fibrosus (46 -50). Those studies using immunohistochemical techniques have specifically been able to identify the presence of sensory afferent fibers in the posterior longitudinal ligament and superficial annular fibers (46, 48). Similar to most human studies, animal studies have been unable to demonstrate the presence of afferent nerve fibers within the inner aspects of the annulus fibrosus and nucleus pulposus. In 1995,Imai et al (47) was able to demonstrate a dual innervation to the posterior longitudinal ligaments in rats. A superficial network on the dorsal aspect of the posterior longitudinal ligament was seen to contain both nociceptive and sympathetic fibers. This dorsal plexus formed a polysegmental innervating system by anastamoses from adjacent upper and lower fibers. A deeper network ventral to the posterior longitudinal ligament was seen to contain only nociceptive fibers. This deeper network did not form connections with adjacent levels at the level of the intervertebral disc, thereby making this ventral network unisegmental in innervation (45). Another study has also promulgated a possible alternate pathway for return of annular sensory nerve fibers through the sinuvertebral nerve, rami communicants, and the lumbar sympathetic trunks (50). This is in contrast to traditional belief that sensory nerve fibers only traveled afferently through the ventral rami, instead of rami communicants and lumbar sympathetic trunk (51).

Based on current data, it is evident the intervertebral disc has a rich nerve supply in its lateral portion. These nerve fibers cover the superficial aspect of the disc and penetrate the annulus to a minimal extent. Thick networks of nerve fibers innervate the posterior longitudinal ligament. This network probably involves a large amount of cross-innervation between neighboring levels. This complex network would then give each posterior longitudinal ligament a diffuse, poly-segmental innervation. In addition, there may exist poly-segmental pathways in which these fibers may return to the spinal cord. The ventral dura also contains a rich polysegmental innervation of both autonomic and nociceptor fibers. This diffuse innervation to the contents of the anterior spinal canal highlights the

difficulty of diagnosing the etiology of low back pain. As well, it reminds us that poorly localized low back pain complaints should be common. This redundancy in innervation may explain why the treatment of low back pain patients continues to be one of the greatest challenges to the pain physician today.

PRACTICAL IMPLICATIONS

♦ Intervertebral discs contain sensory nerve fibers capable of transmitting pain impulses.

♦ Diagnosis of a specific pain generator in the spinal canal is troublesome secondary to its diffuse, polysegmental innervation.

♦ Treatment of anterior canal spinal pain may best be accomplished by ablation of the larger sensory nerve fibers outside the intervertebral foramen.

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