Neural Elements in Human Cervical Intervertebral Discs

TUVIA MENDEL, BSc, CAROLE S. WINK, PhD, and MARILYN L. ZIMNY, PhD

This study attempted to characterize neural elements within the human cervical intervertebral disc. Cervical intervertebral discs were obtained from four adult human subjects at autopsy. Discs were stained in bulk with gold chloride, sectioned, and viewed with the light microscope. Nerve fibers appeared to enter the disc in the postero-lateral direction and course both parallel and perpendicular to the bundles of the annulus fibrosus. Nerves were seen throughout the anulus but were most numerous in the middle third of the disc. Receptors resembling Pacinian corpuscles and Golgi tendon organs were seen in the postero-lateral region of the upper third of the disc. These results provide further evidence that human cervical intervertebral discs are supplied with both nerve fibers and mechanoreceptors. [Key words: cervical intervertebral disc, neural elements]

The innervation of the intervertebral disc (IVD) and other tissues of the spine is of considerable clinical importance. Pain and disorders of the vertebral column are common complaints, and although there have been many clinical and experimental studies on the causes of back and neck pain, there is no consensus on the mechanisms responsible. Nerve fibers have been observed in the anterior and posterior longitudinal ligaments in the lumbar region, and in the outer third of the annulus fibrosus of the lumbar IVD. Malinsky found encapsulated nerve endings as well as nerve fibers in the outer layers of the annulus fibrosus of the lumbar IVD. Horackova and Malinovsky observed nerve fibers and encapsulated nerve endings in the capsules of intervertebral (apophysial) joints, including those in the cervical region. Malinsky recently demonstrated the presence of free nerve endings within the anterior half of the C5–6 disc from two operative specimens. The purpose of the present study was to examine the entire cervical IVD from each vertebral level and further characterize neural elements within the disc.

MATERIALS AND METHODS

Fourteen cervical IVDs from all vertebral levels were obtained from four adult human subjects at autopsy and were immediately frozen in saline. Subsequently, seven discs were thawed and cut into anterior and posterior halves, and each half was cut sagittally into three pieces. The six pieces of discs were then sewn into plastic netting to preserve their original orientation and were stained in bulk by the use of a modified gold chloride method. After staining, the pieces were dehydrated in graded alcohols, embedded in paraffin, and serially sectioned at 30 um. Each disc yielded 40–45 sections. The remaining seven discs were cut into anterior and posterior halves. The halves were frozen and serially sectioned at 100 um on a sliding microtome. Each disc yielded 15–20 sections. The individual sections were placed in compartmentalized Petri dishes to maintain orientation, fixed with lemon juice and formic acid, and stained with gold chloride, as above. All sections were mounted on slides and viewed with the light microscope. Every section of every disc was studied to assess the presence of nerves and mechanoreceptors. The mechanoreceptors were measured with a millimeter ruler on photomicrographs. Using the paraffin sections and the Bioquant Image Analysis Morphometry Program (R & M Biometrics, Inc., Nashville, TN), the diameters of nerves were measured in the following five regions of the disc: posterior, postero-lateral, lateral, anterior, and nerves perpendicular to the anulus.

RESULTS

Nerve fibers appeared to enter the disc in the postero-lateral direction (Figure 1) and course perpendicular to the fibrocartilaginous bundles in the deep layers of the annulus fibrosus (Figure 2) and parallel to the bundles in the more superficial layers of the annulus fibrosus (Figure 3). Nerves were more numerous in the middle third of the disc. Measurements of nerve diameters in five regions of the disc are shown in Table 1. The average diameters ranged from 1.86 to 2.87 um. These diameters fell within the range of the diameters of Type III pain fibers, i.e., 1–6 um. No nerves were seen in the nucleus pulposus. Receptors 130 × 80 um resembling Pacinian corpuscles (Figures 4–5) were found in superficial layers, and receptors 100 × 60 um resembling Golgi tendon organs (Figure 6) were seen in the deeper layers of the annulus fibrosus. Both types of receptors were most prevalent in the postero-lateral regions of the annulus fibrosus. Only three or four mechanoreceptors were identified per disc.

DISCUSSION

The nerve fibers found in the cervical IVD may have been branches from the ventral primary rami (Figure 1). Bogduk et al dissected cervical spines in adult human cadavers and traced nerves going to the discs from sinuvertebral and vertebral nerves, which are branches of the ventral primary rama. Although we did not dissect these nerves from the rami, the neural elements we saw in the discs appeared to enter the annulus fibrosus in the postero-lateral direction, similar to branches of the sinuvertebral and vertebral nerves described by Bogduk et al.

Malinsky reported seeing encapsulated receptors from 110 × 50 um to 180 × 80 um on the surfaces (predominantly the lateral surfaces) of the lumbar IVDs in the adult human. The Pacinian-like receptors (Figures 4–5) seen in the superficial layers of the annulus fibrosus of the cervical IVD in this study were of similar size (130 × 80 um). The receptors resembling Golgi tendon organs seen in the deeper layers of the annulus fibrosus (Figure 6) were about the same size (100 × 60 um) as those seen by Zimny et al in the human medial meniscus (125 × 50 um). Although both large (1,300 × 600 um) and small (97 × 53 um) Pacinian-like corpuscles and large (1,400 × 800 um to 600 × 100 um) Golgi tendon organs have been found in joint capsules, sub-synovial connective tissues, and the connective tissues surrounding musculotendinous junctions, there have been no reports of large receptors within ligaments or menisci. In the present study, only small receptors (130 × 80 um to 100 × 60 um) were seen within the annulus fibrosus of the cervical IVD. The reasons for this are unknown. It may be that large, complex receptors cannot exist among the densely packed fibrous and avascular fibrocartilaginous bundles of ligaments.
Fig 1. Diagram of cervical IVD showing distribution of nerve fibers. It is hypothesized that these were branches from the ventral primary rami (VR). D = dorsal; V = ventral; NP = nucleus pulposus; U = upper (superior) third of disc; M = middle third of disc; L = lower (inferior) third of disc.

Fig 2. Micrograph of horizontal section through posterolateral portion of disc, deep within annulus fibrosus, showing nerve (arrow) passing perpendicular to fibrocartilage bundles (B). Magnification ×150.

Fig 3. Micrograph of horizontal section through posterolateral portion of disc (superficial) showing nerve fibers (arrows) arching parallel to fibrocartilage bundles (B). Magnification ×60.

Fig 4. Micrograph of horizontal section through posterolateral portion of disc. Axon (arrow) ends in Pacinian-like receptors (R). Original magnification ×60.

Table 1. Measurements of Nerve Diameters (Mean ± SD) in Regions of Disc

<table>
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<th>Region</th>
<th>No. of Nerves Measured</th>
<th>Mean Diameter (μm)</th>
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<tr>
<td>Posterior</td>
<td>6</td>
<td>2.37 ± 0.65</td>
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<tr>
<td>Posterolateral</td>
<td>19</td>
<td>2.85 ± 1.83</td>
</tr>
<tr>
<td>Lateral</td>
<td>6</td>
<td>2.87 ± 0.99</td>
</tr>
<tr>
<td>Anterior</td>
<td>47</td>
<td>1.86 ± 0.66</td>
</tr>
<tr>
<td>Perpendicular to annulus</td>
<td>16</td>
<td>2.28 ± 0.91</td>
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Small free nerve endings and their parent nerve fibers, similar to the menisci, and IVDs.7,14 Most receptors seen in this study were in the posterolateral region of the annulus fibrosus, similar in location to those reported by Malinsky in the lumbar IVD.19 There seems to be some agreement in the literature on the classification of sensory receptors based on anatomic and physiologic studies.28 Morphologically, receptors are classified as either encapsulated or nonencapsulated. Nonencapsulated receptors include nonmyelinated free nerve endings and terminals 0.5–1.5 μm in diameter, and are either efferent vasomotor fibers or pain receptors.9 With respect to joints, these fibers are apparently distributed throughout periarticular tissues, including joint capsules, ligaments, menisci, and discs.1,5,10,21–23,25,28–30

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ones reported by Bogduk et al using a cholinesterase stain.4 were seen throughout the annulus fibrosus of the cervical IVD in the present study.

Based on the classification of Freeman and Wyke,3 the Pacinian-like receptors seen in the present study could be classified as Type II receptors. These are described as cylindrical or conical corpuscles, average size 280 × 120 µm, with a thick laminated capsule (up to 10–12 layers) and a single (bifid or trifid) nerve terminal, linked in clusters of two or three corpuscles. They are low-threshold mechanoreceptors and adapt rapidly. The Golgi-like receptors seen could be classified as Type III receptors. These mechanoreceptors are fusiform corpuscles 600 × 100 µm (average size), with high thresholds, and adapt slowly. The other type of encapsulated receptor (Type I—Ruffini), was not seen in the cervical IVD in this study.

Although no definite conclusions can be made from the results of this study as to the functional significance of the neural elements within the cervical IVD, it appears that the disc is supplied with nerve fibers of various sizes and small encapsulated receptors, as suggested by Bogduk et al.4 The presence of neural elements within the IVD indicates that the mechanical status of the disc is monitored by the central nervous system. If the nonencapsulated nerve endings in the annulus fibrosus are pain receptors, their presence may explain the occurrence of neck or shoulder pain when there is dislocation or trauma to the disc. To what degree the encapsulated receptors (mechanoreceptors) may monitor the deformation and position of the disc is not apparent. Both Pacinian corpuscles and Golgi tendon organs are reportedly active in response to changes in tension.

Recent studies have shown that the IVD has a complex structure and mechanical properties that vary from region to region and change with age.16,19,24,26 There is evidence that the disc is capable of some regeneration.25 These findings plus evidence that the disc is innervated suggest that the IVD may be more than a pad that absorbs shock and maintains the spaces between vertebral bodies. The concentration of nerves in the middle third of the disc may be sensing supero-inferior compression or deformation. The circumferential arrangement of the nerve bundles about the disc and the superficial-to-deep location of the mechanoreceptors may enable the IVD to sense peripheral compression or deformation as well as alignment.

ACKNOWLEDGMENTS

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