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Are the nerves supplying the anterior sacroiliac joint nociceptive?

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Background: *Sacroiliac joint (SIJ) pain is often difficult to diagnose. Moreover, while its anatomical characteristics have been well studied, its innervation and the contributions of particular nerves remain controversial, especially in relation to posterior joint innervation. To our knowledge, previous studies have not investigated the presence of nociceptive fibres in the nerves innervating the anterior SIJ.*

Materials and methods: *Eight adult cadaveric sides underwent dissection of the anterior SIJ. Adjacent anterior rami were examined for branches to the anterior SIJ. Any branches contributing to the anterior SIJ were measured and then resected. These samples were fixed in formalin and substance P was identified immunohistologically.*

Results: *On all sides, 1–2 small branches (mean diameter of 0.33 mm) arose from the posterior aspect of the L4 anterior ramus (12.5%), the L5 anterior ramus (62.5%), or simultaneously from both the L4 and L5 anterior rami (25%). These branches had a mean length of 13.5 mm. All histological samples contained nerve tissue. All samples of nerve fibres traveling to the anterior SIJ were positive for diffuse substance P reactivity. There were no histological differences between sides or sex. Each of the branches identified as travelling to the SIJ exhibited similar positivity for substance P.*

Conclusions: *This cadaveric study demonstrates that the anterior SIJ nerve fibres carry pain fibres. This new knowledge has application to patients with SIJ syndrome and to its various treatments including interventional approaches to SIJ pain.* (Folia Morphol 2023; 82, 1: 96–101)

Key words: back pain, sacroiliac joint pain, syndrome, innervation

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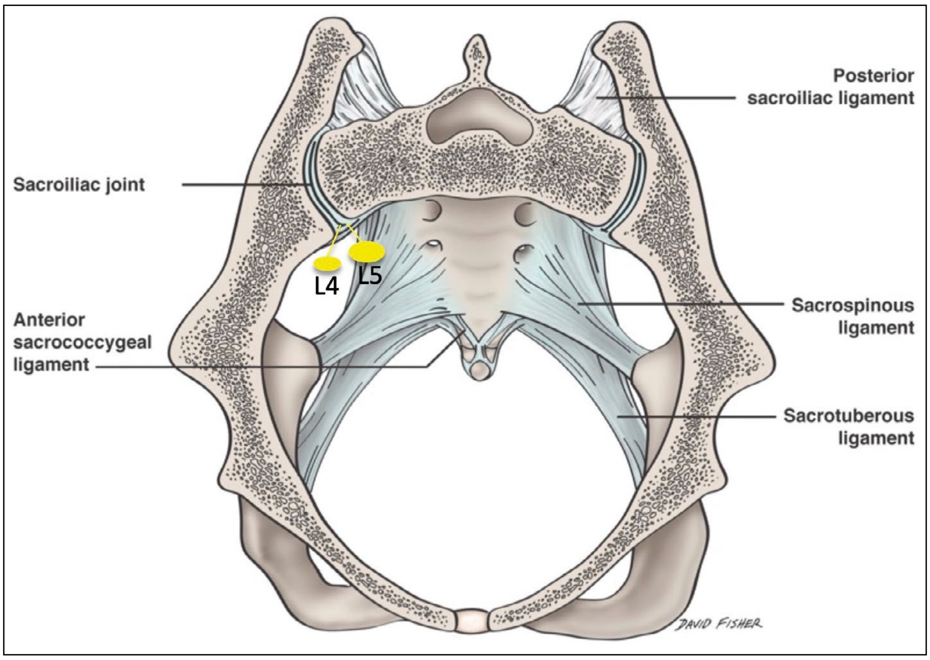

Figure 1. Superior view of the sacroiliac (SI) joint and related ligaments showing contributions from the L4 and L5 anterior rami to SI joint.

INTRODUCTION

The sacroiliac joint (SIJ) connects the sacrum to the ilium and transfers the weight from the spine to the lower extremities. While its anatomical characteristics have been well studied, SIJ innervation and the contributions of particular nerves remain controversial [6]. The SIJ has been identified as a potential cause of low back pain (LBP), and joint degeneration has been shown to be age-related and highly prevalent even in asymptomatic patients [7]. Recently, research on the SIJ as a cause and target of low back pain has intensified. The reported prevalence of SIJ dysfunction as a cause of LBP varies from 15% to 36% [6, 29]. SIJ-related pain is difficult to diagnose, and several different clinical tests and diagnostic blocks are used to confirm a diagnosis [11]. The clinical symptoms range from buttock pain, with or without extension to the posterolateral thigh, to pain in the area of the posterior inferior iliac spine, to lumbar pain, to pain radiating into the groin. There is no real consensus on how to diagnose SIJ-related pain [16, 17, 26, 30]. Furthermore, most clinical tests of the SIJ are limited in their validity and reliability [33]. Therefore, SIJ pain scores have been developed to corroborate a diagnosis. Kurosawa et al. [25] described a score using the following criteria: one-finger test, groin pain, pain while sitting on a chair, SIJ shear test, tenderness of the posterosuperior iliac spine, and tenderness of the sacrotuberous ligament. This score has proven effective for differentiating SIJ pain from any other cause of buttock pain, and provides moderate accuracy in diagnosing it [35].

Several different treatments such as physical therapy, nerve blocks, steroid injections, denervation, and ablation have been described. Treatment success ranges from 30% to 85% [6]. However, since SIJ innervation is still not fully understood, we recently studied the nerve contribution to the anterior SIJ. Previously, we demonstrated that the vast majority of nerve contributions to the anterior SIJ arise from the anterior rami of L4 or L5 (Fig. 1) [7]. However, to the best of our knowledge, there has been no immunohistological analysis of the fibre type in these branches [2, 27, 32, 36]. Therefore, the purpose of this study was to identify the fibre type of the nerve branches supplying the anterior SIJ using immunohistochemistry.

MATERIALS AND METHODS

We dissected 4 fresh-frozen cadavers (8 sides) for this study. The age at death ranged from 67 to 98 years (mean 75 years). Two cadavers were male and two were female. The cadavers were positioned supine and a midline incision was made from the xiphoid process to the pubic symphysis. We split the linea alba from the subjacent peritoneum. The greater omentum was lifted upwards and the intestines and mesentery were retracted. After the retroperitoneal space had been carefully opened, the fascia was removed and the psoas major muscle was identified. Next, the lumbar plexus was visualised by retracting the muscle laterally. Using a surgical microscope (OPMI CS NC31, Carl Zeiss, Germany), we identified the lower lumbar anterior rami (e.g., L4, L5) and upper sacral anterior rami (e.g., S1) and the anterior SIJ. Any branches contributing to the anterior SIJ were measured with microcallipers (Mitutoyo, Japan). These samples were fixed in formalin and substance P was identified immunohistologically. Substance P is found in primary sensory neurons; it is a NK1 receptor agonist and belongs to the tachykinin group, which is released in response to noxious stimuli [30].

Tissue preparation

The specimens were fixed by immersion in 0.1 M phosphate-buffered 4% formaldehyde at 4°C. The samples were cryoprotected with 30% sucrose in phosphate buffer containing 0.9% sodium chloride supplemented with 0.15% sodium azide and were then sectioned at 50 μm intervals. The sections were stored at 4°C pending processing. Following blocking (suppression of non-specific staining) with 2.5% normal horse serum, the sections were incubated with anti-rabbit substance P (Millipore Sigma, Burlington, MA; dilution 1:1000). Following incubation, sections were rinsed with TRIS-HCl buffer, pH 7.6, and treated with 3,3'-diamino-benzidine until the desired colour intensity was reached. Slides were mounted and allowed to dry at room temperature. Once cover-slipped, the slides were examined under a light microscope and representative images photographed.

Statistical analysis between sides and sex was performed using Student t-tests with statistical significance set at $p < 0.05$.

RESULTS

On all sides, 1–2 small branches (Fig. 2) ranging in diameter from 0.28 to 0.47 mm (mean 0.33 mm) arose from the posterior aspect of the L4 anterior ramus (n = 1; 12.5%), the L5 anterior ramus (n = 5; 62.5%), or simultaneously from both the L4 and L5 anterior rami (n = 2; 25%). These branches ranged from 7 mm to 38 mm long (mean 13.5 mm). All histological samples were consistent with nerve tissue. No specimen showed any gross evidence of pathology or previous surgery in the areas dissected. All samples of

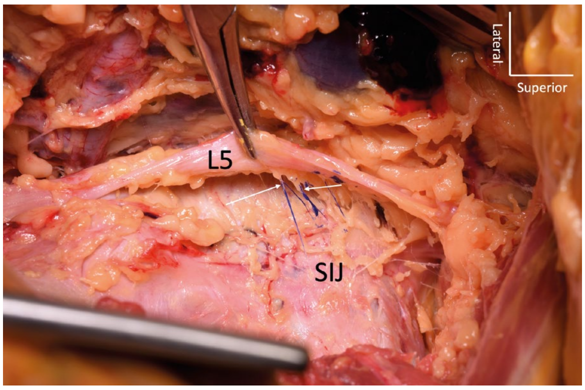

Figure 2. Cadaveric dissection of the left sacroiliac joint (SIJ) and related nerve lumbar anterior rami branches (arrows) to the SIJ.

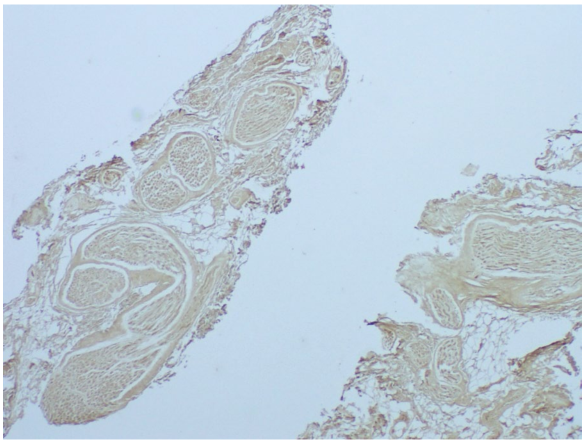

Figure 3. Histological section of two selected sacroiliac joint nerve branches noting positive reactivity for substance P (40×).

nerve fibres travelling to the anterior SIJ were positive for substance P (Fig. 3). There were no histological differences or statistical significance between sides or sex. Each of the branches identified as travelling to the SIJ exhibited similar diffuse positivity for substance P. All controls reacted appropriately.

DISCUSSION

The SIJ is a complex and biomechanically little-understood irregularly-shaped joint. According to Jesse et al. [22], three different surface shapes can be distinguished depending on the alpha angle. The SIJ is important in weight-bearing, load transfer and the structural stability of the pelvic girdle, which is provided mainly by the posterior sacroiliac complex ligaments forming the appearance of a suspension bridge [34]. SIJ pain can result from injury to or loosening of the ligamentous complex after trauma or inflammation [23, 24]. Minor movements resulting in collisions between the articulating surfaces can also regenerate pain [37].

However, innervation of the SIJ is still little understood. It is mostly accepted that the innervation derives from the anterior rami of L4, L5 and the posterior rami of L5-S3 [14, 15]. Ferrante et al. [13] were the first to report radiofrequency ablation to treat SIJ-related pain. They showed that radiofrequency ablation can significantly reduce pain even though only 36% of their patients met the criterion of at least a 50% decrease in the visual analogue pain scale. They denervated the joint by inserting three electrodes at 90° starting at the inferior anterior margin and placing the two other more cephalad at 1 cm distances [13]. Cheng et al. [3] described a modified technique with bipolar radiofrequency by placing a continuous straight strip lesion laterally to the sacral foramina in order to denervate the L5, S1, S2 and S3 posterior rami. They observed a significantly higher rate of pain reduction (> 50%) than with cooled radiofrequency [3]. A randomized prospective study by Dutta et al. [11] compared patients who underwent intraarticular methylprednisolone (n = 15) with those who underwent pulsed radiofrequency (PRF) treatment (n = 15) of the L4 medial branch, L5 posterior rami and the lateral sacral branches. Patients in the PRF group showed more significant pain relief and functional improvement than those in the intraarticular methylprednisolone group [11]. Vallejo et al. [38] reported 22 patients undergoing pulsed radiofrequency of the medial branch of L4, the posterior rami of L5, and the lateral branches of S1 and S2. Sixteen (72.7%) patients reported a "good" result (pain relief > 50% in VAS). However, the duration of pain relief ranged from only 6 to 32 weeks [38]. Ding et al. [8] reported overall efficiencies of 56.3% conventional radiofrequency (CRF) and 31.3% pulsed radiofrequency (PRF) using a continuous lesion lateral to the S1-S3 foramina. Gevargez et al. [18] achieved similar results using computed tomography-guided intervention in 43 patients by applying CRF to the posterior rami of the L5 nerve and to the posterior interosseous sacroiliac ligaments. Significant pain relief was experienced by 31.6% of the patients. Cohen et al. [4] found negative correlations between age, duration of symptoms, and outcome. Patients were subjected to radiofrequency ablation of the L4-L5 posterior rami and S1-S3 lateral branches. Fifty-two per cent were considered successfully treated (pain reduction > 50% for at least 6 months) [4]. Interestingly, van Tilburg et al. [39] could not reject the hypothesis that there is no difference in pain reduction between patients who underwent radiofrequency ablation of the S1-S4 nerve root lateral branches and L5 posterior branch and patients in the placebo-treatment group. They found 42.1% pain reduction in both groups [39].

The SIJ is closely related to the lumbosacral plexus, and while the posterior SIJ is supplied by the lateral branches of the L3/L4-S3 posterior rami, the anterior joint has been said to be innervated by L2-S2 [6]. However, our more recent cadaveric study narrowed this range to L4 and L5 anterior rami and the findings of the present study support these earlier findings. A randomised placebo-controlled trial with 28 patients by Cohen et al. [5] showed that L4 and L5 posterior rami and S1-S3 lateral branch denervation can lead to pain relief and a functional benefit for up to 6 months post-procedure in selected patients. Different rates of success in pain relief have been reported for radiofrequency ablation, which could be related to the different techniques used, including different denervation processes, locations and targeted nerve branches [1].

Specialised peripheral sensory neurons (nociceptors) detect noxious stimuli and mediate pain [10]. Nociceptive fibres are classified according to their sensitivity to heat, cold and noxious mechanical stimuli. Most nociceptors have unmyelinated axons (C-fibres) with small diameter, which is directly correlated with the transmission speed. In contrast, initial 'fast-onset' pain is mediated not by C-fibres, but by A-fibres with myelinated axons [9]. Debate about innervation of the SIJ continues. However, several studies support the assumption that nociceptive signals originate directly from the SIJ. A histological study of neural elements of the human SIJ (n = 6) by Vilensky et al. [40] revealed mechanoreceptors, nerves and nerve fascicles. Grob et al. [19] found myelinated and unmyelinated fibres in the joint. Ikeda et al. [20] reported nerve diameters ranging from 0.2 to 2.5 μm, which puts the nerve in the range of C- and A-delta fibres [37]. There are substance P and calcitonin gene-related polypeptide positive fibres, associated with nociception, in the SIJ and surrounding ligaments. Szadek et al. [32] revealed substance P and CGRP positive fibre-like structures in their cartilage tissue samples from 10 human cadavers. Sakamoto et al. [28] identified mechanosensitive afferent units in the SIJ and adjacent tissues.

Eno et al. [12] showed that SIJ degeneration is age-related and highly prevalent even in asymptotic patients. Furthermore, Suri et al. [31] observed growth of neurovascular tissue in human knees with advanced osteoarthritis. Whether these results are associated with joint degeneration or are valid for non-degenerated SIJs has yet to be determined.

CONCLUSIONS

This cadaveric study demonstrates that the anterior SIJ nerve fibres carry pain fibres. This new knowledge has application to patients with SIJ syndrome and to its various treatments including interventional approaches to SIJ pain.

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Conflict of interest: None declared

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