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Review

# Stretching of roots contributes to the pathophysiology of radiculopathies

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ABSTRACT

*Purpose:* To perform a synthesis of articles addressing the role of stretching on roots in the pathophysiology of radiculopathy.
*Methods:* Review of relevant articles on this topic available in the PubMed database.
*Results:* An intraoperative microscopy study of patients with sciatica showed that in all patients the hernia was adherent to the dura mater of nerve roots. During the SLR (Lasègue's) test, the limitation of nerve root movement occurs by periradicular adhesive tissue, and temporary ischemic changes in the nerve root induced by the root stretching cause transient conduction disturbances. Spinal roots are more frail than peripheral nerves, and other mechanical stresses than root compression can also induce radiculopathy, especially if they also impair intraradicular blood flow, or the function of the arachnoid villi intimately related to radicular veins. For instance arachnoiditis, the lack of peridural fat around the thecal sac, and epidural fibrosis following surgery, can all promote sciatica, especially in patients whose sciatic trunks also stick to piriformis or internus obturator muscles. Indeed, stretching of roots is greatly increased by adherence at two levels.
*Conclusions:* As excessive traction of nerve roots is not shown by imaging, many physicians have unlearned to think in terms of microscopic and physiologic changes, although nerve root compression in the lumbar MRI is lacking in more than 10% of patients with sciatica. It should be reminded that, while compression of a spinal nerve root implies stretching of this root, the reverse is not true: stretching of some roots can occur without any visible compression.


## 1. Spinal radiculopathies are multi-factorial diseases

The pathophysiology of sciatica is not completely understood, although ion channels, such as acid-sensing ion channel 3, Piezo2, and transient receptor potential vanilloid receptor 1 responding to tissue acidosis, mechanical force, and inflammatory mediators, seem the main pathways transducing the subset of pains in sciatica [1]. Accumulating evidence has shown that lumbar radiculopathy may involve almost all types of pain in a single patient, including inflammatory, neuropathic, ischemic, and mechanical pain [1].

All those mechanisms can result from a single inducing factor, like disc herniation. For instance, it has been extensively demonstrated in pig and rodent models that chemical injury by nucleus pulposus induces inflammation surrounding the dorsal roots or dorsal root ganglion (DRG) [2,3]. Furthermore, those neurons sensitized by inflammatory mediators are hypersensitive to otherwise innocuous mechanical force (stretching or compression) [4]. A central sensitization in the spinal cord can also follow, and could favour ongoing allodynia in some patients [1].

However, a histological study of 96 transligamentous disc herniations showed that the importance of cell infiltration by macrophages, T or B lymphocytes, or activated T lymphocytes, was not associated with motor weakness or positivity of straight leg raising (SLR) (Lasègue's test) [5]. The authors concluded that those immune cells, which have been demonstrated in a high proportion of disc herniations, are probably more important for disc tissue resorption processes than for producing sciatica [5].

As diagnoses of radiculopathy following acute or chronic root stretching can be missed or denied when imaging shows no root compression, this review aims to recall that stretching of root could play a leading role in the pathogenesis of some mechanical radiculopathies.

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## 2. Stretching of sticking roots reduces intraradicular blood flow and causes conduction disturbances

In fact, adhesion of roots to herniated materials, leading to repeated stretching, can be pivotal. Indeed, an intraoperative microscopy study of 32 patients with unilateral sciatica showed that in all patients the hernia was adherent to the dura mater of the nerve roots [6]. During the SLR test, the limitation of nerve root movement occurred by periradicular adhesive tissue (granulation with many inflammatory cells) [6]. The amplitude of action potential showed a sharp decrease at the angle that produced sciatica. After removal of the hernia, all the patients showed smooth gliding of the nerve roots during the test, and there was no longer decrease of amplitude [6]. This suggests that temporary ischemic changes in the nerve root induced by the root stretching cause transient conduction disturbances, as already observed in another set of patients with reduction of gliding to only a few millimetres [7]. Indeed, during the SLR test, intraradicular blood flow showed a sharp decrease at the angle that produced sciatica, which lasted for one minute. It decreased by $70.6\% \pm 20.5\%$ in the L5 nerve root, and by $72.0\% \pm 22.9\%$ in the S1 nerve roots relative to the blood flow before the SLR test. After removal of the hernia, all the patients showed smooth gliding of the nerve roots, and there was no marked decrease in intraradicular blood flow during the second intra-operative test [7]. Japanese surgeons similarly measured S1 nerve root blood flow and electrophysiologically evaluated the nerve root using the compound muscle action potentials (CMAPs) from the gastrocnemius muscle after S1 nerve root stimulation during an intraoperative SLR test in patients with sciatica by lumbar disc herniation [8]. Before discectomy, there were sharp decreases in the nerve root blood flow after 1 and 3 minutes of the SLR test ($P < 0.001$), and the amplitudes of the CMAPs deteriorated significantly ($P < 0.001$), with a significant correlations between the two. After discectomy, the blood flow increased significantly ($P = 0.001$), and when the SLR test was performed again, the blood flow showed no significant decreases, while the average amplitudes of the CMAPs were significantly improved ($P < 0.01$) [8].

## 3. Contact with nucleus pulposus is not a prerequisite, and other mechanical stresses can also induce radiculopathy

Therefore, although contact with nucleus pulposus certainly increases the likelihood of nerve root disturbance, it might not be mandatory for the onset of all sciatica. Other conditions leading to repeated mechanical insults and/or root adhesion could also make the root hypersensitive to further triggers. They can also induce radiculopathy, especially if those mechanical stresses also impair intraradicular blood flow, or the function of the arachnoid villi present around spinal roots, and intimately related to radicular veins. Indeed, cerebrospinal fluid absorption occurs not only intracranially, but also along the spinal axis [9,10].

For instance, mechanical stress on roots without disc herniation (as observed in foraminal spinal stenosis) also alters nerve root conduction and compromises the nutritional support of spinal nerve roots and ganglia (through intrinsic and extrinsic vascularity and cerebral spinal fluid percolation), so that mechanical forces alone can lead to intraneural damage and functional changes [11]. Whereas peripheral nerves receive 95% of their nutritional supply from intramural blood vessels, spinal nerve roots and DRGs are surrounded by cerebrospinal fluid and receive 58% of their nutritional supply from cerebrospinal fluid and 38% from intramural blood vessels. Accordingly, DRG are even more sensitive to mechanical stress and consequent ischemic and nutritional changes than nerve roots [1]. This explains why chronic compression of the DRG in the L4/L5 intervertebral foramina by stainless steel rods can be used to simulate the clinical conditions caused by stenosis, such as a laterally herniated disc, or foraminal stenosis. This results in neuronal hyperexcitability, spontaneous action potentials associated with hyperalgesia, spontaneous pain, and mechanical allodynia, mimicking radicular pain in humans [1]. Sciatica due to epidural gas migrating from gas-containing herniated discs with the vacuum phenomenon has even been observed in numerous occasions [12]. Thus, mechanical forces other than disc herniations can promote and sustain sciatica.

## 4. Stretching strains on roots have been disregarded

Although there is a general acceptance that those radiculalgia result from compression of nerve root and/or DRG, other insults, like excessive traction of roots or DRG and overpressure in the peridural space, could be frequently involved in the pathogenesis of radiculopathy. Those disregarded roles of traction stresses and peridural overpressure could account for the frequent mismatch between spinal magnetic resonance imaging (MRI) and symptoms of sciatica, and the observation that nerve root compression in the lumbar MRI is lacking in more than 10% of patients with sciatica [13].

Actually, sciatica, and even cauda equina syndrome, can be observed in patients with spondylolisthesis, or pseudomeningocele without disc herniation [14]. Although the predominance of the literature has addressed nerve root compression as the principal cause of sciatica and other spinal neuropathy, it is equally likely that a stretch mechanism may be responsible for all or part of the pathology [15].

### 4.1. Imaging cannot show excessive traction of nerve roots

The first explanation for this unawareness is that excessive traction of nerve roots and/or hyperpressure in DRG are not shown by imaging, although intra-radicular blood flow is equally affected by excessive traction than by compression [7]. Many physicians-radiologists, and mainly surgeons, have unlearned to think in terms of microscopic and physiologic changes, and just consider the macroscopic changes that can be observed on MRI or CT-scans. This pragmatic and wise attitude is mostly in line with the lack of mechanical root decompression possibility, although the threat of lawsuits following surgeries performed without imaging proof of an extrinsic insult could have also contributed to what may be seen as a step backwards in medical thinking.

### 4.2. Peripheral nerves sustain major stretching stresses

The second reason for minoring the role of stretching in radiculopathy is that in peripheral nerves neurapraxia following excessive stretching of nerves is a rare event at the clinical level, although some pain previously ascribed to entrapment neuropathies have been recently reclassified as traction neuritis (like pain in the lateral forearm due to lateral antebrachial cutaneous nerve traction neuritis [16], or suprascapular nerve neuropathies [17], including those secondary to retracted rotator cuff tears [18]). For instance, the follow-up of 1512 total hip arthroplasty showed that only 51 patients (3.37%) suffered from transient lateral femoral cutaneous nerve neuropraxia (3.37%), 4 from femoral nerve paralysis (3 permanent, 1 transient [0.26%]) and only one of permanent sciatic nerve paralysis (0.06%) [19] with different mechanisms of injuries depending on surgical approach (indirect stretching for anterior approach, versus direct conflict with retractor for most posterior approach).

Peripheral nerves are indeed more extensible and less prone to stretch injuries than spinal roots. In a cadaveric study on 7 specimens performed 7–20 hours after death, a relative strain

deformation of 3%–23% of plexus brachialis was documented during 0° to 180° abduction tests [20]. One nerve sample was studied histologically after 15% stretch on the bench. The mean pressure change in the bundle was 13.6 mm Hg at 90° arm abduction, 53.7 mm Hg at 120°, 73.4 mm Hg at 150°, and 89.0 mm Hg at 180°. Those traction and pressure were considered sufficient to induce lesions in neural bundles of the plexus brachialis [20], but extensive and repeated stretching of peripheral nerves usually do not induce pain. Continuous intraoperative neuromonitoring used to detect imminent injury by traction of some nerves like recurrent laryngeal nerve [21] showed that the mean physiologic limit strain was found to be as high as 15.0%, and histological analysis in a swine model showed no abnormal structural finding [22]. Even after extreme stretches, like those inducing brachial plexus avulsion, only 30–80% of patients develop neuropathic pain in human [23], which is mainly the consequence of root and/or spinal cord lesions, as better studied in animal models [23,24].

## 5. But spinal roots are more frail than peripheral nerves, and are fixed by ligaments

Whereas the nerves and associated structures transmit and absorb large amounts of force, the roots, in comparison, are mechanically frail [25], as they are surrounded by much smaller amounts of connective tissue, so that protection from tension strains depends mainly on dissipation of peripherally applied forces through epineurial and dural structures [26]. Old studies comparing mechanical properties of peripheral nerves and nerve roots confirmed major differences. While nerve root elasticity was comparable to nerve, nerve root strength was only 10% that of nerve, and root stiffness was only 20% of nerve values [26]. This explain why, to protect them from excessive strains, the mobility of the nerve roots is much lower than those of peripheral nerves, as a result of foraminal and extra-foraminal ligaments extending between the spinal nerves and the tissues surrounding the intervertebral foramens, either at the lumbar or cervical levels [27,28]. These foraminal ligaments are of two types: a radiating ligament, which connects the nerve root sleeves to the transverse processes and the walls of the intervertebral foramen, and a trans-foraminal ligament, which connects the structures around the intervertebral ligaments. Foraminal ligaments in the cervical spine limit cervical nerve root displacement and strain during upper limb neural tension testing, and have a protective role in normal conditions [29]. However, although those ligaments usually prevent lateral traction [27,28], the radiating ligaments may also contribute to dura laceration and root lesions during excessive tractions [30].

## 6. Motility and elasticity of the dura mater are also low and weak

The motility and elasticity of the dura mater seems also rather weak. Indeed, the conus medullaris is displaced caudally in the spinal canal by $3.54 \pm 0.87$ mm ($\mu \pm$ SD) with unilateral ($P \leq 0.001$), and $7.42 \pm 2.09$ mm with bilateral SLR ($P \leq 0.001$) [31]. Moerover, this movement seems directly proportional to the sliding of the L5 and S1 neural roots [32]. It has been checked that 90% of conus medullaris displacement in the vertebral canal with SLR is primarily due to transmission of tensile forces through the neural tissues, while 10% only results of reciprocal movements between vertebrae and nerves during the maneuver [33].

A study of cervical nerve root displacement in unembalmed cadavers showed that upper limb neural tension testing resulted in mild but significant inferolateral displacement (average, 2.16 mm–4.32 mm) of cervical nerve roots C5–C8, with a significant difference between the C5 and C6 nerve roots (3.15 mm vs. 4.32 mm, $P = 0.009$). Upper limb neural tension testing also resulted in significant strain (average, 6.80%–11.87%), as well as a significant difference in strain between the C5 and C6 nerve roots (6.60% vs. 11.87%, $P = 0.03$) [34]. This low motility of the spinal roots partly explains why dynamic functional spinal unit that encloses a tethered nerve root can create significant stretching through anterior, posterior, and rotatory olisthesis [15].

## 7. Stretching of nerve roots can result in nerve damage

Numerous studies have demonstrated that stretching can result in roots damage [15]. For instance, in a tethered cord syndrome produced by slow traction in cats through fixation of a filum terminale tractor, histopathological examination revealed an association between the increasing traction in the spinal cord and the increase in impaired nerve cells [35]. The latencies of sensory and motor evoked potentials significantly increased in the tethered cats [35]. In a model of limb lengthening-induced chronic nerve-stretch injury in rats, axonal degeneration of unmyelinated fibers was also observed, and associated with tetrodotoxin-resistant (TTX-R) sodium-channel Nav1.8 mRNA expression [36]. TTX-R expression was restored following cessation of stretch, and conduction block and histological changes recovered after 30 days, but pain threshold did not recovered to the control group level after 30 days [37]. In a model of tibial lengthening in rabbits, a reduction of the number of substance P-positive small cells in the dorsal root ganglia was observed [38]. In rats dorsal lumbar nerve roots, functional nerve root injuries, as evidenced by changes in the conduction velocity, amplitude, and area of the compound action potential, were strain- and rate-dependent [39]. High-tension strains at low rates cause complete conduction block in the roots, but a similar block was also observed at lower strains and higher rate. The extent of impaired axoplasmic transport was concomitant with functional injury [39]. Differences in mechanical behavior of nerve roots were observed among the four root levels (L4 to S1), although a significant interaction effect had previously been observed between nerve root diameter and stretch rates [40]. An in vitro study of 20% tensile strain in human DRG cells showed that this mechanical injury also led to significant neuronal cell death, which was proportional to strain duration. Hypoxia also promoted death of DRG neurons, which was further enhanced when mechanical strain and hypoxia were combined. Total cell death in response to mechanical injury or hypoxia was similar in both non-nociceptive and nociceptive neurons [41].

## 8. Repetated mechanical injury of roots could be sufficient to induce allodynia

In a model of transient and repeated injury of lumbar nerve roots in rats (loose ligation with chromic gut suture) at 0 and 42 days, mechanical allodynia was significantly greater on both the ipsilateral and contralateral sides after reinjury ($P < 0.001$), and the response did not return to baseline after reinjury, as it did with the initial injury [42]. There were also persistent spinal astrocytic and microglial activation and interleukin-1beta expression in spinal cord. This supports the concept that central neuroinflammation plays an important role in chronic radicular pain [42], but also that mechanical stress of roots without disc herniation can by itself induce long lasting allodynia.

## 9. Stretch tests on roots (SLR and femoral stretch tests) are highly specific for lumbar radiculopathies

The most useful and time-honoured tests to distinguish real sciatica and femoral neuralgia from referred pain in the thigh/legs, are

SLR and femoral stretch test, respectively. In disc herniation sciatica, with patients relieved from their pain following surgery as gold standard, sensitivity of the SLR test ranges from 0.87 to 0.95 [43], with an excellent specificity when the test is correctly performed. Although the lumbosacral nerve roots (L4, L5, S1) may require hip motion greater than 60° to produce substantive displacement in the lateral recess [44], significant traction can occur for lower angles, especially when dura mater motion is already impaired, either by disc herniation, spinal stenosis, or adhesion of dura mater to the spinal canal. It has been checked in rats that cauda equina compression by epidural balloon decreased the excursion, and increased the strain of the sciatic nerve in response to a modified SLR test [45].

## 10. Examples of radiculopathy promoted by repeated root stretching

A first frequently overlooked explanation for radiculalgia is arachnoiditis. Lumbar arachnoiditis is characterized by obliterated nerve root sleeves, and the adherence of nerve roots to each other and/or to the thecal sac [46]. Three anatomic groups can be identified on MRI:

- conglomerations of adherent nerve roots residing centrally within the thecal sac (group 1);
- nerve roots adherent peripherally to the meninges, giving rise to an "empty thecal sac" appearance (group 2);
- soft tissue mass replacing the subarachnoid space (group 3) [47].

It can also occur at the dorsal level, where arachnoiditis can induce roots kinking within the thecal sac, or spinal cord kinking due to focal adhesion with dura mater [48]. It is often difficult to recognize, but microsurgical arachnoidolysis can sometimes resolve the spinal cord kinking, without short-term recurrence [48]. Chronic adhesive arachnoditis has been ascribed to prior spinal surgery [49], intrathecal pump implantation [50], prior meningeal inflammation or spinal hemorrhage, epidural blood patches [51], percutaneous fibrin glue treatment of meningeal cyst [52], lumbar epidural anaesthesia, translaminar or caudal epidural steroid injections [53], and even diagnostic lumbar puncture [54], but familial cases have also been reported [55]. It is presumed to be rare, but minor arachnoiditis could be easily overlooked. Indeed, transcutaneous neuroendoscopic inspection of the subarachnoid structures of the lumbar thecal sac (thecaloscopy) [46] showed that arachnoiditis could be much more frequent than deduced only from imaging. Indeed, in 55 patients with chronic pain, using a thin flexible fiberscope to observe subarachnoid spaces, a diagnosis of chronic arachnoiditis was made in 20% (11 patients), that could not be found by magnetic resonance imaging or computed tomography [56].

A second situation is the lack of peridural fat around the thecal sac, which, in patients with very large thecal sac, leads to venous stasis in foraminal veins, excessive pressure in epidural space, and DRGs, together with lack of motility of both, making nerve roots and DRGs more vulnerable to stretching. Although these changes, which are also observed in Tarlov's cysts (found incidentally in 4%–9% of MRI [57]), are not sufficient to induce radiculalgia, they probably increase the risk of root damage following repeated mechanical stretching insults, and are the sole explanation in some cases of radiculalgia. Some of these radiculopathies may even be transiently relieved following cerebro-spinal fluid soustraction, like in some symptomatic perineural cysts [57].

A third possibility is the adhesion between the dura-mater, roots and intervertebral disc and spinal canal, which can induce very sharp back pain, and unexplained limitation when bending forward or backwards, each time the anterior aspect of the dura-mater, which is highly innervated, or roots, can no longer gently glide over the disc or spinal canal. In a finite element analysis model, recent work found a significant stress concentration in the spinal nerves, especially on the DRG, caused by the lack of adaptive displacement between the dura mater and posterior annulus fibrosus [58]. The authors concluded that the increased stress on the spinal nerve might elicit more pain under similar magnitudes of lumbar disc protrusion [58]. In another model, the strength of adhesion of the L5 intraforaminal spinal nerve to the surrounding structures was quantified eight weeks after bilateral L5–L6 laminectomy with right-side L5–6 disc injury in rats. Lumbar intraforaminal spinal nerve adhesion and tethering was demonstrated, supporting the conclusion that post-surgical fibrosis might play a role in recurrent radiculopathy following laminectomy [59].

The pathogenicity of epidural fibrosis following surgery has been extensively reported, and adhesiolysis performed either percutaneously of through spinal endoscopy seems effective to treat chronic refractory low back and lower extremity pain induced by root adhesions. Indeed, a recent meta-analysis concluded, based upon 7 randomized controlled trials showing efficacy, with no negative trials, that there was level I or strong evidence of the efficacy of percutaneous adhesiolysis in the treatment of chronic refractory low back and lower extremity pain [60]. Based upon one high-quality randomized controlled trial, there was also level II to III evidence supporting the use of spinal endoscopy in treating chronic refractory low back and lower extremity pain [60].

## 11. Conclusion

In patients with radiculopathy but no overt discoradicular conflict, a thorough clinical examination is mandatory to discard the possibility of other sources of pain, including spinal cord, plexus or nerve trunk suffering, but a systematic search for subtle changes along the course of spinal roots from the conus medullaris to the extra-foraminal space could also be carried out. This could help in identifying co-factors of root adhesions (like minor arachnoiditis and/or adhesions of large thecal sac to the spinal canal). Indeed, such minor changes may facilitate repeated stress of traction on DRGs, leading to their sensitisation, chronic neuropathic sciatica, and sometimes excruciating pain despite an apparently normal MRI, especially in patients whose sciatic trunks also stick to piriformis or internus obturator muscles. Indeed, stretching of roots might require adherence at two levels, explaining why most patients with large thecal sac or minor arachnoiditis have few if any complaints. This could prevent costly diagnostic wavering, and encourage the search of new procedures to treat those painful and frustrating conditions.

Although it might be a rather rare event, physicians and radiologists should not definitively discard the diagnosis of radiculopathy when no disc herniation or other sources of compression can be found at imaging. Medical students should also be taught that, while compression of a spinal nerve root implies stretching of this root, the reverse is not true: stretching of some roots can occur without any visible compression.

## Disclosure of interest

The authors declare that they have no competing interest.

## References

[1] Lin JH, Chiang YH, Chen CC. Lumbar radiculopathy and its neurobiological basis. World J Anesthesiol 2014;3:162–73.
[2] Olmarker K. Reduction of adhesion formation and promotion of wound healing after laminectomy by pharmacological inhibition of pro-inflammatory cytokines: an experimental study in the rat. Eur Spine J 2010;19:2117–21.

[3] Mulleman D, Mammou S, Griffoul I, et al. Pathophysiology of disk-related sciatica. I. – Evidence supporting a chemical component. Joint Bone Spine 2006;73:151–8.
[4] Kuslich SD, Ulstrom CL, Michael CJ. The tissue origin of low back pain and sciatica: a report of pain response to tissue stimulation during operations on the lumbar spine using local anesthesia. Orthop Clin North Am 1991;22:181–7.
[5] Grönblad M, Virri J, Seitsalo S, et al. Inflammatory cells, motor weakness, and straight leg raising in transligamentous disc herniations. Spine 2000;25:2803–7.
[6] Kobayashi S, Takeno K, Yayama T, et al. Pathomechanisms of sciatica in lumbar disc herniation: effect of periradicular adhesive tissue on electrophysiological values by an intraoperative straight leg raising test. Spine 2010;35:2004–14.
[7] Kobayashi S, Shizu N, Suzuki Y, et al. Changes in nerve root motion and intraradicular blood flow during an intraoperative straight-leg-raising test. Spine 2003;28:1427–34.
[8] Takamori Y, Arimizu J, Izaki T, et al. Combined measurement of nerve root blood flow and electrophysiological values: intra-operative straight-leg-raising test for lumbar disc herniation. Spine 2011;36:57–62.
[9] Tubbs RS, Hansasuta A, Stetler W, et al. Human spinal arachnoid villi revisited: immunohistological study and review of the literature. J Neurosurg Spine 2007;7:328–31.
[10] Berthelot JM, Le Goff B, Maugars Y. The role for radicular veins in nerve root pain is underestimated: limitations of imaging studies. Joint Bone Spine 2011;78:115–7.
[11] Garfin SR, Rydevik B, Lind B, et al. Spinal nerve root compression. Spine 1995;20:1810–20.
[12] Lee CH, Cho JH, Hyun SJ, et al. Symptomatic gas containing herniated disc with the vacuum phenomenon: mechanism and treatment. Case report. Neurol Med Chir (Tokyo) 2012;52:106–8.
[13] Yoshimoto M, Kawaguchi S, Takebayashi T, et al. Diagnostic features of sciatica without lumbar nerve root compression. J Spinal Disord Tech 2009;22:328–33.
[14] Asha MJ, George KJ, Choksey M. Pseudomeningocele presenting with cauda equina syndrome: is a 'ball-valve' theory the answer? Br J Neurosurg 2011;25:766–8.
[15] Kitab SA, Miele VJ, Lavelle WF, et al. Pathoanatomic basis for stretch-induced lumbar nerve root injury with a review of the literature. Neurosurgery 2009;65:161–7.
[16] Brogan DM, Bishop AT, Spinner RJ, et al. Lateral antebrachial cutaneous neuropathy following the long head of the biceps rupture. J Hand Surg Am 2012;37:673–6.
[17] Economides CP, Christodoulou L, Kyriatides T, et al. An unusual case of suprascapular nerve neuropathy: a case report. J Med Case Rep 2011;5:419.
[18] Shi L, Freehill MT, Yannopoulos P, et al. Suprascapular nerve: is it important in cuff pathology? Adv Orthop 2012:516985, http://dx.doi.org/10.1155/2012/516985.
[19] Macheras GA, Christofilopoulos P, Lepetsos P, et al. Nerve injuries in total hip arthroplasty with a mini invasive anterior approach. Hip Int 2016;26:338–43.
[20] Vasilevskis E, Skuja S, Evansa I, et al. Plexus brachialis strain and compression deformation in the costo-axillary-brachial region: a cadaveric study. Medicina (Kaunas) 2011;47:566–72.
[21] Dionigi G, Donatini G, Boni L, et al. Continuous monitoring of the recurrent laryngeal nerve in thyroid surgery: a critical appraisal. Int J Surg 2013;11:S44–6.
[22] Lee HY, Cho YG, You JY, et al. Traction injury of the recurrent laryngeal nerve: results of continuous intraoperative neuromonitoring in a swine model. Head Neck 2016;38:582–8.
[23] Wang L, Yuzhou L, Yingjie Z, et al. A new rat model of neuropathic pain: complete brachial plexus avulsion. Neurosci Lett 2015;589:52–6.
[24] Sindou MP, Blondet E, Emery E, et al. Microsurgical lesioning in the dorsal root entry zone for pain due to brachial plexus avulsion: a prospective series of 55 patients. J Neurosurg 2005;102:1018–28.
[25] Luttges MW, Stodieck LS, Beel JA. Postinjury changes in the biomechanics of nerves and roots in mice. J Manipulative Physiol Ther 1986;9:89–98.
[26] Beel JA, Stodieck LS, Luttges MW. Structural properties of spinal nerve roots: biomechanics. Exp Neurol 1986;91:30–40.
[27] Kraan GA, Smit TH, Hoogland PV. Extraforaminal ligaments of the cervical spinal nerves in humans. Spine J 2011;11:1128–34.
[28] Shi B, Zheng X, Zhang H, et al. The morphology and clinical significance of the extraforaminal ligaments at the cervical level. Spine 2015;40:E9–17.
[29] Lohman CM, Gilbert KK, Sobczak S, et al. 2015 Young Investigator Award Winner: cervical nerve root displacement and strain during upper limb neural tension testing: part 2: role of foraminal ligaments in the cervical spine. Spine 2015;40:801–8.
[30] Zhao Q, Zhong E, Shi B, et al. The morphology and clinical significance of the intraforaminal ligaments at the L5-S1 levels. Spine J 2016;16:1001–6.
[31] Rade M, Schacklock M, Könönen M, et al. Part 3: developing methods of in vivo MRI measurement of spinal cord displacement in the thoracolumbar region of asymptomatic subjects with unilateral and bilateral straight leg raise tests. Spine 2015;40:935–41.
[32] Rade M, Könönen M, Vanninen R, et al. 2014 young investigator award winner: In vivo magnetic resonance imaging measurement of spinal cord displacement in the thoracolumbar region of asymptomatic subjects: part 1: straight leg raise test. Spine 2014;39:1288–93.
[33] Rade M, Könönen M, Martilla J, et al. In vivo MRI measurement of spinal cord displacement in the thoracolumbar region of asymptomatic subjects with unilateral and sham straight leg raise tests. PLoS One 2016;11:e0155927.
[34] Lohman CM, Gilbert KK, Sobczak S, et al. 2015 Young Investigator Award Winner: cervical nerve root displacement and strain during upper limb neural tension testing: part 1: a minimally invasive assessment in unembalmed cadavers. Spine 2015;40:793–800.
[35] Huang SL, Peng J, Yuan GL, et al. A new model of tethered cord syndrome produced by slow traction. Sci Rep 2015;5:9116.
[36] Ohno K, Yokota A, Hirofuji S, et al. Altered expression of sodium channel distribution in the dorsal root ganglion after gradual elongation of rat sciatic nerves. J Orthop Res 2010;28:481–6.
[37] Hirofuji S, Yokota A, Ohno K, et al. Role of sodium channels in recovery of sciatic nerve-stretch injury in rats. Muscle Nerve 2014;50:425–30.
[38] Pap K, Berta A, Szoke G, et al. Nerve stretch injury induced pain pattern and changes in sensory ganglia in a clinically relevant model of limb-lengthening in rabbits. Physiol Res 2015;64:571–81.
[39] Singh A, Kallakuri S, Chen C, et al. Structural and functional changes in nerve roots due to tension at various strains and strain rates: an in vivo study. J Neurotrauma 2009;26:627–40.
[40] Singh A, Lu Y, Chen C, et al. Mechanical properties of spinal nerve roots subjected to tension at different strain rates. J Biomech 2006;39:1669–76.
[41] Gladman SJ, Ward RE, Michael-Titus AT, et al. The effect of mechanical strain or hypoxia on cell death in subpopulations of rat dorsal root ganglion neurons in vitro. Neuroscience 2010;171:577–87.
[42] Hunt JL, Winkelstein BA, Rutkowski MD, et al. Repeated injury to the lumbar nerve roots produces enhanced mechanical allodynia and persistent spinal neuroinflammation. Spine 2001;26:2073–9.
[43] Van der Windt DA, Simons E, Riphagen II, et al. Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain. Cochrane Database Syst Rev 2010;2:CD007431.
[44] Gilbert KK, Brismée JM, Collins DL, et al. 2006 Young Investigator Award Winner: lumbosacral nerve root displacement and strain: part 1. A novel measurement technique during straight leg raise in unembalmed cadavers. Spine 2007;32:1513–20.
[45] Tai TW, Su FC, Chien JT, et al. Changes in excursion and strain in the rat sciatic nerve under cauda equina compression induced by epidural balloon inflation. Spine J 2015;15:329–35.
[46] Di leva A, Barolat G, Tschabitscher M, et al. Lumbar arachnoiditis and thecaloscopy: brief review and proposed treatment algorithm. Cent Eur Neurosurg 2010;71:207–12.
[47] Delamarter RB, Ross JS, Masaryk TJ, et al. Diagnosis of lumbar arachnoiditis by magnetic resonance imaging. Spine 1990;15:304–10.
[48] Miyazaki M, Yoshiiwa T, Ishihara T, et al. Symptomatic spinal cord kinking due to focal adhesive arachnoiditis, with ossification of the ligamentum flavum: a case report. Spine 2014;39:E538–41.
[49] Liu LD, Zhao S, Liu WG, et al. Arachnoiditis ossificans after spinal surgery. Orthopedics 2015;38:e437–42.
[50] Kochany JZ, Tran ND, Sarria JE. Increasing back and radicular pain 2 years following intrathecal pump implantation with review of arachnoiditis. Pain Med 2013;14:1658–63.
[51] Carlswärd C, Darvish B, Tunelli J, et al. Chronic adhesive arachnoiditis after repeat epidural blood patch. Int J Obstet Anesth 2015;24:280–3.
[52] Hayashi K, Nagano J, Hattori S. Adhesive arachnoiditis after percutaneous fibrin glue treatment of a sacral meningeal cyst. J Neurosurg Spine 2014;20:763–6.
[53] Nanjayan SK, Swamy GN, Yallappa S, et al. Arachnoiditis following caudal epidural injections for the lumbo-sacral radicular pain. Asian Spine J 2013;7:355–8.
[54] Gürbüz MS, Erdogan B, Yuksel MO, et al. Postlumbar puncture arachnoiditis mimicking epidural abscess. BMJ Case Rep 2013 [pii:bcr2013200169].
[55] Pasoglou V, Janin N, Tebache L, et al. Familial adhesive arachnoiditis associated with syringomyelia. AJNR Am J Neuroradiol 2014;35:1232–6.
[56] Tobita T, Okamoto M, Tomita M, et al. Diagnosis of spinal disease with ultrafine flexible fiberscopes in patients with chronic pain. Spine 2003;28:2006–12.
[57] Burke JF, Thawani JP, Berger I, et al. Microsurgical treatment of sacral perineural (Tarlov) cysts: case series and review of the literature. J Neurosurg Spine 2016;24:700–7.
[58] Lee N, Ji GY, Yi S, et al. Finite element analysis of the effect of epidural adhesions. Pain Phys 2016;19:E787–93.
[59] Kulkami VA, Massie JB, Zauner F, et al. Novel biomechanical quantification methodology for lumbar intraforaminal spinal nerve adhesion in a laminectomy and disc injury rat model. J Neurosci Methods 2007;166:20–3.
[60] Helm 2nd S, Racz GB, Gerdesmeyer L, et al. Percutaneous and endoscopic adhesiolysis in managing low back and lower extremity pain: a systematic review and meta-analysis. Pain Phys 2016;19:E245–82.