



REVIEW ARTICLE

The role of the peripheral and central nervous systems in rotator cuff disease



Damien Bachasson, PT, PhD^a, Anshuman Singh, MD^b, Sameer B. Shah, PhD^{c,d}, John G. Lane, MD^e, Samuel R. Ward, PT, PhD^{a,c,d,*}

^aDepartment of Radiology, University of California San Diego, La Jolla, CA, USA

^bDepartment of Orthopaedics, Kaiser Permanente Southern California, San Diego, CA, USA

^cDepartment of Orthopaedic Surgery, University of California San Diego, La Jolla, CA, USA

^dDepartment of Bioengineering, University of California San Diego, La Jolla, CA, USA

^eCOAST Surgery Center, San Diego, CA, USA

Rotator cuff (RC) disease is an extremely common condition associated with shoulder pain, reduced functional capacities, and impaired quality of life. It primarily involves alterations in tendon health and mechanical properties that can ultimately lead to tendon failure. RC tendon tears induce progressive muscle changes that have a negative impact on surgical reparability of the RC tendons and clinical outcomes. At the same time, a significant base of clinical data suggests a relatively weak relationship between RC integrity and clinical presentation, emphasizing the multifactorial aspects of RC disease. This review aims to summarize the potential contribution of peripheral, spinal, and supraspinal neural factors that may (1) exacerbate structural and functional muscle changes induced by tendon tear, (2) compromise the reversal of these changes during surgery and rehabilitation, (3) contribute to pain generation and persistence of pain, (4) impair shoulder function through reduced proprioception, kinematics, and muscle recruitment, and (5) help explain interindividual differences and response to treatment. Given the current clinical and scientific interest in peripheral nerve injury in the context of RC disease and surgery, we carefully reviewed this body of literature with a particular emphasis on suprascapular neuropathy that has generated a large number of studies in the past decade. Within this process, we highlight the gaps in current knowledge and suggest research avenues for scientists and clinicians.

Level of evidence: Narrative Review.

© 2015 Journal of Shoulder and Elbow Surgery Board of Trustees.

Keywords: Shoulder; rotator cuff tear; pain; muscle; nerve; spinal cord; brain

The human shoulder complex exhibits a unique anatomic design to allow a wide range of motion at various speed and force levels. The shoulder joint complex has an

unstable bone configuration secured by connective tissues and dynamic stabilizers (rotator cuff [RC] muscles) controlled by a sophisticated neuromuscular system.^{157,161} As a consequence, shoulder structures, particularly RC tendons, are prone to various injuries and degenerative disorders.^{19,121} RC tendon tears are common in the general population^{104,123} and can lead to shoulder pain, impaired functional capacities, and reduced quality of life.^{88,164}

Funding: The source of funding for this study was NIH R01 HD073180.

*Reprint requests: Samuel R. Ward, PT, PhD, 9500 Gilman Drive (mail code 0610), La Jolla, CA 92093, USA.

E-mail address: srward@ucsd.edu (S.R. Ward).

RC tendon tears are not necessarily associated with pain or patient-reported loss of shoulder function^{91,164,165}; however, asymptomatic patients may develop symptoms in a relatively short time.¹⁰⁷ Symptomatic patients usually undergo surgery when nonoperative and pharmacologic options have been exhausted.^{112,130} Surgical management decisions are mainly driven by patients' pain, disability, and functional requirements rather than by the severity of local tissue damage.¹⁵ In the short term, nonoperative treatment may be effective in a fraction of patients,^{35,50,76} but tissue damage and symptoms may progress over time,^{91,107,164} further limiting surgery and rehabilitation.^{79,92,96,98} RC tendon repair is not universally successful; ~25% of repairs fail to re-establish the integrity of the RC⁹⁸ (up to 70% in massively retracted tears³⁶), and patient-reported improvements are limited.^{79,98} Preoperative factors, such as age, chronicity, and severity of muscle-tendon unit impairments, have been repeatedly associated with higher retear rates and poorer clinical outcomes.^{79,98} Paradoxically, 2 recent meta-analyses^{98,130} suggested that patients with intact repairs might not have significant differences in symptom improvement compared with patients with recurrent tears. Another major concern is that muscle impairments do not seem to be reversed, even when repair is intact and function is improved at follow-up.²⁶

During the past decades, RC disease has been extensively investigated within the framework of tendon pathophysiology, tendon to bone healing, and muscle changes after tendon tear.^{30,72} A smaller set of studies have investigated how peripheral, spinal, and central neural factors are likely to contribute to muscle-tendon unit changes, impaired shoulder function, and responses to treatment. Expanding our knowledge, or at least considering the potential involvement of both peripheral and central nervous systems, is critical to improve our understanding of RC disease and our ability to appropriately intervene along the continuum of RC injury processes. Therefore, this review aims to scrutinize and highlight the gaps in current knowledge about the nervous system that may be altered in patients with RC disease from the peripheral receptors to the brain and from the brain to the neuromuscular junction. We summarized how these factors may (1) exacerbate structural and functional muscle changes induced by tendon tear, (2) compromise the reversal of these changes during surgery and rehabilitation, (3) contribute to pain generation and persistence, (4) impair shoulder function by impairing shoulder proprioception, kinematics, and muscle recruitment, and (5) contribute to explain interindividual differences in symptoms and response to treatment. Given the current and lively interest in peripheral nerve injuries in the context of RC disease and surgery, we carefully reviewed this body of literature with a particular emphasis on suprascapular nerve (SSN) injury that has generated a large number of studies in the past decade. Within this process, we highlighted the gaps in

current knowledge and suggested research avenues for scientists and clinicians.

Proprioceptors and related spinal reflexes

Shoulder movements and positional changes induce a deformation of tissues surrounding joints, including skin, muscles, tendons, fascia, joint capsules, and ligaments.^{24,27,47,122,144,156} All these tissues are innervated by mechanically sensitive receptors termed proprioceptors that relay information to the central nervous system about movement, position, and forces exerted on shoulder structures (e.g., muscle spindles, Golgi tendon organs, Ruffini endings, Pacinian and Meissner corpuscles). The distribution and the function of proprioceptors in shoulder joints and soft tissue have been investigated in both animal and human studies.^{40,51,139,141,144,147,156} Glenohumeral joint and ligament receptors probably play a minor role in shoulder proprioception,¹²² as illustrated by the small proprioceptive deficit observed after shoulder arthroplasty.²¹ However, they may act as limit detectors, triggering protective and synergistic reflex muscle activity during movement.^{27,46,64,141,149,158} In RC muscles and tendons, a large concentration of muscle spindles and Golgi tendon organs have been demonstrated in rabbits and rats,^{3,22,105,166} but no human data exist. Current theory suggests that muscle spindles are the most important proprioceptors, especially during movement.¹²² They also play a critical role in regulating muscle contraction through spinal reflexes that are essential for joint stability and accurate motor control.¹⁰¹ Golgi tendon organs are equally important proprioceptors, signaling information about force and mass, and are also involved in the regulation of muscle contraction.¹²²

The effect of tendon disruption on muscle spindles and Golgi tendon organs has been studied in a limited number of animal experiments concerning hindlimb muscles only. After tenotomy, muscle shortening and changes in the surrounding extrafusal tissue modify the morphology of muscle spindles that become slack and distorted.¹⁶⁹ In the chronically tenotomized muscle, atrophy of intrafusal fibers, degeneration of supplying axons, and fibrotic thickening of the capsule have been reported.^{67,95} Functionally, acute tenotomy decreases muscle spindle discharge,^{56,160,169} but interestingly, responsiveness of muscle spindles from the chronically tenotomized muscle has been shown to increase.^{56,57,169} Shortening of intrafusal fibers, increased preliminary stretch caused by kinking of intrafusal fibers, change in passive mechanical properties, and increased sensitivity of spindles have been subsequently proposed as potential explanations for this phenomenon. These increases in muscle-tendon afferent outflow have also been suggested to result from non-proprioceptive discharge.^{57,78} Increase in the amplitude of the monosynaptic reflex has also been repeatedly observed

in the chronically tenotomized muscle,^{10,61,75,160} suggesting adaptive changes in motoneuron excitability consistent with the decrease in muscle mechanical loading.⁹⁹ In the Golgi tendon organs, tenotomy also induces morphologic changes, but the physiologic consequences remain to be investigated.⁶⁷ To the best of our knowledge, only 1 study related to proprioceptor function in RC tendon tear has been conducted and reported that experimentally induced inflammation within rabbit RC sensitizes and increases the firing of mechanical receptors.¹⁶⁶

Based on the findings of these studies, it is reasonable to speculate that RC tendon tear is associated with structural and functional alterations of proprioceptors. Either reduced or inconsistent proprioceptive information from the injured muscle-tendon unit and altered muscle reflex activity may impair shoulder proprioception and contribute to impaired kinematics and muscle recruitment (see also the section on shoulder muscle activity and kinematics). Finally, the effects of tendon repair on the structure and the function of proprioceptors remain entirely unknown. Further experiments are therefore required to assess the relative contribution of these mechanisms to anatomic and clinical impairments associated with RC disease.

Central processing of proprioceptive information

Proprioceptive information from the shoulder and more broadly from the upper limb is conveyed through the spinothalamic tracts and relayed to the somatosensory cortex, where it is referred to a central body map allowing the conscious awareness of arm position and movement in space. Unconscious proprioceptive tracts (i.e., spinocerebellar tracts, projecting in the ipsilateral cerebellum) and the cervical propriospinal system are also involved in the coordination movements involving multiple joints of the arm.^{122,125}

Measurement of errors in the perceived position, movement detection latency, or ability to reproduce a determined force level can be used to globally assess shoulder proprioception.^{6,86,108,126,132} A large fraction of studies involving shoulder proprioception assessment have been conducted in patients with shoulder instability.^{6,108,126} In the overhead athlete with isolated infraspinatus atrophy caused by SSN compression, impaired sense of movement associated with different brain activation patterns has been reported, suggesting an important contribution of RC muscle to shoulder proprioception.¹³² Decreased sense of movement^{4,89,131} and a tendency to overestimate the target during force reproduction tests⁹⁰ have been reported in patients with RC tendinopathy, but no data exist in patients with RC tendon tears. In conditions such as knee disorders, functional brain magnetic resonance imaging demonstrated reduced activation of sensorimotor cortical areas and increased activation in proprioception-related brain regions; however, no data exist

in patients with RC disease.⁷⁰ In healthy subjects, transcranial magnetic stimulation (TMS) combined with peripheral nerve stimulation has been used to assess the modulation of the propriospinal system¹²⁵ of the upper limb, which is an important determinant for synergies between forearm, hand, and shoulder muscles. This system remains to be investigated in patients with RC disease.

Proprioception has been insufficiently assessed in patients with RC disease despite its recognized importance in other musculoskeletal conditions.¹²² Therefore, further studies are required to assess proprioception in patients with RC disease and patients who have undergone RC reconstruction.

Nociceptors and peripheral and central pain processing

Nociceptors are high-threshold receptors that detect signals from damaged tissue or tissue on the verge of damage. They can be found in the shoulder, skin, muscles, joints, soft tissue, and bone.^{32,40,41,51,144,149,150} RC disease is associated with local tissue damage and inflammation within the RC and surrounding structures, which release a variety of substances that sensitize nociceptors by decreasing their activation threshold (peripheral sensitization), resulting in hyperalgesia at the site of injury.^{23,34,41} Prolonged release of neuropeptides by nociceptive afferent fibers at the dorsal horn may sensitize nociceurons and cause long-term changes in pain processing at the spinal level and higher centers that result in pain hypersensitivity within but also outside the original zone of injury.¹⁶³ As previously observed in other musculoskeletal conditions,⁵³ sensory abnormalities have been observed on the injured but also on the noninjured side of patients with RC disease, illustrating the involvement of central mechanisms.^{39,48,55} Interestingly, patients with a RC tendon tear and signs of central sensitization have been shown to have worse clinical outcomes after surgery.⁴⁸ Pain may have profound effects on motor behavior mediated at various levels of the nervous system and have an impact on numerous motor parameters, such as reflex amplitude, muscle activity, kinematics, movement planning, and brain activation⁵ (see section on shoulder muscle activity and kinematics).

Pain remains poorly characterized in patients with RC disease, but the use of existing pain assessment tools and the development of biologic markers have the potential for enhancement of our understanding of pain in RC disease.²⁴ Interindividual differences in the magnitude of these changes and their persistence after local tissue damage has healed may explain differences in clinical presentation and response to therapies.²⁴

Motor nerves and neuromuscular junction

The motor innervation of the RC muscles is achieved by nerves emerging from the posterior and the superior

trunks of the brachial plexus, all originating from the C5-C6 cervical roots and C4 nerve root in some individuals.^{2,81,137,167} The architecture and the high mobility of the shoulder complex predispose nerves to various dynamic or static compressive and traction injuries.¹⁴⁸ Cervical radiculopathy, brachial plexopathy, and peripheral nerve trunk injuries are potential comorbidities of RC tendon tear.^{52,136} Motoneuron damage immediately reduces muscle activation and induces progressive muscle changes proportional to the severity of nerve injury.¹⁴⁶ Over time, the muscle tissue can virtually disappear while connective tissue and fat accumulate,⁸⁵ as recently illustrated in the human supraspinatus.^{14,80,102} A particular interest has been placed on the SSN because it innervates the most affected muscles in RC disease (i.e., supraspinatus and infraspinatus) and because it is particularly prone to entrapment.^{106,136} SSN injury can cause shoulder weakness and pain that overlap with the signs of RC disease.¹⁰⁶

SSN injury associated with RC tendon tear: anatomic studies

SSN injury is possible, given the surgical manipulation of previously retracted muscles during RC repair procedures.¹³⁴ In vivo studies have shown that lateral advancement during supraspinatus repair initiates a stretch of the SSN.^{44,162} The main trunk of the SSN may be prone to damage, but also its smaller branches may be injured.⁴⁴ Following a similar principle, medial retraction of the supraspinatus and infraspinatus muscles caused by tendon tear has been suggested to place excessive traction on the SSN and to promote compressive injuries at the suprascapular or spinoglenoid notch. In cadavers, supraspinatus tenotomy changes the course of the SSN.^{1,94} Various anatomic variations have also been suggested to promote suprascapular entrapment (e.g., deep and narrow suprascapular notch,^{60,109,119,124,151} shape or ossification of the superior transverse scapular ligament,^{118,120,151} arrangements of blood vessels,^{120,168} configuration of the fascia securing the SSN to the supraspinatus fossa,²⁸ close relationship of the subscapularis muscle⁷). However, the incidence of these anatomic predispositions in patients with an RC tendon tear and concomitant neuropathy has never been studied. In addition, the potential occurrence of dynamic stretch or compressive strain of the SSN promoted by biomechanical and kinematic impairments in patients with RC disease should not be neglected.^{20,117}

These anatomic studies must be acknowledged as the original incentive for investigating SSN function in RC tendon tears.¹⁰⁶ However, they have not addressed the question of whether these changes are physiologically relevant and whether smaller nerve branches are also likely to be insulted clinically.

Prevalence of SSN injury in patients with RC tendon tear

In patients, diagnosis of SSN injury is confirmed by electrodiagnosis that combines needle electromyography (EMG) and nerve conduction studies (NCS). Various clinical reports, retrospective studies, and prospective studies of the prevalence and the impact of peripheral nerve injuries before or after surgery have been published (see Table I for supporting material).

After tendon repair, a low risk of iatrogenic nerve injury has been reported,^{25,49,59,170} but comparisons of presurgery and postsurgery EMG/NCS data have not been systematically performed.^{18,42,93,170} Goutallier et al⁴² achieved such comparisons in the largest sample of patients, and findings confirmed the low incidence of SSN dysfunction after RC repair previously reported. In these studies, the long delay between surgery and electrodiagnosis may have allowed nerve recovery. Some case reports also suggested that supraspinatus repair may restore the normal course of the SSN, therefore reducing nerve strain and allowing its recovery, but larger studies are required to prove this concept.^{18,93} The large undocumented occurrence of traumatic events that could have caused direct nerve injury often limits interpretation of the data (Table I).

Studies suggesting a greater prevalence of SSN motor neuropathy in patients with RC tendon tears involve important recruitment bias. In the studies of Boykin et al¹² and Shi et al,¹³⁵ patients were sent for electrophysiologic examination for persistent pain or severe muscle changes; similarly, Costouros et al¹⁸ and Mallon et al⁹³ selected patients with severe muscle atrophy and fatty infiltration. Whereas some studies are consistent with a higher risk of SSN injury in severely vs. slightly retracted tears,^{13,93} the study of Shi et al¹³⁵ involving a larger spectrum of RC tear severity does not support this hypothesis. These data thus call into question the concept of SSN injury as a direct consequence of muscle retraction. Prospective and carefully conducted studies indicate a rare occurrence of isolated motor SSN injury in patients with RC tendon tears, even in massive or traumatic RC tendon tear.^{16,154} Within the largest series of patients in this topic area,¹⁶ peripheral neuropathy was found in 12% of patients, and only 1 patient exhibited positive signs of SSN injury.

Heterogeneous and incompletely documented EMG/NCS methods are also major limitations in comparing results between these studies.^{13,93,135,154} Some categorize EMG findings on the basis of the isolated or combined occurrence of positive EMG signs,¹³⁵ whereas others use graded scoring based on semiquantitative assessments of EMG abnormalities.^{16,18,135} Regarding NCS, some compared latencies with previously published values^{13,16} or the contralateral side,^{16,18,154} whereas others compared latencies of patients with positive and negative EMG findings.¹³ Severe retraction, ultrastructural muscle

Table I Prevalence of suprascapular neuropathy in patients with rotator cuff tears before or after surgical repair

Studies	N	Tear etiology		Tear severity		Time of electrodiagnosis				Prevalence of suprascapular neuropathy	
		Trauma	Chronic	Mild/ partial	Massive/ full	Before surgery	After surgery	Before and after surgery	Time from surgery or trauma (months)	Before surgery	After surgery
Ha'eri and Wiley, ⁴⁹ 1981	5	/	/	/	/	0	5	0	/	/	0% (0/5)
Kaplan and Kernahan, ⁶⁹ 1984	6	6	0	5	1	5	1	1	/	100% (5/5)	100% (1/1)
Zanotti et al, ¹⁷⁰ 1997	10	0	10	0	10	1	10	1	(24-36)	/	10% (1/10)
Goutallier et al, ⁴² 1996	24	/	/	/	/	19	24	19	8.5	/	~ 21% (4/19)
Hoellrich et al, ⁵⁹ 2005	9	0	9	/	/		9		17 (6-28)	/	0% (0/9)
Vad et al, ¹⁵⁴ 2003	25	8	17	17	8	25	0	0	/	8% overall (2/25)	/
Mallon et al, ⁹³ 2006	8	0	8	0	9	8	4	4	6	100% (8/8)	0% (0/6)
Costouros et al, ¹⁸ 2007	26	19	7	0	26	26	6	6	8 (3-12) (trauma) 6 (surgery)	27% (7/26, all trauma)	0% (0/6)
Boykin et al, ¹³ 2011	44	/	/	6	38	44	0	0	/	0% (partial tear) 60% (massive tear)	/
Shi et al, ¹³⁵ 2014	60	/	/	SS (14) IS (15)	SS (46) IS (30)	60	0	0	/	29% overall (26/87) 50% (partial SS tear) 54% (full SS tear/minor retraction) 17% (full SS tear/>5 cm retraction) 20% (partial IS tear) 71% (full IS tear/minor retraction) 23% (full SS tear/>5 cm retraction)	/
Collin et al, ¹⁶ 2014	49	24	25	0	49	49	0	0	/	2%	

SS, supraspinatus; IS, infraspinatus; /, undocumented or unavailable information.

changes, or nonuniform denervation may also complicate EMG/NCS in RC muscles.⁸ Ultrasound imaging¹¹⁴ and multisite EMG assessments may help overcome some of these limitations. Standardization of procedure and quantification methods¹⁷⁰ must be pursued to enhance the sensitivity of EMG. Recent progress in nerve imaging techniques^{82,116,145} may also allow enhancement of our ability to study peripheral nerve injuries in vivo.

Relative contribution of denervation to muscle changes associated with RC tendon tears: clinical data and animal models

In humans, imaging techniques cannot discriminate muscle impairments related to tendon tear or denervation when they happen simultaneously.⁸ EMG/NCS is limited, and an objective test such as nerve biopsy cannot be reasonably performed in patients. Consequently, various animal models of RC disease or nerve injury have been developed to understand cellular and molecular mechanism underlying muscle changes.³⁰

In rabbits and rodents, tenotomy associated with full nerve transection has been shown to produce severe atrophy and fatty infiltration, and these data are frequently used to support the role of SSN injury in human RC muscle changes.^{65,66,73,83,127} However, if nerve injury occurs in humans, denervation is more likely to be incomplete, with higher capacity for recovery. In rabbits, fatty infiltration has been repeatedly observed after isolated supraspinatus tenotomy,^{127,129,153} even in the absence of retraction¹⁵² and independent from denervation,³⁸ further clouding the cause-effect relationship between nerve injury and fatty infiltration. There are many transcriptional pathways that control various aspects of the adipogenic, fibrogenic, and myogenic programs.⁶⁸ However, distinct pathways may be triggered by RC tenotomy or denervation as recently reported in rodents.^{65,83} Although small animal models have a limited ability to replicate human RC disease, previously developed transgenic mice associated with tendon or nerve injury have great potential to further understanding of RC pathophysiologic processes.^{73,84} Increased availability in human tissue may also allow further investigations of muscle impairments and comparison of data obtained in animal models.

Direct consequences of RC tendon tears on nerves and neuromuscular junction

Studies that investigated the consequences of tendon tear on motor nerve and neuromuscular junction provide equivocal results.⁶¹ These effects have been investigated in animal models of RC tendon tears in rabbit only. Signs of degenerative histologic changes in the subscapular nerve after tenotomy of the subscapularis muscle have been reported,¹²⁷ but characteristics of these nerve abnormalities

remain unclear. Gayton et al³⁸ reported that motor end plates were not significantly affected after tenotomy in rabbits; confirmation is required, given the small sample size of this work ($N = 4$). A critical point that has not been addressed is whether neuromuscular junctions are altered in patients with isolated RC tendon tears.

Sensory nerves

Sensory nerve injuries have received less interest than the motor neuropathies discussed before. However, the RC and surrounding structures receive sensory innervation from numerous sensory nerve branches^{29,159} that are equally susceptible to injury. Injury within a peripheral nerve trunk induces a local inflammatory response that causes changes in afferent fibers and in the central nervous system and may lead to neurogenic pain (see section on nociceptors and peripheral and central pain processing and reference 31 for more details). Damage to afferent fibers may also contribute to the impairment of the transduction of proprioceptive information. SSN block has demonstrated effectiveness in the management of postoperative pain,⁶³ and pulsed radiofrequency modulation has been reported to provide promising long-lasting pain relief in experimental models¹⁵⁵ and in patients with shoulder pain.⁶² These data highlight the important contribution of shoulder nerves in the transmission of nociceptive information in patients with RC disease, making them important targets for shoulder pain management.^{63,155}

Shoulder muscle activity and kinematics

Alterations in shoulder muscle activity and kinematics of the glenohumeral and scapulothoracic joints have been widely reported in patients with RC disease.^{87,97,128} One potential contributing factor may be that patients with symptomatic tears display different motor control patterns during movement compared with asymptomatic patients.¹²⁸

Kelly et al⁷¹ observed that symptomatic patients retain supraspinatus and infraspinatus activity despite tendon tears but are unable to activate intact deep muscles (i.e., subscapularis) as efficient co-contractors and that they may preferentially rely on periscapular muscles during elevation. These results have been partially reproduced by Cordasco et al¹⁷ and suggest that symptomatic patients fail to develop alternative muscle activation strategies to compensate for weakened RC muscles and the resulting altered shoulder biomechanics. Importantly, they suggest that RC muscles may continue to be activated despite tendon damage. Shinozaki et al¹³⁸ recently used positron emission tomography with fluorodeoxyglucose^{77,113} to assess shoulder muscle activity differences between asymptomatic and symptomatic patients. They observed increased trapezius activity and lower deltoid activity in the

symptomatic group but no differences in RC muscle activity compared with asymptomatic patients. This technique appears promising, but further developments are required, particularly regarding quantification.

An important issue is whether different muscle activity patterns observed in symptomatic patients are the cause or the result of pain or both. Experimentally induced pain has been shown to increase activity in the antagonist muscle during abduction (i.e., latissimus), probably in an attempt to limit the compression of painful subacromial structures. Similar adaptations have been observed in patients with massive RC tendon tears.^{17,143} Masking pain may reduce these protective mechanisms and further promote local tissue damage. Stackhouse et al¹⁴² reported that pain reduced shoulder strength in external rotation in association with a decrease in voluntary activation when using the twitch interpolation technique.¹⁰³ Sole et al¹⁴⁰ also pointed out that motor adaptation to acute pain may be individual and task specific.⁵⁸ Given the acute nature of experimentally induced pain,⁵ precautions should be taken in trying to generalize these results in patients with chronic RC disease.

In patients with RC disease, pain reduction has been shown to improve glenohumeral motion and to reduce scapular contribution during arm elevation.¹³³ Dramatic increases of peak torque and power have also been reported.⁹ Surprisingly, when it is assessed with isometric contractions, pain reduction has been shown to have no relevant effect on shoulder strength,^{33,115} suggesting that pain-related motor impairments may be particularly visible during movement.

These experiments observed muscle activity pattern changes under pathophysiologic and simulated conditions; however, the relative contribution of muscle-tendon unit impairments, biomechanical abnormalities, pain, impaired proprioception, and deterioration of motor control in shoulder dyskinesia and weakness remains unclear. Poor coping strategies in muscle activation patterns in response to biomechanical changes and pain may contribute to worsen local tissue damage and pain. Interestingly, motor adaptations may also differ between individuals, in particular between symptomatic and asymptomatic patients.

Motor cortical changes

As in various other conditions, RC disease may induce structural and functional changes in the motor cortex that could partly explain changes in motor control and affect muscle activation. Little is known about the cortical organization of motoneurons related to proximal muscles of the arm and even less regarding RC muscles.¹⁰⁰ Functional magnetic resonance imaging has been previously used but is not discriminant for motor cortical mapping of individual RC muscles.⁷⁴ The output of the primary motor cortex (M1) can be objectively measured by motor evoked potentials (MEPs) elicited by TMS, providing direct insight

into the cortical representation and the function of the corticospinal tracts.⁴⁵ Mapping of the infraspinatus muscle has been recently described in healthy subjects,¹¹¹ and the same group observed positive correlation between pain chronicity and reduced M1 excitability in patients with RC disease,¹¹⁰ supporting an indirect inhibitory effect of pain on corticospinal excitability in line with current concepts.⁵ However, the effects of limb disuse and other spinal and supraspinal neural factors cannot be excluded. Similarly,

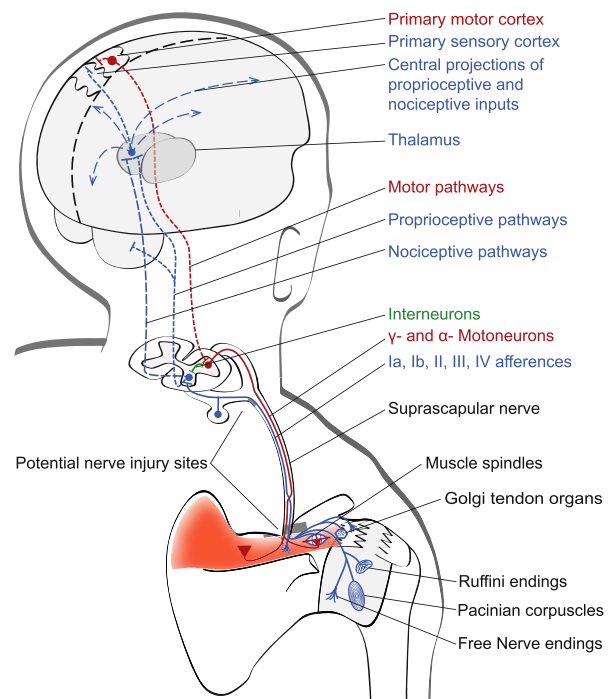


Figure 1 Potential sites for sensory and motor impairments associated with supraspinatus tendon tear. Tendon tear, soft tissue or joint damage, and local inflammatory environment sensitize peripheral nociceptors (mechanical or chemical high-threshold peripheral nociceptors, e.g., free endings) that cause pain and increase the sensitivity of central pain centers (peripheral and central sensitization, respectively). They may also induce impairments in proprioceptive outputs (muscle spindles; Golgi tendon organ, Ruffini endings; Pacinian corpuscles) and in the central processing of proprioceptive information (proprioceptive pathways; primary sensory cortex). Motoneurons innervating both extrafusal and intrafusal muscle fibers (α - and γ -motoneurons, respectively) may equally undergo remodeling and impairments. The neuromuscular junction may also be altered as a result of reduced neural activity, muscle impairments, and central alterations within the motor nervous system. At the nerve level, stretch or compression caused by muscle retraction, mass compression, and manipulation of the previously retracted muscle or direct nerve manipulation during surgery can result in injury of both sensory and motor axons. The suprascapular nerve may be damaged at any point of its path, but the suprascapular notch and the cervical roots are identified as the most common sites for injury. Nerve damage can further increase pain, limit the afferent transduction of proprioceptive information, and aggravate muscle changes.

Table II Suggested deleterious nervous consequences of rotator cuff (RC) disease in studies cited in the current review

Structures/mechanisms	Consequences	Human RC studies	Animal RC studies	Human or animal non-RC studies
Proprioceptors, afferences and related spinal reflexes	Structural/functional impairments of proprioceptors		166	3,22,56,57,78,95,105,160,166,169
Central processing of proprioceptive afferences	↑ Motoneuron excitability	131,132		10,61,75,160
	↓ Sense of position	89		70
	↓ Sense of movement			
	↓ Sense of force	4,90		
Nociceptors and peripheral and central pain processing	Modified brain activity			
	Peripheral sensitization	40,41,150	149	
	Central sensitization	39,48,55		
Motor nerves	± Injury	1,8,13,16,44,49,59,69,	65,66,73,83,84,127,	
	Iatrogenic	93,94,154,162,170	129,152,153	
Neuromuscular junction	Direct consequence of RC disease			
	↓ = Acetylcholine receptors		38,127	61
	↓ Cholinergic/noncholinergic muscle stimulation			
Sensory nerves	± Injury			56,95,160,169
Shoulder muscle activity and kinematics	Modifications of muscle recruitment and kinematics	17,71,87,97,128,133,138,		
	↓ Voluntary activation	140,142,143		
	↑ = Strength with pain reduction	9,33,115		
Cortical changes	↓ Corticospinal excitability	11,110		

↓, decreased; ↑, increased; =, unchanged.

Numbers refer to references; review articles are excluded.

bilateral alterations of corticospinal excitability in the deltoid and the first interosseous muscles have been reported in patients with RC tendon tears.¹¹ However, spinal motoneuron excitability must be properly assessed to verify that the change in size of MEPs is not mediated at the spinal level.³⁷ C3-C4 propriospinal neurons may also influence the excitability of premotoneuronal sites and therefore the amplitude of MEPs.^{43,125} Peripheral nerve stimulation associated with TMS has been used recently in healthy subjects to assess the modulation of afferent signals on M1 output,⁵⁴ thus opening the possibility for its application in patients with RC disease. Further TMS studies are required to confirm the effects of RC disease on the motor cortex and to understand how these alterations may impair muscle activation, motor control, and shoulder function.

Conclusion and perspective

In this review, we identified a large number of neural structures and mechanisms that may contribute to pain and shoulder dysfunction in patients with RC disease. These structures and mechanisms are summarized in Figure 1. However, numerous questions remain unanswered (Table II). Current data suggest that inflammation and muscle-tendon unit impairment disrupt proprioceptive function and reflex muscle activity.

Alterations of proprioceptive afferents may impair proprioception and motor control, therefore contributing to poor muscle activation and impaired shoulder kinematics. However, motor control and proprioception impairments in patients with RC diseases have been insufficiently assessed and require further investigations. Current advances in the understanding of pain pathophysiology encourage the enhancement of pain assessment and sensory abnormalities that remain poorly characterized in the clinical setting in patients with RC disease. Recent experiments suggest that the occurrence of motor nerve injury appears to be less frequent than first assumed, yet peripheral nerve dysfunction remains a non-negligible aggravating factor. Thus, this problem must be considered (perhaps with improved diagnostic tools) in clinical practice and further explored through both anatomic and physiologic studies. Some data also highlight that tendon disruption, disuse, and inflammation may have a direct impact on neuromuscular junction and motoneurons, but further studies are needed for confirmation. Increased availability of human tissue obtained during surgeries and animal models of RC disease will also improve our understanding of RC physiopathology and will help define markers able to improve the detection of muscle denervation processes. Damage inflicted to sensory nerves should not be neglected because it may contribute to the generation of

pain and disrupt the afferent transduction of proprioceptive information. Evidence that RC disease induces significant motor adaptations and the important role of pain in these changes have been clearly demonstrated. However, the contribution of proprioception deficits, motor cortical changes, and modified brain activity in patients with RC disease remains to be explored. The problem of motor nervous system dysfunction is particularly relevant as the field begins to explore the mechanisms of reduced muscle force generation after reconstruction. If these problems are induced or aggravated by poor muscle activation, the nervous system impairments may need to be addressed first, perhaps in a way that is consistent with neurorehabilitation instead of standard musculoskeletal physical therapy. In the clinical setting, all these factors may contribute to explain why clinical presentations and responses to treatments can vary considerably between individuals despite similar peripheral tissue damage. Therefore, our final proposal is that different profiles involving different degrees of biomechanical, motor control, proprioceptive, and nociceptive impairments exist among patients with RC disease. The development of standardized tests achievable in the clinical setting to assess each of these aspects is necessary to provide comprehensive assessment and to refine the management of these patients.

Disclaimer

The authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References

1. Albritton MJ, Graham RD, Richards RS 2nd, Basamania CJ. An anatomic study of the effects on the suprascapular nerve due to retraction of the supraspinatus muscle after a rotator cuff tear. *J Shoulder Elbow Surg* 2003;12:497-500. [http://dx.doi.org/10.1016/S1058-2746\(03\)00182-4](http://dx.doi.org/10.1016/S1058-2746(03)00182-4)
2. Aszmann OC, Dellon AL, Birely BT, McFarland EG. Innervation of the human shoulder joint and its implications for surgery. *Clin Orthop Relat Res* 1996;202-7.
3. Backenkohler U, Halata Z, Strassmann TJ. The sensory innervation of the shoulder joint of the mouse. *Ann Anat* 1996;178:173-81.
4. Bandholm T, Rasmussen L, Aagaard P, Jensen BR, Diederichsen L. Force steadiness, muscle activity, and maximal muscle strength in subjects with subacromial impingement syndrome. *Muscle Nerve* 2006;34:631-9. <http://dx.doi.org/10.1002/mus.20636>
5. Bank PJ, Peper CE, Marinus J, Beek PJ, van Hilten JJ. Motor consequences of experimentally induced limb pain: a systematic review. *Eur J Pain* 2013;17:145-57. <http://dx.doi.org/10.1002/j.1532-2149.2012.00186.x>
6. Barden JM, Balyk R, Raso VJ, Moreau M, Bagnall K. Dynamic upper limb proprioception in multidirectional shoulder instability. *Clin Orthop Relat Res* 2004;181-9.
7. Bayramoglu A, Demiryurek D, Tuccar E, Erbil M, Aldur MM, Tetik O, et al. Variations in anatomy at the suprascapular notch possibly causing suprascapular nerve entrapment: an anatomical study. *Knee Surg Sports Traumatol Arthrosc* 2003;11:393-8. <http://dx.doi.org/10.1007/s00167-003-0378-3>
8. Beeler S, Ek ET, Gerber C. A comparative analysis of fatty infiltration and muscle atrophy in patients with chronic rotator cuff tears and suprascapular neuropathy. *J Shoulder Elbow Surg* 2013;22:1537-46. <http://dx.doi.org/10.1016/j.jse.2013.01.028>
9. Ben-Yishay A, Zuckerman JD, Gallagher M, Cuomo F. Pain inhibition of shoulder strength in patients with impingement syndrome. *Orthopedics* 1994;17:685-8.
10. Beranek R, Hnik P. Long-term effects of tenotomy on spinal monosynaptic response in the cat. *Science* 1959;130:981-2.
11. Berth A, Pap G, Neuman W, Awiszus F. Central neuromuscular dysfunction of the deltoid muscle in patients with chronic rotator cuff tears. *J Orthop Trauma* 2009;10:135-41. <http://dx.doi.org/10.1007/s10195-009-0061-7>
12. Boykin RE, Friedman DJ, Higgins LD, Warner JJ. Suprascapular neuropathy. *J Bone Joint Surg Am* 2010;92:2348-64. <http://dx.doi.org/10.2106/JBJS.I.01743>
13. Boykin RE, Friedman DJ, Zimmer ZR, Oaklander AL, Higgins LD, Warner JJ. Suprascapular neuropathy in a shoulder referral practice. *J Shoulder Elbow Surg* 2011;20:983-8. <http://dx.doi.org/10.1016/j.jse.2010.10.039>
14. Carlson BM, Borissov G, Dedkov EI, Dow DE, Kostrominova TY. The biology and restorative capacity of long-term denervated skeletal muscle. *Basic Appl Myol* 2002;12:247-54.
15. Chaudhury S, Gwilym SE, Moser J, Carr AJ. Surgical options for patients with shoulder pain. *Nat Rev Rheumatol* 2010;6:217-26. <http://dx.doi.org/10.1038/nrrheum.2010.25>
16. Collin P, Treseder T, Ladermann A, Benkalfate T, Mourtada R, Courage O, et al. Neuropathy of the suprascapular nerve and massive rotator cuff tears: a prospective electromyographic study. *J Shoulder Elbow Surg* 2014;23:28-34. <http://dx.doi.org/10.1016/j.jse.2013.07.039>
17. Cordasco FA, Chen NC, Backus SI, Kelly BT, Williams RJ 3rd, Otis JC. Subacromial injection improves deltoid firing in subjects with large rotator cuff tears. *HSS J* 2010;6:30-6. <http://dx.doi.org/10.1007/s11420-009-9127-6>
18. Costouros JG, Porramatikul M, Lie DT, Warner JJ. Reversal of suprascapular neuropathy following arthroscopic repair of massive supraspinatus and infraspinatus rotator cuff tears. *Arthroscopy* 2007;23:1152-61. <http://dx.doi.org/10.1016/j.arthro.2007.06.014>
19. Craik JD, Mallina R, Ramasamy V, Little NJ. Human evolution and tears of the rotator cuff. *Int Orthop* 2014;38:547-52. <http://dx.doi.org/10.1007/s00264-013-2204-y>
20. Cummins CA, Messer TM, Nuber GW. Suprascapular nerve entrapment. *J Bone Joint Surg Am* 2000;82:415-24.
21. Cuomo F, Birdzell MG, Zuckerman JD. The effect of degenerative arthritis and prosthetic arthroplasty on shoulder proprioception. *J Shoulder Elbow Surg* 2005;14:345-8. <http://dx.doi.org/10.1016/j.jse.2004.07.009>
22. de Castro Pochini A, Ejnisman B, de Seixas Alves MT, Uyeda LF, Nouailhetas VL, Han SW, et al. Overuse of training increases mechanoreceptors in supraspinatus tendon of rats SHR. *J Orthop Res* 2011;29:1771-4. <http://dx.doi.org/10.1002/jor.21320>
23. Dean BJ, Franklin SL, Carr AJ. The peripheral neuronal phenotype is important in the pathogenesis of painful human tendinopathy: a systematic review. *Clin Orthop Relat Res* 2013;471:3036-46. <http://dx.doi.org/10.1007/s11999-013-3010-y>

24. Dean BJ, Gwilym SE, Carr AJ. Why does my shoulder hurt? A review of the neuroanatomical and biochemical basis of shoulder pain. *Br J Sports Med* 2013;47:1095-104. <http://dx.doi.org/10.1136/bjsports-2012-091492>
25. Debeyre J, Patie D, Elmelik E. Repair of ruptures of the rotator cuff of the shoulder. *Br J Sports Med* 1965;47:36-42.
26. Deniz G, Kose O, Tugay A, Guler F, Turan A. Fatty degeneration and atrophy of the rotator cuff muscles after arthroscopic repair: does it improve, halt or deteriorate? *Arch Orthop Trauma Surg* 2014;134:985-90. <http://dx.doi.org/10.1007/s00402-014-2009-5>
27. Diederichsen L, Krogsgaard M, Voigt M, Dyhre-Poulsen P. Shoulder reflexes. *J Electromyogr Kinesiol* 2002;12:183-91. [http://dx.doi.org/10.1016/S1050-6411\(02\)00019-6](http://dx.doi.org/10.1016/S1050-6411(02)00019-6)
28. Duparc F, Coquerel D, Ozeel J, Noyon M, Gerometta A, Michot C. Anatomical basis of the suprascapular nerve entrapment, and clinical relevance of the supraspinatus fascia. *Arch Orthop Trauma Surg* 2010;32:277-84. <http://dx.doi.org/10.1007/s00276-010-0631-7>
29. Ebraheim NA, Whitehead JL, Alla SR, Moral MZ, Castillo S, McCollough AL, et al. The suprascapular nerve and its articular branch to the acromioclavicular joint: an anatomic study. *J Shoulder Elbow Surg* 2011;20:e13-7. <http://dx.doi.org/10.1016/j.jse.2010.09.004>
30. Edelstein L, Thomas SJ, Soslowky LJ. Rotator cuff tears: what have we learned from animal models? *J Musculoskelet Neuronal Interact* 2011;11:150-62.
31. Ellis A, Bennett DL. Neuroinflammation and the generation of neuropathic pain. *Br J Anaesth* 2013;111:26-37. <http://dx.doi.org/10.1093/bja/aet128>
32. Elser F, Braun S, Dewing CB, Giphart JE, Millett PJ. Anatomy, function, injuries, and treatment of the long head of the biceps brachii tendon. *Arthroscopy* 2011;27:581-92. <http://dx.doi.org/10.1016/j.arthro.2010.10.014>
33. Farshad M, Jundt-Ecker M, Sutter R, Schubert M, Gerber C. Does subacromial injection of a local anesthetic influence strength in healthy shoulders?: a double-blinded, placebo-controlled study. *J Bone Joint Surg Am* 2012;94:1751-5. <http://dx.doi.org/10.2106/JBJS.K.00855>
34. Franklin SL, Dean BJ, Whewey K, Watkins B, Javaid MK, Carr AJ. Up-regulation of glutamate in painful human supraspinatus tendon tears. *Am J Sports Med* 2014;42:1955-62. <http://dx.doi.org/10.1177/0363546514532754>
35. Fucentese SF, von Roll AL, Pfirrmann CW, Gerber C, Jost B. Evolution of nonoperatively treated symptomatic isolated full-thickness supraspinatus tears. *J Bone Joint Surg Am* 2012;94:801-8. <http://dx.doi.org/10.2106/JBJS.I.01286>
36. Galatz LM, Ball CM, Teefey SA, Middleton WD, Yamaguchi K. The outcome and repair integrity of completely arthroscopically repaired large and massive rotator cuff tears. *J Bone Joint Surg Am* 2004;86:219-24.
37. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev* 2001;81:1725-89.
38. Gayton JC, Rubino LJ, Rich MM, Stouffer MH, Wang Q, Boivin GP. Rabbit supraspinatus motor endplates are unaffected by a rotator cuff tear. *J Orthop Res* 2013;31:99-104. <http://dx.doi.org/10.1002/jor.22192>
39. Ge HY, Fernandez-de-Las-Penas C, Madeleine P, Arendt-Nielsen L. Topographical mapping and mechanical pain sensitivity of myofascial trigger points in the infraspinatus muscle. *Eur J Pain* 2008;12:859-65. <http://dx.doi.org/10.1016/j.ejpain.2007.12.005>
40. Gohlke F, Janssen E, Leidel J, Heppelmann B, Eulert J. Histopathological findings in the proprioception of the shoulder joint. *Orthopade* 1998;27:510-7.
41. Gotoh M, Hamada K, Yamakawa H, Inoue A, Fukuda H. Increased substance P in subacromial bursa and shoulder pain in rotator cuff diseases. *J Orthop Res* 1998;16:618-21.
42. Goutallier D, Postel JM, Boudon R, Lavau L, Bernageau J. A study of the neurologic risk in tendino-muscular advancement of supra-spinatus and infra-spinatus in the repair of large rotator cuff rupture. *Rev Chir Orthop Reparatrice Appar Mot* 1996;82:299-305.
43. Gracies JM, Meunier S, Pierrot-Deseilligny E, Simonetta M. Pattern of propriospinal-like excitation to different species of human upper limb motoneurons. *J Physiol* 1991;434:151-67.
44. Greiner A, Golser K, Wambacher M, Kralinger F, Sperner G. The course of the suprascapular nerve in the supraspinatus fossa and its vulnerability in muscle advancement. *J Shoulder Elbow Surg* 2003;12:256-9. [http://dx.doi.org/10.1016/S1058-2746\(02\)00034-4](http://dx.doi.org/10.1016/S1058-2746(02)00034-4)
45. Gruet M, Temesi J, Rupp T, Levy P, Millet GY, Verges S. Stimulation of the motor cortex and corticospinal tract to assess human muscle fatigue. *Neuroscience* 2013;231:384-99. <http://dx.doi.org/10.1016/j.neuroscience.2012.10.058>
46. Guanche C, Knatt T, Solomonow M, Lu Y, Baratta R. The synergistic action of the capsule and the shoulder muscles. *Am J Sports Med* 1995;23:301-6.
47. Guanche CA, Noble J, Solomonow M, Wink CS. Periarticular neural elements in the shoulder joint. *Orthopedics* 1999;22:615-7.
48. Gwilym SE, Oag HC, Tracey I, Carr AJ. Evidence that central sensitisation is present in patients with shoulder impingement syndrome and influences the outcome after surgery. *J Bone Joint Surg Am* 2011;93:498-502. <http://dx.doi.org/10.1302/0301-620X.93B4.25054>
49. Ha'eri GB, Wiley AM. Advancement of the supraspinatus muscle in the repair of ruptures of the rotator cuff. *J Bone Joint Surg Am* 1981;63:232-8.
50. Harris JD, Pedroza A, Jones GL, Group MS. Predictors of pain and function in patients with symptomatic, atraumatic full-thickness rotator cuff tears: a time-zero analysis of a prospective patient cohort enrolled in a structured physical therapy program. *Am J Sports Med* 2012;40:359-66. <http://dx.doi.org/10.1177/0363546511426003>
51. Hashimoto T, Hamada T, Sasaguri Y, Suzuki K. Immunohistochemical approach for the investigation of nerve distribution in the shoulder joint capsule. *Clin Orthop Relat Res* 1994:273-82.
52. Hattrup SJ, Cofield RH. Rotator cuff tears with cervical radiculopathy. *J Shoulder Elbow Surg* 2010;19:937-43. <http://dx.doi.org/10.1016/j.jse.2010.05.007>
53. Heales LJ, Lim EC, Hodges PW, Vicenzino B. Sensory and motor deficits exist on the non-injured side of patients with unilateral tendon pain and disability—implications for central nervous system involvement: a systematic review with meta-analysis. *Br J Sports Med* 2014;48:1400-6. <http://dx.doi.org/10.1136/bjsports-2013-092535>
54. HENDY KA, Visser A, Hordacre B, Bradnam LV. Afferent inhibition of infraspinatus primary motor cortex by stimulation of the suprascapular nerve. *Brain Stimul* 2014;7:338-9. <http://dx.doi.org/10.1016/j.brs.2013.12.015>
55. Hidalgo-Lozano A, Fernandez-de-las-Penas C, Alonso-Blanco C, Ge HY, Arendt-Nielsen L, Arroyo-Morales M. Muscle trigger points and pressure pain hyperalgesia in the shoulder muscles in patients with unilateral shoulder impingement: a blinded, controlled study. *Exp Brain Res* 2010;202:915-25. <http://dx.doi.org/10.1007/s00221-010-2196-4>
56. Hnik P, Beranek R, Vyklicky L, Zelena J. Sensory outflow from chronically tenotomized muscles. *Physiol Bohemoslov* 1963;12:23-9.
57. Hnik P, Lessler MJ. Alterations in spindle activity during long-term tenotomy in the rat gastrocnemius muscle. *Exp Neurol* 1973;40:232-42.
58. Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. *Pain* 2011;152:S90-8. <http://dx.doi.org/10.1016/j.pain.2010.10.020>
59. Hoellrich RG, Gasser SI, Morrison DS, Kurzweil PR. Electromyographic evaluation after primary repair of massive rotator cuff tears. *J Shoulder Elbow Surg* 2005;14:269-72. <http://dx.doi.org/10.1016/j.jse.2004.09.013>

60. Iqbal K, Iqbal R. Classification of suprascapular notch according to anatomical measurements in human scapulae. *J Coll Physicians Surg Pak* 2011;21:169-70.
61. Jamali AA, Afshar P, Abrams RA, Lieber RL. Skeletal muscle response to tenotomy. *Muscle Nerve* 2000;23:851-62.
62. Jang JS, Choi HJ, Kang SH, Yang JS, Lee JJ, Hwang SM. Effect of pulsed radiofrequency neuromodulation on clinical improvements in the patients of chronic intractable shoulder pain. *J Korean Neurosurg Soc* 2013;54:507-10. <http://dx.doi.org/10.3340/jkns.2013.54.6.507>
63. Jerosch J, Saad M, Greig M, Filler T. Suprascapular nerve block as a method of preemptive pain control in shoulder surgery. *Knee Surg Sports Traumatol Arthrosc* 2008;16:602-7. <http://dx.doi.org/10.1007/s00167-008-0520-3>
64. Jerosch J, Thorwesten L. Proprioceptive abilities of patients with post-traumatic instability of the glenohumeral joint. *Z Orthop Ihre Grenzgeb* 1998;136:230-7.
65. Joshi SK, Kim HT, Feeley BT, Liu X. Differential ubiquitin-proteasome and autophagy signaling following rotator cuff tears and suprascapular nerve injury. *J Orthop Res* 2014;32:138-44. <http://dx.doi.org/10.1002/jor.22482>
66. Joshi SK, Liu X, Samagh SP, Lovett DH, Bodine SC, Kim HT, et al. mTOR regulates fatty infiltration through SREBP-1 and PPAR-gamma after a combined massive rotator cuff tear and suprascapular nerve injury in rats. *J Orthop Res* 2013;31:724-30. <http://dx.doi.org/10.1002/jor.22254>
67. Jozsa L, Kvist M, Kannus P, Jarvinen M. The effect of tenotomy and immobilization on muscle spindles and tendon organs of the rat calf muscles. A histochemical and morphometrical study. *Acta Neuropathol* 1988;76:465-70.
68. Kang JR, Gupta R. Mechanisms of fatty degeneration in massive rotator cuff tears. *J Shoulder Elbow Surg* 2012;21:175-80. <http://dx.doi.org/10.1016/j.jse.2011.11.017>
69. Kaplan PE, Kernahan WT Jr. Rotator cuff rupture: management with suprascapular neuropathy. *Arch Phys Med Rehabil* 1984;65:273-5.
70. Kapreli E, Athanasopoulos S, Gliatis J, Papathanasiou M, Peeters R, Strimpakos N, et al. Anterior cruciate ligament deficiency causes brain plasticity: a functional MRI study. *Am J Sports Med* 2009;37:2419-26. <http://dx.doi.org/10.1177/0363546509343201>
71. Kelly BT, Williams RJ, Cordasco FA, Backus SI, Otis JC, Weiland DE, et al. Differential patterns of muscle activation in patients with symptomatic and asymptomatic rotator cuff tears. *J Shoulder Elbow Surg* 2005;14:165-71. <http://dx.doi.org/10.1016/j.jse.2004.06.010>
72. Killian ML, Cavinatto L, Galatz LM, Thomopoulos S. Recent advances in shoulder research. *Arthritis Res Ther* 2012;14:214. <http://dx.doi.org/10.1186/ar3846>
73. Kim HM, Galatz LM, Lim C, Havlioglu N, Thomopoulos S. The effect of tear size and nerve injury on rotator cuff muscle fatty degeneration in a rodent animal model. *J Shoulder Elbow Surg* 2012;21:847-58. <http://dx.doi.org/10.1016/j.jse.2011.05.004>
74. Kocak M, Ulmer JL, Sahin Ugurel M, Gaggl W, Prost RW. Motor homunculus: passive mapping in healthy volunteers by using functional MR imaging—initial results. *Radiology* 2009;251:485-92. <http://dx.doi.org/10.1148/radiol.2512080231>
75. Kozak W, Westerman RA. Plastic changes of spinal monosynaptic responses from tenotomized muscles in cats. *Nature* 1961;189:753-5.
76. Kuhn JE, Dunn WR, Sanders R, An Q, Baumgarten KM, Bishop JY, et al. Effectiveness of physical therapy in treating atraumatic full-thickness rotator cuff tears: a multicenter prospective cohort study. *J Shoulder Elbow Surg* 2013;22:1371-9. <http://dx.doi.org/10.1016/j.jse.2013.01.026>
77. Kurokawa D, Sano H, Nagamoto H, Omi R, Shinozaki N, Watanuki S, et al. Muscle activity pattern of the shoulder external rotators differs in adduction and abduction: an analysis using positron emission tomography. *J Shoulder Elbow Surg* 2014;23:658-64. <http://dx.doi.org/10.1016/j.jse.2013.12.021>
78. Laurin J, Gondin J, Dousset E, Decherchi P. Effect of tenotomy on metabosensitive afferent fibers from tibialis anterior muscle. *Exp Brain Res* 2008;186:87-92. <http://dx.doi.org/10.1007/s00221-007-1210-y>
79. Le BT, Wu XL, Lam PH, Murrell GA. Factors predicting rotator cuff retears: an analysis of 1000 consecutive rotator cuff repairs. *Am J Sports Med* 2014;42:1134-42. <http://dx.doi.org/10.1177/0363546514525336>
80. Leclere LE, Shi LL, Lin A, Yannopoulos P, Higgins LD, Warner JJ. Complete fatty infiltration of intact rotator cuffs caused by suprascapular neuropathy. *Arthroscopy* 2014;30:639-44. <http://dx.doi.org/10.1016/j.arthro.2014.01.010>
81. Lee HY, Chung IH, Sir WS, Kang HS, Lee HS, Ko JS, et al. Variations of the ventral rami of the brachial plexus. *J Korean Med Sci* 1992;7:19-24.
82. Lehmann HC, Zhang J, Mori S, Sheikh KA. Diffusion tensor imaging to assess axonal regeneration in peripheral nerves. *Exp Neurol* 2010;223:238-44. <http://dx.doi.org/10.1016/j.expneurol.2009.10.012>
83. Liu X, Joshi SK, Samagh SP, Dang YX, Laron D, Lovett DH, et al. Evaluation of Akt/mTOR activity in muscle atrophy after rotator cuff tears in a rat model. *J Orthop Res* 2012;30:1440-6. <http://dx.doi.org/10.1002/jor.22096>
84. Liu X, Laron D, Natsuhara K, Manzano G, Kim HT, Feeley BT. A mouse model of massive rotator cuff tears. *J Bone Joint Surg Am* 2012;94:e41. <http://dx.doi.org/10.2106/JBJS.K.00620>
85. Lu DX, Huang SK, Carlson BM. Electron microscopic study of long-term denervated rat skeletal muscle. *Anat Rec* 1997;248:355-65.
86. Lubiatowski P, Ogradowicz P, Wojtaszek M, Kaniewski R, Stefaniak J, Dudzinski W, et al. Measurement of active shoulder proprioception: dedicated system and device. *Eur J Orthop Surg Traumatol* 2013;23:177-83. <http://dx.doi.org/10.1007/s00590-012-0950-y>
87. Ludewig PM, Reynolds JF. The association of scapular kinematics and glenohumeral joint pathologies. *J Orthop Sports Phys Ther* 2009;39:90-104. <http://dx.doi.org/10.2519/jospt.2009.2808>
88. MacDermid JC, Ramos J, Drosdowech D, Faber K, Patterson S. The impact of rotator cuff pathology on isometric and isokinetic strength, function, and quality of life. *J Shoulder Elbow Surg* 2004;13:593-8. <http://dx.doi.org/10.1016/j.jse.2004.03.009>
89. Machner A, Merk H, Becker R, Rohkohl K, Wissel H, Pap G. Kinesthetic sense of the shoulder in patients with impingement syndrome. *Acta Orthop Scand* 2003;74:85-8. <http://dx.doi.org/10.1080/00016470310013716>
90. Maenhout AG, Palmans T, De Muynck M, De Wilde LF, Cools AM. The impact of rotator cuff tendinopathy on proprioception, measuring force sensation. *J Shoulder Elbow Surg* 2012;21:1080-6. <http://dx.doi.org/10.1016/j.jse.2011.07.006>
91. Mall NA, Kim HM, Keener JD, Steger-May K, Teefey SA, Middleton WD, et al. Symptomatic progression of asymptomatic rotator cuff tears: a prospective study of clinical and sonographic variables. *J Bone Joint Surg Am* 2010;92:2623-33. <http://dx.doi.org/10.2106/JBJS.I.00506>
92. Mall NA, Tanaka MJ, Choi LS, Paletta GA Jr. Factors affecting rotator cuff healing. *J Bone Joint Surg Am* 2014;96:778-88. <http://dx.doi.org/10.2106/JBJS.M.00583>
93. Mallon WJ, Wilson RJ, Basamania CJ. The association of suprascapular neuropathy with massive rotator cuff tears: a preliminary report. *J Shoulder Elbow Surg* 2006;15:395-8. <http://dx.doi.org/10.1016/j.jse.2005.10.019>
94. Massimini DF, Singh A, Wells JH, Li G, Warner JJ. Suprascapular nerve anatomy during shoulder motion: a cadaveric proof of concept study with implications for neurogenic shoulder pain. *J Shoulder Elbow Surg* 2013;22:463-70. <http://dx.doi.org/10.1016/j.jse.2012.04.018>
95. Matsumoto DE, Baker JH. Degeneration and alteration of axons and intrafusal muscle fibers in spindles following tenotomy. *Exp Neurol* 1987;97:482-98.

96. Matthews TJ, Hand GC, Rees JL, Athanasou NA, Carr AJ. Pathology of the torn rotator cuff tendon. Reduction in potential for repair as tear size increases. *J Bone Joint Surg Br* 2006;88:489-95. <http://dx.doi.org/10.1302/0301-620X.88B4.16845>
97. McClure PW, Michener LA, Karduna AR. Shoulder function and 3-dimensional scapular kinematics in people with and without shoulder impingement syndrome. *Phys Ther* 2006;86:1075-90.
98. McElvany MD, McGoldrick E, Gee AO, Neradilek MB, Matsen FA 3rd. Rotator cuff repair: published evidence on factors associated with repair integrity and clinical outcome. *Am J Sports Med* 2015;43:491-500. <http://dx.doi.org/10.1177/0363546514529644>
99. McNeil CJ, Butler JE, Taylor JL, Gandevia SC. Testing the excitability of human motoneurons. *Front Hum Neurosci* 2013;7:152. <http://dx.doi.org/10.3389/fnhum.2013.00152>
100. Melgari JM, Pasqualetti P, Pauri F, Rossini PM. Muscles in "concert": study of primary motor cortex upper limb functional topography. *PLoS One* 2008;3:e3069. <http://dx.doi.org/10.1371/journal.pone.0003069>
101. Mense S. Functional anatomy of muscle: muscle, nociceptors and afferent fibers. In: Mense S, Gerwin RD, editors. *Muscle pain: understanding the mechanisms*. Berlin: Springer; 2010. p. 17-48. http://dx.doi.org/10.1007/978-3-540-85021-2_2
102. Midrio M. The denervated muscle: facts and hypotheses. A historical review. *Eur J Appl Physiol* 2006;98:1-21. <http://dx.doi.org/10.1007/s00421-006-0256-z>
103. Millet GY, Bachasson D, Temesi J, Wuyam B, Feasson L, Verges S, et al. Potential interests and limits of magnetic and electrical stimulation techniques to assess neuromuscular fatigue. *Neuromuscul Disord* 2012;22(Suppl 3):S181-6. <http://dx.doi.org/10.1016/j.nmd.2012.10.007>
104. Minagawa H, Yamamoto N, Abe H, Fukuda M, Seki N, Kikuchi K, et al. Prevalence of symptomatic and asymptomatic rotator cuff tears in the general population: from mass-screening in one village. *J Orthop* 2013;10:8-12. <http://dx.doi.org/10.1016/j.jor.2013.01.008>
105. Minaki Y, Yamashita T, Takebayashi T, Ishii S. Mechanosensitive afferent units in the shoulder and adjacent tissues. *Clin Orthop Relat Res* 1999;349:56.
106. Moen TC, Babatunde OM, Hsu SH, Ahmad CS, Levine WN. Suprascapular neuropathy: what does the literature show? *J Shoulder Elbow Surg* 2012;21:835-46. <http://dx.doi.org/10.1016/j.jse.2011.11.033>
107. Moosmayer S, Tariq R, Stiris M, Smith HJ. The natural history of asymptomatic rotator cuff tears: a three-year follow-up of fifty cases. *J Bone Joint Surg Am* 2013;95:1249-55. <http://dx.doi.org/10.2106/JBJS.L.00185>
108. Myers JB, Wassinger CA, Lephart SM. Sensorimotor contribution to shoulder stability: effect of injury and rehabilitation. *Man Ther* 2006;11:197-201. <http://dx.doi.org/10.1016/j.math.2006.04.002>
109. Natsis K, Totlis T, Tsikaras P, Appell HJ, Skandalakis P, Koebke J. Proposal for classification of the suprascapular notch: a study on 423 dried scapulas. *Clin Anat* 2007;20:135-9. <http://dx.doi.org/10.1002/ca.20318>
110. Ngomo S, Mercier C, Bouyer LJ, Savoie A, Roy JS. Alterations in central motor representation increase over time in individuals with rotator cuff tendinopathy. *Clin Neurophysiol* 2015;126:365-71. <http://dx.doi.org/10.1016/j.clinph.2014.05.035>
111. Ngomo S, Mercier C, Roy JS. Cortical mapping of the infraspinatus muscle in healthy individuals. *BMC Neurosci* 2013;14:52. <http://dx.doi.org/10.1186/1471-2202-14-52>
112. Oh LS, Wolf BR, Hall MP, Levy BA, Marx RG. Indications for rotator cuff repair: a systematic review. *Clin Orthop Relat Res* 2007;455:52-63.
113. Omi R, Sano H, Ohnuma M, Kishimoto KN, Watanuki S, Tashiro M, et al. Function of the shoulder muscles during arm elevation: an assessment using positron emission tomography. *J Anat* 2010;216:643-9. <http://dx.doi.org/10.1111/j.1469-7580.2010.01212.x>
114. Padua L, Martinoli C. From square to cube: ultrasound as a natural complement of neurophysiology. *Clin Neurophysiol* 2008;119:1217-8. <http://dx.doi.org/10.1016/j.clinph.2008.02.005>
115. Park JY, Lee WS, Lee ST. The strength of the rotator cuff before and after subacromial injection of lidocaine. *J Shoulder Elbow Surg* 2008;17:8S-11S. <http://dx.doi.org/10.1016/j.jse.2007.06.010>
116. Pham M, Baumer T, Bendszus M. Peripheral nerves and plexus: imaging by MR-neurography and high-resolution ultrasound. *Curr Opin Neurol* 2014;27:370-9. <http://dx.doi.org/10.1097/WCO.0000000000000111>
117. Plancher KD, Luke TA, Peterson RK, Yacoubian SV. Posterior shoulder pain: a dynamic study of the spinoglenoid ligament and treatment with arthroscopic release of the scapular tunnel. *Arthroscopy* 2007;23:991-8. <http://dx.doi.org/10.1016/j.arthro.2007.03.098>
118. Polgaj M, Jedrzejewski K, Podgorski M, Majos A, Topol M. A proposal for classification of the superior transverse scapular ligament: variable morphology and its potential influence on suprascapular nerve entrapment. *J Shoulder Elbow Surg* 2013;22:1265-73. <http://dx.doi.org/10.1016/j.jse.2012.11.017>
119. Polgaj M, Jedrzejewski K, Podgorski M, Topol M. Morphometric study of the suprascapular notch: proposal of classification. *Arch Orthop Trauma Surg* 2011;33:781-7. <http://dx.doi.org/10.1007/s00276-011-0821-y>
120. Polgaj M, Rozniecki J, Sibinski M, Grzegorzewski A, Majos A, Topol M. The variable morphology of suprascapular nerve and vessels at suprascapular notch: a proposal for classification and its potential clinical implications. *Knee Surg Sports Traumatol Arthrosc* 2015;23:1542-8. <http://dx.doi.org/10.1007/s00167-014-2937-1>
121. Prescher A. Anatomical basics, variations, and degenerative changes of the shoulder joint and shoulder girdle. *Eur J Radiol* 2000;35:88-102.
122. Proske U, Gandevia SC. The proprioceptive senses: their roles in signaling body shape, body position and movement, and muscle force. *Physiol Rev* 2012;92:1651-97. <http://dx.doi.org/10.1152/physrev.00048.2011>
123. Reilly P, Macleod I, Macfarlane R, Windley J, Emery RJ. Dead men and radiologists don't lie: a review of cadaveric and radiological studies of rotator cuff tear prevalence. *Ann R Coll Surg Engl* 2006;88:116-21. <http://dx.doi.org/10.1308/003588406X94968>
124. Rengachary SS, Neff JP, Singer PA, Brackett CE. Suprascapular entrapment neuropathy: a clinical, anatomical, and comparative study. Part 1: clinical study. *Neurosurgery* 1979;5:441-6.
125. Roberts LV, Stinear CM, Lewis GN, Byblow WD. Task-dependent modulation of propriospinal inputs to human shoulder. *J Neurophysiol* 2008;100:2109-14. <http://dx.doi.org/10.1152/jn.90786.2008>
126. Rokito AS, Birdzell MG, Cuomo F, Di Paola MJ, Zuckerman JD. Recovery of shoulder strength and proprioception after open surgery for recurrent anterior instability: a comparison of two surgical techniques. *J Shoulder Elbow Surg* 2010;19:564-9. <http://dx.doi.org/10.1016/j.jse.2009.09.010>
127. Rowshan K, Hadley S, Pham K, Caiozzo V, Lee TQ, Gupta R. Development of fatty atrophy after neurologic and rotator cuff injuries in an animal model of rotator cuff pathology. *J Bone Joint Surg Am* 2010;92:2270-8. <http://dx.doi.org/10.2106/JBJS.1.00812>
128. Roy JS, Moffet H, McFadyen BJ. Upper limb motor strategies in persons with and without shoulder impingement syndrome across different speeds of movement. *Clin Biomech (Bristol, Avon)* 2008;23:1227-36. <http://dx.doi.org/10.1016/j.clinbiomech.2008.07.009>
129. Rubino LJ, Stills HF Jr, Sprott DC, Crosby LA. Fatty infiltration of the torn rotator cuff worsens over time in a rabbit model. *Arthroscopy* 2007;23:717-22. <http://dx.doi.org/10.1016/j.arthro.2007.01.023>
130. Russell RD, Knight JR, Mulligan E, Khazzam MS. Structural integrity after rotator cuff repair does not correlate with patient function and pain: a meta-analysis. *J Bone Joint Surg Am* 2014;96:265-71. <http://dx.doi.org/10.2106/JBJS.M.00265>
131. Safran MR, Borsa PA, Lephart SM, Fu FH, Warner JJ. Shoulder proprioception in baseball pitchers. *J Shoulder Elbow Surg* 2001;10:438-44.

132. Salles JI, Cossich VR, Amaral MV, Monteiro MT, Cagy M, Motta G, et al. Electrophysiological correlates of the threshold to detection of passive motion: an investigation in professional volleyball athletes with and without atrophy of the infraspinatus muscle. *Biomed Res Int* 2013;2013:634891. <http://dx.doi.org/10.1155/2013/634891>
133. Scibek JS, Mell AG, Downie BK, Carpenter JE, Hughes RE. Shoulder kinematics in patients with full-thickness rotator cuff tears after a subacromial injection. *J Shoulder Elbow Surg* 2008;17:172-81. <http://dx.doi.org/10.1016/j.jse.2007.05.010>
134. Scully WF, Wilson DJ, Parada SA, Arrington ED. Iatrogenic nerve injuries in shoulder surgery. *J Am Acad Orthop Surg* 2013;21:717-26. <http://dx.doi.org/10.5435/JAAOS-21-12-717>
135. Shi LL, Boykin RE, Lin A, Warner JJ. Association of suprascapular neuropathy with rotator cuff tendon tears and fatty degeneration. *J Shoulder Elbow Surg* 2014;23:339-46. <http://dx.doi.org/10.1016/j.jse.2013.06.011>
136. Shi LL, Freehill MT, Yannopoulos P, Warner JJ. Suprascapular nerve: is it important in cuff pathology? *Adv Orthop* 2012;2012:516985. <http://dx.doi.org/10.1155/2012/516985>
137. Shin C, Lee SE, Yu KH, Chae HK, Lee KS. Spinal root origins and innervations of the suprascapular nerve. *Arch Orthop Trauma Surg* 2010;32:235-8. <http://dx.doi.org/10.1007/s00276-009-0597-5>
138. Shinozaki N, Sano H, Omi R, Kishimoto KN, Yamamoto N, Tashiro M, et al. Differences in muscle activities during shoulder elevation in patients with symptomatic and asymptomatic rotator cuff tears: analysis by positron emission tomography. *J Shoulder Elbow Surg* 2014;23:e61-7. <http://dx.doi.org/10.1016/j.jse.2013.06.009>
139. Snow BJ, Narvy SJ, Omid R, Atkinson RD, Vangsness CT Jr. Anatomy and histology of the transverse humeral ligament. *Orthopedics* 2013;36:e1295-8. <http://dx.doi.org/10.3928/01477447-20130920-23>
140. Sole G, Osborne H, Wassinger C. Electromyographic response of shoulder muscles to acute experimental subacromial pain. *Man Ther* 2014;19:343-8. <http://dx.doi.org/10.1016/j.math.2014.03.001>
141. Solomonow M, Guanche C, Wink C, Knatt T, Baratta RV, Lu Y. Mechanoreceptors and reflex arc in the feline shoulder. *J Shoulder Elbow Surg* 1996;5:139-46.
142. Stackhouse SK, Eisennagel A, Eisennagel J, Lenker H, Sweitzer BA, McClure PW. Experimental pain inhibits infraspinatus activation during isometric external rotation. *J Shoulder Elbow Surg* 2013;22:478-84. <http://dx.doi.org/10.1016/j.jse.2012.05.037>
143. Steenbrink F, de Groot JH, Veeger HE, Meskers CG, van de Sande MA, Rozing PM. Pathological muscle activation patterns in patients with massive rotator cuff tears, with and without subacromial anaesthetics. *Man Ther* 2006;11:231-7. <http://dx.doi.org/10.1016/j.math.2006.07.004>
144. Steinbeck J, Bruntrup J, Greshake O, Potzl W, Filler T, Liljenqvist U. Neurohistological examination of the inferior glenohumeral ligament of the shoulder. *J Orthop Res* 2003;21:250-5. [http://dx.doi.org/10.1016/S0736-0266\(02\)00155-9](http://dx.doi.org/10.1016/S0736-0266(02)00155-9)
145. Subhawong TK, Wang KC, Thawait SK, Williams EH, Hashemi SS, Machado AJ, et al. High resolution imaging of tunnels by magnetic resonance neurography. *Skeletal Radiol* 2012;41:15-31. <http://dx.doi.org/10.1007/s00256-011-1143-1>
146. Sulaiman W, Gordon T. Neurobiology of peripheral nerve injury, regeneration, and functional recovery: from bench top research to bedside application. *Ochsner J* 2013;13:100-8.
147. Tamai M, Okajima S, Fushiki S, Hirasawa Y. Quantitative analysis of neural distribution in human coracoacromial ligaments. *Clin Orthop Relat Res* 2000;125-34.
148. Tapadia M, Mozaffar T, Gupta R. Compressive neuropathies of the upper extremity: update on pathophysiology, classification, and electrodiagnostic findings. *J Hand Surg Am* 2010;35:668-77. <http://dx.doi.org/10.1016/j.jhsa.2010.01.007>
149. Tarumoto R, Murakami M, Imai S, Maeda T, Hukuda S. A morphometric analysis of protein gene product 9.5-, substance P-, and calcitonin gene-related peptide immunoreactive innervation in the shoulder joint of the Japanese macaque. *J Shoulder Elbow Surg* 1998;7:522-8.
150. Tosounidis T, Hadjileontis C, Georgiadis M, Kafanas A, Kontakis G. The tendon of the long head of the biceps in complex proximal humerus fractures: a histological perspective. *Injury* 2010;41:273-8. <http://dx.doi.org/10.1016/j.injury.2009.09.015>
151. Tubbs RS, Nechtman C, D'Antoni AV, Shoja MM, Mortazavi MM, Loukas M, et al. Ossification of the suprascapular ligament: a risk factor for suprascapular nerve compression? *Int J Shoulder Surg* 2013;7:19-22. <http://dx.doi.org/10.4103/0973-6042.109882>
152. Uthoff HK, Coletta E, Trudel G. Intramuscular fat accumulation and muscle atrophy in the absence of muscle retraction. *Bone Joint Res* 2014;3:117-22. <http://dx.doi.org/10.1302/2046-3758.34.2000275>
153. Uthoff HK, Matsumoto F, Trudel G, Himori K. Early reattachment does not reverse atrophy and fat accumulation of the supraspinatus—an experimental study in rabbits. *J Orthop Res* 2003;21:386-92. [http://dx.doi.org/10.1016/S0736-0266\(02\)00208-5](http://dx.doi.org/10.1016/S0736-0266(02)00208-5)
154. Vad VB, Southern D, Warren RF, Altchek DW, Dines D. Prevalence of peripheral neurologic injuries in rotator cuff tears with atrophy. *J Shoulder Elbow Surg* 2003;12:333-6. [http://dx.doi.org/10.1016/S1058-2746\(03\)00040-5](http://dx.doi.org/10.1016/S1058-2746(03)00040-5)
155. Vallejo R, Tilley DM, Williams J, Labak S, Aliaga L, Benyamin RM. Pulsed radiofrequency modulates pain regulatory gene expression along the nociceptive pathway. *Pain Physician* 2013;16:E601-13.
156. Vangsness CT Jr, Ennis M, Taylor JG, Atkinson R. Neural anatomy of the glenohumeral ligaments, labrum, and subacromial bursa. *Arthroscopy* 1995;11:180-4.
157. Veeger HE, van der Helm FC. Shoulder function: the perfect compromise between mobility and stability. *J Biomech* 2007;40:2119-29. <http://dx.doi.org/10.1016/j.jbiomech.2006.10.016>
158. Voigt M, Jakobsen J, Sinkjaer T. Non-noxious stimulation of the glenohumeral joint capsule elicits strong inhibition of active shoulder muscles in conscious human subjects. *Neurosci Lett* 1998;254:105-8.
159. Vorster W, Lange CP, Briet RJ, Labuschagne BC, du Toit DF, Muller CJ, et al. The sensory branch distribution of the suprascapular nerve: an anatomic study. *J Shoulder Elbow Surg* 2008;17:500-2. <http://dx.doi.org/10.1016/j.jse.2007.10.008>
160. Vrbova G. Changes in the motor reflexes produced by tenotomy. *J Physiol* 1963;166:241-50.
161. Ward SR, Hentzen ER, Smallwood LH, Eastlack RK, Burns KA, Fithian DC, et al. Rotator cuff muscle architecture: implications for glenohumeral stability. *Clin Orthop Relat Res* 2006;448:157-63.
162. Warner JP, Krushell RJ, Masquelet A, Gerber C. Anatomy and relationships of the suprascapular nerve: anatomical constraints to mobilization of the supraspinatus and infraspinatus muscles in the management of massive rotator-cuff tears. *J Bone Joint Surg Am* 1992;74:36-45.
163. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain* 2011;152:S2-15. <http://dx.doi.org/10.1016/j.pain.2010.09.030>
164. Yamaguchi K, Ditsios K, Middleton WD, Hildebolt CF, Galatz LM, Teefey SA. The demographic and morphological features of rotator cuff disease. A comparison of asymptomatic and symptomatic shoulders. *J Bone Joint Surg Am* 2006;88:1699-704. <http://dx.doi.org/10.2106/JBJS.E.00835>
165. Yamamoto A, Takagishi K, Kobayashi T, Shitara H, Osawa T. Factors involved in the presence of symptoms associated with rotator cuff tears: a comparison of asymptomatic and symptomatic rotator cuff tears in the general population. *J*

- Shoulder Elbow Surg 2011;20:1133-7. <http://dx.doi.org/10.1016/j.jse.2011.01.011>
166. Yamashita T, Minaki Y, Takebayashi T, Sakamoto N, Ishii S. Neural response of mechanoreceptors to acute inflammation in the rotator cuff of the shoulder joint in rabbits. *Acta Orthop Scand* 1999;70:137-40.
167. Yan J, Horiguchi M. The communicating branch of the 4th cervical nerve to the brachial plexus: the double constitution, anterior and posterior, of its fibers. *Arch Orthop Trauma Surg* 2000;22:175-9.
168. Yang HJ, Gil YC, Jin JD, Ahn SV, Lee HY. Topographical anatomy of the suprascapular nerve and vessels at the suprascapular notch. *Clin Anat* 2012;25:359-65. <http://dx.doi.org/10.1002/ca.21248>
169. Yellin H, Eldred E. Spindle activity of the tenotomized gastrocnemius muscle in the cat. *Exp Neurol* 1970;29:513-33.
170. Zanotti RM, Carpenter JE, Blasier RB, Greenfield ML, Adler RS, Bromberg MB. The low incidence of suprascapular nerve injury after primary repair of massive rotator cuff tears. *J Shoulder Elbow Surg* 1997;6:258-64.