

# What Role Does the Sympathetic Nervous System Play in the Development or Ongoing Pain of Adhesive Capsulitis?

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**Abstract:** While there have been numerous attempts in the literature to explain adhesive capsulitis (AC), many questions remain with respect to the aetiology, pathogenesis, and pain-generating mechanisms of AC. Conflicting results of treatment approaches may be due to the failure to appreciate at which stage of the disease process that the AC is in at the time of intervention (i.e., stages I-IV). Alternatively AC may not be a true single etiology, but rather it may have several forms or combinations of pathology. Sympathetic nervous system involvement, for example, could in part be responsible for the production and maintenance of pain associated with recalcitrant AC shoulders.

**Key Words:** Adhesive capsulitis, Allodynia, Hyperalgesia, Hyperpathia, Neuropathic Pain, Sympathetic Nervous System

**A**dhesive capsulitis, or frozen shoulder, constitutes a medical, social, and economic challenge to society. According to Van der Heijden<sup>1</sup> patients with shoulder disorders are the third largest group of those with musculoskeletal disorders in primary health care, following only patients with lower back and neck disorders. First described in 1945 by Neviaser<sup>2</sup>, the aetiology of the disease remains illusive, and consequently an effective treatment approach has still not been found<sup>3-7</sup>. Given that AC is an idiopathic condition, diagnosis of AC is usually made when other causes of pain and ROM loss have been eliminated<sup>7</sup>. Recently several authors have begun to link AC as a complication of a neuropathic process<sup>8-11</sup>. Where a

neurological component, as opposed to soft-tissue pathology, was determined to be the predominant factor in AC, especially in the early stages, then appropriate treatment would be required to address this factor.

In this review, the mechanism and source of sympathetically originated or maintained pain will be investigated, followed by histopathology of adhesive capsulitis and more recent views of the pathology. Finally, possible connections between the two, i.e., AC and sympathetically maintained pain (SMP), will be discussed.

It is now generally recognized that in mammals, pain is a normal sensory modality signalling tissue damage or pathology to an organism<sup>12,13</sup>. Pain is caused by activation of A-delta (thinly myelinated fibers) or C-fibers (unmyelinated nociceptor units)<sup>14,15</sup>. The A-delta fibers are responsible for sharp, lancinating, well-localized first pain, whereas C-fibers encode slow, poorly localized, diffuse, burning second pain<sup>12</sup>. Noxious stimuli co-activate different pain and somatosensory tissue receptors, whose summated activity results in a blended sensation. Therefore, burning or cold pain is a combination of A-delta cold receptors and C-fiber nociceptors<sup>12</sup>. Following peripheral tissue damage and inflammation or post-nerve

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injury, a state of excessive sensitivity can develop. Low intensity stimuli can initiate pain, which will help prevent injury while recuperation or healing occurs<sup>14</sup>. Sensitisation is not always adaptive, however, and when it is produced after the initial damage has healed, or following nerve injury, it can result in pain of no apparent benefit to the sufferer<sup>14</sup>. If roots, plexi, nerves, or central pain pathways are damaged, pain persistently generated is of no benefit and is termed neuropathic pain<sup>12-14</sup>. Peripheral or central sensitisation can occur, and although neuropathic pain syndromes include a number of different conditions<sup>15</sup>, and arise from a variety of aetiology and pathogenesis, many share common clinical phenomena such as mechanical and thermal hyperalgesia and hyperpathia<sup>12,14-16</sup>.

Neuropathic pain can present in several different forms. Allodynia refers to pain provoked by an innocuous mechanical or thermal stimulus; hyperalgesia is an exaggeration in the response to the activation of high-threshold afferents and therefore enhanced pain perception<sup>12,14</sup>. Hyperpathia reflects a disordered central pain processing in which there is an increased pain threshold; once exceeded, the pain sensation is more severe than expected<sup>12,14,15</sup>.

Under normal physiological conditions in man, sympathetic neurons have little or no effect on the activity of peripheral afferent receptors. However, this may change after trauma, according to Blumberg and Janig<sup>17</sup>. They cite trauma as the most important initiating event in their hypothesis of sympathetically maintained pain<sup>17</sup>. Whilst their hypothesis contains several components, those most relevant to this review are as follows. Afferent neurons (particularly nociceptive ones) may be sensitised as a result of the initial trauma, generating ongoing activity and subsequent abnormal reaction to mechanical, thermal, and chemical stimulation<sup>17</sup>. Sympathetic postganglionic fibers may also sensitise afferent receptors via an inflammatory process<sup>17</sup>. Following trauma, direct chemical coupling between sympathetic and efferent nerve terminals, both distally and centrally, can occur, and produce abnormal afferent impulse traffic to the spinal cord<sup>17</sup>. This continuous nociceptive activity generates spontaneous pain and leads to sensitisation of dorsal horn neurons, resulting in various forms of allodynia and hyperalgesia. Blumberg and Janig<sup>17</sup> maintain that increased or altered sympathetic activity is not necessary for the generation of sympathetically maintained pain.

Adhesive capsulitis is generally recognized as an insidious painful condition of the shoulder, characterized by progressive loss of range of motion<sup>5-7,10,11,18</sup>. Women are more frequently affected than men, and the nondominant side is more frequently involved<sup>3,5,7</sup>. Of those affected, 20-30% will also develop the condition in the opposite shoulder<sup>3,7</sup>. The development of AC is often associated with trauma, age 40 years and greater, diabetes, thyroid disease, prolonged immobilization, stroke or myocardial

infarction, auto-immune disease, cervical disc disease, head injury, tendonitis, bursitis, hormonal changes, suprascapular compression neuropathy, and autonomic neuropathy<sup>4-8</sup>.

Controversy reigns regarding diagnosis, pathophysiology and treatment<sup>1,5,7</sup>. Essentially no completely reliable or pathognomic sign exists for AC, and actual diagnosis remains clinical in nature<sup>7</sup>. Traditionally the causative factors have led to the further classification of primary and secondary AC. Primary AC is characterized by idiopathic, progressive, painful loss of active and passive shoulder motion<sup>5,19</sup>; secondary AC has a similar histopathological appearance<sup>7</sup> but results from a known intrinsic or extrinsic cause<sup>5,19</sup>.

To date, there remains disagreement in the literature regarding whether the underlying pathological process is an inflammatory condition<sup>11,18</sup> or a fibrosing condition<sup>8</sup>. However, there is growing evidential support for the hypothesis that the underlying pathological changes in AC are synovial inflammation with subsequent reactive capsular fibrosis, making adhesive capsulitis both an inflammatory and a fibrosing condition, dependent on the stage of disease process<sup>3,4,7</sup>.

Increased vascularity and hypertrophy of the synovial membrane is a common feature of AC<sup>3,4,7,18,20</sup>. The acute stage is usually associated with intense pain, reflex myospasm, and restriction of movements of the glenohumeral joint. Historically it has been thought that due to lack of movement the synovial fluid does not circulate and becomes sticky, and walls of the axillary fold begin to adhere. The "intra-articular" adhesions formed reduce the capacity of the joint capsule and, therefore, restrict movement of the humeral head<sup>3,4</sup>. Reduction in the capacity of the glenohumeral joint to less than 10ml in AC has been verified by arthrography by several authors<sup>4,5,8,21</sup>. Neviaser<sup>2</sup> first described "intra-articular" adhesions in adhesive capsulitis; he found proliferative synovitis and early adhesion formation occurred during stage II of the disease process, with adhesions becoming fully matured and causing marked restriction by stage IV.

Mao, Jaw, and Chery<sup>5</sup> referred to the "adhesive nature" of the capsule and axillary fold in AC, but they do not describe the presence of any adhesions as such. Poehling cited in Burkhart<sup>22</sup> described intra-articular adhesions between the anterior capsule and intra-articular subscapularis tendon in AC, yet other authors report finding no such adhesions. Rizk, Gavant, and Pinals<sup>8</sup> described the typical radiographic appearance of AC as restriction of joint volume, failure to fill the biceps tendon sheath, and partial obliteration of subscapular and axillary recesses.

More frequently reported than adhesions during arthroscopy is a thickened, contracted capsule<sup>7,8,18,21</sup>. Rizk, Gavant, and Pinals<sup>8</sup> described generalized capsular thickening, little synovial fluid, normal articular cartilage, and little synovial cell hyperplasia; however, they failed to describe the stage of AC during the investigation.

It is commonly accepted that AC progresses through four stages<sup>5,7</sup>. Many of the articles researching, describing, and testing treatments fail to clarify or distinguish the stage at which AC is evolving when under investigation, a point noted by Hannafin and Chiaia<sup>7</sup>, who maintained that this in itself may explain a lot of the contradictory findings of various researchers investigating AC.

Note: Although AC can be broken down into four stages, it is important to remember that these stages represent a continuum of disease rather than discrete well-defined stages.

### *Stage I*

Patient presents with pain (typically dull on rest and sharp at end ROM) of less than 3 months duration, reporting a progressive loss of active ROM. Passive ROM is usually near normal, as the majority of motion loss is secondary to painful synovitis versus true capsular contraction.

Arthroscopic examination reveals a hypertrophic vascular synovitis coating the entire capsular lining<sup>2,7</sup>. Biopsy specimens show rare inflammatory infiltrates, a hypervascular synovitis, and normal morphologic characteristics<sup>7</sup>.

### *Stage II*

Patient presents with persistence of the pain pattern as above, present for 3-9 months with progressive loss of ROM. Passive ROM exhibits partial improvement only under local anesthetic, and loss of ROM here reflects a loss of capsular volume and response to painful synovitis. Arthroscopic examination reveals a dense, proliferative, hypervascular synovitis<sup>2,5,7</sup>. A capsular biopsy specimen reveals hypervascular synovitis with perivascular scar formation and capsular fibroplasia with deposition of disorganized collagen fibrils and hypercellular appearance, but no presence of inflammatory infiltrates<sup>7</sup>.

### *Stage III*

At this point, patient presents with a history of painful stiffening of the shoulder and significant loss of ROM, with symptoms changing over the previous 9-14 months resulting in a relatively pain-free but stiff shoulder. Neviasser<sup>2</sup> noted this as the stage of maturation with loss of axillary fold. Arthroscopic examination during this phase is unremarkable when compared with stages I and II, with patchy synovial thickening without hypervascularity. Capsular biopsy specimens reveal a dense, hypercellular collagenous tissue<sup>7</sup>.

### *Stage IV*

This final or "thawing" stage is characterized by slow,

steady recovery of ROM resulting from capsular remodeling in response to using the shoulder.

As patients in this stage rarely undergo surgery, no arthroscopic or histological data is available<sup>7</sup>.

Hannafin and Chiaia<sup>7</sup> and Hazelman (1972, cited in Hannafin & Chiaia<sup>7</sup>) both assessed the use of intra-articular corticosteroid for treating AC. Both found that the success of treatment was dependant on the duration of the symptoms. Patients treated within 3 months of the onset of symptoms reported a significant improvement in symptoms, whereas patients whose symptoms had exceeded 5 months had a more delayed recovery. This evidence supports the hypothesis that AC is an inflammatory and fibrotic condition; early on, a hypervascular synovial hyperplasia is present, which results in eventual fibrosis of the sub-synovium and capsule<sup>7</sup>.

When discussing AC, most researchers focus on the histopathology for treatment directions<sup>18</sup>. Several have also examined the pathomechanics of AC, noting a decrease in joint play or normal arthrokinematic motion, most notably a decrease in humeral-head inferior-glide limiting abduction<sup>4,19</sup>. The current classification of AC acknowledges various aetiologies<sup>1,4-8</sup>. Clinically and surgically, it can be difficult to specify pathology, and it may vary in combination with other pathologies in any given patient<sup>6,10,23</sup>. A few researchers have considered the feasibility of whether a neurological component may be the predominant factor in some cases of AC as opposed to inflammatory and fibrotic soft tissue changes<sup>3,4,9-11,24,25</sup>.

Butler and Slater<sup>25</sup> believed there to be considerable clinical, neuroanatomical, and pathologic evidence for a hypothesis that loss of the normal movement and tension requirements of the sympathetic nervous system may be the cause of sympathetically maintained pain. Just as a limited and painful straight leg raise can be indicative of mechanical compromise of the normal movement and tension requirements of the sciatic nerve, they maintained that where the sympathetic nervous system stands apart, e.g., the sympathetic trunks, neural tissue may be vulnerable to mechanical interference from pathologic changes in interfacing tissues. They upheld that clinically, impairment of intervertebral thoracic joint mechanics can appear to be linked with pain and sympathetic epiphenomena that can be relieved by treatment, and many clinicians are aware of this; less frequently is abnormal sympathetic neurodynamics considered due to compromise of the sympathetic trunk<sup>25</sup>.

In the thorax, the sympathetic trunks lie on or just lateral to the costovertebral joints<sup>25,26</sup>. Taking into consideration the neuroanatomy of the sympathetic trunks and their probable neurodynamics, these sympathetic chains appear to undergo mechanical deformation during trunk and body movement<sup>25</sup>. Preganglionic sympathetic neurons for the upper limb arise from T1 to T9<sup>25</sup>, yet in the literature search on AC or sympathetically maintained pain, very little was found that mentioned assessment of

thoracic posture or mobility, either static or dynamic, along with its potential effect on the sympathetic nervous system. Butler and Slater maintained that careful enquiry and physical examination to identify any associated abnormal sensitivity of thoracic neural structures may uncover a minor neuropathy of the sympathetic trunks, particularly in patients whose sole symptom is pain that is slow to resolve or is out of proportion to the initial pain-producing stimulus<sup>25</sup>.

Menck, Requejo and Kulig<sup>26</sup> described a case study of a patient with thoracic spine dysfunction in upper-extremity complex regional pain syndrome type 1 (CRPS-1). Their purpose was to demonstrate a relation between the distal symptoms of CRPS-1 and the thoracic spine, and to describe the use of thoracic spine manipulation in the management of patients with CRPS-1 in the arm. They found segmental hypomobility in the thoracic spine, along with localized allodynia, decreased temperature of the limb, and abnormal posturing of the thoracic spine. Thoracic manipulation of the most restricted and symptomatic thoracic vertebral segment resulted in improved joint mobility (of thoracic spine and shoulder), and increased sympathetic outflow (immediate normalisation of skin temperature and colour, as well as a significantly decreased allodynic response to light touch along the arm and thoracic spine). Unfortunately, the positive outcome of this approach must be devalued because of concurrent treatment of psychological counselling and drug therapy. Nonetheless, positive outcome measures of reduced pain, improved autonomic symptoms, increased ROM and ADL should encourage further researchers to evaluate thoracic spine dysfunction in cases of sympathetic dysfunction of the upper limb, particularly where pain is out of proportion and possibly sympathetically maintained.

Slater<sup>9</sup> assessed function of the sympathetic nervous system in patients with frozen shoulder. The experience of pain and altered sympathetic function is well recognized, and sympathetic outflow may aggravate or maintain apparent activity in nociceptive neurons via several different mechanisms<sup>9</sup>, including peripheral and central sensitisation.

Slater<sup>9</sup> also clinically observed that the experience of pain accompanying frozen shoulder is sometimes found to alter with manual treatment directed at the thoracic spine (sympathetic outflow to the upper limbs). She proposed that sympathetic dysfunction might contribute to the aetiology of AC, and investigated the physiological effects of the sympathetic slump on peripheral sympathetic nervous system function, as well as the relationship between changes in peripheral sympathetic nervous system activity and clinical correlates (pain perception, pressure pain threshold, and ROM). Results indicated that the application of the sympathetic slump produced substantial increases in sudomotor function consistent with sympatho-excitatory effects in patients with AC in the study.

In describing chiropractic treatment of a single case

of frozen shoulder, Polkinghorn<sup>3</sup> stated that there is sufficient evidence to suggest that different forms of this condition exist. He proposed that particularly in the early stages, a neurological component could be the predominant factor. Based on this concept, a treatment protocol for AC included chiropractic adjustments to correct subluxations found in the cervical thoracic spine and shoulder girdle region, therefore addressing any dysfunctional neurological components.

Unfortunately Polkinghorn presented no scientific evidence to support the existence of a neurological component to early AC. As a single case study, external validity is limited, and reproducibility is difficult as his description of methodology is poor and contains obvious omissions. Treatment interventions were multi-faceted and, by the author's own admission, unique not only to each patient presenting with AC but even on subsequent visits with the same patient. One "common denominator" between patients, however, which Polkinghorn highlighted is subluxation of the T2 rib head<sup>3</sup>. Unfortunately, this was an empirical observation only, and the author made no attempt to offer an explanation as to the relevance of this finding.

Muller, Muller, Happ, and Kerschbaumer<sup>11</sup> proposed that frozen shoulder, or AC, is an algoneurodystrophic process. They quoted several references making similar assumptions as well as detailed diagnostic evidence of their own of dystrophic changes in shoulders affected by AC to support their hypothesis. They compared diagnostic and clinical features of frozen-shoulder syndrome and Sudeck Syndrome, another recognised clinical syndrome attributable to autonomic dysfunction. These authors measured and compared the bone mineral density of affected humeral head with the unaffected side in three groups of patients with frozen shoulder (n=12); an immobilized control group with rotator cuff, calcifying tendinitis, and shoulder instability (n=12), and a group of healthy participants (n=20). There was a decrease of greater than 21% in the bone density in the humeral head of the affected shoulder in 10 of the first group, but in only one case each of the subsequent two groups<sup>11</sup>. This was a well-designed trial, with sound methodology, good external and internal validity, description, and tabulation of results. The authors included a case report demonstrating the clinical application of their findings and proposed future research directions.

Thermography, (skin temperature measurement), reflects cutaneous blood flow changes—an indication of the level of sympathetic activity, and is an adjunct to clinical diagnosis in algoneurodystrophy<sup>11</sup>. It has been used by several researchers investigating the role of sympathetically mediated pain in the onset of AC<sup>4,24,27</sup>. Vecchio, Adebajo, Chard, Thomas, and Hazelman<sup>27</sup> used thermography to compare 28 patients with unilateral AC and 86 patients with unilateral rotator cuff lesions. The authors demonstrated differences in skin-temperature distribu-

tion in 82% of subjects with AC, nearly three-quarters of whom had reduced skin temperature<sup>27</sup>. There was no such pattern found in patients with rotator cuff tendinitis, demonstrating the role of sympathetic dysfunction in AC in the dermatome subserving the pain-affected area.

Jeracitano and Cooper<sup>24</sup> also used computer-assisted thermography to compare shoulder-skin vasomotor control in 11 patients with AC and 17 matched control subjects without shoulder pain, before and after application of an ice pack. They too demonstrated a significant temperature difference between the two groups, suggesting a sympathetic dysfunction in the dermatome associated with pain sensation from the affected shoulder<sup>24</sup>, but could not establish whether these abnormalities were primary or secondary.

Mani, Cooper, Kidd, Cole, and Cawley<sup>28</sup> used laser Doppler flowmeter to measure reflex changes in the cutaneous microcirculation in the C5 dermatome on the outer aspect of the shoulder. Normal laser Doppler flowmeter to inspiration/expiration responses were measured in all controls and in 22 of the patients with AC. However, the remaining 16 patients had no laser Doppler flowmeter responses to inspiration/expiration, a recognized clinical test of autonomic dysfunction. The authors therefore concluded that sympathetic fibers in the ventral cervical nerve root might alter the vascular supply to the shoulder and result in atrophic changes in the perivascular tests.

Simotas and Tsairis<sup>10</sup> noted that historically, AC has seemed to develop as a complication of a neuropathic process, referring in particular to cervical radiculopathy (nerve root compression) and neuralgic amyotrophy (clinical syndrome involving pain about the shoulder girdle followed by weakness and atrophy)<sup>10</sup>. Cervical radiculopathy has been associated with AC but cases are poorly documented<sup>10</sup>, whilst they refer to one study where two cases had neuralgic amyotrophy, complicated by reflex sympathetic dystrophy as well as AC (Billey et al 1992 cited in Simotas & Tsairis<sup>10</sup>).

According to Simotas and Tsairis<sup>10</sup>, AC and neuralgic amyotrophy are both painful processes affecting the shoulder girdle and surrounding muscles. Aetiology and pathogenesis of both conditions are unknown, and both are characterized by the initial onset of usually poorly localized severe shoulder pain. Neuralgic amyotrophy typically involves atrophy of cervical spinatii, deltoid, and serratus anterior muscles. They described a case study of a patient presenting with AC and neuralgic amyotrophy. While the authors discussed the patient's symptoms and each condition in detail, they proposed no hypothesis or conjecture in support of their statement that AC developed as a result of the neuropathy.

Other researchers have also investigated the role of autonomic dysfunction in the aetiopathology of AC. Rizk, Gavant, and Pinals<sup>8</sup> mentioned autonomic neuropathy (among others) as a possible cause of AC, but they elabo-

rated no further. Wassef<sup>29</sup> based his treatment approach of AC on the assumption that frozen shoulder is associated with reflex sympathetic dystrophy. This concept arises from the fact that the suprascapular nerve contains a high proportion of sympathetic fibers supplying the shoulder joint. In this trial, Wassef administered a suprascapular nerve block 2-4 times. The efficacy of the block was measured by comparing subjective pain scores and passive ROM before the first block and after the final one. Highly significant improvements were obtained<sup>29</sup>.

Waldburger, Meier, and Gobelet<sup>30</sup> found an increased radioisotope uptake in the affected shoulder girdle without involvement of the ipsilateral carpus in 82% of idiopathic AC patients. Physical treatment associated with administration of subcutaneous salmon calcitonin had a statistically significant increased effect on pain compared with physiotherapy alone. The authors concluded that the adhesive phase of AC corresponds to the retractile phase of a reflex sympathetic dystrophy syndrome.

Wohlgethan<sup>23</sup> studied a patient who presented with bilateral frozen shoulders and unrecognised hyperthyroidism. In both of these conditions, dysfunction of the autonomic nervous system is thought to be of pathogenic importance. The author postulated that the close resemblance of hyperthyroidism to activation of the sympathetic nervous system may underlie its association with frozen shoulder.

In his attempt to gain more understanding of the pathogenesis of pain, Woolf<sup>14</sup> focused attention on the dorsal horn. Accepting that the somatosensory system is not in a fixed or static state is central to understanding the role of the dorsal horn in the pain mechanism (perception); e.g., a stimulus generating an innocuous sensation on one occasion may reproduce pain on another<sup>14</sup>. On this basis, Woolf maintained that it is inadequate to study the system in one state, e.g., the control situation, and then attempt to use this information to fully explain the mechanism in play in another state, e.g., a patient with intractable pain following peripheral nerve damage. He described four states or modes of the dorsal horn. In brief, Mode I is the control or physiological state of the dorsal horn; Mode II is a suppressed state; Mode III is the sensitised state of increased excitability of the dorsal horn; Mode IV represents a reorganized state of the synaptic circuitry. In chronic neuropathic pain states, disorder in processing of nociceptor impulses at the dorsal horn is the dominant mechanism underlying neuropathic pain<sup>12,14</sup>. His description of mode III represents a state of hypersensitivity, and Woolf lists as one of the syndromes that can result as peripheral neuropathic pain. In this sensitised state, low-intensity stimulus acting via low-threshold afferents (normally an innocuous sensation) generates pain, what is called the phenomenon of allodynia<sup>14,15</sup>. Alternatively, a decrease in the threshold of high threshold of nociceptors due to peripheral sensitisation can lead to primary hyperalgesia, resulting in low-inten-

sity stimuli generating pain<sup>14-16</sup>. Sensitisation of the dorsal horn can occur following peripheral tissue injury, peripheral inflammation, and damage to the peripheral and central nervous system<sup>14,15</sup>.

Cousins<sup>16</sup> stated that central sensitisation response can outlast the afferent input by a substantial period of time and is truly a pathological process. It is evoked by A-delta low-threshold mechano-receptors, which usually do not produce sensations<sup>16</sup>. As described earlier, during stage I of AC, biopsy specimens have shown rare inflammatory infiltrates and a hypervascular synovitis<sup>7</sup>. Cousins described a "sensitising soup" released by inflammation in the periphery that increases the sensitivity of nociceptors. These include traditional inflammatory mediators as well as cytokines and nerve growth factor<sup>16</sup>. Levels of nerve growth factor are significantly elevated at sites of inflammation, and direct evidence exists that nerve growth factor plays a pivotal role in mediating inflammatory hyperalgesia<sup>31</sup>. Could this inflammatory stage of AC be the trigger leading to sensitisation of the dorsal horn and pre-disposing the patient to developing sympathetically maintained pain?

Woolf acknowledged several researchers who have demonstrated that dorsal horn neurons, including spinothalamic tract neurons, can be "sensitised" following activity in nociceptors, and that this is almost certainly responsible for mechanical allodynia and hyperalgesia<sup>14</sup>. What is less certain is the role that this sensitisation plays in the sensory abnormality accompanying chronic pain states. Acute tissue damage and inflammatory states will lead directly or indirectly to activation of nociceptors, which will induce central sensitisation. With recovery, however, the stimulus source is removed and hyperalgesia and allodynia commonly disappear within several hours or days. Neuropathic pain, in contrast, is typically persistent and intractable.

Sensitised dorsal horn neurons increase their receptive fields<sup>14,16,32</sup>. A prominent feature of the receptive field of dorsal horn neurons is the large number of wide-dynamic range cells responding to low- and high-threshold peripheral stimuli<sup>14,32</sup>. It has been demonstrated that these wide-dynamic range cells are likely responsible for conscious appreciation of pain and not nociceptive specific cells<sup>14</sup>. Roberts<sup>32</sup> refined the concept and proposed that sympathetically maintained pain results from tonic activity in myelinated mechanoreceptor afferents. This activity is induced by sympathetic efferent actions in sensory receptors, and this afferent input causes tonic firing in previously sensitised wide-dynamic range neurons that are part of a central nociceptive pathway<sup>32</sup>. Roberts pro-

posed that the process occurs as follows: trauma or inflammation in peripheral tissue activates unmyelinated (C) nociceptors that excite and sensitise wide-dynamic range neurons. If this sensitisation persists, these neurons can continue to give a vigorous response to mechanical stimulation of low-threshold A-fiber mechano-receptors (not nociceptors) even after healing is complete, leading to allodynia. A-fiber mechano-receptors can also be activated by sympathetic efferent actions in the periphery with the same painful result, i.e., sympathetically maintained pain<sup>32</sup>. This hypothesis does not require an abnormality in the sympathetic nervous system, peripheral nervous, or other tissues, only a peripheral sensitisation of wide-dynamic range neurons; this hypothesis provides further potential that the pain associated with AC is sympathetically maintained<sup>32</sup>.

Many questions remained to be answered with respect to the aetiology, pathogenesis, and pain-generating mechanisms of AC. Testaments to this are the volumes of articles in the literature investigating, exploring, and explaining AC. Perhaps the key to this mysterious condition lies in the fact that it is not a single aetiology, but rather that it presents in different forms and combinations of pathology. This would in part explain conflicting results in the research. One such variable may be the degree to which the sympathetic nervous system is involved in the pain of AC. If so, is it only involved in the acute, inflammatory stages of AC, and/or is it involved via a different mechanism (sensitisation) in the chronic pain of stage II AC?

Cohen<sup>33</sup> suggested that the recognition of secondary hyperalgesia should prompt an end to "chasing" nociception in the area of pain, both diagnostically and therapeutically. Instead, the concept of central sensitisation should prompt a search for remote but neuroanatomically related sites of ongoing nociception or mechanoreception that may be maintaining the changed neuronal activity as its clinical correlate of hyperalgesia<sup>33</sup>.

Perhaps suggestions by Slater<sup>9</sup>, and Muller, Muller, Happ and Kerschbaumer<sup>11</sup>, that arthroscopic and histological changes observed in shoulders of patients with AC are not primary but indeed secondary are correct, and they occur because of synovial fluid stasis, fibrosis, and inactivity of a painful joint sensitised by an over-active sympathetic nervous system.

Does, in fact, the focus of future research on AC need to change in the direction of neuropathology to unlock the puzzle presented by AC? If this is the case, then the sympathetic nervous system may eventuate as a major role player in the scenario of nociception and AC. ■

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