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Pathophysiology of Reflex Sympathetic Dystrophy

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Reflex sympathetic dystrophy (RSD) usually develops in a limb after an injury. It is characterized by constant burning pain, allodynia, hyperalgesia, swelling, vasomotor and sudomotor changes. Once RSD is established, successful outcome depends upon early recognition and therapy. The therapies include sympathetic blockade, myofascial trigger point injection, physical therapy, oral corticosteroid, etc. Many hypotheses have been proposed to explain the mechanism responsible for RSD. However, no single hypothesis proposed to date explains all of the features of RSD. It has been recognized for decades that pain may in certain instances be dependent on sympathetic innervation of the area afflicted with pain. Sympathetically maintained pain (SMP), a term that describes the intimate interrelationship of pain and autonomic dysfunction, is recognized by many to be an aspect (or even a defining characteristic) of causalgia and RSD. It seems that alpha-1 receptors expressed on the terminals of sensory nerve fibers develops the capacity, when activated, to evoke pain. Further studies are needed to elucidate the pathogenesis of the RSD. (J Rehab Med Assoc ROC 1997; 25(1): 1 - 11)

Key words: sympathetic dysfunction, pain, myofascial trigger point, electromyography

INTRODUCTION

Reflex sympathetic dystrophy (RSD) usually develops in a limb after an injury which may be relatively minor. It is characterized by constant burning pain, hyperalgesia, allodynia and vasomotor disturbances. Trophic changes in the skin and bone of the affected extremity are commonly observed if appropriate treatment is not instituted early. The symptoms and signs are often exacerbated after muscular exercise or by sympathetic arousal, such as emotional stress, urination and defecation [1].

RSD has been given various names, depending on precipitating factor, the country concerned, or the specialty treating the patient: reflex sympathetic dystrophy in English-speaking, Sudeck’s atrophy in German-speaking, and algodystrophy in French-speaking countries; causalgia after nerve injury; postinfarction sclerodactyly by cardiologists; Pourfour du Petit syndrome by anaesthesiists; and peripheral trophicneurosis, or Babinsky-Froment sympathetic paralysis by neurologists [1].

DEFINITION

According to the International Association for the Study of Pain (IASP), RSD has been defined as a constant pain in a portion of an extremity after trauma which may include fracture but does not involve a major nerve,
associated with sympathetic hyperactivity [3]. The consensus report of an ad hoc committee of the American Association for Hand Surgery (AAHS) agreed on the following definition: a diffuse pain syndrome in which the pain is accompanied by loss of function and evidence of autonomic dysfunction [3]. The first criterion is diffuse pain, often nonanatomic, and frequently out of proportion to the initiating injury or factor. The pain may develop at any time. Most typically, the pain can be described as hyperalgesia, hyperpathia, or allodynia. The second criterion is loss of function, which can include any activity or motion impairment associated with the pain. The third criterion includes some objective evidences of significant autonomic dysfunction as reflected by temperature changes, hyperhidrosis, hair growth changes, nail growth changes, edema, blood flow increase or decrease, or Sudeck’s osteoporosis. All three criteria must be present to confirm a diagnosis.

By the IASP definition, the causalgia involves an established nerve lesion, but the RSD does not. However, nerve injuries are sometimes associated with RSD and this may cause considerable confusion in terminology. Lehman (1934) has indicated that when RSD is precipitated by a peripheral nerve injury, the symptoms quickly spread outside the distribution of the damaged nerve [4]. Lankford and Thompson have described major causalgia as RSD associated with injury to a major mixed nerve and minor causalgia as RSD associated with an injury to a sensory (cutaneous) nerve. The AAHS [3] has recommended that causalgia implies pain from nerve injury and may or may not be associated with RSD. Kozin [9], whose criteria for diagnosis are most widely quoted, has suggested that it is essential to recognize the existence of different forms of RSD. “Definite” RSD is identified by diffuse pain and tenderness in an extremity associated with symptoms or signs of vasomotor instability (particularly temperature or color changes), and generalized swelling in the same extremity. “Probable” RSD is defined as a painful, tender part with allodynia or hyperpathia, but without other clinical features. “Possible” RSD is characterized by the presence of vasomotor and sudomotor changes but little or no pain or tenderness. “Doubtful” RSD is represented by diffuse pain and tenderness of unexplained etiology. Sympathetically maintained pain syndrome, a term that describes the intimate interrelationship of pain and autonomic dysfunction, is currently favored by many pain researchers and may replace the preceding term in general usage in the future [9].

**Etiology**

RSD is associated with wide variety of precipitating factors, including soft-tissue injury, fracture, arthritis, infection, operative procedure, venous or arterial thrombosis, immobilization with cast or splint, CVA, brain tumor, severe head injury, poliomyelitis, prolonged bedrest, vasculitis, myocardial infarction, malignancy, idiopathic, etc [7]. The means by which all of these events cause the same clinical syndrome is not yet known, but the common mechanism may be injury to either central or peripheral neural tissue including the autonomic nervous system. The symptoms may begin gradually, days or weeks after the injury, or may manifest within a few hours. In 10-26% of cases, no precipitating factor can be identified [1].

**Symptoms and signs**

Patients with RSD typically complain of burning pain which usually begins within the first 24 hr of injury but may be delayed in onset by weeks or months [309]. Initially, the pain is usually located in the distal portion of an extremity but extends proximally over time and may ultimately involve other, uninjured extremities [109]. Rarely, the syndrome spreads to include the entire body [111].

The other cardinal clinical features of RSD include allodynia, hyperalgesia, swelling, vasomotor and sudomotor changes. Allodynia is pain produced by a stimulus that is not normally painful. Hyperalgesia is increase of pain produced by a noxious stimulus. Cutaneous hypersensitivity may be so extreme that the patients will protect the affected limb from any contact all the time.

At onset, the skin was warm, red and dry; later, the skin may appear cold, sweaty and cyanotic. Sudomotor (sweat gland and hair follicle) effects may be observed as hyperhidrosis or hypotrichosis. Swelling is common and may be pitting or non-pitting. The nails are often brittle and crack easily.

In a prospective study of 829 patients referred over eight years to a tertiary referral center, Veldman et al [1]
paid particular attention to early signs and symptoms of RSD. The report showed that pain was present in 93% of all cases, 91% had discoloration of skin; 92% had altered skin temperature; edema was present in 69%, and limited active range of movement in 88%. In 96% of patients, the above signs and symptoms appeared or increased in severity after exercising the affected limb, while 4% were unable to exercise at all. Neurological manifestations included sensory changes, typically with a glove- or stocking-like distribution. In the first 2 months of RSD, hypoesthesia was found in 69%, hyperpathy in 75%. With time, tissue atrophy may occur as well as involuntary movements, muscle spasm, or pseudo-paralysis. Tremor was found in 49% and muscular incoordination in 54% of patients. Tissue dystrophy, atrophy, or hyperhidrosis was infrequent and therefore had no diagnostic value. Besides, there was no leucocytosis or fever found in the RSD patients, nor was the increased sedimentation rates or the specific antigens or auto-immune antibodies in blood or tissue found.

Patients with RSD seem emotionally unstable, anxious, and socially withdrawn. Chronic invalidism, drug addition, suicide, and psychiatric commitment occur. These lead many physicians to think that the pain is psychogenic. However, in a literature reviewed on psychological aspects of RSD, Lynch has concluded that the emotional and behavioral changes seen in patients with RSD are probably the result of pain, and that there is no worthwhile evidence supporting the notion that psychological factors or certain personality traits are predispositional factors for the development of RSD [12].

Staging

Three stages of severity have been described [13]:

(a) Stage I (Acute) — The pain is out of proportion to any injury and aggravated by physical contact or emotional upset. Swelling, mottling, hyperthermia or hypothermia, and increased hair and nail growth occur in the affected part. Bony changes may be present on roentgenograms.

(b) Stage II (Dystrophic) — Stage II is characterised by persistence of pain and disability with increasing dystrophy. The edematous tissue becomes indurated and the skin is cool and hyperhidrotic, with livedo reticularis or cyanosis. Hair loss occurs. The nails are ridged, cracked, and brittle.

(c) Stage III (Atrophic) — The pain spreads to involve the entire limbs. Irreversible trophic changes occur. The skin is thin and shiny, and the fingertips are wasted. The fascia becomes thickened, and flexion or Dupuytren’s contractures may occur. Roentgenograms show marked bony demineralization and ankylosis.

However, the study by Veldman et al, did not confirm this chronological progression, but revealed that patients could be divided into “warm” or “cold” on the basis of relative skin temperature in the affected limb. The longer they had RSD, the more likely they were to have a cold limb. Despite this, 13% of patients examined very early in the condition had a cold limb, and warm limbs were found in patients who had had RSD for many years. Tissue atrophy was a rare and late finding in their study [11].

Treatment

A wide variety of therapies have been recommended for the treatment of RSD. Most of the therapies that have proved effective are aimed at blocking the effects of sympathetic hyperactivity, including regional intravenous block with guanethidine sulfate [14,15], or reserpine [16], paravertebral sympathetic ganglion block [17,18], paravertebral sympathetic gangliectomy [19,20], or oral antisypathetic agents [21]. There were many uncontrolled studies offering subjective and objective evidences of improvement with various methods of sympathetic blockade. However, controlled studies are rare. Regardless of the form of treatment, it is important to interrupt the sympathetic supply to the injured extremity early in the course of the disease. Many clinicians have noted that if therapy is delayed, the pain may become refractory to any type of treatment [8,10,22,23].

Physical therapy alone has been showed to be effective in the treatment of RSD. The exercises are directed toward improving the mobility of the affected extremity. If the lower extremity is involved, therapy involves gradually increasing the weight-bearing capability of the limb. However, patients are usually in too much pain to participate in physical therapy unless adequate pain relief can be obtained prior to the initiation of activity. Transcutaneous electrical nerve stimulation (TENS) is postulated to relieve pain by an artificially
generated barrage of nerve impulses in large axons. One study on eight patients revealed that TENS provided long-lasting relief in 2 patients, transient relief in 4 patients, and no relief in 2 patients [24]. Another study of 54 patients with RSD compared exercises and cryotherapy either with or without galvanic stimulation, and reported a significant therapeutic effect in both treatment groups [25]. However, there were no controlled groups involved in these studies.

The effectiveness of treatment with oral corticosteroids has been investigated in several studies. The dosage varied from 20 mg/d for 10 to 70 weeks to 200 mg/d for two weeks, then tapered gradually. In general, the rates of effectiveness ranged from about 60 percent to as high as 90 percent [5-7]. Unfortunately, few of these studies have been placebo-controlled. These studies indicate that prolonged treatment with high-dose corticosteroids should be considered for patients who refuse or cannot tolerate treatments that directly block sympathetic activity.

**PATHOPHYSIOLOGY**

Many hypotheses have been proposed to explain the mechanism responsible for RSD. However, no single hypothesis proposed to date can explain all of the features of RSD.

**Electric ephaptic transmission**

In the 1940s, it was believed that sympathetic fibers could cross-excite pain afferents electrically. In 1943, Livingston proposed the so-called “theory of reverberating circuits” in the spinal cord to explain the phenomenon of RSD. Intense, painful stimuli may initiate these reverberating circuits in the internuncial neuron pools of the spinal cord which later can be triggered by normal stimuli [29]. Doupe et al proposed that the pain of RSD was caused by activation of sensory fibers by sympathetic effects [27]. Nathan presented the hypothesis that abnormal stimulation of somatic sensory axons occurs in the area with partial nerve injury [29]. This stimulation is caused by efferent impulses from preganglionic sympathetic nerves. He has suggested that artificial synapses are formed at the site of the lesion and allow ephaptic transmission to occur between efferent and afferent fibers.

Drucker et al observed that RSD could be resulted from minor soft tissue injuries as well as clinically demonstrable nerve injury [29]. The clinical manifestations were the same in these two conditions. They considered that ephaptic transmission between sympathetic efferents and sensory afferents could also be formed if the minuscule peripheral-nerve twigs in the soft tissue were injured. This ephaptic transmission might increase the activity of the internuncial neuron pool in the spinal cord, which could further stimulate the sympathetic efferents and formed a vicious cycle of pain.

**Chemical ephaptic transmission**

Hannington-Kiff reported that 17 consecutive cases of Sudeck’s atrophy were treated successfully with intravenous regional guanethidin [14]. In his method, guanethidin was injected intravenously into a limb, to which an arterial tourniquet was applied until the drug had been fixed in the tissues (about 10 min). Guanethidin displaces noradrenaline (NE) from stores in the sympathetic nerve endings and its persistent accumulation at these sites prevents the usual re-uptake of noradrenaline. Thus, the first effect of guanethidin is to release NE, which exacerbates the pain, and its second effect is to produce prolonged regional sympathetic block lasting several days. In contrast, bretazenil does not have this biphasic effect. The relief of causalgia in the extremity by guanethidin blockade when the site of nerve damage is proximal to the tourniquet suggests that the previous simple ephaptic explanation is incorrect. Hannington-Kiff has suggested that superficial pain and hyperpathia in Sudeck’s atrophy are due to the NE overdrive of damaged sensory nerves or nerve endings [14-16].

In 1983, Devor showed that the primary change in sensory fibers of damaged nerves was their transformation from impulse conductors to impulse generators [20]. Adrenaline or noradrenaline injected at low doses close-arterially, or at higher doses systemically, usually produced an increase in discharge rate of sensory fibers. The response to adrenaline was mimicked by brief tetanic (but not single-pulse) stimulation of preganglionic sympathetic efferents, or the lumbar sympathetic trunk at levels corresponding to the hindlimb. Electrical
stimulation of sympathetic efferents in patients with causalgia has been reported to increase pain. Devor has proposed the hypothesis that any form of injury or inflammation which damages Schwann’s cells or the axons themselves may result in local demyelination or spout outgrowth. The spout or demyelinated segment incorporates excessive numbers of sodium and calcium channels as well as $\alpha$-adrenergic receptors and results in an ectopic pacemaker. This ectopic pacemaker may discharge spontaneously as well as in response to the circulating catecholamines or those released from sympathetic efferent spouts. In short, chemical, rather than electrical (epiphaptic) cross-talk is the mechanism responsible for the activation of high threshold afferents by sympathetic efferents in regions of nerve injury in causalgia.

The neuroma studies in animal models have also shown that neuromas generate abnormal spontaneous afferent activity and this activity may be increased in response to a variety of stimuli including hypoxia, ischemia [31], mechanical stimulation [32], and alpha agonists [31,32]. Electrical stimulation of the paravertebral sympathetic nerve chain causes an abrupt increase in afferent neuroma activity [32,33]. The response of fibers in experimental neuromas to adrenalin and to sympathetic trunk stimulation can be blocked by the $\alpha$-adrenergic antagonist phentolamine but not by the $\beta$-antagonist propranolol. All the evidences including that the regional effectiveness of sympathetic trunk stimulation, the equivalent dose for systemic versus close-arterial injection of adrenalin (about 10:1), and the persistence of adrenalin chemosensitivity after the neuroma has been decentralized proximal to the recording point, have indicated that the adrenergic chemosensitivity resides in the region of the neuroma itself. Could the response of neuroma to adrenalin, however, be secondary to partial ischemia caused by local vasoconstriction? Two lines of evidences, however, indicate that the adrenalin effect is not due to ischemia. First, after virtually complete block of the vascular supply by arterial clamping, the response of neuroma fibers to close-arterial injection of adrenalin below the clamp persists. Second, the responses to clamp ischemia and to systemic adrenalin are frequently qualitatively different. The response to arterial clamping is almost always slower in onset than that to adrenalin or sympathetic stimulation [34]. Nor does the clinical manifestation of RSD favor the vasoconstriction as an etiologic factor. First, if sympathectomy produces its beneficial effects by correcting the vasoconstriction, why does the vasodilation achieved by methods other than the interruption of sympathetic pathways fail to relieve the pain? Second, in many cases there is no vasoconstriction but vasodilation instead. The relief that follows sympathectomy in these cases cannot be attributed to vasodilation because this condition already existed before the operation. At last, the vasodilation after sympathectomy is transitory, however, the pain is usually permanently cured by the operation [30]. Between the neuromas and the sympathetic efferents, no synaptic complexes or other junctional specializations associated with transmitter release have been found in the neuroma studies [33]. However, there were many studies showed that sympathetic effects occur at the receptor end in skin and muscle, at the central axon terminal in the spinal cord and at the level of the cell soma in the dorsal root ganglion. Devor did not suspect that the occurrence of adrenergic receptors in sensory afferents is a de novo phenomenon related to nerve injury [30]. Rather, he considered that these receptors appear to be a normal part of afferent fiber economy since that sympathetic outflow has a modulatory role in the normal physiology of many primary afferent neurons.

**Sympathetically maintained pain**

Roberts proposed the term, sympathetically maintained pain (SMP) to include a family of disorders including causalgia, reflex sympathetic dystrophy, minor causalgia, Sudeck’s atrophy, and even post-herpetic neuralgia [69]. These pain syndromes were characterized by: (a) a history of physical trauma in the painful area; (b) the presence of a continuous burning pain together with mechanical allodynia; and (c) relief from the pain during sympathetic block. Neither dystrophic tissue nor nerve injury is required. It is proposed that trauma in some peripheral tissue first activates unmyelinated (C) nociceptors. This activity excites wide-dynamic-range (WDR) neurons in the spinal cord and also causes these neurons to become more responsive to all subsequent afferent inputs (sensitized). If this sensitization of WDR neurons is persistent over time, then the WDR neurons
will continue to give a vigorous response to mechanical stimulation of A-fiber mechanoreceptors even after healing is complete, leading to touch-evoked pain or allodynia. A-fiber mechanoreceptors can also be activated by sympathetic efferent actions in the periphery or in a neuroma with the same painful result. The only abnormal neuronal state required is a persistent sensitization or increased gain of WDR neurons. This hypothesis is in part similar to previous proposals by others in that it assumes prior sensitization of central nociceptive neurons. It deviates from most previous proposals in that mechanoreceptors, not nociceptors, are proposed as the afferent fibers which evoke the painful sensation.

Several lines of evidence in human studies suggest that alpha-adrenergic receptors play a critical role in SMP: (a) Drugs that deplete norepinephrine from the sympathetic nerve terminals (e.g., regional guanethidine or bretylium) have been used successfully for the treatment of RSD [14,16]; (b) Oral alpha-adrenergic antagonists such as phenoxybenzamine and prazosin decrease pain in SMP disorders [21,37]; (c) In SMP patients, temporary relief of their causalgia, hyperalgesia is rekindled by local iontophoresis or intradermal injection of norepinephrine into the originally painful area [18,39]; (d) Perineuronal injection of epinephrine (5μg), but not normal saline, in a blinded manner caused an intense increase in reported pain with subjects often commenting that the appendage was “on fire”[39].

Treede et al recently defined SMP as “all pain syndromes that can be relieved by sympathetic blockade” [40]. Being less invasive than ganglion block, phenolamine (alpha-1 and alpha-2 adrenergic blockers) sympathetic block (PSB) is often considered a crucial test in the diagnosis of SMP in patients with chronic painful conditions associated with seemingly neuropathic sensory, motor, or neurovascular symptoms [41]. Attempting to determine the contribution of alpha-1 and alpha-2 adrenergic receptors in SMP, Davis, et al examined the effects of local application of adrenergic agents in patients with SMP [42]. The alpha-2 adrenergic agonist clonidine, available as a transdermal patch, was delivered topically to the patients’ hyperalgesic skin. In four patients with SMP, clonidine eliminated or substantially reduced hyperalgesia to mechanical and cold stimuli. In three of these patients, the effects were confined to the skin region beneath the patch, suggesting a peripheral but not a central effect. It is likely that clonidine locally blocks the release of norepinephrine via activation of alpha-2 receptors on the sympathetic terminals. The authors have suggested, therefore, that SMP is mediated via alpha-1 adrenergic receptors located in the affected tissue. Campbell et al [43,44] have proposed a model of pathogenesis of SMP:

(a) An injury that results in a barrage of activity in nociceptors may lead to the sensitization of central-pain-signaling neurons that inputs from low-threshold mechanoreceptors impart pain.

(b) Sympathetic efferent fibers activate nociceptive fibers via an alpha-1-adrenergic receptors that develops on the terminals of nociceptive fibers.

(c) Aside from evoking pain, this nociceptor activation serves to maintain the central-pain-signaling neurons in a sensitized state.

(d) A sympathetic block eliminates activation of the nociceptors, the central sensitization is eliminated, and thus ongoing pain and touch-evoked pain are eliminated.

Campbell postulated that the alpha-1 adrenergic receptors is the pathophysiologic key in SMP.

However, Verduco and Ochoa [45-47] argued that prior demonstrations of SMP are flawed because controls for placebo effects were not instituted properly. They stated that it was improper to investigate the pathophysiology of RSD with the neuroma animal model, since, according to the IASP definition, RSD does not involve any nerve lesion. In their double-blinded study, none of the beneficial responses was legitimately attributed to a specific effect of the sympathetic blocks through intravenous phenolamine [40]. They questioned the existence of “sympathetically maintained pain” and suggested that the concept of SMP should be “eradicated”.

**Adrenergic supersensitivity to reduced sympathetic outflow**

It has been assumed that an increase in sympathetic outflow causes sweating and changes in peripheral blood flow in RSD. [22]. In fact, the basis of current treatment for this condition centres around reducing sympathetic outflow to the affected limb. However, this view is
widely challenged by a lot of experimental studies. If there is increased sympathetic activity in the affected limb, it would be possible to find increased concentrations of adrenaline or noradrenaline. It seems that the reverse is the case. In a study by Drummond et al. [48], venous blood was collected from painful and unaffected limbs of 26 patients with RSD, and levels of plasma adrenaline and noradrenaline and its intracellular metabolite, 3,4-dihydroxyphenylethylenglycol (DHPG), were measured by combined gas chromatography/mass spectrometry. Plasma DHPG was lower on the painful side. Concentration of plasma noradrenaline was also lower on the painful side in patients with widespread allodynia, and in those with hyperhidrosis in the affected hand or foot. These findings suggest that sweating and changes in peripheral blood flow in RSD may result from supersensitivity to sympathetic neurotransmitters rather than overactivity of the sympathetic system. Furthermore, other studies showed that vasoconstrictor tone was reduced rather than increased in symptomatic areas [49], and resting sympathetic discharge was unchanged in the affected skin based on multi-unit micro-electrode recordings [50-51]. Rosén et al reported that nailfold-skin capillary blood cell velocity and skin blood flow through the affected finger, assessed by laser Doppler flowmetry, were lower in 12 patients with RSD than in controls [52]. In addition, reflexes to skin cooling and postural changes were impaired in the affected fingers, indicating reduced sympathetic function [52]. Drummond et al suggested that after tissue injury, a local decrease in release of sympathetic neurotransmitters could induce adaptive supersensitivity in blood vessels and sweat glands [48]. Similarly, afferent neurons or their sensory receptors could also develop supersensitivity to adrenergic substances. They have proposed that adrenergic supersensitivity aggravates the primary pain-producing mechanism in RSD, either in the periphery or in the spinal cord.

Myofascial trigger point and RSD

The clinical observation of autonomic phenomena associated with active myofascial trigger points (MTrPs) has been well documented [53]. MTrPs have been found to be a complication (or a manifestation) of RSD [54]. Furthermore, trigger point injection is an effective way to treat muscle pain in RSD patients [53].

The diagnosis of MTrP was based on a tender spot in a palpable taut band with typical referred pain patterns as described by Travell and Simons [53]. Two important clinical characteristics of MTrP, referred pain (ReP) and local twitch response (LTR), can be elicited by mechanical stimulation (pulpation or needling). Referred autonomic phenomena (vasoconstriction, coldness, sweating, pilomotor response, piosis, hypersecretion, etc.) may also occur in the zone of the reference. MTrP is usually activated by acute or chronic injury to a muscle, tendon, ligament, joint, disc, or nerve. Recent human and animal studies have suggested that the pathogenesis of either ReP or LTR is related to integration in the spinal cord [56-58]. Hong has proposed that there are multiple sensitive loci in a MTrP region [59-60]. Recent electrophysiological studies have demonstrated that spontaneous electrical activity (SEA) can be recorded from active loci in the region of a MTrP in humans or in a trigger spot (similar to human MTrP) in rabbits [61-64]. In an ongoing study on the morphological nature of the active locus, it was frequently found that a small nerve was in the immediate vicinity of where SEA could be recorded [65]. It has been suggested that a sensitive locus may contain one or more sensitized structures (free nerve endings?) [66-68]. Furthermore, the amplitudes (the average of integrated areas) of the SEA were reduced by the intra-arterial injection of an adrenergic antagonist phenolamine [69]. Hubbard used needle electromyographically-guided injection of trigger points in patients with chronic and recurrent muscle pain associated with MTrPs and showed that intramuscular injections of alpha-adrenergic antagonists phenolamine or phenoxybenzamine eliminate EMG spike activity recorded by needle EMG in the nidi of MTrPs and significantly reduced subjective report of pain arising in MTrPs [80]. Intravenous phenolamine also resulted in eliminated MTrP-EMG (i.e. SEA) during the infusion. He proposed that SEA arises in muscle spindles and MTrP pain arises in the spindle capsule due to increased pressure, initiated by traumatic and/or repetitive hyperextension of the spindles and sustained by sympathetically-mediated factors. On the contrary, Simons proposed that the active loci of myofascial MTrPs are in the immediate vicinity of extramuscular motor
endplates and that SEA represents abnormal extrafusal endplate activity due to release of greatly increased numbers of acetylcholine packets. However, he did not exclude the important observation that MTrPs are closely associated with sympathetic activity. It is possible that one type of RSD is caused by severe MTrPs, or vice versa. When mild MTrPs are not appropriately treated in the early stage (shortly after an injury), the MTrPs may spread out through the spinal cord mechanism. Concomitantly, the sympathetic outflow may be induced by the same injury, and may be aggravated by the same spinal cord mechanism which causes the spread of MTrPs. Inactivation of MTrPs by MTrP injection may also eliminate the sympathetic outflow, and thus, may reduce the symptoms and signs of RSD. In this way, the muscle pain caused by RSD can be effectively controlled by MTrP injection.

CONCLUSION

It seems that alpha-1 receptors are expressed on the terminals of nociceptive fibers in the skin, subcutaneous tissue, blood vessels, sweat glands, muscle fibers (intrafusal or extrafusal?), ligament, tendon, and joint capsule. Alpha-adrenergic supersensitivity may develop after trauma in these sites and this impulse may ascend and spread out at the spinal cord level. When the blood vessels and sweat glands are significantly involved, then the clinical picture of RSD may evolve. When the muscle fibers are predominantly affected, muscle pain associated with myofascial trigger point is the main clinical picture. Further studies are needed to elucidate the pathogenesis of the RSD, sympathetically-maintained pain and other muscle pain associated with myofascial trigger point.

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交感神經反射失養症常發生於外傷之後，它的臨床症狀包括了肢體持續性的燒灼痛，觸、痛覺敏感，腫脹，皮膚顏色及溫度改變，流汗改變及關節活動度受限等。較有效的治療方法包括了早期交感神經阻斷，肌膜引誘點局部注射，口服類固醇及物理治療等。其致病機轉目前仍不清楚，但認為和交感神經活性過高有關；早期的研究以為於神經受損處形成感覺神經和交感神經突觸，並造成神經反射異常，如此形成立性循環所致。之後的研究則認為可能是感覺神經末稍阿爾法-1受體(alpha-1)被活化，並發展出對交感神經傳導物質過度敏感性，此種變化並可往上升至脊髓，造成神經反射異常。臨床上，交感神經反射失養症常見合併有肌膜引誘點，而肌膜症候群亦可見交感神經反射異常之現象；肌膜引誘點局部注射對交感神經反射失養症亦是一相當有效的治療方法。目前的研究認為肌膜引誘點和交感神經反射失養症，於致病機轉及臨床表現方面有相關性，它們均和交感神經及神經反射異常有關。但二者詳細的作用機制仍須要進一步的研究探討。（中華復健醫學 1997; 25(1): 1 - 11）

關鍵字：交感神經痛(sympathetic pain)，肌膜引誘點(myofascial trigger point)，肌電圖(electromyography)