Spinal Neuroplasticity in Chronic Pain

By Eric B Shay

Faculty Advisor: Rodger Tepe, PhD

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ABSTRACT

Background Research abounds on changes to our brain both the good and the bad. Neuroplasticity, or the brain's adaptive response to change is a rapidly developing area of research. With today's technology we are learning more new things about ourselves as a species than any other time in history. The intent here is not to present a comprehensive review of pain induced plasticity but to assess the literature on neuroplasticity in the spinal cord, and allow us to evaluate what we know about similar events and nervous system responses primarily in the brain. This review uses a model that is hypothesized by the author that there is a loop within the spinal cord somatic pain path that contributes to many chronic pain syndromes and experiences.

Objective: This literature review provides an overview of pain processes and neuroplastic changes to our nervous system as a result.

Methods: MANTIS, PubMed, and Google Scholar searches for spinal neuroplasticity and chronic pain. Special attention was given to articles since 2009, as much as 30% of the literature has been since then.

Results: Seven hundred and seventy five sources searched for "spinal neuroplasticity" have been published since 2009. Of these just two hundred and twenty two discuss pain. Furthermore, just eighty three discuss chronic pain, the bulk of which were selected for review..

Conclusion: The chiropractic adjustment, or Spinal Manipulative Therapy (SMT) (or otherwise known as Chiropractic Manipulative Therapy (CMT) is described in the literature as moving spinal joints with the intent of positively effecting dysfunction. SMT increases GABA, which reduce nociception and mechanoreception inhibits nociception. This process is activated by the mechanical effects of SMT. Just as these plastic and neural responses perpetuate the pain cycle, these same feedback loops can also be used to adapt positively. As the spinal dorsal horn is bombarded the spill over effects and "Volume Transmission" perpetuate the pain cycle. Much of today's research is poses with questions related to what drugs do to "manipulate" these natural physiological process. More research is needed about how understanding neuroplasticity can lead to new pain management strategies.

Key Indexing Terms: *Spinal Neuroplasticity, Chronic Pain, Spinal Manipulation, Chiropractic*

Introduction

In today's world people recognize the word inflammation. Do they know just what it means? They may have even heard of neuroplasticity. One word we all know is pain. How does all this sum up to the issues we have today? How does it all lead up to chronic pain?

The aim of this paper is to sum it all up and provide the lay person and health practitioner a plausible explanation as to what is going on, what we know about it and what we can or should do about it. We have reviewed the past and current literature to gain an understanding of just what we know about spinal neuroplasticity and chronic pain.

Materials and Methods

The author has been studying the mind-body connection for 20+ years and has an extensive personal library. He has used his personal notes, textbooks and personal communications to fill in the gaps. The bulk of his review has come from scouring the research archives via MANTIS PubMed.

Results (data)

PubMed queries revealed the following

	All Time	Since 2009
Spinal neuroplasticity	2,526	757
Spinal neuroplasticity + pain	681	222
Spinal neuroplasticity + pain + chronic	230	83

It is this authors aim to show how spinal manipulation and chiropractic are beneficial in helping those that suffer from Chronic Pain. Additional queries were made.

Spinal neuroplasticity + pain + chronic + manipulation 3

Spinal neuroplasticity + pain + chronic +chiropractic 1

It is this author's hope that these numbers will significantly increase in the years to come as people are looking for safe and effective ways to deal with their pain.

Discussion

Research abound on changes to our brain both the good and the bad. The plasticity, or adaptive response to the brain is fascinating. With technology today we are literally learning new things about ourselves as a species than any other time in history. Perhaps what we are learning is we know less than we thought we did. It may seem the more we know the less we understand. For instance a simple question such as "Hey Doc, why do I hurt?" should be fairly easy to answer. When it is repeatedly asked without sufficient answers, or more importantly, resolution, life is dramatically different. No one understands this more than someone in chronic pain.

Pain is processed in our brain as a result of our experiences. Simple survival adaptability and plasticity at its finest is in knowing not to touch a hot stove. Why not? Because it is hot. How do you know? At some point you experienced personally or via someone else that touching a hot stove results in pain and injury.

If pain is in the brain, why does my hand hurt after I touch a hot stove? Pain is the brain's calculation that tissue damage is occurring. Various pain receptors in our body, in this case our hand; know that hot metal on skin causes damage. Via various functioning systems, as will be

reviewed later in this article, communicate: stove hot – skin burns – pull hand away. Your brain knew it was hot before you even touched it. It is easy to see how a hot stove equates to pain. Let's get back to chronic pain. You or someone you know may have chronic back pain. You have tried everything to no avail. What is spinal pain? If pain is in the brain, is spinal pain an oxymoron? What is pain before it gets to the brain? Is it pain if it never reaches the brain? This is one of those philosophical rhetorical questions like "if a tree falls in the woods and no one is there to hear it does it make a sound?" Anyone in chronic pain does not care what it is called they just want it to stop.

What is Pain?

The intent here is not to present a comprehensive review of pain – induced plasticity but to assess the data on neuroplasticity in the spinal cord, and allow us to compare with what we know are similar events and nervous system responses primarily in the brain. While beyond the scope of this review, we have come a long way in understanding the processes and events involved via breakthroughs in functional magnetic imaging (fMRI)

Chronic pain may simply be a malfunctioning in pain signals. Prolonged pain and injury can induce several types of responses to and changes in perception of neurological, mechanical, chemical, and temperature stimuli. The most common of which may be hyperalgesia. This is defined as pain elicited by a noxious stimulus. Primary hyperalgesia occurs in the region of tissue damage. One can point and say, "it hurts here!" Secondary hyperalgesia occurs in the surrounding region. One can not pinpoint an exact location but will rub there entire shoulder or low back and may even still say, "it hurts right here!"

Allodynia is the good old fashioned pain or "owie". It is invoked by a normally innocuous stimulus and is normally expected after injury or inflammation brought on by our body's stress response. This increased sensitivity to external stimulus serves to protect the injured area and allow the healing to begin. Built into this protective mechanism is memory of painful events. "Don't touch the hot stove. Remember, it hurts?" With this memory recorded in the central nervous system we do not reach out our hand and avoid the hot stove. These pain pathways and the changes in perception of the signals are what plasticity is all about.

Our joints have receptors to help the nervous system keep everything in check. Integrity is maintained when the neuromusculoskeletal system is running as designed. Interesting is that many of the things that ail us today and cause pain is in fact this system working as designed to maintain integrity. The old joke, "hey doc, it hurts when I do this. Well don't do that!" is funny because there are many times that we simply do not know why it hurts. The joint itself may be fully functional. There is a pain memory and we may avoid using a fully functional joint. Our adaptive (read: plastic) nervous system responds to our environment. If a joint is not moving, there must be a reason for it. Our brain will only allow muscles to fire to move a joint that it trusts. It is hard to develop trust when there is a perception of danger. Be it real or exaggerated pain is a signal of danger.

Low back pain is something much of society can relate to. Practically every anatomical structure of the lumbar motion segment is capable of producing pain. Chronic pain is responsible for many of the aches and pains we experience. We are constantly in a fight or flight mode of protection, pain avoidance, and survival. In this "danger" or stress response our adrenals are jacked up to prepare us to run from or face and fight the danger. If we come face to face with a tiger, we had better run or fight. We know from experience, be it our own or another's, that tigers can hurt and

hurt is bad. Tigers are danger. Danger is bad. We have a physiological response to the impending danger. Our body will use all the chemicals released and energy created to run, fight, and do all that is necessary to maintain safety. When the tiger leaves, as perhaps he was not interested in eating us this day, our system must now respond and reverse the cascade of stress response processes. We take a deep breath and realize we are safe. Chronic aches and pain may be stored "pent up" energy never used to fight off tigers that never existed. Our body reacts to stress the same way each and every time. It is very efficient in this. It does not judge the type of stress, be it a tiger or looming mortgage payment, when the system detects stress the cascade begins.

Stress Response

Stress is a survival response. It is not a healing response. We go into stress response to bide survival time until we can change environment and allow healing to begin. Stress delays healing. As our body goes through the 3 stages of healing we physiologically adapt accordingly, The initial stage is inflammatory. This stage is physiologically designed to last up to 72 hours as the injured area is bombarded with the cascade of events that kick off the inflammatory response. We then begin the next stage of repairing injured tissue. This can take anywhere from 72 hours to six weeks, depending on the tissue damaged and the extent of damage. Finally we enter the last stage of healing and we begin to remodel the damaged tissue. This can take from three weeks to twelve months. Stress delays healing. Like a broken record, stress may skip healing stages and start again inducing the inflammatory stage.

The sympathetic nervous system is responsible for our physiological response to stress. The fight or flight response, as it is known, increases our ability to perform vigorous muscle activity. This

most basic of our animal instincts help us, in an instant, decide whether to stand and fight or turn and run. Both of which require a great deal of energy. To prepare us our arterial pressure increases and blood flow to active muscles are increased while blood flow to other organs such as gastrointestinal tract, kidneys, and anything not needed for rapid motor activity are diminished. Blood is shunted from these organs. Cellular metabolism throughout the body is increased to expend more needed energy. Our blood glucose concentration increases and the liver and muscle increase glycolysis as muscle strength and mental activity increase the demand for glucose and glycogen. The rate of blood coagulation increases in the event we are injured and literally will not have time to bleed. (Guyton, AC, Hall JE 2006) This is a physiological response to our environment.

Increased blood pressure, diminished digestive systems and kidneys, increased blood sugar, increased mental activity, and sticky blood; Sound like anyone you know? These are all natural occurrences in time of stress or life threatening danger. Show me someone in chronic pain and I will show you someone with a nervous system on full alert. As seen in the physiological response to our environment we can see that our body is doing exactly what it was designed to. The nervous system has no conscious, does not care if pleasure or pain. Once the "pain" cycle starts, the body will do what it can to allow pain to travel. The body is very efficient and it will release more neurotransmitters and increase receptors and decrease GABA. Getting a patient out of pain is very beneficial. The quicker you break the pain cycle the better. The longer nociceptive afferentation is allowed to progress the more the condition will persist. Nociception is the "pain signal" input. As we learned previously physiological pain is necessary and beneficial. It is a normal response to adverse stimuli. Our excited state is facilitation to a well functioning system.

With regards to neck and back pain, we are familiar with shooting pain in our arms and legs. This type of process is referred to as radiculopathy and has a whole other related yet different physiological response that is a little easier to determine the "source of pain" or more precisely neurological deficit. The focus of this article is the more elusive chronic pain that is found in an excited yet functioning system as explained above.

What's pain got to do with it?

The Melzack-Wall Pain Gate Control theory is based on inhibitory neurons known as A-beta nerve fibers. The brain's perception of pain is dependent (to an extent) on the interaction (within the laminae of the spinal cord) of C and A-delta nerve fibers with the inhibiting, non-pain transmitting, A-beta fibers. Which when activated will "close" the pain gate and pain signals are not sent to the brain. Analgesics, such as biofreeze, Ice-Hot and Ben-Gay, illicit this response to delay or minimize pain.

Pain is a complex sensation, in that a noxious stimulus leads not only to a perception of where it occurred, but also increased attentive, emotional, reactive, autonomic responses and a greater likelihood that the event and resulting circumstances will be remembered. Don't touch the hot stove. (Nolte, J 2002 p 242) The A-delta pain fibers are responsible for an OWIE! They are rapid signaling and adapting, due to their thin myelination. The sensation is sharp and well localized. (Nolte, J 2002 p 208) It has been said, and much of the literature can attest, The gate Control Theory revolutionized our thinking with regards to chronic pain syndromes. According to the theory stimulating low-threshold primary afferent fibers could result in the central suppression of nociceptive influence. Ruffini endings in skin are activated by touch. When you rub the owie it helps to suppress the nociceptive fibers sending pain signals to the brain.

Physiological pain is crucial to our survival and health. An event occurs, damage is done, repairs are made and a link to the pain memory is made to avoid the event in the future and/or to keep the body from more injury to a "painful" area.

The theory gave merit to the CNS (Brain & Spinal Cord) as essential components in pain processes. The cord – specifically the dorsal horns – were no longer seen as passive and empty stations along the pain path, but dynamic and bustling hubs responsible for inhibition, excitation and modulation of pain signals.

This review uses a model that is hypothesized by the author that there is a loop within the spinal cord somatic pain path that contributes to many chronic pain syndromes and experiences. Neuroplastic changes play an important role in the generation and maintenance of chronic pain syndromes. Such changes occur at all levels of the neuraxis, from the peripheral terminals of primary sensory neurons to the cerebral cortex. Changes observed in the spinal dorsal horn in particular provide a mechanistic basis for many of the characteristics of chronic pain syndromes.

Psychological pain is a result of fear avoidance. We remember how a certain movement hurt and we do not want to feel the pain again. The joint and tissue may be healed but we still do not want to move it. This creates a debilitating loop. Joints are designed to move. Immobilized joints hurt when you move them. We experience pain. We change our motor behavior to avoid the pain. We have more pain from not moving.

It is hypothesized that plasticity in both connective tissue and nervous systems are linked to each other though changes in motor behavior; this connection plays a key role in the natural history of chronic low back pain. (Caruso, 2009)

In addition to abnormal movement patterns, patients with chronic low back pain have been shown to have generalized increased pain sensitivity and cortical activation patterns which

implies abnormal central pain processing. It is important to remember that actual pain occurs in the brain and not at the level of the tissue feeling the pain. (Seaman D, Cleveland III C. 1999)

'Nociception" is an important term referring to the neuronal signal carried along the nociceptive pathway. Chronic pain is associated with widespread neuroplastic changes at multiple levels within the nervous system. Nociceptive pain is a vital early warning device that helps protect us from the dangerous environment in which we occasionally find ourselves. The sensation of pain must be an unpleasant experience in order to allow us to react in the appropriate manner to avoid any further harm from our environment. (Boersma K, Linton SJ.2005)

Neuropathological pain is long-term change after injury and is the result of an error somewhere in the nervous system; it is frequently described as a burning sensation, or an electric shock. Unlike nociceptive pain, it occurs in response to noxious stimulus causing nervous tissue inflammation and injury, or nervous system structural and /or functional damage. Neuropathic pain also has the features of both spontaneous pain that arises without any apparent peripheral stimulus, and hypersensitivity to that stimuli. (Boersma K, Linton SJ.2005)

Clinical exams to investigate a patient's complaint often include a neurological exam. The aim is to ensure the neurological system is in tact. The challenge lies when one must determine if the pain reported by the patient is in deed pain. The nervous system can provide the clinician clues. The neurological exam focuses on three categories of nervous system functions: sensory, motor and reflex. Each of these functions correlates with different parts of the nervous system. The sensory functions can be the least reliable as it is the most subjective. Feedback depends on what the patient tells you based on the questions the clinician asks. Sensory or "perception" is difficult and unreliable. However, in the investigation of pain complaints the sensory nervous system is of chief concern. It can be separated into two distinct types of sensory receptors based on function

and fiber types. Nociceptors are comprised of A-delta and C fibers. Mechanoreceptors are primarily A-beta fibers.

The intent of the neurological exam is to identify a lesion or deficit in the nervous system. It is more reliable to rely on results of the motor and reflex exams as these are objective findings the motor strength and tone is present or is not. The patient's reflexes are intact or they are not. Evidence of neurological deficit, in both central and peripheral nervous systems are indicative of a lesion.

The patient presents with pain. Is it caused by a neurological deficit? Pain is a normal sensation wherever there is damage to tissue. Pain is generally not result of neurological lesion more than 90% of the time. Pain is afferent (impulse toward the CNS) "pain shooting down the leg" is an oxymoron. Nociception is detection of tissue damage not just pain i.e. tingling. The chief complaint can be complicated by phantasia (imagined and/or exaggerated) and inertia (lack of movement or activity especially when movement or activity is wanted or needed) Many people in pain are told it is in their head. Well, yes pain is in deed located in the head. What are these "pain" signals doing before they get to the head?

The spinothalamic tract, or more formally the spinoreticulothalamic tract carries the fibers from the cord up to the thalamus where pain perception is realized. Awareness is manifested but discrimination does not take place until it gets to the cortex. (parietal lobe – Post Central Gyrus SSA1 Somatic Sensory Area 1) C-fibers for the most part do not go past the thalamus. On their way to the thalamus they branch out to reticular formation. The RAS (reticular activating system) keeps us "awake". Chronic pain often keeps people up at night. This is the Limbic system and the seat of our emotions.

The Central Excitatory State

This has long been described in the literature and physiology textbooks as an area of the cord in a facilitated or "lowered threshold" state. This has been referred to as Central Sensitization. No matter what it might be called it is a result of biochemical release in the nervous system. Biochemically sensitized neurons are brought closer to threshold. In reality, this refers to an area, or segment, of the cord into which a great deal of sensory input, referred to as afferentation, has been transmitted from either visceral or somatic structures. In order for this "state" to develop, the afferentation must be constant and long-lasting. This would require that the afferentation be from "C" fibers, because these fibers do not adapt. "A" delta pain would be substantial, but not long-lasting. "C" fiber nociception is the most commonly accepted etiology of the excitatory state and may be derived from either somatic structures or viscera. All sensation enters the cord through the dorsal horn, so the dorsal horn is the site that initially receives the afferentation. From here it is transmitted to tract fibers (spinothalamic, spinoreticulothalamic) and to the interneuronal pool. Once the interneurons have been stimulated by the prolonged and constant afferentation, the excitation will now be transmitted to other areas of the cord, namely the lateral and ventral horns. As a result of this transmission to other areas of the cord, the effects of nociceptive stimulation on the cord will now be manifested by sympathetic and motor stimulation. There is a "diffusion of electrochemical signals via the extracellular medium" (Cailliet, 1993) which would allow neurotransmitter chemicals to stimulate numerous postsynaptic receptors, leading to the term transmitter-receptor mismatch. This form of transmission is called "volume transmission" and explains the older term "spillover" which was

used to describe the phenomenon of abundant neurotransmitter release at the dorsal horn (and elsewhere) resulting from constant afferentation into the cord. This abundance of neurotransmitter release at the dorsal would then be able to stimulate neighboring pools of interneurons and thereby transmit excitation to other areas of the cord. "In the volume transmission concept the chemical neurotransmitters leave the synapse and are free to find their receptors wherever they are and as numerous as they may be" (Cailliet,1993 p17). Thus, when the dorsal horn receives constant and long-lasting afferentation from either a visceral or somatic source, the results of this afferentation are far-reaching and may involve visceral as well as somatic function.

Fortunately, researchers have shed light on the molecular mechanism of painful chronic conditions for both inflammatory and neuropathic pain through recent animal studies. Through these studies, researchers have discovered that the spinal cord is an important relay center to integrate peripheral painful inputs and propagate signals to the brain. In painful conditions, peripheral nociceptors transmit afferent painful signals to the dorsal horn by releasing neurotransmitters from presynaptic terminals. These neurotransmitters cross the synapse and activate the corresponding receptors on the postsynaptic terminals of neurons and glial cells in the dorsal horn. These events induce multiple inflammatory and neuropathic processes in the dorsal horn, as well as trigger modification and plasticity of local neural circuits. In addition, the activation of glial cells, including astrocytes and microglia in dorsal horn, contribute to the persistence of increased nociception through the enhancement of local actions of cytokines and chemokines. As a result of such molecular modifications, painful signals are often amplified and prolonged. (Dauch JR, Hsinlin TC)

Sensitization is manifested as an increased response of neurons to a variety of inputs following intense or noxious stimuli. It is one of the simplest forms of learning and synaptic plasticity and it represents an important feature of nociception. In the spinal cord, repeated stimulation (at constant strength) of dorsal root afferents including nociceptive C fibres can elicit a progressive increase in the number of action potentials generated by motoneurons and interneurons. This phenomenon is termed "action potential windup" and is used as a cellular model of pain sensitization developing at the level of the central nervous system. (Baranauskas G, Nistri 1998) Understanding the mechanisms responsible for windup generation might allow clarification of the cellular mechanisms of pain signaling and development of new strategies for pain treatment. (Baranauskas G, Nistri 1998)

This process of central sensitization is an important aspect of neuroplasticity in that it contributes to upregulation of the nociceptive system in response to injury This process may provide a link between the pain in the motor system and autonomic dysfunction in patients with musculoskeletal disorders. Central sensitization describes changes occurring at the cellular level to support the process of plasticity occurring in the neurons of the spinal cord and in the supraspinal centers, as a result of activation of the nociceptive system. (Woolfe 1994)). If "central sensitization is (to be) defined as an increased excitability of nociceptive neurons in the central nervous system" (Caillet 1993) then a facilitated/hyperstimulated central nervous system may lead to an overload or volume transmission in the interneuronal pool of the spinal cord. Too much overload in the interneuronal pool may lead to a spillover effect to the lateral horn. This increase of activity in the lateral horn leads to increased sympathetic activity and release of norepinephrine at its terminal endings. (Coderre T 1993) (Denslow J 1942)

With regards to how central sensitization has been shown to be involved in many chronic pain states Charles Davis D.C. performed a review of the literature on chronic pain/dysfunction in whiplash disorder. He concluded that chronic pain indicates increased sensitivity to low threshold A-B fiber inputs and low levels of afferent activity which are sufficient to maintain a state of central sensitization responsible for sensory changes. This repetition of low level stimulation can result in an integration of neural responses and cause severe pain in whiplash patients. He found from his literature search that patients suffering from chronic whiplash and fibromyalgia have a central hyper-excitability contributing to their chronic pain state. (Davis C 2001)

Although neurogenic inflammation plays a role in inducing a state of central sensitization, researchers have found that injury decreases the central inhibitory processes. The disinhibition leads to a state of hyperalgesia and central sensitization. Cortical disinhibition occurs through loss of the inhibitory control of the central nervous system by the opiodergic, noradernergic, and serotonergic receptors on the dorsal horn. It has been noted that some patients are predisposed to have fewer of these receptors in the dorsal horn, thus leading to a greater perception of pain in that patient. (Elenkov IJ. 2000)

Meanwhile back at the spine…

As we have established "pain" travels to the cord via A-delta and C fibers. You may recall that C fiber pain does not generally travel to the SomatoSensory Area I (SSA I) for somatotopic discrimination and remains as dull achiness. The patient can not localize and pinpoint the pain. C fibers tend to stimulate a particular pain tract in the cord called the "spinoreticulothalamic" tract and ultimately send pain signals to the SSA II which is not capable of somatotopic

discrimination. A-delta fibers tend to stimulate the lateral spinothalamic tract in the cord whose signals are then transmitted to the cortex (SSA I). The spinoreticulothalamic tract travels to the reticular formation first where it may stimulate the RAS (reticular activating system). This particular system effectively keeps an individual awake. Thus, chronic pain may result in a patient's complaint of difficult sleeping. Additionally, before reaching the thalamus, the spinoreticulothalamic tract will synapse on neurons from the Limbic system which is the seat of our emotions. In general, it is believed that the signals transmitted to the thalamus via the spinoreticulothalamic tract are not transmitted on to the cortical area SSA I. These deep, dull achy pains which are poorly localized are not cortically discriminated in SSA I, but rather are being perceived in SSA II. Stimulation of proprioceptors (large A-beta fibers) will greatly assist in the abatement of these poorly discriminated C fiber pain patterns. (Christy 2007)

The cord may be legitimately divided into three specific areas - the dorsal horn, lateral horn, and ventral horn. The dorsal horn is the seat of sensory manifestations, the lateral horn is the site of sympathetic innervation, and the ventral horn is the area of motor stimulation to skeletal muscle. Excitation of each of these areas will provide different signs and symptoms. Let's examine what happens as each area of the cord is excited.

Dorsal Horn Excitation

All sensory bombardment (afferentation) enters the cord through the dorsal roots and terminates in the area of the cord known as the dorsal horn. If the sensation is of short duration it will be transmitted to particular ascending tracts and the patient may experience certain pain sensations or mechanical sensations such as movement, or pressure. Problems arise when the sensations (sensory bombardment) are constant and of long duration. This central excitation or facilitation

creates increased stimulation to the interneuronal pool through volume transmission and involves the associated visceral and muscular components of the cord.

What effects of this "spillover" or volume transmission might be exerted on the dorsal horn itself? Remember, this is the seat of sensory input to the central nervous system. At any particular segment, there are body tissues and viscera which send sensory input (nociception) into that specific cord level. Many decades ago, investigators such as Feinstein and Inman proposed that stimulation of multiple interneurons at the dorsal horn would give the patient a false sense of pain coming from multiple body areas. They called this phenomenon *sclerotome pain*. All of us understand that a pain source (such as a tendinitis) commonly "spreads" and gives us a sense of pain from other areas of the body. We are all familiar with cardiac pain (angina) being perceived not only in the chest but also down the arm and into the neck and jaw. These pains are often called "referred" pains. Feinstein and Inman recognized a segmental relationship between the pain source and the site of referral. They quickly established known patterns of pain referral known as sclerotomes. For example, pain from the supraspinatus tendon could refer pain into the entire shoulder girdle as well as into the interscapular area. This is because the rhomboid muscles are innervated from C5, just as most of the shoulder structures. The rhomboids send pain fibers into the cord through C5. Therefore, when pain from the supraspinatus tendon is severe and long-lasting, the volume transmission at the dorsal horn from the lesioned tendon (nociceptive afferentation) will excite neighboring interneurons which normally would be receiving input from other C5 structures (such as the rhomboids). When these interneurons fire, the pain message would be transmitted to the thalamus (probably over the spinoreticulothalamic tract), and the patient would insist that there is pain between the shoulder blades. It is true that the patient does experience real pain between the shoulder blades, but on

examination the clinician would see that there is no painful lesion at this site. Poking and prodding the interscapular tissues would not create the pain nor exacerbate the pain. In fact, the tissues which are located in the areas of referred pain would test as totally intact and normal – no evidence of dysfunction coming from the referred areas of pain. Feinstein and Inman strongly suspected the cord as the site of "spillover" and cited it as the etiology of "sclerotome pain referral."

In the late 70's a very important paper entitled "The Facet Syndrome" by Mooney and Robertson brought back the concepts of sclerotome pain which Feinstein and Inman had studied many years prior. In the Mooney study, volunteers allowed themselves to be injected with irritating saline solutions into spinal ligaments and facet joints. Within minutes the pain patterns would be documented. The pain patterns described were reminiscent of the sclerotome pain patterns illustrated by Feinstein and Inman. The study pointed out that purely somatic lesions, especially when near the spine, were capable of referring pain peripherally. The importance of this was the fact in the late 70's, the most common surgery was discectomy for low back pain. The Mooney and Robertson study provided conclusive evidence that peripheralizing pain could occur without nerve entrapment (neuropathy). This conclusion was very threatening to those who performed thousands of disc surgeries for back pain with peripheralizing pain patterns. Indeed, this study also provided strongly supported mechanisms for relief of back pain through manual or manipulative manuevers to the facet joints. (Christy 2006)

Lateral Horn Excitation:

Involvement of this area will stimulate the autonomic nervous system. When the afferentation reaches the cord and creates great stimulation of the dorsal horn, by volume transmission the

excitation will be transmitted to other areas of the cord via the interneurons. Interneurons from the dorsal horn connect with the preganglionic fibers whose cell bodies are in the lateral horn. These are the beginnings of the sympathetic nervous system. The preganglionic fibers are myelinated (white) and exit the cord along with the ventral root. Once outside the IVF, the preganglionic fiber leaves the root (white ramus) and enters a sympathetic ganglion where it synapses on a secondary fiber. This secondary fiber is called the postganglionic fiber and is not myelinated (gray). It leaves the ganglion (gray ramus) and reconnects with an exiting nerve. The lateral horn is part of the cord from the low cervical spinal area to L2. The upper thoracic preganglionic fibers, after they exit the IVF, will ascend to join with one of three cervical ganglia. There they synapse on postganglionic sympathetic fibers which leave the ganglia to innervate structures in the face, arm, and certain viscera (heart). (Christy 2006)

The neurotransmitter secreted by the preganglionic fiber in the ganglion is acetylcholine (nicotinic). The acetylcholine will stimulate the postganglionic fiber. The postganglionic fiber will then travel long distances to various visceral structures throughout the body, sweat glands, smooth muscle, and to essentially every structure in the body. The postganglionic fiber will secrete norepinephrine as its neurotransmitter. (Christy 2006)

A study of the effects of sympathetic stimulation must include the works of "Irwin Korr, PhD" who published much information regarding norepinephrine and its increased production in various tissues. Many years prior to Dr. Korr's studies, Dr. Laura Burns published research from an Osteopathic College in which animals were "subluxated" artificially and later autopsied. Visceral pathologies were documented which were segmentally related to the levels of subluxation. Dr. Burns later reversed artificially subluxated areas of the spine and waited to see whether or not visceral pathology could be stopped or reversed. She found on autopsy of these

animals that, indeed, pathophysiology was evident on microscopic examination of the segmentally involved tissues, but not to the degree that the previous animals had demonstrated whose subluxations had not been reversed. One can say from Dr. Burns' studies that there appears to be a strong link between the subluxation and visceral function. The connection is, obviously, the sympathetic nervous system.

Dr. Korr carried on the original work and determined in the 60's and 70's that there is indeed a strong link as reported by Dr. Burns. However, Dr. Korr proposed that the neurotransmitter, norepinephrine, is the cause of tissue changes. In essence, he proposes that norepinephrine will "enhance" tissue function, but too much will ultimately lead to tissue damage. He did not propose any mechanisms, but merely indicated that norepinephrine will be implicated in tissue dysfunction. Dr. Korr coined the term "sympatheticotonia" to indicate an increase in sympathetic conduction which would lead to an increase in norepinephrine delivery to tissues. Dr. Korr's research primarily centered on sympatheticotonia and the effects of excessive norepinephrine on tissue function. Enhancement of tissue function may appear to be a good thing. However, anything in excess can be troublesome. For example, a mucus gland is designed to produce mucus. This is necessary in the airways, but excessive mucus production as a result of sympatheticotonia is damaging to airways. Smooth muscles in the airways also need to constrict on occasion, but excessive constriction under the influence of norepinephrine is debilitating. Sympathetic stimulation to the heart when necessary is a good thing, and the heart beats faster and more powerfully. Chronic sympathetic stimulation, however, will lead to cardiac damage and conduction disturbances. Simply stated, too much of a good thing is not good. (Christy 2007)

Caillet places great emphasis on the role of norepinephrine in creating and maintaining pain states. “During a state of anxiety, the locus coeruleus (control of the final common pathway of sympathetic release) is maintained at a constant alert. This … may lead to a condition termed sympatheticotonia, which is considered prevalent in many disease states, including chronic pain states.” (Cailliet 1993, p. 36).

Anterior Horn Excitation

This is the area of motor involvement. Alpha and gamma motor neurons both reside in the anterior (ventral) horn of the cord. The alpha motor neuron exits the cord through the IVF and ultimately synapses with a skeletal muscle cell at the myoneural junction. The neurotransmitter released at the neuromuscular junction is acetylcholine (muscarinic). When an alpha motor neuron fires a muscle fiber contracts. Prolonged contraction is labeled a spasm. It seems reasonable to state that whatever has the ability to stimulate an alpha motor neuron will cause a muscle spasm. The pain fibers from the injured tissue enter the cord and synapse on interneurons which synapse on the motor neurons of the anterior horn. The motor neurons fire and create a muscle contraction. The pain from the injury keeps the cord excited (central excitatory state) and, thus, the muscle spasm continues. (Christy 2006

Dr. Barry Wyke, known as the Father of Articular Neurology, is credited with researching and promoting the facet joint as a major source of afferentation which would lead to muscle spasms. Dr. Wyke researched the innervation of the facet capsule and discovered that it contained three fiber types – two mechanoreceptor and one nociceptor. He labeled the two mechanoreceptors as “Type I and Type II” fibers; the nociceptor was labeled as “Type IV” The mechanoreceptors are divided into “tonic” and “phasic” – those which fire fast and quickly adapt and those which fire

constantly, providing a background "tone" of excitation to the muscle fiber. Dr. Wyke theorized that fixation of spinal joints would essentially reduce firing from the type I and II mechanoreceptors. This loss of mechanoreception would provide easy access to the CNS for nociception. Because of loss of mechanoreception, the inhibition of nociception was compromised, thereby lowering the threshold of nociceptors entering that particular segment. This afferentation would then be transmitted via interneurons to the anterior horn where motor neurons would then be stimulated. A somatosomatic reflex was now firmly established. According to Dr. Wyke, spinal manipulation is a viable solution to the loss of motion at the spinal segments. He states that reestablishing mechanoreception is one of (if not the most) important answer to effective management of musculoskeletal disorders. He indicates that mechanoreception from a variety of sources is helpful, such as skin stimulation through a TENS unit, acupuncture, or massage. Manipulation of the vertebral joint complex would restore the needed mechanoreception, inhibit the nociception, reduce the central excitation, and relieve the muscle spasms. The mechanoreception must be delivered to the proper segment in order to relieve the excitation at that particular segment.

Dr. Wyke further noted that inflammation of the joints or immobilization of several weeks will destroy the Type I and Type II neurons. Once lost, the mechanoreceptors do not return. In this case, the joint will remain painful on palpation, and motion will always be met with pain and resistance. Therefore, the need for motion to be maintained is without dispute. Other researchers, such as Travell, have recommended the use of a rocking chair for low back pain. The mechanism behind such therapies lies in maintaining mechanoreception from the spinal joints and soft tissues

Pain Begets Inflammation

When in an inflammatory state normally innocuous stimuli produce pain. It is widely understood that the nervous system poses an array of responses to different conditions (neural plasticity and neural memory) Since the Melzach-Wall gate theory posed in 1965 research has been concerned with the mechanisms by which these neural responses occur. Of special interest is the key peripheral mechanisms by which inflammatory mediators interact with neurons to produce the hypersensitivity state that accompanies inflammation. (Kidd, BL.,Urban, LA 2001) "Peripheral tissue inflammation leads to prolonged central sensitization characterized by an enhanced neuronal activity in the spinal dorsal horn." (Ren K 1996)

Subluxation complex releases sup-p to "innocent" areas inducing the bodies natural inflammatory response – mast cells and macrophages stimulate destruction and inflammation. This begins with nociceptor afferentation – if we can block Glutamate and Sub-p we can come along way to relieve pain. How do we do that? Let's look further in to the subluxation complex, inflammation and the joint complex itself.

Back to the Spine

David Seaman so eloquently covers this in almost all of his material. Why more chiropractors and health care professionals can not "understand" this is beyond me. Hippocrates has been accredited with stating "Look well to the spine for the cause of disease." What is it about the spine that literally divides professions, theories, and philosophies regarding the human condition and more importantly, pain?

To help us understand this Seaman focuses on the neuropathophysiology of subluxation. We need to be aware of the innervation of the spinal joint complex. Nociceptors and

mechanoreceptors are the primary sensory receptors that innervate joint structures, including synovia, joint capsules, bone, ligaments, tendons, muscles, and blood vessels. The predominant receptor is the nociceptor. More than 90 percent of joint innervation is nociceptive, originally determined by animal studies, (Hanesch U 1996) then confirmed in studies with human spinal joint capsules.(McLane 1994) The clue lies in the anatomical fact that here is a considerable less mechanoreception of the joint capsule, and an abundance of nociceptive innervations. Seaman reminds us using any basic anatomy text book that "There seems to be less nociceptive innervation of muscle (and that) we have about an equal balance of nociceptive and mechanoreceptive receptors, which means that nociceptive innervation of muscles is still significant. Clearly, the afferent innervation of the spinal joint complex favors nociceptive receptors."

This heavy concentration of nociceptive fibers in joints suggests that we are basically built to experience joint pain. "Doc, it hurts when I do this" Yes it does. Don't do that.

As we have pointed out through out this paper, nociceptors are activated by tissue injury and the chemical mediators that cause inflammation. Keep in mind mechanoreceptors are stimulated by normal movements. Spinal injury is likely to increase the firing of nociceptors however, the activity of mechanoreceptors is likely to be reduced because with injury, inflammation, nociception and pain, there will be less movement afforded to the injured joint and therefore, less mechanoreceptor activation. Increased nociception and reduced mechanoreception can cause pain, visceral symptoms, problems with motor control and proprioception.(Seaman DS, Winterstein JF 1999)

What have we learned?

The chiropractic adjustment, or Spinal manipulative therapy or otherwise known as Chiropractic Manipulative Therapy (CMT) are many ways the literature describes moving spinal joints with the intent of positively effecting a dysfunction. This increases GABA, which will reduce nociception. Mechanoreception inhibits nociception. This is activated when we rub the booboo. Just as these plastic and neural responses perpetuate the pain cycle, these feedback loops can also be used to adapt positively. As the spinal dorsal horn is bombarded we have discussed the spill over effect and "Volume Transmission" which perpetuate the pain cycle.

Much of today's research is posed with the questions related to what drugs can they use to "manipulate" these natural physiological process as we have described. More research is needed posing the questions as to how we might break the pain cycle naturally.

"A new appreciation of the significance of plasticity in the development of persistent pain has underscored the general recommendation that early therapeutic intervention should be utilized to interrupt (or even preempt) the start up of sensitized (hyperexcitability) states in patients, thus decreasing the likelihood of developing of persistent pain condition. (Merskey H, Bogduk N 1994)

CMT has been demonstrated to have excellent clinical results for the treatment of chronic and acute back pain. CMT is theorized to increase joint motion at segments which are not moving properly. (Jay S, 2009) By inducing motion into the hypomobile areas, mechanoreception is stimulated. By increasing mechanoreception to the involved area, gamma-aminobutyric acid (GABA) is released into the surrounding tissue thereby inhibiting substance-P. (Gatterman, 2005)

In addition to increasing mechanoreception, it is thought the afferent impulses resulting from CMT affect the central nervous system, and alter t he ascending and descending pain-modulating

characteristics of the nervous system. (Lane C. 2007) (Harris RE 2009) This is crucial for areas that have been sensitized through plastic changes. By inputting new, normalized afferent impulses, it could be possible to alter the cycle of hyperexcitation (Seaman 1999)

In a review done by Seaman and Winterstein they found in the latest research that C-fibers (the small unmyelinated pain carrying fibers) can produce extended excitation of the cord. It was also found that the C-fibers also cause a profound change in the receptive field properties of the dorsal horn. In later studies, they found researchers focusing on how input can change the plasticity of the cord in the development of central sensitization. This plasticity is now agreed upon as an increased spontaneous activity, reduced thresholds or increased responsiveness to afferent inputs which are prolonged after discharge from repeated stimulation of the afferent fibers. Seaman and Winterstein conclude their review on this topic with researchers currently hypothesizing that plastic changes in the cord are due to an increase in excitatory inputs and/or a loss of inhibitory inputs, which result in a net excitation of the dorsal horn. (Seaman DR., Winterstein JF 1998)

Michael Patterson, Ph.D. in his article, "The Spinal Cord: Participant in Disorder," published in Spinal Manipulation, 1993 states: "Studies have shown that relatively short inputs to the spinal cord can produce long-last alterations in the excitability of the spinal reflexes that do not depend on higher brain structures and are sufficiently robust to outlast days of intervening activity. … It is now becoming evident that dramatic changes occur in the characteristics of interneurons of the spinal cord … Thus, the neurons of the spinal cord undergo a massive increase in excitability. … The use of adjustment therapies to reduce motion restrictions, increase proper fluid infusion, and decrease nociceptive inputs to the spinal cord seems to be an effective way to decrease the hyperexcitable central state that leads to further alterations in spinal function.

To summarize, the concept of increased sympathetic or parasympathetic conduction is not new. The pathological conditions which may result from continuous activity of these pathways are relatively new to traditional medical reviews and are at present few in number. Nevertheless, significant research has provided sufficient evidence to promote the role of the autonomic system in establishing dis-ease and disease states. The theory of subluxation-induced excitation of the nervous system is quite old and is repeated in the early works of Palmer. Modern concepts include the central excitatory state, sensitization of central neurons, volume transmission, and a host of other similar descriptors. We must recognize that afferentation, primarily nociceptive, will initiate the eventual irritation to the sympathetic preganglionic neurons housed in the lateral horn of the cord. Subsequently, the sympatheticotonia may contribute significantly to tissue responses which include spasm, overproduction of endocrine and exocrine factors, vasoconstriction, hyperalgesia, increased heart rate, sweating, neurogenic inflammation, etc… etc… The loss of motion at the segmental level contributes to the central excitation by the loss of mechanoreception which would normally block the nociceptive afferentation from ever manifesting at the cord level. Restoration of motion will help eliminate the excitatory state within the cord and assist in returning the sensory, autonomic and motor areas of the cord to their natural balance (homeostasis). (Christy 2007)

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