PSYCHOSOCIAL CORRELATES OF SENSITIZATION IN CHRONIC PAIN: AN

EXPLORATORY ANALYSIS

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Abstract

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Assessments of tenderness to palpation (touch) and thresholds for pain are physiological assessments frequently used in chronic pain research. These measurements are generally believed to index pain regulatory systems. However, given the large body of research supporting the high correlation between certain psychiatric symptoms (such as anxiety and depression) and chronic pain disorders (such as tension-type headache), it is reasonable to hypothesize that these physiological measures could assess physiological vulnerability related to both the physical experience of pain and the psychological distress that may accompany this experience. The current research hopes to clarify the physiological vulnerability often found in individuals with chronic pain and the association this vulnerability may have to measures of psychological distress using a novel design that recruited participants from the entire population of undergraduate females rather than recruiting participants based upon their report of having a chronic pain disorder (as is typically done in research in tenderness/pain thresholds). Participants underwent several physiological measures designed to evaluate various aspects of pain sensitization and the participant's physiological reaction to stress. Participants also complete several pen and paper questionnaires to assess psychiatric symptoms (in particular, anxiety and depression), stress, pain, coping, family history, and physical

symptoms. Results showed that participants with high levels of muscle tenderness were significantly different from their low tender peers on measures of pain threshold, tolerance, and widespread sensitivity. Highly tender participants also reported significantly more symptoms of depression, anxiety, stress, poor pain coping, and family history of chronic pain problems. It is believed that the results of this study could help to clarify the physiological mechanisms believed to play a role in both pain and affect regulation and assist future researchers in developing studies to better examine the etiology and possible treatments for disorders of these systems (i.e., chronic pain and psychiatric symptoms).

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Introduction

Chronic pain disorders are associated with significant negative impact upon general health (Becker, Thomsen, Olsen, Sjogren, Bech & Eriksen, 1997), psychological health (Magni, Marchetti, Moreschi, Merskey, & Luchini, 1993), and social and economic well-being (Becker et al., 1997; Latham & Davis, 1994). Community research studies have found rates of self-reported chronic pain among adults in the general population to be as high as 46.5% (Elliot, Smith, Penny, Smith, & Chambers, 1999) with back pain, arthritis, and headaches among the most frequently reported complaints. Worldwide epidemiological studies suggest that on average 22% of primary care patients present with a complaint of persistent pain, often in the presence of other physical complaints and accompanied by psychosocial complications including a diagnosis of anxiety or depression, significant limitations in activity, and less than favorable health perceptions (Gureje, Simon, & Von Korff, 2001; Gureje, Von Korff, Simon, & Gater, 1998). Out of the individuals who present to primary care centers for pain complaints, back pain, headache, and joint pain have been found to be the most commonly reported difficulties with more than 40% of these primary care patients reporting pain in at least one of these areas. These survey studies often suffer from several limitations including the use of non-specific measurement instruments that do not allow for easy cross-study comparisons, instruments that are not validated for use in different cultures, and difficulty in setting specific criteria for defining/diagnosing pain and its chronicity. Despite these limitations, together these studies point to the fact that chronic pain is associated with significant individual and societal costs.

Despite the significant cost and burden of chronic pain, researchers in this area are just beginning to understand the nature of these disorders. Our growing understanding of pain transmission and pain modulation in the central nervous system in recent years, through advances in both basic and clinical research, has pointed to the role central sensitization plays in a number of pain disorders. Recent research suggests that dysfunctions in endogenous pain regulatory systems play a central role in the development and maintenance of chronic pain. In much of this research, sensitization is measured through assessing participant's reported sensitivity to manual palpation. Three areas of investigation where these measures are frequently used both in research and clinical practice are headache, fibromyalgia, and temporomandibular disorder. In each of these disorders, researchers have utilized measures of manual palpation to hypothesize about the role of central sensitization in these disorders.

While it has been hypothesized that a dysfunction in central pain processing plays an important role in many chronic pain disorders, the ability to precisely identify the central and peripheral mechanisms underlying specific pain disorders has made limited progress. Recent advances in assessment techniques along with an improved understanding of pain mechanisms are making it possible to more precisely examine of the role of central and peripheral factors in chronic pain disorders. Nonetheless, we currently have little knowledge about the prevalence of abnormalities in pain processing and/or sensitization in the general population, whether such abnormalities (if present) are always associated with a pain disorder, and how these abnormalities are associated with psychological findings such as the presence of a mood or anxiety disorders, pain coping mechanisms, and family history of pain disorders.

This study will attempt to clarify the prevalence of one pain processing abnormality—central sensitization as indexed by manual palpation of the pericranial muscle tenderness—in the general population of undergraduate females, and the association of this abnormality with clinical and psychophysiological findings. A two-stage design will be used. First, the presence of sensitization in the general population will be assessed using a brief assessment of pericranial muscle tenderness and the psychological and family history correlates of sensitization will be examined. Correlates to be examined during this first phase of the study include presence of a mood or anxiety disorder, pain coping strategies, evaluation of present levels of stress, family history, and personal history of pain and psychiatric problems. In the second phase of the study, individuals who are found to be "high-sensitive" or "low-sensitive" on the measure of pericranial muscle tenderness during the first phase of the study will be asked to return for an additional examination. At this point additional psychophysiological variables will be assessed and a more detailed clinical evaluation will be conducted.

The following review will briefly discuss the major pathways in pain transmission, how and why these pathways can become sensitized, methods for examining sensitization in both research and clinical settings, and finally how sensitization presents itself in various chronic pain disorders. The discussion of chronic pain disorders will focus on tension-type headache, fibromyalgia, and temporomandibular disorder, all conditions that frequently utilize measures of manual palpation in research and clinical diagnosis. And, finally the current review will conclude by examining the psychological correlates of these three chronic pain disorders.

Pain Modulation: Major Pain Pathways

Pain transmission takes place along nociceptive fibers through the dorsal horn of the spinal cord and trigeminal nucleus caudalis to higher (supraspinal) central nervous system areas. In order to understand the dysregulation believed to occur in the presence of a chronic pain disorder (sensitization), it is important to understand how the system functions normally and the differences between chronic and acute pain. While chronic and acute pain share the same pain transmission pathways, these pathways function quite differently in each case. In the case of acute pain, injury will activate and alter the nervous system within the injured area, but the body's natural healing mechanisms eventually restore the body to a pre-injured state. In the case of chronic pain, the central systems that influence the transmission, modulation, and expression of pain become altered and do not demonstrate the same reparative mechanisms that occur in acute injury. The following section will discuss the important differences between acute and chronic pain and review the systems by which pain transmission is believed to occur.

Chronic Versus Acute Pain

In order to understand sensitization and the role it plays in chronic pain, it is important to understand the difference between acute and chronic pain. Acute, localized pain is characterized by tissue damage elicited by the injury of body tissue and involves activation of nociceptive transducers at the site of damage (Loeser & Melzack, 1999). The acute injury alters the characteristics of the nociceptors, their central connections, and the nervous system in the injured region but does not overwhelm the body's reparative mechanisms for healing. Acute pain serves as a key physiological protective mechanism to help an organism avoid physical damage, elicit reflex and behavioral

avoidance, and seek healing (Wall & Melzack, 1999). Thus, in the case of acute pain, an injury occurs and the body responds, but as the healing process progresses in a normal fashion the body will no longer continue transmitting the acute pain signal. Indeed, healing will often occur without medical intervention and reports of pain may cease long before the healing process has been completed (Wall & Melzack, 1999).

In contrast, chronic pain persists after healing has occurred and after the adaptive function of the pain ceases to serve any adaptive purpose. Chronic pain can be triggered by injury or disease, but is often perpetuated by factors other than the original cause of pain. In such a case, the injury may exceed the individual's capacity for healing and the nervous system may be altered by the initiating event such that it cannot restore itself to its original, pre-injured state (Skevington, 1995). However, it is also important to recognize that chronic pain syndromes may also occur spontaneously in the absence of any sign of injury, suggesting that other factors besides obvious injury may serve as initiating events. Indeed, it seems likely that in many cases a complex interplay among individual physiological factors, psychological, social, cognitive, and cultural influences (Gatchel & Blanchard, 1993) may result in the development and maintenance of a chronic pain disorder.

Neurophysiology of Pain Transmission

One of the most vital functions of the nervous system is to provide information about possible or actual injury to the organism. The aversive sensation of pain contributes to this function and, in the case of chronic pain, the central systems that influence the transmission, modulation, and expression of pain may be altered. Pain, defined by the International Association for the Study of Pain, is an "unpleasant sensory and emotional

experience associated with actual or potential tissue damage, or described in terms of

such damage" (Merskey & Bogduk, 1994). Nociception is a broad category with the

larger concept of pain that can be defined as the detection of tissue damage by specialized

receptors attached to certain fibers. These receptors may be biased by inflammatory and

neural changes in their immediate environment, such as the presence of an anti-

inflammatory medication (Loeser & Melzack, 1999). As an understanding of central

systems and the nociceptive process are important in understanding the pathophysiology

of chronic pain, this discussion will begin with an overview of major pain transmission

pathways.

Pain at the peripheral level is typically moderated by two distinct kinds of pain

receptors activated by nociceptive input from somatic or visceral tissues. These include

low-threshold nociceptors connected to fast conducting, thin myelinated (Aδ) fibers and

high-threshold nociceptors that conduct impulses in slow, unmyelinated C fibers. Thick

myelinated Aα and Aβ fibers normally mediate innocuous sensations, such as light

pressure, and tend to inhibit the response of spinal cord cells to noxious sensations when

injury occurs. Thus, in normal tissue Aδ and C fibers are the principal transmitters of

impulses experienced as pain, though other categories of nociceptive fibers may be

involved (Besson & Chaouch, 1987). Activated Aδ and C fibers tend to overlap in

sensitivity and may respond to one type of stimulation or be polymodal, responding to

varying degrees of pressure, heat, cold and chemicals (Treede, Meyer, Raja, & Campbell,

1992).

Within the dorsal horn of the spinal cord, these pain fibers synapse with

nociceptor-specific neurons or wide-dynamic range neurons before they transmit to

higher central nervous system areas such as the somatosensory cortex and the thalamus.

Figure 1 demonstrates the synapse between these fibers (A-beta, A-delta, and C) and

wide-dynamic range neurons. Mechanosensitivity is one criterion by which the response

properties of nociceptive neurons at the level of the dorsal horn of the spinal cord can be

classified (Willis, 1989). Low threshold neurons respond to weak mechanical stimuli

with response saturation below the noxious range, thus they are activated by innocuous

stimuli and do not normally mediate pain. Wide dynamic range neurons also respond to

weak mechanical stimuli but encode stimulus intensity throughout the noxious range.

High threshold neurons respond only to noxious mechanical stimuli, thus they require

noxious intensities of stimulation for activation (Treede et al., 1992). Both high threshold

and wide dynamic range neurons signal input from primary afferents to blunt pressure

stimuli.

Figure 1.
Synapse between pain fibers (A-beta, A-delta, and C fibers) & wide dynamic range
neuron.
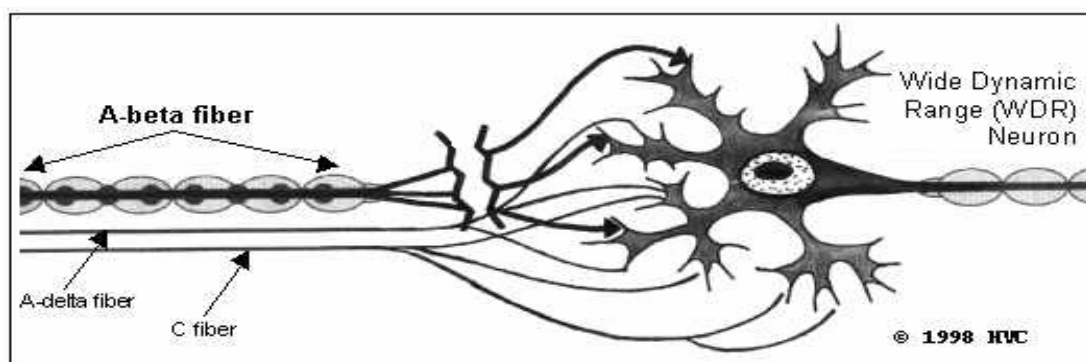
Note. Retrieved July 18, 2004 from http://www.painphysician.com/Presentations/PainMgt.htm.

In normal sensibility a low-intensity stimulus, of sufficient energy to only activate low-threshold primary afferent neurons (Aβ fibers), will produce a sensation that is always interpreted as being innocuous. A high-intensity stimulus sufficient to activate high-threshold primary afferent nociceptors but not produce tissue injury (Aδ, C fibers) will produce transient localized pain. In this normal mode, low-intensity stimuli evoke innocuous sensations such as touch, vibration, pressure, warmth and cold, while high-intensity stimuli evoke pain. This normal sensibility is the consequence of the activation of distinct neural substrates specialized to encode the different kinds of stimuli and provide information on the intensity, duration, and location of the stimuli as well as their modality (Wall & Melzack, 1999). This state operates in healthy individuals as a way to distinguish between damaging and non-damaging stimuli. Reactions to noxious stimulation are a key physiological protective mechanism warning of possible tissue damage and eliciting reflex and behavioral avoidance responses.

The cell bodies of primary sensory neurons are located in the dorsal root ganglion and the first stage of sensory processing for the somatosensory system is performed in the dorsal horn of the spinal cord. The dorsal horn consists of the central terminals of primary sensory neurons, intrinsic dorsal horn neurons and inputs from and outputs to the rest of the central nervous system (Wall & Melzack, 1999). The central terminals of primary afferents (Aβ, Aδ, and C fibers) occupy highly ordered spatial locations in the dorsal horn. In the laminar plane, this order reflects the threshold sensitivity of the afferents, with specific termination sites for functionally distinct afferent types. From the perspective of nociception, high-threshold C and Aδ nociceptors terminate predominantly

in laminae I and II with some contribution to lamine V while low-threshold Aβ

mechanoreceptors terminate in deeper laminae. From here, projection neurons send their

axons upward forming the spinothalamic and spinoreticular tracts, the two major

ascending systems of the anterolateral quadrant of the spinal cord. Certain collaterals of

these tracts terminate in spinobulbar regions involved in descending control and

maintaining homeostasis while the majority of these tracts continue on via the thalamus

to somatosensory and other cortical areas (Treede, Kenshalo, Gracely, & Jones, 1999).

As previously discussed, nociceptive neurons in the dorsal horn of the spinal cord can be

classified by their response patterns of mechanosensitivity (Willis, 1985). Both high-

threshold and wide dynamic range dorsal horn neurons signal input from primary

afferents to blunt pressure stimuli and the discharge of spinal neurons reflects the

integrated response of all primary afferent connections (Cervero & Laird, 1988).

In the ascending spinothalamic track, there is crude somatotopic organization as

the fibers ascend through the medulla, pons, and lateral pathways to the mesencephalon

to the thalamus where the spinothalamic tracks terminate in six distinct regions (Wall &

Melzack, 1999). Spinobulbar nociceptive projections appear to terminate in four major

areas of the brainstem including the periaqueductal grey (PAG), an area recently

receiving much research in the literature on pain processing. The PAG, with both

ascending and descending projections, is a major integration site for homeostatic control

and limbic motor output. Research suggests that spinal input to the PAG may be

integrated as part of descending antinociceptive modulation of the spinal cord (Depaulis,

Keay, & Bandler, (1994). Additionally, the same portions of the PAG that receive spinal

input also have ascending projections to the hypothalamus and the thalamus (Reichling &

Basbaum, 1991), suggesting that spinal input to the PAG may also influence brainstem

modulation of forebrain processing. Thus, these pathways appear to operate as part of the

descending and ascending system of pain sensation broadly illustrated in Figure 2.

While the above discussion focuses on non-craniofacial pain pathways, evidence

suggests that pain processing in the trigeminal system appears to follow a similar if not

identical process (Dostrovsky, 1993). The sensory afferents that innervate the craniofacial

region terminate primarily within the trigeminal brainstem complex consisting of the

main sensory nucleus and the spinal tract nucleus. The major termination site for small-

diameter trigeminal primary afferents is the subnucleus caudalis (SNC), which is

structurally and functionally very similar to the spinal dorsal horn with which it merges in

the upper cervical cord (Light, 1992). As does the spinal cord, there is a differential

distribution of neurons in the different layers of the SNC. Similar to the spinothalamic

tract, the SNC has major projections to the thalamus, brainstem structures, and possibly

to the hypothalamus. Many of the nociceptive neurons in the SNC receive inputs from

non-cutaneous tissues including muscle, temporomandibular joints, corena, and

intracranial blood vessels (Dostrovsky, Davis, & Kawakita, 1991).

Summary

Pain processing takes place along nociceptive fibers, through the dorsal horn of

the spinal cord, and beyond to higher central nervous system areas with little, if any,

demonstrated difference in pain processing at both craniofacial (trigeminal) and non-

craniofacial areas (dorsal horn). There are important differences in how pain is processed

within this system in the case of acute versus chronic pain. While the above discussion

focuses on how pain is processed normally, the following discussion will focus on how

Figure 2.
Ascending/descending system of pain sensitization.
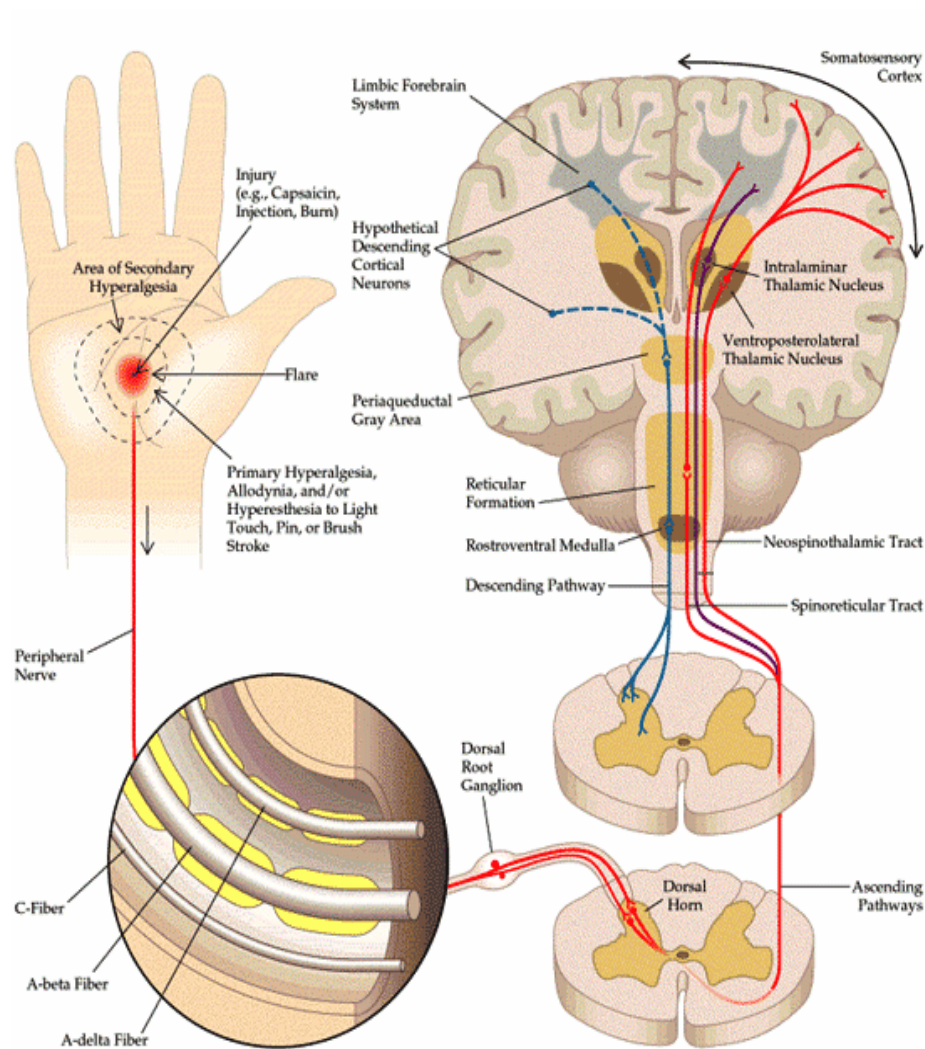
Note. Retrieved July 17th, 2004 from www.medscape.com/viewarticle/460306_2.

the body's pain processing system can become altered or 'sensitized' in the case of chronic pain.

Abnormal Pain Transmission: Sensitization

Definition and Characteristics of Sensitization

The term "sensitization" refers to the state of increased pain sensitivity to nociceptive input. Tissue sensitization after injury is a recognized and expected reaction to the pain experienced from an injury; however the sensitization that occurs in chronic pain disorders lasts long beyond any experienced injury and frequently includes both hyperalgesia and allodynia. Peripheral sensitization is defined as a reduction in the threshold of nociceptive afferent receptors caused by a local change in the sensitivity of sensory fibers initiated by tissue damage (Treede et al., 1992). Such sensitization usually depends upon local inflammation that can lead to decreased nociceptor thresholds. Primary hyperalgesia (pain to stimuli within the injured area) occurs at least in part by sensitization of these peripheral nociceptors (LaMotte, Thalhammer, & Robinson, 1983). Hyperalgesia can also be defined as a leftward shift of the stimulus-response function that relates the magnitude of pain to stimulus intensity. Typically, noxious stimuli evoke more pain than normal in this sensitized state, a state of primary hyperalgesia, where the sensation no longer matches the stimulus in a normal way. Thus, when an individual experiences an injury, it is expected that a change in the sensitivity of sensory fibers at the area of that injury would occur initiated by any damage caused by the injury. Local inflammation and tissue damage at the site of the injury leads to decreased nociceptor thresholds and thus results in pain at the site of the injury. Minor tissue injuries, including

burns, abrasions, and infections can cause a reduction in the threshold of nociceptor

endings, thus sensitizing them. Additionally, as demonstrated in recent experimental

designs, chemical inflammatory mediators—such as capsaisn—can also trigger this

sensitization directly (LaMotte, Shain, Simone, & Tsai, 1991). Once sensitized,

nociceptors also respond to weak, non-noxious stimuli and read these as painful.

Tenderness that results from this state is termed primary allodynia—pain to light touch or

other stimuli that would not typically be considered noxious—and appears to be mediated

by central sensitization to the input from non-nociceptive Aß afferents (Torebjork,

Lundberg, & LaMotte, 1992).

However, primary hyperalgesia and its accompanying peripheral sensitization of

peripheral nociceptors does not appear to play a central role in chronic pain disorders

such as fibromyalgia and tension-type headache where secondary hyperalgesia and

allodynia are frequently present and have been described as important features of central

sensitization. Acute tissue damage and inflammatory states will directly and indirectly

lead to the activation of nociceptors that will induce central sensitization. However, upon

recovery the source of input during the central changes is removed and the primary

hyperalgesia and allodynia commonly disappear shortly thereafter. By contrast, the pain

sensitivity believed to be associated with central sensitization is persistent. Secondary

hyperalgesia (pain to stimuli outside the area of injury) involves increased excitability of

spinal cord neurons and central sensitization appears to be much more relevant in chronic

pain disorders than sensitization at the peripheral level. Central sensitization can be

defined as the enhanced excitability of dorsal horn neurons of the spinal cord

characterized by increased spontaneous neuronal activity, enlarged receptive fields, and

augmented stimulus responses transmitted by afferent fibers (Li, Simone, & Larson, 1999), or, rather, central sensitization can result from abnormal signal processing in the central nervous system and allodynia and hyperalgesia can result (Hardy, Wolff, & Goodell 1952; Woolf, 1991). There is significant evidence that in the presence of central sensitization peripheral input to the central nervous system along non-nociceptive, thickly myelinated Aβ touch afferents may evoke pain—that is neuronal inputs that previously evoked sensations of touch now evoke pain responses (Torebjork et al., 1992). Central sensitization leads to enlargement of mechanical receptive fields, which could explain the local spreading of tenderness found in hyperalgesia, but widespread or generalized tenderness could also be due to alterations in descending pathways from the brainstem (Ren, Zhuo, & Willis, 2000). Thus, in the case of central sensitization there appears to be an increase in the number and magnitude of responses evoked by natural stimuli, or rather central sensitization can be ascribed to increased excitability of spinal and supraspinal neurons. More simply, central sensitization appears to result in an individual experiencing what would usually be considered non-painful sensations as pain and typically painful sensations with increased pain.

Laboratory studies have repeatedly demonstrated that dorsal horn neurons, including spinothalamic tract neurons, can be 'sensitized' following brief bursts of activity in nociceptors. Strong nociceptive input has been found to be one of the factors that can trigger central sensitization and research has demonstrated that central sensitization can be generated by prolonged nociceptive inputs from the periphery (Li et al., 1999). This mechanism is particularly likely to be of importance in those diagnosed with chronic muscular pain as inputs from muscle nociceptors are more effective in

initiating changes in the behavior of dorsal horn neurons than are inputs from cutaneous

nociceptors in animal models (Wall & Woolf, 1984). Again, it should be noted that pain

processing and the process of sensitization in craniofacial pain pathways (the trigeminal

system) is analogous to pain processing in non-craniofacial pathways (dorsal horn). Thus,

the dorsal horn is analogous in structure and function to the trigeminal nucleus (with

which the trigeminal pathway merges in the upper cervical cord). In a state of

sensitization, dorsal horn excitability or trigeminal nucleus excitability is increased and as

a consequence the response of the dorsal horn or trigeminal nucleus to sensory input is

facilitated. A thalamic correlate of the sensitization of dorsal horn neurons to Aβ fiber

input has not yet been documented, but it is theorized that sensitization also involves

supraspinal structures.

Central sensitization can manifest in one of three ways: (1) a reduction in the

threshold of dorsal horn neurons; (2) an increase in the responsiveness of dorsal horn

neurons; (3) as the expansion of the extent and the recruitment of novel inputs to

receptive fields (Woolf, 1983; Hu, Sessle, Raboisson, Dallel, & Woda, 1992). Changes in

receptive field properties are due to the recruitment of previously subthreshold

components of the receptive field as a result either of increased synaptic output or

increased excitability of the postsynaptic cell (Woolf, 1991). In this case, the receptive

field "grows" as it begins to include components that were not part of the original

receptive field. For example, in central sensitization afferent fibers that normally would

only signal non-painful sensations such as touch have been "recruited" to signal painful

sensations. Normally, only C-fiber input can initiate central sensitization, a phenomena

that has been observed in human volunteers following the application of C-fiber irritants

such as capsaicin (Koltzenburg, Lundberg, & Torebjork, 1992). Following either nerve injury and peripheral inflammation, however, the propensity of primary afferent to induce central sensitization increases because some A fibers undergo chemical alteration such that low-intensity stimulation begins to induce prolonged excitability and changes in the dorsal horn neurons that would never typically occur in a normal animal (Neuman, Doubell, Leslie, & Woolf, 1996). The behavioral manifestation of this is progressive tactile allodynia, a centrally mediated progressive increase in pain sensitivity initiated by repeated touch stimulation of inflamed skin (Ma & Woolf, 1996). Thus, prolonged or repeated activation of the nociceptive C fibers produces central sensitization such that noxious stimuli produce more intense pain (hyperalgesia) and innocuous stimuli produce pain (allodynia) and central sensitization can occur in any situation with prolonged or intense C-fiber input (the latter phenomenon also known as wind-up). Additionally, activity in large-diameter, low-threshold Aβ mechanoreceptors becomes capable of generating pain as demonstrated by the fact that the previously non-noxious stimuli, in a state of central sensitization, produce pain.

Animal Models of Sensitization

Animal experimentation has done much to help us better understand research conducted on humans on central sensitization. For example, in animal studies with rats Yu & Mense (1990) have demonstrated that high-threshold mechanosensitive dorsal horn neurons have a positively accelerating stimulus-response function while the low-threshold mechanosensitive neurons have an approximately linear stimulus-response function, a finding that has been critical in understanding differences in human studies examining pressure pain thresholds in tender versus non-tender muscles. Extensive

animal experimentation has demonstrated that hyperexcitability of dorsal horn neurons may be a possible cause of the hyperalgesia found in individuals with chronic pain. Studies with animals also have demonstrated that the development of new and/or expansion of existing receptive fields by noxious muscle stimuli can result in central sensitization. In animal models it appears that strong inputs from the peripheral nociceptors can rewire the circuitry of the dorsal horn by unmasking previously ineffective synapses and by then forming new synaptic connections between low-threshold afferents and dorsal horn neurons that normally receive input from high-threshold afferents (McMahon, Lewin & Wall, 1993; Mense, 1993).

To study mechanisms of hyperalgesia, allodynia, and central sensitization animal models have been established that frequently employ chemical irritants to produce tissue inflammation and exaggerated responses to a variety of noxious stimuli. Among the chemical irritants, mustard oil (allyl isothiocyanate) is considered to activate C-fiber nociceptors selectively (Woolf and Wall, 1986); cause neurogenic inflammation (Fitzgerald and Gibson, 1984); produce hyperalgesia to thermal, mechanical and electrical stimuli (Woolf and Wall, 1986); result in activation of silent C-nociceptors (Schmidt et al., 1995); and produce hyperalgesia (Koltzenburg & Wahren, 1994). Other irritants, including capsaicin injection (Simone et al., 1991), have also been used to examine sensitization in animal models and demonstrate many of these similar properties.

Using flexor reflexes (motor response, which can be elicited by pinch or heat stimuli) in decerebrate rats, Woolf (1984) found that these reflexes were markedly facilitated by stimuli that activate C-fibers (topical burn, injection of mustard oil, electrical stimulation). This facilitation of the flexion reflex was independent of changes

in the excitability of the primary afferents and of motor neurons. Similarly, Cook et al. (1987) found that C-fiber strength conditioning stimuli also produced substantial increases of the receptive field size in rat dorsal horn neurons. Some of these neurons initially responded only to noxious mechanical stimuli, but eventually the rats developed sensitivity to brushing and touching stimuli following the conditioning stimuli suggesting both hyperalgesia and allodynia. In many of these animal studies examining neuronal excitability in rats, C-fiber stimulation of the nerves of the skin had little effect while stimulation of deeper tissues such as muscle led to long-lasting changes. This suggests that, for the changes believed to occur in a state of central sensitization, repetitive sensory stimulation is required to take place in deeper tissues. A similar facilitation of A-fiber responses, such as that found by Cook et al. (1987) in rats, elicited by C-fiber input has also been seen in spinalized cats (Behrends, Schomburg, & Steffens, 1983).

Evidence for central sensitization has been found in dorsal horn neurons in both monkey and rats as both demonstrate changes in the receptive field size and threshold after injury. For example, experimental burn injuries inside the receptive field of the monkey spinothalamic tract neurons has been found to cause a shift of the stimulus-response function such that mechanical stimulation outside the injured skin area led to increased responses to noxious and non-noxious stimuli (Kenshalo, Leonard, Chung, & Willis, 1982). A similar expansion of the receptive field of rat dorsal horn neurons has been found with application of mustard oil outside of the receptive field (Woolf & King, 1990). Mechanical injury within the receptive field of rat dorsal horn neurons have led to expansions of the receptive field into uninjured skin (Laird & Cervero, 1989). Injection of capsaicin has been found to lead to increased responses to stroking and a decrease in

the threshold for mechanical stimuli away from the injection site and sensitization to near-threshold electrical stimulation that (assumedly) only activated Aß fibers (Simone et al., 1991). Changes in the receptive field size of spinal neurons suggest the importance of sensory integration at the supraspinal level. Additionally, there is direct evidence from animal studies to suggest that supraspinal changes occur during the process of central sensitization. For example, thalamic neurons in anesthetized rats exhibit enhanced responses to mechanical stimuli remote from the injury site (Guilbaud, Kayser, Benoist, & Gautron, 1986), but it is unclear what the human psychophysical correlate of these changes might be.

Summary

Chronic pain disorders such as tension-type headache and fibromyalgia are characterized by aberrant pain processing such that noxious stimuli produce more intense pain (hyperalgesia) and innocuous stimuli produce pain (allodynia). Both hyperalgesia and allodynia are signs of the central sensitization that is believed to accompany chronic pain disorders. In terms of neurophysiology, central sensitization can manifest itself either by a reduction in the threshold of dorsal horn neurons, an increase in the responsiveness of dorsal horn neurons, or as the expansion of the extent and the recruitment of novel inputs to receptive fields. It is believed that this process occurs as the result of prolonged nociceptive input from periphery fibers. Thus, as the result of this prolonged nociceptive input from the periphery, input to the dorsal horn becomes 'amplified' in such a manner that previously non-painful stimuli begins to produce pain and painful stimuli will produce more intense pain.

Standardized Assessment of Sensitization

While the above section discussed the definition and characteristics of

sensitization, the following section will outline how sensitization can be measured and

utilized as a valid technique for understanding central sensitization within a research

setting. Experimentally, sensitization can be assessed utilizing a number of standardized

techniques designed to measure how an individual processes noxious and non-noxious

sensations such as light touch and deep pressure. Mechanical pressure stimulus is widely

used in studies examining sensitization in tension-type headache, fibromyalgia, and

temporomandibular disorders. Furthermore, assessments of muscle tenderness via manual

palpation are used in the clinical diagnosis of fibromyalgia and have been suggested for

diagnostic use in tension-type headache. The following discussion will focus on a review

of mechanical pressure as a standardized assessment of sensitization and discuss recent

developments in technology and research design that have increased the reliability of

assessment via manual palpation.

Mechanical Pressure and the Assessment of Sensitization

In both research and clinical practice, pain is frequently measured as tenderness

upon blunt pressure palpation of various areas of the body. Tenderness, a very common

sign in medical practice, may be defined as pressure-induced pain. It may be a normal

physiological sign—such as tenderness following strenuous exercise. Or, tenderness may

signal some underlying pathology—such as inflammation in an arthritic joint. Manual

palpation can provide a clinically relevant method for the evaluation of tenderness and is

an important tool in pain research as a means by which to measure sensitization (Mense,

1990). The stimulus-response functions that can be plotted using data collected via

manual palpation can provide important information about central sensitization at the level of the dorsal horn/trigeminal nucleus. Individuals who demonstrate the sensitization believed to accompany chronic pain disorders such as tension-type headaches and fibromyalgia have frequently been found to demonstrate abnormalities in pain sensitivities to mechanical pressure.

Mechanical stimulation is one method for exciting muscle nociceptors and pressure algometry is the most generally applied technique for quantification of tenderness, which in clinical practice is assessed by palpation. However, using this technique it can be difficult to distinguish between peripheral and central sensitization unless the sensitization is restricted to a single muscle/joint. Stimulus-response functions, which can be assessed using mechanical stimulation, can provide important information on muscle hyperalgesia and the presence of higher order central sensitization. Important differences have been found between the stimulus-response functions in normal muscle/individuals and those with chronic pain. Generally, this data suggests that those diagnosed with a chronic pain disorder demonstrate abnormal stimulus-response functions suggestive of changes in neuronal behavior at the spinal dorsal horn/trigeminal nucleus. Or rather, they demonstrate increased tenderness to mechanical stimulation in comparison to healthy controls. This research will be discussed at greater length in the following sections on findings of sensitization in chronic pain disorders.

In studies involving mechanical pressure, pain sensations are evoked by deformation of the skin by von Frey hairs, needles, and by application of gross pressure. Spring-loaded dolorimeter/algorimeters or digitally controlled palpometers may also be used. Current research paradigms often use pressure to a finger joint, muscles or deep

tissue (Jensen, 1990; Lautenbacher, Rollman, & McCain, 1994). Mechanical methods for assessing pain have the potential to produce a wide range of pain intensities and durations, however it can be difficult to control the mechanical stimulus as tissue elasticity and stimulating area, rate and degree of compression can all influence results. Thus, it is important to control for as many of these factors as possible when conducting mechanical stimulation via pressure. Pressure that is exerted onto the skin may activate nociceptive afferents in several tissues depending on the configuration of the object used to exert the pressure. Thus, the diameter of the algometer is important as there is not necessarily a simple relation between diameter and threshold as spatial summation plays an important role for pain. Contact with a punctuate object such as a small diameter needle may exclusively activate intraepidermal nerve endings. Since deformation of the epidermis can be achieved with very small forces, these stimuli have little to no effect on afferents in deeper, muscular tissues. And, as was discussed in the previous section, activation of deeper tissues appears to be a critical component in measuring central sensitization. A preferential activation of deep afferents is possible if pressure is exerted on a large skin area (i.e., 1 cm^2) and the contact surface is rounded or cushioned. Cutaneous afferents do not appear to be involved in contact with a large, blunt probe such as this (Kosek, Ekholm, & Hansson, 1995).

However, precise quantification of tenderness to manual palpation can be difficult. The degree of tenderness is presumed to be dependent on the pressure exerted during palpation, but until recently there was no way to reliably standardize the pressure of palpation. In previous studies, the reliability of manual palpation has been reported to be low (Kopp & Wenneberg, 1983; Levoska, Keinanen Kiukaanniemi, & Bloigu, 1993)

to acceptable (Cott, Parkinson, & Bell, 1992; Jacobs, Geenen, van der Heide, Rasker, &

Bijlsma, 1995; Tunks, McCain, & Hart, 1995). Several factors could contribute to the

variability found in the evaluation of tenderness including the intensity of the palpation

pressure and the scoring of the tenderness rating (Jensen, Rasmussen, Pedersen, Lous, &

Olesen, 1992; Wolfe, Smythe, & Yunus, 1990). One difficulty with early studies

examining tenderness to palpation was the fact that there was no means to standardize the

pressure used in palpation, thus likely resulting in the lower reliabilities found in these

studies. Additionally, several of the more recent studies have controlled for observer bias

by utilizing blind comparisons in which all examinations are done by the same observer.

Often, pressure pain thresholds are assessed clinically by palpation by the

examiner's thumb or forefinger as is done in the manual survey of 9 bilateral locations

used in the diagnosis of fibromyalgia (Wolfe et al., 1990). Clearly, this technique is

subject to significant sources of variance. In research settings, quantitative measurement

of pain to blunt pressure is most frequently performed using pressure algometry with the

aid of a hand-held device such as the Pressure Threshold Meter/Algometer that has

become widely available. These devices consist of a circular rubber pad of approximately

1 cm^2 connected to a dial readout that measures pressure in both kilograms and pounds.

Threshold values at various sites for healthy individuals (Fischer, 1993; Jensen, et al.,

1992) and those diagnosed with various chronic pain disorders have been documented

(Jensen, Rasmussen, Pedersen, & Olesen, 1993; Norregaard, Bendtsen, Lykkegaard, &

Jensen, 1997; Granges & Littlejohn, 1993) and will be further discussed in the following

sections.

As a means of addressing the problem of experimental variance in myofascial pain research, the palpometer was developed in order to more accurately measure the pressure intensity exerted during palpation (Bendtsen, Jensen, Jensen, & Olesen, 1994). The palpometer consists of a thin pressure-sensitive plastic film connected to a LED read-out and the pressure exerted during palpation is measured in arbitrary units on a scale. The relation between the forces applied to the plastic film and the palpometer output has been found to be approximately linear and the intra- and interobserver variation of exerted force at a given palpometer value has been found to be acceptably low (Bendtsen et al., 1994). Additionally, palpation pressure has been found to be stable within observers from week to week. Thus, Bendetsen et al. (1994) concluded that the palpometer is a valuable tool for the measurement of the pressure intensity exerted during palpation as it allowed researchers a means by which to standardize the pressure applied during pericranial examination.

In headache research, manual palpation is most often performed according to the procedure outlined by Langemark & Olesen (1987) and later adapted by Bendtsen et al. (1995) to include the use of a palpometer. In this method, the palpation is performed bilaterally to a fixed pressure of approximately 500 grams/centimeter in the pericranial muscles with small rotating movements of the second and third fingers. The induced tenderness is scored according to the Total Tenderness Scoring system. The Total Tenderness Scoring system scores tenderness on a four-point combined behavioral and verbal scale (0= denial of tenderness and no visible reaction; 1 = verbal report of discomfort or mild pain, no visible reaction; 2 = verbal report of moderate pain, with or without visible reaction; 3 = verbal report of marked pain and visible expression of

discomfort). The values from both sides are summed to create a Total Tenderness Score. Previous research has found this technique to be reliable (Bendtsen, Jensen, Jensen, & Olesen, 1995). In one study, the measurement of non-instrumental palpation resulted in significantly different measurements of tenderness between two observers; however this difference was eliminated during pressure-controlled palpation by using a palpometer. Additionally, tenderness scores did not differ significantly within observers from week to week even without control of palpation pressure. Thus, this supports the idea that palpation pressures are stable within observers over time as suggested by Langemark & Olesen (1987).

Gender and Sensitization

Several studies have found that females exhibit greater sensitivity to laboratory pain when compared to males, that this increased sensitivity does not appear to be site specific, and that differences in sensitivity occur most when pain inductions mimic those experienced in a natural environment (Fillingim & Maixner, 1995). Several other studies have found similar conclusions that females demonstrate significantly greater pain sensitivity compared to males in their perception of noxious experimental stimuli (Berkley, 1995; Riley, Robinson, Wise, Myers, & Fillingim, 1998). Additionally, increased sensitivity in females has been found in measures of pressure pain threshold (Chesterton, Barlas, Foster, Baxter, & Wright, 2003) and pericranial muscle tenderness (Jensen et al., 19992). Thus, researchers utilizing measures of pain sensitivity should carefully consider the influence of gender when designing studies and evaluating outcomes of experimental pain and sensitization.

Limitations of Standardized Assessment of Sensitization

While efforts have been made to standardize assessments of sensitization through the use of careful experimental control and new technologies such as the palpometer, these measures remain somewhat indirect assessments of sensitization—a construct that despite much research remains not entirely well understood. Most simply, sensitization can be defined as increased pain sensitivity. Though many hypotheses have been formulated as to how sensitization occurs and why it is such a significant concept in chronic pain research, these are frequently based upon assessment techniques that use participant's self-report. As such, assessments of sensitization are subject to the same biases inherent in all self-report measures. Despite this, these limitations and biases are rarely considered in the literature on sensitization.

Summary

Manual palpation has proved useful in the assessment of sensitization in chronic pain disorders and standardized assessments using mechanical pressure are frequently used to assess sensitization in both tension-type headache and fibromyalgia research. Recent developments in both technology and research design—such as the development of the palpometer—have increased the reliability of assessment via manual palpation by allowing researchers to reliably standardize the pressure of palpation. While the above section focuses primarily on how manual palpation has been used to assess sensitization in chronic pain disorders, the information gained from utilizing assessments such as these has helped researchers better understand the central sensitization and the role of the dorsal horn/trigeminal nucleus in such sensitization. Thus, the following section will

review these and other findings of sensitization in chronic pain disorders with a particular

focus on the areas of tension-type headaches and fibromyalgia.

Findings of Sensitization in Chronic Pain Disorders

Research on sensitization in chronic pain has focused on disorders that utilize

manual palpation as part of diagnostic assessment, including conditions such as

headache, fibromyalgia, and temporomandibular disorder. Much of what is currently

known about sensitization is the result of research in one of these three disorders, each of

which has significant individual and societal impact. For example, prevalence rates of

fibromyalgia in the general population are estimated at 2%, affecting women (3.4%) at a

higher rate than men (0.5%) (Wolfe et al, 1995), and fibromyalgia has been found in

countries worldwide (White & Harth, 2001). Comparatively, prevalence rates of chronic

headache in the United States have been estimated at 2.2% for tension-type headache and

up to 38.3% for episodic tension-type headache (Schwartz et al., 1998). Similar to

fibromyalgia, tension-type headache has been found in countries worldwide (Rasmussen,

1995; Merikangas et al.,1993; Gobel, Petersen-Braun, & Soyka, 1994) and prevelance

rates are consistently found to be higher in females than males. Finally, the prevelance of

temporomandibular disorder signs and symptoms has been estimated to as high as 60% in

non-patient populations (Dimitroulis, 1998; Dworkin, Le Resche, Von Korff, Truelove,

& Sommers, 1990) though it is estimated that only 5% of people with one or more signs

of the disorder actually seek treatment (Hannson & Milner, 1975; Dworkin et al., 1990;)

and females outnumber males by at least four to one in presenting for treatment (Dworkin

et al., 1990). Thus, these three conditions—headache, fibromyalgia, and

temporomandibular disorder—all account for significant disability. And, as these

disorders are perhaps among the most prominent in sensitization research, the following discussion will focus on reviewing the findings of sensitization in the areas of headache, fibromyalgia, and temporomandibular disorders.

Tension-type Headaches

As discussed previously, manual palpation is frequently used as a means to assess sensitization in chronic pain disorders, in particular to assess such sensitization in the research on tension-type headaches. Taken together, studies that utilize manual palpation as a means of assessing tenderness in tension-type headache suggest that perhaps the most common clinical finding in patients with tension-type headaches is increased tenderness to palpation of the myofascial tissues. Importantly, this abnormality has been found in individuals diagnosed with both chronic and episodic tension-type headache (Jensen et al., 1993; Jensen, Bendtsen, & Olesen, 1998), suggesting that even individuals who experience only a few headache days per month can demonstrate increased tenderness. In these individuals diagnosed with tension-type headache, tenderness has been found to be uniformly increased throughout the pericranial region and both muscles and tendon insertions have been found to be excessively tender (Langemark & Olesen, 1987; Jensen et al., 1993; Bendtsen, Jensen, & Olesen, 1996). This suggests that increased tenderness is not localized to the particular pericranial area where individuals experience their headache most. More interestingly, evidence suggests that individuals who experience increased pericranial muscle tenderness do so even when they are headache-free.

It is not specifically known whether the increased tenderness in tension-type headache is primary or secondary to the headache, but currently available evidence

indicates that such tenderness is not the byproduct of a headache episode but rather suggestive of altered pathophysiology in those who experience tension-type headaches. Pericranial tenderness in patients diagnosed with tension-type headache alone has also been found to be increased not only on days with headache but also on days without headache (Lipchik, Holroyd, Talboy, & Greer, 1997) and this increased tenderness has been associated with both the intensity and frequency of tension-type headaches (Jensen et al., 1993). This suggests that the pericranial tenderness demonstrated in these individuals is not solely the product of a headache episode. Rather, the elevated pericranial muscle tenderness found in individuals diagnosed with tension-type headache could suggest a possible sensitization of pain transmission circuits at the trigeminal nucleus and dorsal horn (Bendtsen, Jensen, & Olesen, 1996), suggesting a more central rather than peripheral mechanism in tension-type headache.

Central mechanisms: Increased pain sensitivity. It seems likely that central mechanisms are more important in the pathophysiology of tension-type headache than the sensitization of peripheral nociceptors in the pericranial muscles. Central mechanisms are complex and can be difficult to investigate, however such investigation is necessary to examine whether the knowledge gained in research on conditions such as headache and fibromyalgia is valid in patients with chronic pain more generally, and in order to further our understanding of the central mechanisms leading to this and other chronic disorders. Additionally, it is important that we fully understand the various biopsychosocial factors that contribute to central sensitization.

The abnormal pericranial tenderness observed in patients with tension-type headache could be related to an increased sensitivity in the central nervous system to

nociceptive stimuli from the periphery. Pain sensitivity has been extensively studied in headache. Pressure pain detection thresholds—the lowest pressure stimulus perceived as painful—have been found to be normal in some studies with participants diagnosed with episodic tension-type headaches (Jensen et al., 1993; Gobel, Weigle, Kropp, & Soyka, 1992) and in groups of mixed episodic and chronic tension-type headache patients (Jensen, 1996; Bovim, 1992). Other studies have found pressure pain detection thresholds decreased in patients with chronic tension-type headache (Schoenen, Bottin, Hardy, & Gerard, 1991; Bendetsen et al., 1996) and inversely related to Total Tenderness Scores (recall, these scores are the sum of tenderness ratings at five bilateral sites in a measure of pericranial muscle tenderness) in both episodic and chronic tension headache sufferers (Jensen & Rasmussen, 1996). The pressure pain tolerance threshold—the maximal pressure stimulus tolerated—has also been compared between chronic tension-type headache patients and healthy controls. In one study, pressure pain tolerance thresholds in both the finger and at the temporalis were significantly lower in chronic tension-type headache patients than in healthy controls (Bendtsen et al., 1996). Janke & Holroyd (2002) also found pressure pain tolerance thresholds to be lower in headache-prone individuals when compared to healthy controls at both the finger and temporalis. This lowered pressure pain detection and tolerance thresholds at both cephalic and extra-cephalic locations indicate the presence of both allodynia (pain elicited by stimuli that are not usually perceived as painful) and hyperalgesia (increased sensitivity to painful stimuli) in patients with chronic tension-type headache, both suggestive of central sensitization. Thus, measurement of pressure pain thresholds have been proved useful and reliable in developing hypothesis regarding the nature of pain processing in tension-

type headache (Bendtsen, 2000; Jensen & Rasmussen, 1996; Fischer, 1993), but population studies that combine manual palpation and pressure pain thresholds have been rarely conducted and no previously published study examines these variables with in the context of psychosocial variables such as psychiatric diagnosis and family history.

Though mechanical stimuli are most commonly used in examining sensitization in tension-type headache, individuals diagnosed with chronic tension-type headache also have been found to be hypersensitive to stimuli beyond pressure including both thermal and electrical pain thresholds. In general, research has found that those diagnosed with a chronic pain disorder such as tension-type headache demonstrate reduced pain thresholds and tolerances to both heat and cold stimuli when compared to healthy controls, however these results are somewhat mixed and appear to be at least partially mediated by disease severity and modality of thermal stimulation utilized in the research design. For example, in comparing those diagnosed with episodic tension-type headaches, chronic tension-type headaches, and healthy controls, Jensen et al. (1997) found that mechanical pain thresholds and tolerances differed between groups of patients diagnosed with chronic tension-type headache (CTTH), episodic tension-type headaches (ETTH), and a group of healthy controls with CTTH participants having the lowest scores, followed by the ETTH group, followed by the healthy control group with the highest. However, there were few significant differences between the three groups on thermal pain tolerance thresholds both at cephalic and extra-cephalic locations. Recall from previous sections that activation of deeper tissues appears to be a critical component in measuring central sensitization, and preferential activation of deep afferents is more likely with mechanical stimuli. Activation of cutaneous afferents by typical thermal stimuli may render

differences in pain tolerance thresholds less obvious and in part explain why the authors found significant differences in mechanical pain thresholds but not thermal pain thresholds. In contrast to Jensen et al.'s findings, Langemark et al. (1989) found a significant decrease pain detection threshold to thermal stimuli in patients with chronic tension-type headache when compared to healthy controls. This discrepancy in these two findings could be explained several ways. It is possible disease severity mediates thermal pain thresholds and that the headache-prone participants in Langemark et al.'s study were more symptomatic than those in Jensen et al.'s study. Or, thermal stimulus modality (hot vs. cold) and/or the ability to carefully control stimulus temperature changes could also have resulted in the discrepant results. Finally, both the pain detection threshold (Bendtsen et al., 1996) and the pain tolerance threshold (Langemark, Bach, Jensen, & Olesen, 1993) to electrical stimuli have been found decreased in patients diagnosed with tension-type headache. Sensitivity to several different stimulus modalities including pressure, thermal, and electrical have been found to be increased at both cephalic and extra-cephalic locations (Langemark, Jensen, Jensen, & Olesen, 1989; Schoenen, Gerard, DePasqua, & Sianard-Gainko 1991; Langemark et al., 1993; Bendtsen et al., 1996). However, it should be noted that significantly more research has been conducted in tension-type headache utilizing mechanical pressure to assess sensitization rather than thermal or electrical stimuli. Thus, the evidence for differences between healthy participants and those diagnosed with tension-type headaches on mechanical pain thresholds is more salient than differences found to date in thermal or electrical pain thresholds. However, increased sensitivity in those diagnosed with tension-type

headaches across stimulus modalities would be suggestive of central dysregulation in pain processing.

Several well-designed studies have examined mechanical pain in tension-type headache patients. Bendetsen et al. (1996) report pressure pain detection and pressure pain tolerance thresholds were decreased in chronic tension-type headache patients when compared with healthy controls. Bendtsen et al. (1996) recruited 40 patients diagnosed with tension-type headache from a local headache clinic and an equal number of age and gender matched healthy controls. Patients were examined during a typical headache episode and pericranial muscle tenderness ratings (Total Tenderness Score) and pressure pain thresholds at both the middle phalanx and anterior temporalis were taken. Pressure pain detection and tolerance thresholds recorded in the finger were significantly lower in patients than controls, and a nonsignificant similar trend was observed in the temple. Additionally, the two thresholds were significantly correlated both in the finger and in the temporal region in headache patients with significant inverse correlations between the pressure pain thresholds and Total Tenderness Scores. Thus, the increased tenderness in patients with tension-type headache appears to be widespread and not localized to certain myofascial tissues or certain locations. These data suggest that pain detection and pain tolerance in different areas of the body are modulated by a common central factor in patients with chronic tension-type headache (Bendtsen et al., 1996). However, this study had the drawback of examining patients during a headache episode and comparing these results with those of healthy controls who were examined outside of a headache episode, which could have resulted in increased discrepancies on these measures between the two groups. Since all the participants in the headache group were recruited from a headache

clinic, the severity of their headaches were likely greater than that found in the general population of headache suffers. Additionally, clinic patients such as those recruited for this study could likely differ from other headache-prone individuals on measures beyond headache severity, including psychosocial history and physiological variables such as pain tolerances, thresholds, and overall muscle tenderness. Finally, one might expect an individual during a headache episode to demonstrate increased tenderness as found by Bendetsen et al. (1996), particularly in the pericranial region, but a finding of increased tenderness in headache patients while they are outside of a headache episode makes a stronger case for central sensitization in tension-type headache. Similarly, Jensen et al. (1998) also found a significant negative correlation between Total Tenderness Scores and both pressure pain detection and pressure pain tolerance thresholds in patients with chronic tension-type headache, but not in patients with episodic tension-type headache. Once again, all the participants in the headache group were recruited from a local headache clinic, however all participants were examined in a headache-free state.

Langemark et al. (1989) also found a significant negative correlation between pressure pain detection thresholds in the temporal region and Total Tenderness Scores in patients diagnosed with chronic tension-type headache and found greater tenderness in headache patients when compared to healthy controls. Again, all the participants included in the headache group for this study were recruited from local headache clinics and hospitals and the experimenters did not report controlling for the presence of a headache during the physiological examination. Additionally, Langemark et al. found that some of the control patients demonstrated severe tenderness in the absence of a headache and that some headache patients demonstrated no tenderness at all, but they were unable to

explain these findings. The fact that a finding of tenderness is associated with but not limited to a diagnosis of tension type headache suggests that other variables beyond headache could be responsible for this tenderness. While previous research has established that there is a correlation between psychosocial variables and a diagnosis of tension-type headache, few studies to date have examined the possible impact these variables could have on ratings of muscle tenderness and pain thresholds.

Pain sensitivity: Spinal dorsal horn/trigeminal nucleus. Jensen (1990) suggested that myofascial tenderness found in tension-type headache could be the result of a lowered pressure pain threshold, a stronger response to pressure in the noxious range, or a combination of both. Until the palpometer was developed as a way to standardize pressure, it was not possible to effectively study the relationship between palpation pressure and pain. Using this instrument, the stimulus-response function for pressure and pain was investigated in patients with chronic tension-type headache and in healthy controls as a way to test this hypothesis (Bendtsen, 1996). Interestingly enough, the stimulus response function found in normal muscle can be accurately described by a power function. However, in highly tender muscle the stimulus-response function was found to be linear and displaced towards lower pressures, thus qualitatively different from that in normal muscle. Figure 3 displays the stimulus-response functions found for both normal and tender muscle. When headache patients and healthy controls in one study were sub-grouped on the basis of their report of tenderness, Bendtsen et al. (1996) found that the stimulus-response function (as measured via manual palpation) was nearly linear in the most tender patients and well-described by a power function in the least tender patients. Thus, the abnormal stimulus-response

Figure 3.
Stimulus-response functions: Trapezius muscle in headache patients (circles, top line) and controls (triangles, bottom line).
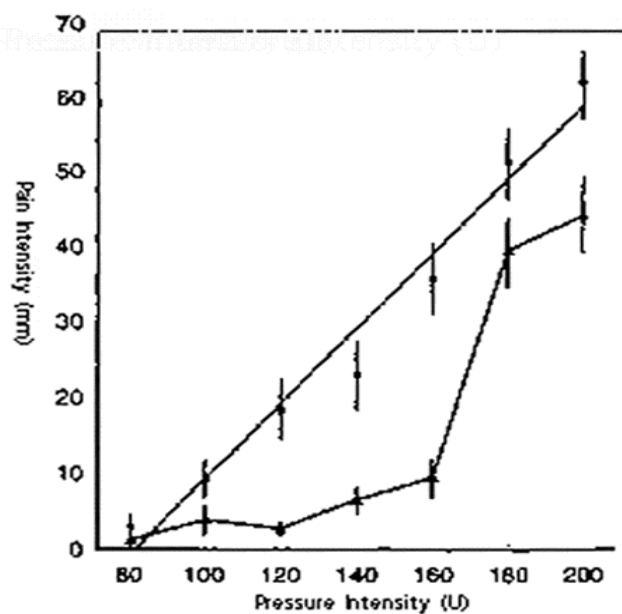
Note. From Bendtsen, Jensen, and Olesen (1996).

function was related to the degree of tenderness and not to the diagnosis of tension-type headache. A subsequent study confirmed this finding (Bendtsen, Norregaard, Jensen, & Olesen, 1997) in patients diagnosed with fibromyalgia. In these participants, the relation between pressure and pain in the trapezius muscle was almost perfectly linear and not slightly curved as in patients with chronic tension-type headache. This concurs with the finding that the trapezius muscle in those diagnosed with fibromyalgia was more tender than in those diagnosed with tension-type headache. This finding of a qualitatively altered response to nociceptor stimulation in tender muscles indicates that myofascial pain, and the widespread non-specific pain experienced in fibromyalgia, is at least partly caused by qualitative changes in the processing of sensory information (Bendtsen et al., 1996; Bendtsen et al., 1997).

As previously discussed, spinal dorsal horn neurons that receive inputs from deep myofascial tissues can be classified as either high threshold (HTM) or low threshold (LTM) mechanosensitive neurons. High-threshold mechanosensitive neurons require noxious intensities of stimulation for activation while low-threshold mechanosensitive neurons are activated by innocuous stimuli (Mense, 1993). This suggests that the linear stimulus-response function found by Bendtsen et al. (1996, 1997) in tender human muscle may be caused by activity in LTM afferents. Such a finding seems to run counter to the evidence that LTM afferents have been found to modulate innocuous stimuli. However, Woolf (1983) has demonstrated that a prolonged noxious input from the periphery is capable of sensitizing spinal dorsal horn neurons such that LTM afferents can mediate pain. Similar findings have been found in human studies. Torebjork et al. (1992) found similar changes in the central processing of inputs from LTM afferents in

humans following the intradermal injection of capsaicin. Thus, it seems likely that the abnormal stimulus-response function in tender muscle can be explained by changes in neuronal behavior at the spinal dorsal horn/trigeminal level (Bendtsen et al., 1996; Bendtsen, 2000). A decrease of the supraspinal descending inhibition probably does not explain the finding of abnormal stimulus-response functions, as it has been reported that the descending inhibition acts via a decreased slope of the stimulus-response curve (Yu & Mense, 1990) while not changing the shape of the stimulus-response curve as seen in Bendtsen's research. Thus, the finding of qualitatively altered nociception from tender human muscles indicates that the central nervous system is sensitized at the level of the spinal dorsal horn/trigeminal nucleus in patients with chronic myofascial pain. While this sensitization likely accounts for part of the increased tenderness demonstrated in patients with tension-type headache, it should be noted that this does not necessarily imply that spinal mechanisms are more important than supraspinal mechanisms in chronic pain. The relative importance of spinal and supraspinal pain mechanisms and the interaction between these is not well understood at this point.

Peripheral mechanisms leading to central sensitization. As previously outlined, it seems likely that the central nervous system is sensitized at the level of the spinal dorsal horn/trigeminal nucleus in individuals diagnosed with chronic tension-type headaches. The process by which this sensitization is theorized to occur will be discussed here. Research cited above by Jensen et al. (1998) that compared pain perception in tension-type headache with and without increased muscular tenderness found significantly lower pressure pain detection thresholds and tolerances in both cephalic and extra-cephalic locations in all patients with a diagnosis of chronic tension-type headache with abnormal

tenderness compared to those who did not exhibit abnormal tenderness. This difference was not found when individuals with episodic tension-type headaches with and without tenderness were compared with each other. Additionally, it was found that chronic tension-type headache patients with abnormal tenderness tended to have lower mechanical pain thresholds than healthy controls, while patients without abnormal tenderness had significantly higher pain thresholds than controls. Thus, this study suggests that central pain sensitivity is increased only in chronic tension-type headache patients with increased pericranial tenderness. Though this relation between pericranial muscle tenderness and central sensitization does not demonstrate a cause-effect relationship between these factors, since evidence suggests patients with episodic tension-type headache have increased pericranial tenderness but normal central pain sensitivity and since chronic tension type headache usually evolves from the episodic form (Langemark, Olesen, Poulsen, & Bech 1988), it is a likely hypothesis that the central sensitization in patients with chronic tension-type headache is induced by prolonged nociceptive inputs from myofascial tissues as previously suggested (Bendtsen et al., 1995; Bendtsen et al., 1996; Bendtsen, 2000).While it is possible the sensitization is secondary to the pain itself, this is most unlikely since the central nervous system does not appear to be sensitized in patients with chronic tension-type headache who are not tender to palpation (Jensen et al., 1998).

Central sensitization in tension-type headache. Bendtsen (2000) proposes a pathophysiological model for chronic tension-type headache that suggests the primary problem in chronic tension-type headache is the sensitization of dorsal horn neurons due to increased nociceptive inputs from pericranial myofascial tissues and decreased

inhibition and increased facilitation of pain transmission from supraspinal structures. Pain processing is modulated by multiple pathways broken down in this model into three main areas: supraspinal structures, brain stem/spinal cord, and pericranial myofascial tissues. In normal individuals, the periaqueductal grey (PAG) in the midbrain has inhibitory pathways descending to the spinal dorsal horn while the rostral ventromedial medulla (RVM) in the brainstem has "off-cells" that inhibit nociceptive transmission and "on-cells" that facilitate nociceptive transmission in the spinal dorsal horn. Bendtsen proposes that these supraspinal and peripheral pathways become rewired to facilitate pain processing in certain susceptible individuals exposed to prolonged or intense myofascial pain and/or muscle activity.

Bendtsen suggests that under certain conditions a painful stimulus from the pericranial myofascial tissues may be more prolonged or intense than normal caused by increased muscle activity or possibly the release of various chemical mediators secondary to local pathological conditions. In this model, increased muscle activity secondary to psychogenic stress could be of particular importance at this stage as psychogenic stress could cause a prolonged increase of muscle tension while at the same time potentiating pain facilitation from the brain stem to the spinal dorsal horn (Wall & Melzack, 1999). Some individuals, due to certain protective factors that at this time are not well understood, may only experience frequent headache episodes for a limited period of time during such a period of psychogenic or physical stress. However, in certain predisposed individuals the prolonged nociceptive input from the pericranial myofascial tissues may lead to sensitization of nociceptive second order neurons at the level of the spinal dorsal/trigeminal nucleus. The pathophysiological basis for increased susceptibility to

central sensitization is not well understood, but possible mechanisms include impaired supraspinal inhibition of nociceptive transmission in the spinal dorsal horn due to a serotonergic dysfunction. Previous research has found that there is a significant negative correlation between plasma 5-HT and headache frequency in patients with chronic tension-type headache (Bendtsen, Jensen, Hindberg, Gammeltoft, & Olesen, 1997). This could suggest that patients with chronic tension-type headache demonstrate an impaired ability to increase plasma 5-HT. Extending this hypothesis to supraspinal function, it could be possible that those with tension-type headache also have an impaired ability to increase synaptic 5-HT levels in response to increased nociceptive inputs from the periphery. However, this is only a tentative hypothesis that assumes that peripheral changes in 5-HT levels actually reflect similar central mechanisms, though it could help account for the high correlation between tension-type headache and depression (as will be discussed in the following sections) and findings that a diagnosis of depression can increase one's vulnerability to developing a tension-type headache following a laboratory stressor (Janke & Holroyd, 2001).

In the sensitized state that results in certain individuals following prolonged nociceptive input, the afferent Aβ-fibers that normally inhibit Aδ- and C-fibers by presynaptic mechanisms in the dorsal horn will now stimulate the nociceptive second order neurons. Additionally, the effect of Aδ- and C-fiber stimulation of the nociceptive dorsal horn neurons will be potentiated and the receptive fields of the dorsal horn neurons will be expanded (Coderre, Katz, Vaccarino, & Melzack, 1993). Thus, the nociceptive input to supraspinal structures will be considerably increased. This increase could result in increased excitability of supraspinal neurons as has been found in animal research

(Lamour, Guilbaud, & Willer, 1983). Increased nociceptive input could also result in decreased inhibition or increased facilitation of nociceptive transmission in the spinal dorsal horn (Wall & Melzack, 1999). Finally, supraspinal structures such as the PAG and RVM could become sensitized such that inhibitory processes are decreased and facilitation of pain transmission is increased. These changes could also result in increased drive to motor neurons which results in somewhat increased muscle activity, thus initiating a self-sustaining cycle of chronic muscle activity and peripheral and central sensitization.

Summary: Tension-Type Headache. Taken together the above mentioned studies suggest that individuals who experience chronic, and perhaps even episodic, tension-type headaches demonstrate increased sensitivity to pain and decreased pain thresholds believed to be associated with central deregulation of pain modulating systems. The finding that pain hypersensitivity has been demonstrated for mechanical pressure stimuli (and some evidence for both electrical and thermal experimental stimuli) when applied at both cephalic and at extra-cephalic, non-symptomatic locations strongly indicates that the pain sensitivity in the central nervous system is increased in patients with chronic tension-type headache (Bendtsen, 2000). From this evidence, one could hypothesize that the primary problem in chronic tension-type headache is the sensitization of dorsal horn neurons due to increased nociceptive inputs from pericranial myofascial tissues and decreased inhibition and increased facilitation of pain transmission from supraspinal structures. While some argue that there is a relationship between the central hypersensitivity and the increased pericranial myofascial tenderness in patients with chronic, but not episodic, tension-type headache (Bendtsen, 2000; Jensen et al., 1998), at

this time there is not enough evidence to clearly state the differences in pain processing between those who experience chronic tension-type headaches and those who experience episodic tension-type headaches and what additional factors, such as psychosocial functioning, could be related to these differences.

While the association between central pain processing dysfunction, increased muscle tenderness/decreased pain thresholds, and tension-type headaches seems a likely hypothesis, there is also evidence to suggest that certain individuals who experience tension-type headaches demonstrate neither increased pericranial muscle tenderness nor decreased pressure pain thresholds. Certain studies have found that some individuals diagnosed with tension-type headache do not demonstrate pericranial muscle tenderness or pressure pain thresholds different than controls and that this "non-tender" group does not differ from a tender group on reports of headache severity (Langemark & Olesen, 1987; Schoenen et al., 1991). Thus, while it is clear that most patients diagnosed with tension-type headache demonstrate increased pericranial tenderness and some degree of widespread tenderness, some do not. Furthermore, while most healthy control patients do not demonstrate increased pericranial tenderness and widespread tenderness, some do. Since it appears that tenderness is mostly but not always associated with a headache diagnosis, it is possible that other factors not measured in previous research designs examining muscle tenderness and tension-type headache could account for this variability in tenderness in both patients and healthy controls. However, at this time it is unclear exactly what factors differentiate between tender and non-tender headache groups and non-tender and tender healthy control groups. Finally, the evidence is mixed as to whether individuals diagnosed with episodic tension-type headaches experience a similar

pattern or degree of widespread tenderness associated with tension-type headache. Thus, it seems general hypersensitivity and central sensitization can explain only a part of the increased pericranial tenderness in some patients with tension-type headache and it is likely that other factors could contribute to the variability in tenderness in both headache and healthy control groups. While research at this time links tension-type headaches to a central dysfunction in pain processing, no research to date has examined other factors beyond pain that could be related to, a cause of, or a consequence of this disorder. If we are correct in assuming a central process is involved that includes a dorsal horn/trigeminal nucleus sensitization modulated by both peripheral and supraspinal structures, then it seems reasonable that such a process would not only manifest itself as pain. However, there are no studies currently examining what, if any, other factors could be involved.

Fibromyalgia

Centrally modulated pain dysfunction such as that believed to occur in tension-type headache has also been implicated in other pain syndromes, such as fibromyalgia. Fibromyalgia is a syndrome of unknown origin that displays allodyna, deep pain, and hyperalgesia to deep and superficial stimuli, however there are no distinctive muscle changes that define fibromyalgia in terms of specific muscle pathology (Simms, 1998). According to the criteria of the American College of Rheumatology, fibromyalgia (FM) is defined by chronic diffuse musculoskeletal pain combined with a low mechanical pain threshold at so-called tender points (Wolfe et al., 1990). In two multicenter studies (Wolfe et al., 1990; Okifuji, Turk, Sinclair, Starz, & Marcus, 1997), the best discrimination between fibromyalgia and patients with other chronic pain conditions

could be achieved with two criteria: (1) widespread pain, above and below the waist, right and left side of the body, and axial, of at least a three month duration and (2) presence of pain upon palpation of at least 11 of 18 specific locations (tender points). Pain threshold at these points is assessed by manual palpation and tender point counts are used for patient classification. Lowered pressure pain threshold at tender points have been illustrated in studies that have measured these thresholds with calibrated devices (Tunks, McCain, & Hart, 1995; Granges & Littlejohn, 1993; Lautenbacher et al., 1994), but several findings suggest that fibromyalgia is characterized by a more generalized increase in pain sensitivity. Pressure pain thresholds in fibromyalgia patients have also been found to be lowered in areas not designated as tender points and pain sensitivity has been found to be increased for heat and electrical stimulation.

Despite extensive research, no definitive organic pathology of fibromyalgia has been identified and there are no universally effective treatments for the syndrome. Fibromyalgia often includes a range of comorbid symptoms that frequently includes recurrent headaches. Some studies have found up to 91% of fibromyalgia patients may have a positive history of primary headache (Nicolodi, Volpe, & Sicuteri, 1998) and approximately 30% report a concurrent headache disorder (Wolfe et al., 1990). In one study where a tender point examination was applied to patients with recurrent headache and those with fibromyalgia, while a substantial number of headache patients met the tender point criterion for fibromyalgia syndrome, the patients with fibromyalgia consistently reported greater numbers of positive tender points and greater pain sensitivity even in the trapezius and occipital sites (Okifuji et al., 1997). Interestingly, it was required that none of the participants in the headache group reported widespread pain

of at least three months' duration ensuring that this group was diagnostically different from the fibromyalgia group. Yet, even upon examination many of the headache patients reported widespread pain as that found in fibromyalgia. These results suggest that while tension-type headache and fibromyalgia may demonstrate similarities in pain processing, perhaps the increased pain sensitivity found in some patients with fibromyalgia indicates an even greater vulnerability to central sensitization than that found in tension-type headache. Some researchers have proposed that a similar mechanism of abnormal pain processing could underlie both headache and fibromyalgia (Nicolodi & Sicuteri, 1996) and research to date suggests that the pain experienced by patients with fibromyalgia is at least partly the result of disordered sensory processing at the central level (Bennett, 1999). In comparison to controls, those with fibromyalgia display lower pain thresholds for mechanical, heat, and electrical stimuli (Granges & Little john, 1993; Lautenbacher et al., 1994; Kosek, Ekholm, & Hansson, 1996; Arroyo & Cohen, 1993). Thus, it has been suggested that the widespread pain and tenderness in fibromyalgia are consequences of a dysfunction of central pathways involved in pain modulation (Mense, 2000). Descending pain modulatory pathways can be inhibitory as well as excitatory (Ren et al., 2000) and reduced activity in the former or increased activity in the latter could lead to generalized pain of the kind that is seen in fibromyalgia.

In part because no organic pathology has been identified, researchers have proposed that fibromyalgia is related to deregulated pain modulation in the central nervous system. A consistent feature of fibromyalgia is a hyperalgesic response that suggests abnormal nociceptive processing at the level of the central nervous system. Indeed, the presence of generalized hyperalgesia in fibromyalgia is one of the cardinal

features of the syndrome and comparisons of pain sensitivity in patients diagnosed with

the disease to those diagnosed with other pain syndromes frequently demonstrate

differences. In one study evaluating the pain ratings of 178 patients including 53

fibromyalgia patients, 46 chronic back pain patients, 41 chronic headache patients, 38

rheumatoid arthritis patients, and 20 pain-free controls who underwent a standardized

tender point examination protocol. The protocol examines pain responses at both tender

points and non-tender point areas on a scale of 0 (no pain) to 10 (worst pain) and

additionally totals the number of painful tender points. Patients with fibromyalgia

reported significantly higher levels of pain than other groups for both tender point and

control points while patients with the other three chronic pain diagnoses each reported

significantly higher levels of pain compared only to healthy controls at both tender points

and non-tender points. Thus, while patients diagnosed with other chronic pain disorders

demonstrated more tenderness than healthy control participants, the fibromyalgia patients

reported the greatest level of tenderness (Okifuji et al., 1997). However, it should also be

noted that within this study there was a wide variety in both the number of tender points

reported by patients with fibromyalgia and the severity of pain ratings at these points. It is

unclear at this time what, if any, other factors could account for the variability in tender

point ratings found within individuals diagnosed with fibromyalgia, though it seems

possible that other measures of general distress and psychopathology may play some role

in the disparity among tenderness.

In another study using an electric dolorimeter recording the participant's

assessment of pain intensity on a 0-10 visual analogue scale at varying levels of applied

force, distinctly different response curves were obtained for fibromyalgia patients than

for healthy controls (Bendtsen et al., 1997). Figure 4 demonstrates these stimulus-response curves. In pain-free controls, there was found to be a threshold at about 160 dolorimeter units beyond which there was an almost linear increase in pain intensity. In comparison, fibromyalgia participants exhibited a linear increase in pain from the baseline dolorimeter force of 80 units. Such a difference between these two groups is suggestive of qualitatively altered nociception in fibromyalgia and additionally suggests that fibromyalgia patients differ from pain-free participants in their processing of sensory information.

Figure 4.
Stimulus-response functions: Trapezius muscle in fibromyalgia patients (circles, top line) and controls (triangles, bottom line).
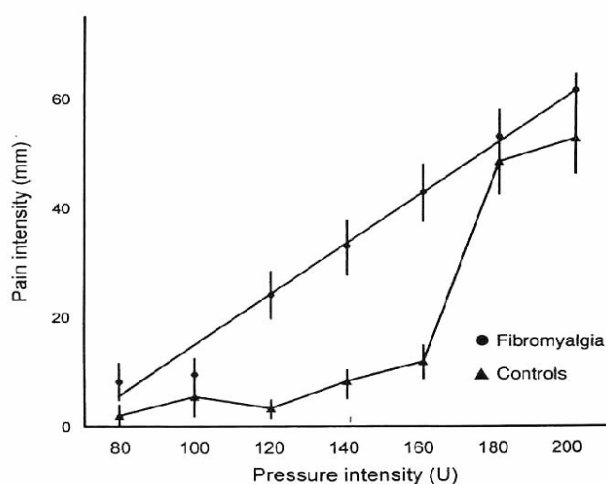
Note. From Bendtsen, Jensen, and Olesen (1996).

Several studies to date suggest that as self-reports of pain and symptoms of distress in fibromyalgia patients increase other measures hypothesized to index central modulation of pain also increase. In one study, a stratified random sample of adults

selected on the basis of their pain complaints were categorized into one of three groups: (1) chronic widespread pain (pain for more than three months affecting the axial skeleton and at least two contralateral quadrants of the body); (2) regional pain (pain during the previous month lasting for longer than 24 hours); (3) no pain during the previous month. Tender point counts were higher in those with pain than in those who had no pain and in those with widespread pain compared with those with regional pain. However, 60% of the participants with chronic widespread pain had fewer than 11 tender points and there were two participants (out of 50) with counts of 11 tender points or more in the group reporting no pain. As tender point count rose, mean symptom scores for depression, fatigue, and sleep problems significantly increased with these trends being independent of pain complaints. As a result, the authors argue that tender point counts are not solely a measure of current pain but are a measure of distress and separately related to central modulators of the experience of pain. While they did not specifically explain the presence of tender point counts greater than 11 in those reporting no pain, their results suggest that other factors including depression and fatigue could account for this finding (Croft, Schollum, & Silman, 1994).

In a similar study (Carli, Suman, Biasi, & Marcolongo, 2002), patients from a Rheumatology Clinic were divided into five main groups: (1) fibromyalgia patients; (2) secondary-concomitant fibromyalgia patients; (3) patients with widespread pain but who did not reach the criterion of tender points to be diagnosed as fibromyalgia; (4) patients with diffuse multiregional pain but who also did not reach the criteria for a diagnosis of fibromyalgia; (5) and patients with multiregional pain associated with at least 11 positive tender points. Pain thresholds were then assessed using mechanical pain, thermal pain,

and ischemic pain assessment techniques. Mechanical pain was assessed with deep pressure algometry to determine pressure pain thresholds at both tender points and non-tender points. Thermal pain was assessed with a thermal stimulator to determine both heat and cold pain thresholds. Ischemic pain was induced by the cold pressor test and the submaximal effort tourniquet test to determine pain thresholds and pain tolerances. For each assessment, patients with widespread pain and patients with multiregional pain demonstrated similar pain thresholds. The thresholds in patients with diffuse multiregional pain and multiregional pain associated with at least 11 tender points differed from those in the fibromyalgia and secondary-concomitant fibromyalgia patients, with the latter generally demonstrating lower pain thresholds and pain tolerance levels. Thus, increased sensitivity to the somatic stimuli utilized in this study and perceived as painful may only occur in certain patient groups. The authors interpreted the results to suggest that dysfunction in the nociceptive system is already present in patients with multiregional pain with a low tender point count, however the dysfunction appears to become more severe as the positive tender point count and pain extent increase and is maximal in fibromyalgia patients. However, the authors found that in fibromyalgia patients, and in each of the four additional patients groups utilized in the study, tender point count was correlated with present pain, fatigue, and stiffness. In the fibromyalgia group, patients who complained and patients who did not complain of ongoing pain displayed similar pain thresholds and pain tolerance at similar sites.

Summary: Fibromyalgia. Fibromyalgia is a syndrome of unknown origin that displays allodynia, deep pain, and hyperalgesia to both deep and superficial stimuli though there are no distinctive muscular changes that define the disease in terms of

specific muscle pathology. While fibromyalgia is often found comorbid with pain disorders such as tension-type headache, two criteria have been established to help diagnostically differentiate between fibromyalgia and other chronic pain conditions: widespread pain and presence of pain upon palpation at 11 of 18 specific locations (tender points). Lowered pressure pain threshold at tender points have been illustrated in studies measuring these thresholds with calibrated devices, but several findings suggest that fibromyalgia is characterized by a more generalized increase in pain sensitivity as pressure pain thresholds in fibromyalgia patients have been found to be lowered in areas not designated as tender points and pain sensitivity has also been found to be increased for heat and electrical stimulation. Thus, it has been argued that centrally modulated pain dysfunction such as that implicated in tension-type headache is also a cardinal feature of fibromyalgia. Finally, it should be noted that there is some evidence to suggest that tender point counts are associated not only with a diagnosis of fibromyalgia and chronic widespread pain, but possibly also to other psychosocial variables. For example, Croft et al. (1994) found participants who did not report widespread pain but who did have tender point counts similar to those diagnosed with fibromyalgia and suggest that this finding could be related to variables such as depression and fatigue. Carli et al. (2002) found variability in the tender point ratings among individuals diagnosed with fibromyalgia. Thus, while centrally modulated pain dysfunction is a likely hypothesis to explain at least part of the increased widespread tenderness found in patients with fibromyalgia, it also seems likely that other factors could contribute to the variability in tenderness ratings found in this research. While research at this time links fibromyalgia to a central

dysfunction in pain processing, little research to date has examined other factors beyond

pain that could be related to, a cause of, or a consequence of this central sensitization.

Temporomandibular Disorder

Temporomandibular disorder (TMD) can be distinguished from fibromyalgia and

tension-type headache, though both conditions can and often do occur in the same

patient. Temporomandibular disorder is characterized by pain in the masseter or temporal

area associated with a history of masticatory dysfunction but without a dysfunction of the

temporomandibular joint (Dworkin & LeResche, 1992). Muscle tenderness of masseter

and temporalis muscles is a salient feature of this disorder and pressure pain threshold

measurement has demonstrated reliability and validity as a diagnostic tool in this

condition (Ohrbach & Gale, 1989; Farella, Michelotti, Steenks, Romeo, Cimino, &

Bosman, 2000). Pain is characteristically aggravated by manipulation or function, limited

range of motion, asymmetric mandibular movement and/or locking and joint sounds.

Within recent years, it has been argued that various subgroups of TMD patients represent

distinct diagnostic groups that can be classified on the basis of physical findings and

psychosocial variables. However, diagnostic criteria remain unclear at this time and the

underlying etiology or pathophysiology mediating TMD has not been identified.

However, several recent studies support the view that TMD is a psychophysical disorder

involving central nervous system pain-regulatory systems that results in maladaptive

emotional, physiological, and neuroendocrine responses to emotional and physical

stressors. Up to 80% of patients with TMD also suffer from a multitude of other

psychobiological disorders and it appears that sensory responses of TMD patients to

noxious stimulation are significantly different than control participants. Malow et al.

(1980) reported that TMD patients with myalgia and no organic pathology have lower finger pressure pain thresholds and are less able to discriminate varying intensities of pressure compared to controls. Similarly, Molin, Edman, & Schalling (1973) reported patients with TMD have significantly lower electric pain thresholds than control participants. Maixner et al. (1995) found that TMD patients had significantly lower thermal pain thresholds, ischemic pain thresholds, and ischemic pain tolerance values relative to control participants which led them to conclude that TMD patients are more sensitive to noxious stimuli than pain-free controls and in support of the finding that TMD is a psychophysiological disorder of the CNS. All these results suggest that the greater sensitivity to pain-evoking stimuli found in TMD is a psychophysiological disorder associated with an impaired pain-regulatory system.

In both Ortbach & Gale (1989) and Farella et al. (2000), the reliability of pressure pain threshold measures was shown to be greater than the reliability of other signs and site-specific symptoms in diagnosing TMD. The positive predictive value of pressure pain thresholds has been reported as 68% for the masseter muscle and 74% for the temporalis muscle (Farella et al., 2000) and pressure pain threshold reliability is considered superior than other methods in the diagnosis of this condition. Reduced pressure pain thresholds have been demonstrated on the painful side in masticatory muscles of patients with TMD with pressure pain thresholds being significantly lower at painful sites than at the non-painful contralateral muscle (Ohrbach & Gale, 1989; Farella et al., 2000). However, significantly reduced pressure pain thresholds in patients with TMD compared with control participants have also been shown in the same muscles on the contralateral, non-painful side and in remote muscle sites in these individuals

(Ohrbach & Gale, 1989; Farella et al., 2000; Svensson et al., 2001) suggesting that more generalized, likely central mechanisms also play a part in the pain experienced in this condition. The hypersensitivity in remote muscles may appear to be similar to fibromyalgia but patients with TMD do not normally fulfill the diagnostic criteria of fibromyalgia (Svensson et al., 2001). Thus, while TMD seems to share some of the same signs of central pain dysfunction found in both tension-type headache and fibromyalgia and it appears that each of these disorders could vary in the degree of central sensitization, it is still unclear the role central sensitization plays in these disorders.

However, the justification for segregation of temporomandibular myofascial pain and dysfunction from other myofascial pain disorders of a more generalized type, such as primary fibromyalgia and tension-type headache, has been questioned by some on the basis that these disorders reflect a similar pathology of central sensitization (Widmer, 1991). Muscle tenderness such as that in tension-type headache is a frequent finding in TMD patients (Clark, Green, Dornan, & Flack, 1987) and patients with TMD report a significantly higher incidence of tension-type headache than controls (Watts, Peet, & Junipter, 1986). Additionally, there are several striking similarities between TMD and fibromyalgia. Blasberg and Chalmers (1989) retrospectively reviewed a series of TMD patients for evidence of generalized musculoskeletal pain and concluded that there are great similarities between these and primary fibromyalgia patients. Thus, though it seems that there is evidence suggesting multiple similarities between TMD and other pain disorders, TMD remains a diagnostically distinct concept.

Summary: TMD. Temporomandibular disorder is characterized by pain in the masseter or temporal area associated with a history of masticatory dysfunction but

without any dysfunction of the temporomandibular joint. Muscle tenderness of the masseter and temporalis muscles is a salient feature of this disorder and pressure pain threshold measurement has demonstrated reliability and validity as a diagnostic tool in this condition. While the underlying etiology or pathophysiology mediating TMD has not been identified, recent studies suggest those diagnosed with TMD demonstrate significantly lowered pain thresholds compared to healthy controls and provide support for the hypothesis that TMD is a disorder involving central nervous system pain-regulatory systems. TMD is often found to be comorbid with both fibromyalgia and tension-type headache, and some researchers have questioned whether TMD should be treated as a distinct disorder on the basis that it demonstrates a similar pathology of central sensitization as found in these other chronic pain conditions. While there are similarities between pain processing in TMD and other pain disorders, currently TMD remains diagnostically distinct from these disorders.

Summary: Sensitization in Chronic Pain Disorders

The above sections discuss findings of altered muscle tenderness and pressure pain thresholds associated with sensitization in tension-type headache, fibromyalgia, and TMD. Generally, researchers have found that individuals diagnosed with these disorders demonstrate increased muscle tenderness and decreased pressure pain thresholds at both symptomatic and non-symptomatic sites and have used this evidence to argue for the presence of centrally modulated pain dysfunction in these disorders. Two additional points may be drawn from the above review. First, each of these disorders often includes a range of comorbid symptoms. For example, fibromyalgia is often found to be comorbid with either a history of primary headache or a concurrent headache disorder (Nicolodi et

al., 1998; Wolfe et al., 1990) and other symptoms of distress including depression,

fatigue, and sleep problems (Croft et al., 1994). Similarly, there is evidence suggesting

multiple similarities between TMD and both fibromyalgia and tension-type headache

(Watts et al., 1986; Blasberg & Chalmers, 1989). Secondly, research has found some

variability in the presence of both muscle tenderness and decreased pressure pain

thresholds such that while most individuals diagnosed with chronic pain disorders

commonly express one if not both of these, there are some who demonstrate neither. In

addition, some individuals who have not been diagnosed with a chronic pain disorder

have been found to have increased muscle tenderness and decreased pain thresholds. For

example, certain studies have found that some individuals diagnosed with tension-type

headache do not demonstrate pericranial muscle tenderness or pressure pain thresholds

different than controls and that this "non-tender" group does not differ from a tender

group on reports of headache severity (Langemark & Olesen, 1987; Schoenen et al.,

1991). Additionally, some research has also found that a few healthy control participants

demonstrate increased muscle tenderness and decreased pressure pain thresholds in the

absence of any headache diagnosis. A similar phenomenon has been noted in the

fibromyalgia literature where it has been found that patients diagnosed with fibromyalgia

report a wide variety in both the number of tender points and the severity of pain ratings

at these points (Okifuji et al., 1997). Research to date has not directly addressed what, if

any, other factors could account for this variability; however, it seems possible that

general distress, comorbid symptoms, and/or psychopathology—given the high

correlation of these with the chronic pain disorders discussed above—may play some role

in the disparity among tenderness and pressure pain ratings used to index central

sensitization. As such, the following section will review psychological factors commonly associated with these chronic pain disorders.

Psychological Factors and Chronic Pain Disorders: Correlates of Sensitization

Psychological Factors and Tension-type Headache

It has been found that stress is one of the most common precipitating factors in the development of tension-type headache (Rasmussen, 1993; Scharff, Turk, &Marcus, 1995). Several experimental studies have demonstrated that tension-type headaches can be induced via psychological stress (Jensen & Olesen, 1996;Gannon, Haynes, Cuevas, & Chavez, 1987; Hatch, Moore, Borcherding, Cyr-Provost, Boutros, & Seleshi, 1992), and psychological and behavioral therapies appear to be quite effective for the treatment of tension-type headaches (Holroyd, O'Donnell, Stensland, Lipchik, Cordingly, & Carlson, 2001). In both clinical and non-clinical samples, individuals with frequent tension-type headaches obtain higher scores on psychological symptom measures and on daily life stress measures than do healthy controls (Andrasik, Blanchard, Arena, Teders, Teevan, & Rodichok, 1982; Penzien, Rains, & Holroyd, 1993; Holm, Holroyd, Hursey, & Penzien, 1986). The mechanisms by which psychological stress plays a role in tension-type headache are not currently well known, but central factors including involuntary contractions of the cephalic muscles, a decrease in supraspinal descending pain-inhibitory activity, and supraspinal hypersensitivity to nociceptive stimuli may be involved (Merskey, 1999). Thus, while psychological stress is of importance to the development of tension-type headache, the exact mechanism by which such stress generates, exacerbates, and maintains headache remains unclear.

Research has consistently supported a link between chronic pain disorders—

including chronic tension headaches—and the diagnoses of anxiety and depression. Verri

et al. (1998) found that in a sample of 88 patient being treated for chronic daily headache

at a headache clinic, 90% of these patients could be diagnosed with a psychiatric disorder

with the most common diagnosis being a comorbidity of anxiety and mood disorders.

Estimates of the prevalence of depression in chronic pain patients vary greatly and range

from 31% to 100% (Romano & Turner, 1985) while the estimated prevalence of pain

complaints in patients diagnosed with depression ranges from 34% to 66% (Smith, 1992).

Several studies have supported a link between chronic tension headaches and depression

suggesting individuals who suffer from chronic tension headaches are more likely to

report symptoms of depression and anxiety on measures such as the MMPI and the

MMPI-2 (Inan, Soykan, & Tulunay, 1994; Kudrow & Sutkus, 1979; Sternbach, Dalessio,

Kunzel, & Bowman, 1980) or to be diagnosed with a mood or anxiety disorder (Verri,

Checchini, Galli, Granella, Sandrini, & Nappi, 1998). In both clinical and non-clinical

samples, those with frequent tension-type headaches score higher on measures of

psychological distress and symptomotology and on daily life stress measures than healthy

controls (Penzien, Rains, & Holroyd, 1993). In subspecialty headache treatment centers,

half or more of chronic tension-type headache sufferers may receive anxiety or mood

disorder diagnoses (Adler, Adler, & Packard, 1987).

In one recent study utilizing both self-report measures and diagnostic interviews

with 245 patients who underwent assessment as part of a larger treatment study, patients

diagnosed with chronic tension-type headaches were found to have significantly higher

scores on self-report measures of depression, trait anxiety, and daily hassles than healthy

controls (Holroyd et al., 2000). Additionally, tension-type headache participants were significantly more likely to have a PrimeMD diagnosis of either a mood or anxiety disorder (45.5%) with 28.9% of the patients having a prime mood disorder and 34.7% of the patients having a prime anxiety disorder. Thus, almost half of the headache patients while less than 10% of the healthy control participants met the diagnostic criteria for an anxiety or mood disorder in this sample. However, this study also found that many of the patients who were diagnosed with an affective disorder were often in the mild to moderate range of severity, suggesting that these symptoms are subtle and have the opportunity to be easily overlooked in a clinical setting.

Headache patients demonstrate significant elevations on scales believed to measure, in part, symptoms of depression and anxiety when compared with healthy controls on the MMPI-2. In a sample of patients drawn from a university headache clinic, Ziegler and Paolo (1995) found that headache patients scored significantly higher than control participants on Hypochondriasis, Depression, Hysteria, Psychastenia, and Social Introversion scales. While these findings are similar to those from previous studies involving clinic populations, this study included participants with diagnoses of both migraine and mixed headaches in the experimental headache group but did not find any differences between these two diagnoses on these measures. This study did not include participants with diagnoses of tension-type headache, thus it is difficult to generalize these findings to tension-type headache sufferers but it seems likely that similar findings would occur in this group.

Finally, a prospective, longitudinal epidemiological study of a cohort of 19- and 20-year-olds using both self-report measures and a diagnostic interview to determine the

presence of pathology among groups of participants with migraine and tension-type headache found that only migraineurs demonstrated increased levels of psychopathology including affective and anxiety disorders when compared to healthy controls (Merikangas, 1994). Tension-type headaches did not differ from controls in rates of psychopathology; however, it should be noted that this study focused on an episodic tension-type headache population (who only experience occasional headaches) and may provide limited implications about what could be observed in frequent tension-type headache sufferers. Thus, while there is some conflicting evidence, the majority of the research suggests a likely link between psychopathology (particularly depression and anxiety) and tension-type headache, though the nature of this link is not yet well understood.

Various theories have speculated as to the nature of the relationship between tension-type headaches and depression. Banks & Kerns (1996) argue that the stress (diathesis-stress) of having a chronic pain disorder may lead to the higher rates of depression in those with pain disorders. Others argue the opposite, that depressed mood can lead to decreased pain tolerance (Zelman, Howland, Nichols, & Cleeland, 1991) and the development of a chronic pain disorder (Mangi et al. , 1994). A third hypothesis is that chronic pain disorders are variants of depression, a kind of "masked depression" (Lesse, 1974); or, it is also possible that a common genetic vulnerability leads to both disorders. Finally, it has also been suggested that different hypotheses may apply for different types of chronic pain disorders and different types of depression (Fishbain, Cutler, Rosomoff, & Rosomoff, 1997). However, research to date does not provide unequivocal support for any specific causal link between pain and depression.

Additionally, while a large body of correlational research establishes a link between depression and chronic pain disorders including tension-type headaches, little research examines the psychophysiological mechanisms that might mediate this relationship.

While the comorbidity of chronic pain and depression is well documented (Holroyd et al., 2000; VonKorff & Simon, 1996), few studies have attempted to examine the relationship between pain and depression in a laboratory setting using a psychological or physical stressor. Pinerua-Shuhaibar et al. (1999) found that while measures of pain threshold, pain intensity, and pain unpleasantness during sustained ischemic pain produced by a maximal effort tourniquet procedure were similar in depressed and non-depressed individuals, overall pain ratings during the task were 28% higher and pain tolerance was 44% lower in depressed participants when compared to controls. This study is limited in its generalizabity to those with tension-type headaches in that these ratings are for acute pain only and none of the participants in this study were diagnosed with a chronic pain disorder. In a sample of undergraduates who underwent a cold-pressor task, it was found that pain expectancies partially mediated the relation between scores on the Beck Depression Inventory and self-reported pain experience (Sullivan, Rodgers, Kirsch, 2001). In another study examining two groups of patients diagnosed with temporomandibular disorders—one "pain sensitive" group and another "pain tolerant" based on their response to an ischemic arm task—the pain sensitive group demonstrated greater sensitivity to thermal pain and reported greater clinical pain but did not differ from the pain tolerant group on psychosocial measures of anxiety, coping, and mood (Fillingim, Maixner, Kincaid, Sigurdsson, & Harris, 1996). However, none of these studies utilized a chronic pain or depressed/anxious population.

Other research suggests that while depressed individuals may self-report more overall daily pain sensitivity, they actually exhibit increased pain thresholds in response to experimental pain. Lautenbacher, Spernal, Schreiber, & Krieg (1999) found that individuals diagnosed with depression have higher pain thresholds to experimental pain induced by heat and pressure when compared to healthy controls, but that these same depressed individuals were reporting more pain sensitivity and unpleasantness in their daily lives. In contrast, Zelman et al. (1991) found that when a depressed mood was induced immediately prior to exposure to a cold pressor task, pain tolerance was decreased while pain reports of those in an induced depressed mood remained no different from those in a neutral mood. However, neither of these studies utilized depressed patients who also were diagnosed with a chronic pain disorder and it is unlikely that the induced depressed mood in the Zelman et al. (1991) study is analogous to clinical depression. Additionally, the experimental method in each of these studies only allowed for the examination of immediate reactions to acute pain.

Many of the studies to date examining the relationship between psychopathology and headaches have serious drawbacks. First, they often do not report diagnostic criteria used to determine either the presence of a headache disorder or the presence of a psychiatric disorder. In many cases, the presence of a psychiatric disorder is determined either by self-report alone or by predetermined cutoff scores on self-report measures used to place participants into the appropriate experimental groups. More recently, studies have begun using diagnostic interviews to determine the presence of pathology and/or headache diagnosis however the criteria by which diagnosis is made is not always clear. Finally, research conducted at subspecialty centers that finds psychiatric disorders to be

highly comorbid in those diagnosed with tension-type headaches may be a function of the kinds of patients seen at these centers. These patients may have been referred because of their headaches and are unlikely to be representative of tension-type headache sufferers seen in primary care or in the general population.

Psychological Factors and Fibromyalgia

Many patients with fibromyalgia report that their symptoms started following physical or emotional stress (Clauw & Chrousos, 1997; Turk, Okifuji, Starz, & Sinclair, 1996; Woolf et al., 1990). There is little doubt that living with fibromyalgia and related symptoms serves as an ongoing stressor, in particular because fibromyalgia may adversely affect quality of life (Burckhardt, Clark, & Bennett, 1993). Patients who suffer from fibromyalgia may demonstrate reduced functional capacity that affects both their work and leisure activities and physical capacity in these patients tends to be low. Thus, these patients are less able to engage in pleasurable, stress-reducing activities and more often encounter daily activities that are likely to increase their levels of stress. Furthermore, many patients with fibromyalgia identify that stress is an aggravating factor for their condition. For example, as part of a treatment outcome study 97 patients were asked to specify what factors were associated with exacerbation and improvement of their symptoms (Kurtze, Gundersen, & Svebak, 1999). The majority (65%) of the patients perceived stress as an aggravating factor of fibromyalgia. On the other hand, stress-reducing strategies, such as taking a warm bath and relaxing were considered as ameliorating factors.

Patients diagnosed with fibromyalgia are likely to present with diverse psychological factors associated with characteristics of pain patterns and fatigue that are

not all consistent with the diagnostic criteria of fibromyalgia. Thus, fibromyalgia can be difficult to diagnose when confounding factors such as psychosocial abnormalities are prominent and some research suggests that levels of anxiety and depression are additively associated with pain and fatigue (Wolfe, 1994). Patients with fibromyalgia report a greater level of emotional distress than do individuals who are healthy when comparing self-report scores of mood disturbance (Krag, Norregaard, Larsen, & Danneskiold-Samsoe, 1994; Uveges, Parker, Smarr, et al., 1990). These reports indicating a high degree of emotional distress in fibromyalgia may reflect the difficulties of these patients to adapt to their condition. From a clinical perspective, these additive effects to the severity of the disease are important in part because these are treatable conditions and also in part because they can have deleterious effects on the patient's ability to cope with the symptoms of fibromyalgia. For example, Kurtze et al. (1999) found that quality of life was relatively high in patients who scored low on self-report measures of anxiety and depression. Additionally, psychological distress in fibromyalgia may in part determine who becomes a patient. Clark et al. (1985) found no differences in tests of state and trait anxiety and depression in participants attending a general medical clinic who did not have fibromyalgia and participants meeting criteria for fibromyalgia who were not seeking treatment for their pain and a more recent study supported these findings (Aaron, Bradley, Alarcon, Alexander, Triana-Alexander, Martin, & Alberts, 1996).

Depression has been found to be more common in fibromyalgia patients than healthy controls (Katz & Krazits, 1996). Concurrent depression is diagnosed in 14–71% of patients with fibromyalgia, far exceeds the prevalence of depression in the healthy community populations, and appears to exceed prevalence rates in other chronic pain

disorders (Ahles, Khan, Yunus, Spiegel, & Masi, 1991; Alfici, Sigal, & Landau, 1989;

Walker, Keegan, Gardner, Sullivan, Katon, & Bernstein, 1997). However, the evidence

suggesting whether individuals diagnosed with fibromyalgia experience significantly

higher rates of depression and anxiety than other disorders or that symptoms of

anxiety/depression are beyond that which can be accounted for by experienced pain is

mixed. Some research suggests there is little evidence for an additive effect of depression

and anxiety upon pain in fibromyalgia (Kurtze et al., 1999). In at least four studies

depression was found more common in fibromyalgia than rheumatoid arthritis (Hudson,

Hudson, Pliner, Goldenberg, & Pope, 1985; Uveges et al., 1990; Hawley & Wolfe, 1993;

Alfici et al., 1989), but in another three studies no difference was found between these

two populations (Kirmayer et al., 1988, Dailey et al., 1990, Ahles et al, 1991). In a study

comparing female patients with fibromyalgia to those diagnosed with myofascial pain,

there were no significant differences on self-report measures of psychological functioning

(Roth, Horowitz, & Bachman, 1998). Importantly, there is some evidence to suggest that

fibromyalgia is not common in patients with major depression, even those depressed

individuals who complained of pain did not have multiple tender points (Fassbender,

Samborsky, Kellner, Muller, & Lautenbacher, 1997).

An additional study (Krag et al., 1994) evaluated the presence of psychopathology

in 49 fibromyalgia patients compared with control groups of 27 patients with rheumatoid

arthritis and 9 patients with lumbar herniation. Participants were interviewed and

completed several self-report measures of depression, anxiety, and general stress. Pain at

the time of interview was scored on a visual analogue scale. Participants with

fibromyalgia scored significantly higher than controls on scales of melancholia, atypical

depression, and anxiety. Additionally, participants with fibromyalgia also scored significantly higher on measures of pain than did controls. Wolfe (1997) examined the relationship between pain thresholds and symptoms of distress as reflected in self-report measures of anxiety, depression, and function disability. Number of tender points was linearly related to fibromyalgia variables and distress. Thus, it appears that tender point counts for some fibromyalgia patients may be related to both the experience of widespread pain and psychosocial distress.

Psychological Factors and TMD

While early studies emphasized the contribution of psychological factors to TMD, more recent research suggests that the comorbidity of psychopathology and TMD may be less than originally believed. Currently, how and if psychosocial factors are related to TMD is of great debate, perhaps to an extent greater than in the literature on tension-type headache and fibromyalgia (Dworkin & LeResche, 1995). Marbach & Lund (1981) found no significant difference in depression and anhedonia between TMD patients and a normal, non-patient group. However, other psychological studies have shown that patients with TMD have greater levels of anxiety, depression, and other emotional disorders than controls (Speculand, Goss, Hughes, Spence, & Pilowsky, 1983). Research using the MMPI and MMPI-2 suggests that clinical psychopathology is present in an appreciable number of patients with TMD who present for medical treatments (Deardorff, Chino, & Scott, 1995) with most common elevations on Hypochondriasis, Depression, and Hysteria scales. Research with the Symptom Checklist-90 suggests that in comparisons of TMD patients to psychiatric populations, patients with TMD could be distinguished by reports of psychological distress limited to somatic as opposed to

emotional or cognitive symptoms of anxiety and depression (Wilson, Dworkin, Whitney, & LeResche, 1994). Additionally, this research has found appreciable psychological distress occurs in samples of patients at TMD clinics and there is a poor relationship between physical signs of jaw impairment and extent of psychological distress in patients with TMD. In a population-based survey of a random sample of 4,000 adults, high levels of psychological distress were strongly associated with increased likelihood of reporting both oralfacial pain and widespread pain with those with the highest levels of distress more than twice as likely to report each pain syndrome (Turner, Chino, & Scott, 2000).

Summary: Psychological Factors

The studies reviewed in the above section clearly suggest that there is much correlational data to support a link between chronic pain disorders and psychopathology, in particular depression and anxiety. The previous section on sensitization in chronic pain disorders demonstrated that there is also a significant correlation between the diagnosis of a chronic pain disorder and increased muscle tenderness to manual palpation, believed to be indicative of the dysregulation of pain modulation systems hypothesized to occur in these disorders. While there is a documented link between chronic pain and psychopathology as well as between chronic pain and increased muscle tenderness, no one has previously examined whether there could possibly be a link between psychopathology and muscle tenderness. Only one previous study has begun to address this question by comparing muscle tenderness and headache frequency among healthy controls, individuals diagnosed with tension-type headache but not depression, and individuals diagnosed with both tension-type headache and depression (Janke & Holroyd, 2002). In this study, participants in all three groups underwent an hour-long laboratory

stressor and muscle tenderness and headache frequency was measured both before and after exposure to this stressor. Participants diagnosed with both depression and tension-type headache demonstrated significantly more headache activity for the 24 hours post-task than did either the healthy control group or the group diagnosed with tension-type headache but not depression. More interestingly, participants who were both depressed and headache-prone demonstrated significantly more pericranial muscle tenderness than the group who was headache-prone but not depressed both before and after the laboratory stressor. Additionally, these depressed and headache-prone participants also demonstrated significantly reduced pressure pain thresholds at both cephalic and extra-cephalic locations both before and after the laboratory stressor. Thus, it seems that depression increased the participant's vulnerability not only to developing a headache post-stressor but also to demonstrating significantly higher levels of pericranial muscle tenderness and lower pressure pain thresholds than the group that was headache-prone but not depressed. While this study suggests a link between psychological variables such as depression and muscle tenderness as measured by palpation, there are currently no other studies to support or clarify this finding. This research suggests that depression is associated with the same tenderness found in chronic pain. Other research has found that some individuals demonstrate muscle tenderness in the absence of a chronic pain disorder. Additionally, some studies suggest that certain individuals diagnosed with a chronic pain disorder exhibit no or little tenderness. Psychological variables could help to explain this variability in tenderness. The presence of depression or other psychological variables could explain why allodynia occurs in the absence of a chronic pain disorder. Psychological variables could also explain why some individuals diagnosed with chronic

pain disorders do not exhibit allodynia. While there is evidence supporting a correlation between psychopathology and chronic pain disorders and a correlation between chronic pain disorders and central sensitization as measured by muscle tenderness to manual palpation, no researcher to date has examined how psychopathology could be (or even if it is) related to muscle tenderness believed to index central sensitization.

Limitations of Previous Research

While research aimed at understanding the process of sensitization as it occurs in chronic pain disorders has made strides in clarifying the role of central and peripheral processes in the development and maintenance of a chronic pain disorder, much work still needs to be done. Until now, research in this area has typically followed a predictable experimental paradigm in which participants are grouped on the basis of their report of having a chronic pain disorder and this chronic pain group is then compared against a group of healthy control participants. While this experimental design has allowed researchers to effectively demonstrate important differences between healthy individuals and those diagnosed with a chronic pain disorder, it also has certain inherent limitations.

First, because of the manner in which experimental designs typically focus on one chronic pain condition and comparing a group of individuals diagnosed with this condition to a group of healthy controls, there is little overlap work done with different pain disorders. As previously discussed, it is believed that similar pain processing mechanisms are at work in several different chronic pain conditions. However, the extent of the similarities, the degree to which sensitization among these conditions might be different, and the possible reasons to explain these differences are not well examined. Thus, while it is generally agreed that deregulation of central pain mechanisms is

implicated in many chronic pain disorders, how and why this deregulation is different across these disorders (or rather, the same) is not well understood as current experimental paradigms do not allow for easy comparisons across disorders.

Secondly, the method of examining a chronic pain group versus a healthy control group has led to the fact that very little is known about the presence of sensitization in the general population. One previous study has examined cephalic muscle tenderness and pressure pain thresholds in the general population (Jensen et al., 1991) and a follow-up to this study examined the relationship between headache diagnosis, tenderness, and pain thresholds in this population (Jensen et al., 1992), but these researchers did not examine what other variables beyond headache could be associated with tenderness and altered pain thresholds. While our knowledge has grown of how sensitization in groups of individuals diagnosed with certain chronic pain disorders differs from healthy participants, we have little knowledge of what sensitization may look like in the general population and no knowledge of what variables beyond the presence of a chronic pain disorder could be associated with this sensitization. Sensitization has nearly always been examined in the presence of a chronic pain disorder and how these scores on measures of sensitization differ from a healthy individual. As previously discussed, experimenters have frequently found significant differences between healthy controls and experimental groups on these measures. As a result, researchers have assumed that signs of sensitization are directly related to the chronic pain disorder they are examining. While the hypothesis linking signs of sensitization to the presence of a chronic pain disorder is likely correct, it is also possible that sensitization is also linked to other factors that have simply not yet been examined (such as the psychosocial measures included in the current

research). This possibility has not been well considered in part because experimental designs have not allowed this question to be easily pursued. The experimental designs used to examine sensitization are constructed such that the hypothesis linking sensitization to chronic pain disorders is a natural conclusion given a finding of significant differences between groups because these two groups (chronic pain vs. healthy control) are the only ones being examined and often the variables measuring signs of sensitization and intensity of pain symptoms are the only ones being statistically examined. However, several experiments discussed in previous sections found that while reports of pain and signs of sensitization are frequently correlated, there appear to be other factors that may account for signs of sensitization (or protection from sensitization) in certain individuals. For example, Okifuji et al., (1997) found the there was a wide variety in both the number of tender points and the severity of pain ratings at these points reported by patients with fibromyalgia and they suggest (but do not examine) that measures of general distress and psychopathology may play some role in this disparity. In their examination of tenderness and pain thresholds in tension-type headache patients, Langemark et al. (1989) found that some patients demonstrated little tenderness while other healthy control participants demonstrated severe tenderness, but could not explain this finding. Thus, it seems likely that other factors beyond chronic pain disorders could play a role in the process of sensitization, but little is known about the prevalence of sensitization in the general population and whether it is always associated with a pain disorder or other findings.

Finally, there are several methodological problems in the research conducted on sensitization. Diagnostic criteria are not always clearly used and often self-report

measures are used as proxies for an actual diagnostic interview. Thus, it is difficult to

know in some studies what criteria have been used to determine either the presence of a

chronic pain disorder or the presence of a comorbid psychiatric disorder. Second,

research examining signs of sensitization in chronic pain patients often recruits

participants from subspecialty clinics or hospital populations. It is unclear whether these

patients are representative of the larger population of pain sufferers, though it seems

likely that these participants may present as more severe than those seen in primary care

and those who do not seek treatment at all. Third, research in this area has also found

difficulties in standardizing the assessments used to assess sensitization. Pain thresholds

and tolerances are the most frequently used signs of sensitization in the experimental

literature, however the means by which these are assessed have only recently been

standardized. However, even with recent advances in technology, pain threshold and

tolerance methodology are problematic as both these are single measures usually

confounded with time or increasing intensity. A participant could be easily biased to

respond sooner or later or to a lower or higher intensity. Pain thresholds imply a

judgment about the quality of a sensation that is always present and such a judgment may

be made on the basis of irrelevant stimulus features. Tolerance measures share this same

problem but additionally tolerance of a painful stimulus has been shown to be related to a

separate endurance factor that is not associated with sensory intensity (Wall & Melzack,

1999). Thus, multidimensional assessment of the pain sensation is recommended to help

control for some of these biases.

Hypotheses

This study is somewhat exploratory in nature. As no previous studies have

examined the possible psychosocial correlates of muscle tenderness to manual palpation,

this study is designed to be a starting point from which future studies and hypothesis can

be generated. The current study was designed in two-parts to better address some of the

limitations found in previous research. The first part of the study collected data on

pericranial muscle tenderness, pressure pain thresholds, and psychosocial variables in the

population of undergraduate females. The second part of the study recruited individuals

who are "high-sensitive" or "low-sensitive" on the measure of pericranial muscle

tenderness used during the first phase and assessed these individuals on other

psychophysiological variables. In particular, the present study hoped to address the

question of what other factors, besides the presence of chronic pain, could account for the

sensitization found in and most often associated with chronic pain by examining the

correlates of pericranial muscle tenderness.

In the first part of the present research, females were recruited from the

undergraduate population to undergo a standardized assessment of pericranial muscle

tenderness that served as the single independent variable for this study. The assessment of

pericranial muscle tenderness is one widely used in the research on tension-type headache

and individuals diagnosed with tension-type headaches have been found to demonstrate

increased sensitivity on this measure when compared to healthy controls. These results

have been used to argue for the presence of central sensitization in headache patients. The

additional measures used during the first and second parts of the study will be examined

as multiple correlates of pericranial muscle tenderness. The following bulleted points

outline the four correlates of pericranial muscle tenderness that were proposed to be assessed in this study:

    • Psychiatric symptoms & disorders. Previous research has established a relationship between psychiatric symptoms and chronic pain disorders (e.g., pp. 65-69, 71-75). While there is limited data to suggest that these variables could be related to increased pericranial muscle tenderness (because the question has rarely been examined), psychiatric symptoms have been shown to be highly correlated with chronic pain thus suggesting these as a good 'starting point' from which to conduct an exploratory analysis. Additionally, pilot data collected to aid in designing this proposed research also suggests measures of depression and anxiety are related to measures of pericranial muscle tenderness, indicating these as variables worthy of further study as correlates of pericranial muscle tenderness.

    To measure the presence of psychiatric symptoms and disorders, during the first session participants underwent a standardized clinical interview designed to assess the presence of anxiety and/or depression. At that time, participants also completed self-report questionnaires designed to measure the presence of symptoms of anxiety and depression.

    • Pain complaints. Previous research has established a relationship between chronic pain complaints—in particular a diagnosis of tension-type headache—and pericranial muscle tenderness (e.g., pp. 36-44, 53-63). Thus, headache diagnosis and presence of widespread pain were assessed as correlates of pericranial muscle tenderness. During the first session, participants completed self-report questionnaires designed to assess the presence of a headache disorder and also the presence of widespread general

pain. Those who participated in the second session were interviewed to confirm and clarify their answers to these questionnaires.

• Psychosocial variables. Various psychosocial variables have been found to be correlated with chronic pain disorders. In particular, stress and coping have been implicated as possible factors in the development and maintenance of these disorders (e.g., pp. 65-69, 71-75). Thus, during the first session, participants completed self-report questionnaires designed to measure subjective and objective stress and pain coping style as possible correlates of pericranial muscle tenderness.

•Physiological variables. Previous research indicates that those diagnosed with a chronic pain disorder demonstrate both increased muscle tenderness and decreased pain thresholds (e.g., pp. 36-44, 53-63). Thus, during the second experimental session participants underwent several different examinations to assess both muscle tenderness and pain thresholds as correlates of pericranial muscle tenderness. First, participants repeated the assessments of pericranial muscle tenderness and pressure pain thresholds (assessed at both the temporalis and the finger) taken during the first session. Participants then underwent a standardized tender point assessment such as that commonly used in the research on fibromyalgia. Finally, participants completed a five-minute ischemic arm task designed to assess pain thresholds and tolerances during a stressor that is more analogous to the experience of chronic pain.

Generally, it was expected that individuals who demonstrate high levels of pericranial muscle tenderness may also demonstrate a greater prevalence of psychiatric symptoms and diagnoses, more pain complaints, more stress, and lowered pain thresholds and increased tenderness as measured by the physiological variables used in this study.

Those who demonstrate low levels of pericranial muscle tenderness were expected to present with fewer psychiatric symptoms and diagnoses, fewer pain complaints, less stress, and higher pain thresholds and less tenderness than those with higher levels of pericranial muscle tenderness. The following bulleted points outline the expected relationship, given the limited available data, between pericranial muscle tenderness and each of the four correlates of this tenderness measured in the presented research:

• Psychiatric symptoms & disorders. Due to the high correlation of psychiatric symptoms with diagnoses of chronic pain disorders (e.g., pp. 65-69, 71-75), it was expected that psychiatric symptoms could be associated with measures of muscle tenderness used to index central pain modulation. Thus, it was hypothesized that those who demonstrate higher levels of pericranial muscle tenderness could present with more psychiatric symptoms than those with lower levels of pericranial muscle tenderness.

• Pain complaints. It was expected that those who demonstrate higher levels of pericranial muscle tenderness will demonstrate higher levels of headache frequency compared to those who have lower levels of pericranial muscle tenderness. Previous research has found that one of the most consistent findings in individuals with tension-type headache is increased sensitivity of the pericranial muscles (e.g., pp. 36-44). Thus, it was hypothesized that participants who report higher levels of symptoms associated with tension-type headaches would also demonstrate increased pain sensitivity as measured by pericranial muscle tenderness. Additionally, given the frequent finding of widespread pain among chronic pain disorders (e.g., pp. 53-63), it was also expected that those who demonstrate higher levels of pericranial muscle tenderness will also demonstrate a greater

likelihood of having more widespread pain complaints than those with lower levels of pericranial muscle tenderness.

• Psychosocial variables. Stress appears to play an important role in chronic pain disorders (e.g., pp. 65-69, 71-75). Thus, it was hypothesized that individuals who demonstrate higher levels of pericranial muscle tenderness will also demonstrate higher levels of stress than those with lower levels of pericranial muscle tenderness.

• Physiological variables. Individuals diagnosed with chronic pain disorders are frequently found to exhibit increased muscle tenderness and decreased pain thresholds and tolerances when compared to healthy controls (e.g., pp. 53-63). Thus, it was hypothesized that those who demonstrate greater tenderness on the pericranial muscle assessment will also demonstrate lower pressure pain thresholds at both cephalic and extra-cephalic locations, greater tenderness as measured by the standardized tender point survey, and lower pain thresholds and tolerances on an ischemic arm task than those with lower pericranial muscle tenderness.

Method

Participants

Participants were recruited in a manner commonly used to recruit participants for psychology experiments at Ohio University. For the first session of this two-session study, participants were recruited from Ohio University's Psychology 101 classes using either advertisements/posters hung in the designated area for such recruitment or an online recruitment and tracking website run by the Psychology Department. Recruitment advertisements briefly described the study ("This study involves filling out several forms, a brief interview, and a short muscle assessment of the head, neck, and shoulders. You

will receive 1 credit for your participation.") and participants could schedule their participation time and date for the initial session by either signing the appropriate location on the recruitment flyer or using their unique login on the online system. Participants who completed the first session of this experiment earned one experimental credit; those who participated in the second session earned two credits.

It was expected that participants would be between the ages of 18 and 25 due to the nature of the undergraduate population being examined. It was also expected that the majority of participants would be white/non-Hispanic for this same reason. However, no participants were excluded based on age or ethnicity, and recruitment materials made every attempt to recruit from a wide range of ages and ethnicities.

Research examining gender differences in lab-based experimental designs using pressure pain thresholds as an outcome measure have found that females consistently report lower pressure pain thresholds than males across a number of sites (Chesterton et al., 2003). Previous research has found females demonstrate significantly greater pain sensitivity compared to males in their perception of noxious stimuli across a variety of experimental designs (Fillingim & Maixner, 1995; Riley et al., 1998). Thus, to control for these effects, only female participants were recruited. Additionally, any participant who reported she had experienced an acute injury of a severity great enough to require medical attention during the past six months was excluded due to the possible effects such an injury could have on the physiological measures used in this study.

A Priori power analyses suggested that the minimum total number of participants needed given the proposed analyses was approximately 200, however a total of 302 participants were recruited in an attempt to fill the two smaller experimental groups.

During the first session, participants completed several pen and paper forms designed to assess both psychosocial and pain status; a brief structured diagnostic interview (Prime-MD); and were assessed for pericranial muscle tenderness and pressure pain thresholds. Participants who demonstrated either high or low levels of pericranial muscle tenderness at this first session were asked to return for a second assessment session. Cutoffs for determining placement in high or low group were based upon pilot data described in following sections (pp. 102-104). Low pericranial muscle tenderness was defined as having a total score of zero across the ten pericranial muscles measured. High pericranial muscle tenderness was defined as a score equal to or greater than three at three or more individual pericranial muscle sites and having a total tenderness score summed across all 10 pericranial muscles of 15 or higher. Pilot data (see following sections) suggested that these cutoffs are appropriate to accurately capture individuals who demonstrate low/high pericranial muscle tenderness.

Procedure

The experiment was conducted in two sessions during a period of approximately one to two weeks. The schedule of sessions is shown in Table 1. During the first session, participants were provided an overview of the study, a brief structured diagnostic interview, psychosocial questionnaires, symptom questionnaires, and the initial physiological assessments. At that time, informed consent was also obtained.

After participants were thoroughly briefed about the study and consent was obtained, they began completing the psychosocial and symptom questionnaires. These questionnaires consisted of the following and were presented to the participants in this exact order: the symptom questionnaire from the Prime-MD; the McGill Pain

Questionnaire—Short Form (including the spatial distribution of pain); a Symptom

Questionnaire assessing the presence of headache symptoms and personal and family

history of both psychiatric and chronic health conditions; the Beck Depression Inventory;

the Beck Anxiety Inventory; the Coping Strategies Questionnaire; the Pain

Catastrophizing Questionnaire; and the Undergraduate Stress Questionnaire.

Upon completing these questionnaires, participants were led into a separate,

private room where the physiological assessments and the structured diagnostic interview

were completed. A graduate student, trained in assessing pericranial muscle tenderness

and pressure pain thresholds, completed both these physiological assessments with the

participant. After completing these physiological assessments, the same graduate

Table 1
Outline of experimental sessions

Session One (approximately one hour)	Session Two (approximately one hour)

1. Informed Consent
2. Psychosocial & Pain Questionnaires:
   a. Prime-MD Symptoms Checklist
   b. McGill Pain Questionnaire-SF
   c. Headache & Symptom Questionnaire
   d. Beck Depression Inventory
   e. Beck Anxiety Inventory
   f. Pain Catastrophizing Scale
   g. Coping Strategies Questionnaire
   h. Undergraduate Stress Questionnaire
3. Pericranial Muscle Tenderness & Pressure Pain Thresholds
4. Prime-MD diagnostic interview
5. Debriefing and schedule for session 2 if subject meets criteria
6. Award one experimental credit
	1. Informed Consent
	2. Pericranial Muscle Tenderness & Pressure Pain Thresholds repeated
	3. Manual Tender Point Survey
	4. Ischemic Arm Task
	5. Retrospective questionnaires on ischemic arm pain including:
	   a. McGill Pain Questionnaire-SF
	   b. Pain Catastrophizing Survey
	   c. Coping Strategies Questionnaire
	6. Debriefing: award two experimental credits for participation

student—also trained in the use of the Prime-MD and in the diagnosis of psychological disorders according to DSM-IV criteria—completed the structured diagnostic interview (Prime-MD).

Following completion of these assessments, participants who qualified as having low or high scores on pericranial muscle tenderness (low = a total score of zero across the ten pericranial muscles measured; high = a score equal to or greater than three at three or more individual pericranial muscle sites and having a total tenderness score summed across all 10 pericranial muscles of 15 or higher) were asked to schedule a second experimental session. This experimental session was scheduled for a time not longer than one week following the first session. Upon completion of the first session, participants were debriefed, provided with referral for treatment (if appropriate/requested), and awarded one experimental credit for their participation. During the second session after obtaining informed consent, a graduate student trained in conducting the physiological measures used in this phase of the study assessed the participants on these measures. First, pericranial muscle tenderness and pressure pain thresholds as assessed during the first session were repeated. Second, the participant was asked to change into an examination gown and was assessed using the manual tender point survey. Finally, participants underwent a brief forearm ischemia task during which they provided numerical ratings of their pain at scheduled intervals until they reached their pain tolerance or five minutes, whichever came first. After the ischemic arm task, participants were asked to complete a retrospective McGill Pain Questionnaire-Short Form, the Pain Catastrophizing Survey, and a Coping Strategies Questionnaire specifically about the "arm pain experienced while the cuff was inflated on your upper arm." Upon completion

of the task, participants were debriefed, referred for treatment (where appropriate and/or requested), and given two experimental credits.

Psychological Measures

Primary Care Evaluation of Mental Disorders

The Primary Care Evaluation of Mental Disorders (Prime-MD, Spitzer, Williams, Kroenke, Linzer, deGruy, Hahn, Brody, & Johnson, 1994) is a structured interview originally designed for rapidly diagnosing mental disorders in primary care settings. The Prime-MD utilizes a patient checklist where the respondent is asked about the presence of various key symptoms followed by a clinician administered structured interview that yields a subset of diagnoses. Diagnoses assessed include mood, anxiety, alcohol, and eating disorders. A list of these diagnoses appears in Appendix A. Research supports the use of the Prime-MD as an effective tool for diagnosing mental disorders suggesting an overall accuracy rate of 88% between Prime-MD diagnoses and those of independent mental health professionals (kappa = .71) (Spitzer et al., 1994).

McGill Pain Questionnaire—Short Form

The McGill Pain Questionnaire—Short Form (MPQ-SF; Melzack, 1987) was developed for use in time-limited research settings. It consists of 15 representative words from the Sensory and Affective categories of the standard MPQ. It includes a Present Pain Intensity (PPI) index and a visual analogue scale to provide indices of overall pain intensity. Additionally, the MPQ-SF as used in the present study also includes a human figure upon which participants may indicate the presence of external or internal pain at various locations across the body. The 15 descriptors used in the MPQ-SF were selected on the basis of their frequency of endorsement by patients with a variety of acute,

intermittent, and chronic pains. Each descriptor is ranked by the participants on a four-point intensity of 0 (none) to 3 (severe) and participants were asked to rate the extent to which each word describes their physical feelings or sensations at the time they completed the questionnaire by marking the appropriate value. A total score was then computed by summing these rankings. Additionally, information provided on the human figure drawing was used to confirm the presence of the participant's self-reported experience of pain complaints. The MPQ-SF correlates very highly with the major Pain Rating Indices of the MPQ (Dudgeon, Ranbertas, & Rosenthal, 1993; Melzack, 1987). Concurrent validity of the MPQ-SF with the MPQ has been found to be high (Dudgeon et al., 1993). A copy of the MPQ-SF is included in Appendix A.

Symptom Questionnaire

This symptom questionnaire is a modified version of the Structured Diagnostic Interview for Headache, Brief Version (Penzien, Rains, & Holroyd, 1990). This instrument is based on the diagnostic criteria established by the Headache Classification Committee of the International Headache Society (IHS; 1988) and includes questions regarding pain quality, headache location, chronicity, frequency, duration, intensity, associated symptoms, medication usage, and information regarding their menstrual cycle. It also has been expanded to include questions about the participant's history of chronic and acute physical complaints and psychiatric history in addition to the participant's family history among first-degree relatives regarding the presence of headaches, psychiatric complaints, and chronic physical complaints. The data collected in this questionnaire was used to determine headache frequency (number of headaches/month), headache diagnosis (according to IHS criteria), family medical and psychiatric history,

and presence of any general pain complaints for analyses described further in subsequent sections. Participants who return for a second session were interviewed by a graduate student to confirm their answers to this questionnaire (originally completed by them at session 1), and the interview questions are nearly identical to this printed questionnaire. However, since the instrument has been altered there are no psychometrics available for this measure in the form used for the present study. A copy of this symptom questionnaire is presented in Appendix A.

Beck Depression Inventory

The Beck Depression Inventory (BDI) is a 21-item, clinically derived, self-report instrument used to measure symptoms believed to be associated with depression. The items on the BDI focus on the cognitive, affective, behavioral, and somatic symptoms of depression and participants choose one of a set of four possible responses (scored 0-3) that indicate the severity with which the individual is currently experiencing a particular symptom. Scores from each individual item are summed to yield a total score. Research supports the construct validity of the scale in psychiatric populations with a split-half reliability estimate of $r = .86$ and point biserial correlations of .67 and .65 between BDI scores and clinical ratings made by four psychiatrists (Beck, Ward, Mendelson, Mock, & Erlbaugh, 1961). It is important to note that chronic pain patients typically report higher levels of depression than the general population and that scores on the BDI for individuals with chronic tension headaches may be inflated due to higher scores on the somatic questions on the BDI (Holm, Penzien, Holroyd, & Brown, 1994). An updated version of the BDI, the BDI-II (Beck, Steer, & Brown, 1996), was utilized in the present research and a copy of the BDI is included in Appendix A.

Beck Anxiety Inventory

The primary aim of the Beck Anxiety Inventory (BAI) was to provide a simple measure that could discriminate anxiety from depression (Beck, Epstein, Brown, & Steer, 1988; Beck and Steer, 1990). It is a 21-item Likert scale, self-report questionnaire that measures common symptoms of clinical anxiety. Each symptom is rated on a four-point scale ranging from 1 (not at all) to 4 (severely) by which participants indicate the degree to which they are bothered a symptom and these ratings were summed to create a total score. Thirteen items assess physiological symptoms, five cognitive aspects, and three both somatic and cognitive symptoms. The BAI is internally consistent with psychiatric outpatients (α = .92, Beck et al., 1988). Concurrent validity is high with the SCL-90-R (Derogatis & Cleary, 1977) anxiety subscale (r = .81; Steer, Rissmiller, Ranieri, & Beck, 1993) and moderate with the Hamilton Anxiety Rating Scale in 367 outpatients with anxiety disorders (r = .56; Beck, Epstein, Brown, & Steer, 1990). The BAI is superior to the STAI in discriminant validity (Creamer, Foran, & Bell, 1995). Common cutting scores of 10 suggest mild anxiety, with 19 reflecting moderate anxiety. A copy of the BAI is included in Appendix A.

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS; Sullivan, Bishop, & Pivik, 1995) consists of 13 items that describe different thoughts and feelings individuals may experience when they are in pain. Instructions on the PCS ask participants to reflect on past painful experiences and to indicate the degree to which they experienced each of the 13 thoughts or feelings when experiencing pain on 5-point scales from 0 (not at all) to 4 (all the time). In addition to a total score that is the sum of the participant's rankings, the PCS also

yields three subscale scores assessing rumination, magnification and helplessness. The PCS has been shown to have adequate to excellent internal consistency, coefficient alphas: total PCS = 0.87, rumination = 0.87, magnification = 0.66, and helplessness = 0.78 (Sullivan et al., 1995). A copy of the PCS is included in Appendix A.

Coping Strategies Questionnaire

The Coping Strategies Questionnaire (CSQ; Rossenstiel & Keefe, 1983) assesses six cognitive coping strategies and one behavioral coping strategy for pain. Items for each coping strategy subscale are rated as to the frequency with which they are used on a seven-point scale (from 0 = "never" to 6 = "always") and these ratings can be summed to create a total score. The subscales for cognitive coping strategies include Diverting Attention, Reinterpreting Pain, Coping Self-Statements, Ignoring Pain, Praying or Hoping, and Catastrophizing. The behavioral coping subscale is Increasing Activity. Additionally, there are two self-efficacy items that reflect "perceived control over pain" and "ability to decrease pain." The internal reliability of the CSQ subscales is in the good range (α = .78 to .89; Keefe et al., 1987). The CSQ has also been shown to be internally reliable when used to assess pain coping strategies used among young adults (Keefe et al., 1987). A copy of the CSQ is included in Appendix A.

Undergraduate Stress Questionnaire

The Undergraduate Stress Questionnaire (USQ) is an 83-item, self-report checklist of life events designed to measure stress among undergraduates. The participant is asked to rate various events according to the following scale: (0) Did not happen (1) Happened, not stressful; (2) Slightly stressful; (3) Moderately stressful; (4) Very stressful; and (5) Extremely stressful. The USQ has subscales for both Objective and

Subjective stress. The Objective score is considered the sum of all items that were reported to have happened (any item a participant scores above a 1). The Subjective score is the sum of the ratings of all reported items. The internal reliability of the USQ has been reported to be good, r = .80. Test-retest reliability is only moderate, r=.50. Research suggests the USQ is sensitive to changes in the amount of stress experienced by undergraduates between the middle and end of a term (Crandall, Priesler, & Aussprung, 1992). A copy of the USQ is included in Appendix A.

Psychophysiological Assessment

Pericranial Muscle Tenderness

Pericranial muscle tenderness (PMT) was assessed by manual palpation using the procedure developed by Langemark and Olesen (1987) and described within the introduction, modified to include the use of a fingertip palpometer (Dolorimenter Systems Inc, Victoria, BC). The standardization of manual palpation by use of a palpometer has increased the reliability and utility of manual palpation as a research tool in myofascial pain disorders (Bendtsen et al., 1995). In this procedure five bilateral pairs of pericranial muscles (suboccipital, posterior cervical, middle trapezius, masseter, and temporalis) are palpated using fingertip pressure of 500g/cm as measured by the palpometer. The participant was asked to report their tenderness for each palpation site on a scale of 0 (no pain) to 10 (worst pain imaginable). The sum of the ratings (total tenderness score: TTS) for the 10 sites was used as the PMT score for each assessment giving the TTS a range of 0-100. Previous research has found this total tenderness score to be reliable (Bendtsen et al., 1995). The TTS was also be used to determine which participants are asked to return for a second session. Participants who, during the initial

screening session, demonstrated either high or low TTS were asked to participate in a second session. Low TTS was defined as having a score of zero at all 10 pericranial sites. High TTS was defined as having a score of three at three or more individual pericranial sites and a TTS of 15 or higher. Pilot data described below and other information collected in this laboratory (Janke & Holroyd, 2002) suggests these to be appropriate cutoffs for determining high/low TTS.

Pressure Pain Thresholds

Pressure pain thresholds (PPT) were be measured at two bilateral points—the anterior temporalis and the middle digit—using a hand-held pain threshold meter (Pain Diagnostics and Thermography, Great Neck, NY). This device consists of a spring-loaded dial that registers pressure applied to the 1cm rubber tip of the instrument as it is pressed into the tissue and it is commonly used in muscle pain assessments (Fischer, 1993). The body of the anterior temporalis was located by palpation, and pressure was then applied and increased at a constant rate of about 1.0 kg/s (Langemark, Jensen, Jensen, & Olesen, 1989). Similarly, pressure will be applied and increased to the fat pad of the middle digit. The participant was asked to indicate when the pressure first became painful. Pressure was immediately released when the participant verbally indicates pain. The maximum force applied was then read from the dial with a maximum reading of 25kg. The average of three bilateral readings at both sites taken 5-10 seconds apart was be used as the PPT score.

Manual Tender Point Survey

The Manual Tender Point Survey (MTPS; Okifuji, Turk, Sinclair, Starz, & Marcus, 1997) is a standardized tender point assessment protocol most often used as a

diagnostic procedure to evaluate the tender point criterion for fibromyalgia syndrome (Wolfe et al., 1990). In this procedure a total of 9 bilateral survey points are located for palpation. These points include the following and were examined in this order: Occiput, trapezius, supraspinatus, gluteal, low cervical, second rib, lateral epicondyle, greater trochanter, and the knee. The precise location of each survey site was determined using soft tissue and bony landmarks. The participant and examiner were positioned specifically to permit standard effects of spinal loading, muscle tension, ease of access, and efficiency. Participants were instructed to rate each palpation on an 11-point scale, from 0 (no pain) to 10 (worst pain ever experienced), similar to that used in the pericranial muscle assessment described above. The examiner asked for the participant's response after each palpation. Pressure was applied perpendicularly, gradually increasing by 1 kg force/second over a period of 4 seconds, by use of a dolorimeter. Individual participant's scores at each site were summed to create a total tenderness score for the MTPS. For the current analyses, readings from the two muscle groups that overlap the PMT assessment (occiput & trapezius) were removed to eliminate the possible confound of examining the muscle group twice.

Forearm Tourniquet Ischemia

The Forearm Tourniquet Ischemia task is a modified version of a task used by Maixiner, Fillingim, Booker, & Sigurdsson (1995) and similar to a task used by France & Suchowiecki (2001). This task was used to assess the participant's report of pain intensity, coping, and catastrophizing following a painful stressor. In this task, participant's maximum non-dominant grip strength was first assessed using a hand dynamometer. Participants were then instructed to begin two minutes of non-dominant

forearm muscle exercise in which they repeatedly compressed a hand dynamometer to 50% of their maximum grip at a rate of one compression per second. After two minutes of forearm exercise, participants raised their non-dominant arm for fifteen seconds to allow for exsanguination and a blood pressure cuff was applied over this same bicep proximal to the elbow and inflated to 220mmHg. Participants then rested their arm on their chair. The cuff remained inflated for five minutes unless a participant indicated that they reached their pain tolerance threshold, at which time it was immediately removed. During this forearm ischemia period, participants were asked to rate the intensity of their arm pain using a numerical rating scale where 1 = sensory threshold, 5 = pain threshold, and 10 = maximum tolerable. Using tape-recorded instructions, numerical ratings were requested at 30, 90, 150, 210, 270, and 300 seconds into the forearm ischemia procedure. If a participant reached her tolerance threshold before the five minutes have elapsed, the bicep cuff was deflated and a maximum pain rating value was assigned for the remaining intervals. Upon completion of the forearm ischemia task, participants were asked to complete retrospective ratings of forearm pain using the MPQ-SF, the PCS, and the CSQ for the "arm pain experienced while the cuff was inflated on your upper arm."

<div align="center">Pilot Data</div>

Pilot data was collected to assist in estimation of cutoffs for high and low pericranial muscle tenderness (PMT) groups, and to determine whether further investigation of this variable divided into such groupings was even feasible. Additionally, as no previously published research has established a direct relationship between PMT and the psychosocial variables utilized in this study, the pilot data was utilized to determine whether further investigation of these relationships would be appropriate and

warranted. Finally, piloting the study also allowed the experimenter to gain practice with the multi-step protocol.

Pilot data was generally collected according to the methods described in the previous sections. A total of 37 individuals participated in data collection and had a mean age of 18.81 (.91). Mean scores on total tenderness ratings (TTS) were 9.57 (9.67). Frequencies of TTS ratings were examined to determine appropriate cutoffs for constructing high and low PMT groups. This revealed that eight participants (approximately 20%) had PMT ratings equal to zero while ten participants had PMT ratings equal to 15 or above (approximately 25%).

Both a-priori power analyses (alpha = 0.05) using data collected during this pilot study to estimate effect sizes and conventions for selecting sample sizes (Green, 1991) suggested a minimum 200 participants should be recruited to participate during this first phase of the study. Additionally, a-priori power analyses (alpha = 0.05) and conventions for selecting sample sizes also suggest an N = 70 (35 per group) in order to have appropriate power for proposed analyses involving data collected from participants during the second experimental session.

Combining the information collected regarding the frequencies of TTS in the pilot data set with the power analyses conducted to estimate required sample sizes, it was approximated that zero would be a feasible cutoff for the low PMT group while 15 would be a feasible cutoff for the high PMT group. A cutoff of zero for the low PMT group had the additional advantage of insuring that the low PMT individuals are exhibiting no tenderness and, thus, are truly different that a group of individuals that are reporting tenderness. To insure that the high PMT participants would be representative of

individuals with tenderness in more than one or two isolated muscle groups, an additional requirement was added to stipulate that high PMT participants must have a TTS of 15 and report a tenderness rating greater than three for three or more muscle sites.

Results

Participant Characteristics

Participant's demographic characteristics by group are presented in Table 2. A total of 302 participants completed session one, 100 participants beyond the proposed N of 200. The additional participants were recruited to fulfill the proposed N of 35 for the high PMT group. Despite recruitment of the additional participants, only 24 participants completed session two for the high PMT group. A total of 36 participants completed session two for the low PMT group, one participant greater than the proposed N of 35. Twelve participants who completed session one self-report questionnaires did not complete the session one physiological assessment as they reported headache pain greater than two. Finally, an additional 13 participants qualified for the second session (4 for high PMT, 9 for low PMT), but chose not to participate in session two.

As Table 2 demonstrates, the participants were predominately white/non-Hispanic with a mean age of 19.05 (1.6) and in their freshman year of college. Participant's ages ranged from 17 to 36 and as proposed all participants were female. A demographic pattern such as this is not unexpected given the population of undergraduate females from which this sample was drawn. Statistical analyses revealed that the two smaller

experimental groups (low PMT and high PMT) did not significantly differ in

demographic characteristics of age[1], ethnicity[2], or year[3] in school ($p \geq .50$).

Table 2
Demographic characteristics by group

	Session 1 Participants (N = 302)	Session 2 Participants	
		High PMT (N = 24)	Low PMT (N = 36)
Age	19.05 (1.60)	18.97 (1.03)	19.29 (2.46)
Self-identified ethnicity			
White/non-Hispanic	281	33	20
Black	9	2	2
Asian	6	-	1
Native American	4	-	-
Other	2	1	1
Year in school			
Freshman	225	26	20
Sophomore	53	7	3
Junior	17	2	1
Senior+	7	1	-

[1] Test for age: $t = -.70, p = .50$
[2] Test for ethnicity: $X^2 = 3.6, p = .73$
[3] Test for year in school: $X^2 = 2.27, p = .89$

Psychophysiological Measurements

Pericranial Muscle Tenderness

Figure 5 presents the frequency distribution of total tenderness scores (TTS) of pericranial muscle tenderness (PMT) collected during session one. As the graph demonstrates, the distribution is skewed to the right with nearly one-quarter of the participants exhibiting TTS of zero at session one. By contrast, approximately 10 percent of participants exhibited TTS of 15 or greater. Table B1 in Appendix B presents frequency distributions and relative frequencies of TTS for all participants.

Table 3 presents the means and standard deviations for total tenderness scores (TTS) from the pericranial muscle tenderness (PMT) assessment. The table presents data collected during the first experimental session for the larger group of session one participants as well as data for the two smaller experimental groups.

Participants in the high PMT group had significantly higher TTS scores at session two than the low PMT group. A Mann-Whitney U test was conducted to determine the presence of any significant differences between the low and high groups on TTS ratings collected during this second session. This analysis revealed that high PMT participants had significantly higher TTS scores than the low PMT group ($U = .50, p < .001$) at session two.

To determine whether TTS scores remained stable from session one to session two, a two Group (high PMT & low PMT) by two Time (session one & session two) mixed model ANOVA was conducted. However, diagnostic tests revealed significant violations of test assumptions. Thus, nonparametric tests were used to examine between and within-subject differences on these variables.

Figure 5.
Distribution of total tenderness scores across all participants: Session one.
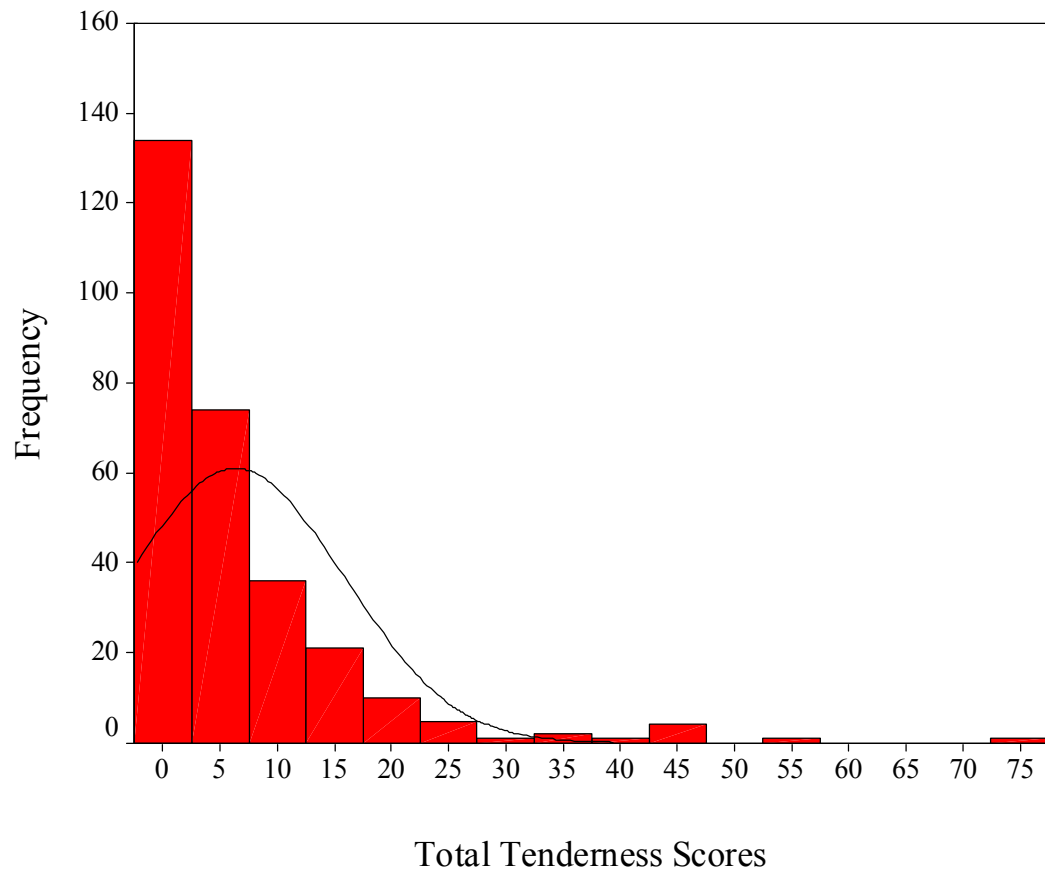
Table 3
Means and standard deviations of TTS for session one and session two by group

	All Participants (N = 290)	High PMT (N = 24)	Low PMT (N = 36)
Total Tenderness Score (0-100)			
Session One	6.41 (9.54)	30.00 (14.67)	0
Session Two	-	27.25 (15.13)**	.08 (.37)

Note. ** Indicates significantly different from low PMT Group, *p* < .001.

To compare TTS at the session one and session two assessments, a Friedman Test (alpha = .01) was conducted to examine whether significant within-subject differences existed for each of the two experimental groups (high PMT & low PMT). For both groups, no significant within-subject differences were found on TTS from session one when compared with TTS scores from session two[1]. Non-parametric correlations were also conducted to examine stability of TTS scores from session one to session two. A significant positive correlation at the $p < .001$ level was found between session one and session two TTS scores across all participants who participated in the second session (Rho = .95), indicating that TTS scores were stable from session one to session two.

Group differences in TTS scores were compared at the session one and session two assessments using a Kurskal-Wallis One Way Analysis of Variance (alpha = .01). Significant between-group differences were found on these measures[2] revealing that the high PMT group had TTS significantly higher than the low PMT group at both experimental sessions.

Dependent Psychophysiological Measures: PPT & MTPS

Table 4 presents the means and standard deviations for finger and temporalis pressure pain thresholds (PPT); total tenderness scores (TTS) for pericranial muscle tenderness (PMT) are also included for ease of reference. The table presents data collected during the first experimental session for the larger group of session one participants as well as data for the two smaller experimental groups.

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[1] High PMT: χ^2 (1, $N = 24$) = 2.13, $p = .14$. Low PMT: : χ^2 (1, $N = 36$) = 2.0, $p = .16$.
[2] Session one: χ^2 (1, $N = 60$) = 54.20, $p < .001$. Session two: χ^2 (1, $N = 60$) = 51.83, $p < .001$.

Table 4

Means and standard deviations of TTS and PPT scores from session one by group

	Session 1 Participants (N = 290)	Session 2 Participants[1]	
		High PMT (N = 24)	Low PMT (N = 36)
Total Tenderness Score (0-100)	6.41 (9.54)	30.00 (14.67)	0
Pressure Pain Thresholds (kg)			
Finger	10.64 (3.80)	8.24 (2.69)**	12.28 (4.45)
Temporalis	5.18 (1.55)	4.42 (1.15)**	6.21 (2.27)

Note. ** Indicates significantly different from low PMT Group, $p < .001$.

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[1] As proposed, session two membership was determined by session one TTS scores. Thus, according to pre-determined cutoffs, the Low PMT group would be expected to have a TTS of zero and the high PMT group would be expected to have a TTS score not less than 15.

A Mann-Whitney U test was conducted to determine the presence of any significant differences between the low and high PMT groups on PPT ratings collected during session one. This analysis revealed that high PMT participants had significantly lower finger PPT ($U = 189, p < .001$) and temporalis PPT ($U = 179, p = .001$) compared to the low PMT group at session one.

To assess the degree of relationship among TTS and PPT at both the finger and temporalis, Spearman's Rho correlation coefficients were calculated among TTS and the mean values of each PPT site from data collected during session one. Table 5 presents the correlation coefficients for the three variables. As the table presents, significant correlations were found to exist among the three variables at the $p < .001$ level. Significant negative correlations were found between TTS and both finger and temporalis PPT. A significant positive correlation was found between finger PPT and temporalis PPT.

Finger pressure pain thresholds (PPT), temporalis pressure pain threshold (PPT), and manual tender point survey (MTPS) total tenderness scores from data collected at session two are presented in Table 6. Again, total tenderness scores (TTS) from session two are also included for ease of reference. Similar to session one data, participants in the high PMT group continued to exhibit lower finger PPT and lower temporalis PPT than the low PMT group at session two. A Mann-Whitney U T-test was conducted to determine the presence of any significant differences between the low and high groups on PPT and MTPS ratings collected during this second session. This analysis revealed that high PMT participants had significantly lower finger PPT ($U = 189, p < .001$) and

Table 5
Spearman's Rho correlation coefficients for TTS and PPT from session one

	Total Tenderness Scores	Pressure Pain Thresholds	
		Finger	Temporalis
Total Tenderness Score	-	-	-
Pressure Pain Thresholds		-	-
Finger	-.27**	-	-
Temporalis	-.29**	.66**	-

Note. ** Indicates significance $p < .001$.

Table 6
Mean and standard deviations of TTS, PPT, and MTPS scores from session two by group

	Session 2 Participants	
	High PMT (N = 24)	Low PMT (N = 36)
Total Tenderness Score (0-100)	27.25 (15.13)**	.08 (.37)
Pressure Pain Thresholds (kg)		
Finger	8.41 (3.74)**	12.59 (4.77)
Temporalis	4.65 (1.27)**	6.25 (2.07)
MTPS Total Tenderness Scores[1] (0-140)	68.92 (20.37)**	9.91 (13.57)

Note. ** Indicates significantly different from low PMT Group, $p \leq .002$

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[1] The MPTS total tenderness score is the sum of participant's report of pain to palpation (0 to 10 scale) taken at 7 bilateral points.

temporalis PPT ($U = 224$, $p = .002$) compared to the low PMT group. High PMT

participants also had significantly higher MTPS scores than the low PMT group ($U = 23$,

$p < .001$).

To determine whether PPT scores remained stable from session one to session

two, a two Group (high PMT & low PMT) by two Time (session one & session two)

mixed model ANOVA was conducted. However, diagnostic tests revealed significant

violations of test assumptions. Thus, nonparametric tests were used to examine between

and within-subject differences on these variables.

To compare finger PPT and temporalis PPT at the session one and session two

assessments, a Friedman Test (alpha = .01) was conducted to examine whether significant

within-subject differences existed for each of the two experimental groups (high PMT &

low PMT). For both groups, no significant within-subject differences were found on

either finger PPT[1] or temporalis PPT[2] from session one when compared with PPT scores

from session two. Non-parametric correlations were also conducted to examine stability

of PPT scores from session one to session two. Significant positive correlations were

found between session one and session two finger PPT and session one and session two

temporalis PPT across all participants who completed the second session ($p < .001$; finger

PPT Rho = .81; temporalis PPT Rho = .70). Significant positive correlations were also

found among these variables when data from high PMT participants were considered

alone ($p < .001$; finger PPT Rho = .72; temporalis PPT Rho = .76) and when data from

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[1] High PMT: χ^2 (1, $N = 24$) = .39, $p = .53$. Low PMT: : χ^2 (1, $N = 36$) = .47, $p = .49$.
[2] High PMT: χ^2 (1, $N = 24$) = .18, $p = .67$. Low PMT: : χ^2 (1, $N = 36$) = 1.0, $p = .32$.

low PMT participants were considered alone ($p < .001$, finger PPT Rho = .81; temporalis PPT Rho = .64).

To examine possible group differences on finger PPT and temporalis PPT, a Kurskal-Wallis One Way Analysis of Variance (alpha = .01) was conducted and found significant between-group differences on all three measures revealing that the high PMT group had lower finger PPT[1] and temporalis PPT[2] than the low PMT group at both experimental sessions.

Psychological Measures

Mean values and standard deviations for the psychological measures collected during session one are presented in Table 7. These included self-report measures of symptoms of depression and anxiety, pain, pain coping, and subjective stress. Values are presented both for all participants assessed during session one as well as the high and low PMT groups. Independent samples T-tests were conducted to examine whether any significant group differences existed on these measures between the low and high PMT groups. Overall, the high PMT group demonstrated significant differences when compared with the low PMT group on nearly every psychological measure taken during session one. When compared to the low PMT group, the high PMT group had significantly higher scores on the BDI, BAI, MPQ-SF, PCS, and USQ at the $p < .001$ level. On subscales of the CSQ, the high PMT group had significantly higher scores on the Praying or Hoping subscale and the Catastrophizing Subscale ($p \leq .005$).

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[1] Session one: χ^2 (1, $N = 60$) = 13.45, $p < .001$. Session two: χ^2 (1, $N = 60$) = 13.45, $p < .001$.
[2] Session one: χ^2 (1, $N = 60$) = 14.58, $p < .001$. Session two: χ^2 (1, $N = 60$) = 9.85, $p = .002$.

Table 7

Means and standard deviations of psychological measures collected during session one by group

| | Session 1 Participants | Session 2 Participants | | |
		High PMT	Low PMT	*t(df)*
Beck Depression Inventory	7.84 (6.77)	12.04 (11.35)**	5.67 (5.58)	$t(58) = -2.89$
Beck Anxiety Inventory	6.79 (6.70)	11.00 (7.76)**	4.14 (4.18)	$t(31.99)^1 = -3.97$
McGill Pain Questionnaire-SF	3.53 (3.86)	7.08 (5.57)**	1.61 (1.78)	$t(43.68)^i = -4.66$
Pain Catastrophizing Scale	10.14 (8.74)	13.71 (8.86)**	7.44 (8.50)	$t(58) = -22.75$
Undergraduate Stress Questionnaire	66.40 (49.94)	71.92 (29.39)**	47.61 (24.88)	$t(58) = -3.45$
Coping Strategies Scale				
Diverting Attention	12.33 (8.16)	15.13 (8.54)	12.81 (8.45)	$t(58) = -1.04$
Reinterpreting Pain	4.72 (5.98)	8.33 (7.56)	4.31 (5.96)	$t(58) = -2.30$
Coping Self-Statements	18.13 (8.23)	22.50 (6.64)	17.64 (7.79)	$t(58) = -2.51$
Ignoring Pain	13.85 (8.73)	16.33 (7.97)	13.33 (9.58)	$t(58) = -1.27$
Praying or Hoping	9.70 (8.19)	14.54 (8.61)*	8.14 (7.68)	$t(58) = -3.01$
Catastrophizing	5.81 (6.02)	10.63 (9.27)*	4.00 (4.32)	$t(29.74)^i = -3.27$
Increased Activity	13.18 (7.39)	16.08 (7.49)	12.53 (6.67)	$t(58) = -1.93$

Note. * Indicates significantly different from low PMT Group, $p \leq .005$. ** Indicates significantly different from low PMT Group, $p < .001$.

[1] Equal variances not assumed.

PrimeMD Diagnosis

Participants were assessed during session one using the PrimeMD, a structured clinical interview designed to evaluate for the presence of common psychological diagnoses according to DSM-IV criteria. Table B2 in the appendix presents the frequency of each PrimeMD diagnosis by experimental group. Data on participant's PrimeMD diagnosis was pooled to create a single dichotomously coded variable (1 = positive PrimeMD diagnosis, 0 = no PrimeMD diagnosis) to examine whether there were any significant group differences in PrimeMD diagnosis by group. A chi-square analysis revealed that individuals in the high PMT group were significantly more likely to have a PrimeMD diagnosis than individuals in the low PMT group (X^2 (2, N = 60) = 20.39, $p <$ .001) with only 8% (3 of 36) of the low PMT participants qualifying for a PrimeMD diagnosis compared to 50% (12 of 24) of those in the high PMT group. In the high PMT group, 41.7% (10 of 24) of participants were diagnosed with a mood disorder and 29.2% (7 of 24) of participants were diagnosed with an anxiety disorder. Additionally, 16.7% (4 of 24) of those in the high PMT group qualified for both an anxiety and a mood diagnosis. By comparison, in the low PMT group only 2.8% (1 of 36) of participants were diagnosed with a mood disorder while 5.6% (2 of 36) of these participants were diagnosed with an anxiety disorder. Only 2.8% (1 of 36) of those in the low PMT group qualified for both an anxiety and mood diagnosis.

Headache Ratings

Participant's self-reported headache characteristics as collected during session one are presented in Table 8. These include headache frequency in months, headache

intensity on a 0 to 10 scale, headache duration in hours, and headache chronicity in months. Information collected during session one on headache symptoms was also analyzed to determine a headache diagnosis for each participant based on International Headache Society classification criteria, and this information is also presented in Appendix B as Table B3. Diagnoses considered for this analysis include migraine headache, infrequent episodic tension-type headache, frequent episodic tension-type headache, and chronic tension-type headache (IHS, 2004). Data is presented for the larger group of individuals who completed session one and the two smaller experimental groups.

An independent samples T-test was conducted to determine if any significant differences existed between the high PMT and low PMT groups on the participant's self-reported headache characteristics. It can be seen from the data presented in Table 8 that the high PMT group reported a history of significantly more intense headaches ($t(58) = -4.07, p < .001$). On average, the high PMT group reported headaches of an intensity at least 1.5 units greater than the low PMT group on a scale of 0 to 10. Of note, the high PMT and low PMT groups did not significantly differ on frequency of headaches per month, nor did they differ on duration of headaches in hours. Also of interest is the fact that, while nearly every subject reported at least an occasional headache , the symptoms reported did not allow for clear classification according to IHS criteria in most cases as accurate diagnosis would have required all subject to be interviewed.

Table 8

Headache characteristics and headache diagnosis by group

	Session 1 Participants (N = 299)	Session 2 Participants	
		High PMT (N = 24)	Low PMT (N = 36)
Headache Characteristics			
Frequency (per month)	5.57 (5.98)	5.47 (4.63)	3.73 (5.50)
Intensity (0 – 10 scale)	4.53 (1.73)	5.39 (1.54)**	3.64 (1.68)
Duration (hours)	4.81 (8.21)	5.67 (7.86)	3.44 (4.81)
Chronicity (months)	41.42 (35.13)	46.74 (35.47)	29.69 (22.99)

Note. ** Indicates significantly different from low PMT Group, $p < .001$

Report of Ongoing Pain

Participants were also asked to report on whether they experienced persistent and/or frequent pain in certain body areas as outlined in the symptoms questionnaire completed during session one. Participant's responses were examined and any participant who reported having pain in at least one body area for a duration of more than 12 months and of an intensity greater than 2 on a 0 to 10 scale was considered to have ongoing pain. This information was pooled to create a dichotomously coded variable to examine whether there were any significant group differences in ongoing pain between the two experimental groups. A chi-square analysis revealed that individuals in the high PMT group were not more likely to report ongoing pain than individuals in the low PMT group. Overall, 19.4% (7 of 36) of the low PMT participants met study criteria for ongoing pain compared to 37.5% (9 of 24) of those in the high PMT group. Of those nine participants in the high PMT group who reported ongoing pain, all but one also met criteria for a PrimeMD disorder. However, 45.8% (11 of 24) of the high PMT participants had neither a PrimeMD disorder or reported ongoing pain.

Family History

During session one, participants were asked to report whether any of their first degree relatives were diagnosed with either a psychiatric disorder or a chronic pain disorder. Table 9 presents number of participants by group reporting a positive family history of either a psychiatric disorder or chronic pain disorder. A chi-square analysis was performed on each of these variables to examine for any significant group differences on these family history variables between the two experimental groups. The analysis

revealed that individuals in the high PMT group were significantly more likely to have a family history of a chronic pain disorder (X^2 (2, N = 60) = 13.21, $p < .001$) than those in the low PMT group. More than half of the individuals in the high PMT group reported a positive family history of chronic pain while only one-fifth of those in the low PMT group had any family history. There were no significant group differences on family history of a psychological disorder with an equal percentage in both groups reporting a positive family history.

Table 9
Family history of chronic pain disorder and psychological condition by group

	Session 1 Participants (N = 302)	Session 2 Participants	
		High PMT (N = 24)	Low PMT (N = 36)
Family History of Chronic Pain	135 (44.7%)	13 (54.2%)**	8 (22.2%)
Family History of Psychological Condition	79 (27.3%)	4 (16.7%)	6 (16.7%)

Note. ** Indicates significantly different from low PMT Group, $p = .001$.

Ischemic Arm Task Ratings

Participant's pain ratings were taken at six intervals during the ischemic arm task. In order to examine within and between subject differences in these pain ratings, a 2 Group (high PMT & low PMT) by 6 Time mixed model ANOVA was conducted. Time served as the within-subjects factor and Group served as the between-subjects factor.

Because diagnostic tests revealed violations of the sphericity assumption (Mauchly's Test $X^2 = 250.91$, $p < .001$), a Geisser-Greenhouse correction was implemented. Table 10 summarizes these results, Figure 5 presents a graph of pain ratings by group over time.

A significant main effect was found for Time ($F\,[1.73, 100.20] = 34.84$, $p < .001$). Follow-up post-tests revealed that ischemic arm task pain ratings progressively and regularly increased through the first five assessment periods such that the second assessment had higher pain rating scores then the first, the third had higher pain rating scores than the second, and so on through the first five assessments ($p < .001$). There was no significant difference between pain ratings taken during the fifth and sixth assessment interval.

There was also a significant main effect for Group ($F\,[1, 58] = 32.96$, $p < .001$). Follow-up post-tests revealed that the high PMT group reported significantly higher pain ratings than the low PMT group at all six assessments ($p < .001$).

Mean values and standard deviations for session two psychological measures—those collected following the ischemic arm task—are presented in Table 11. Data presented includes measures of pain and pain coping collected following the ischemic arm task (PCS, CSQ, and MPQ-SF). Independent samples T-tests were conducted to examine whether any significant group differences existed on these measures between the low PMT and high PMT groups. The high PMT group had significantly higher scores on the post-ischemic arm task MPQ-SF and PCS questionnaires ($p < .001$) with MPQ-SF scores nearly twice that of the low PMT group and PCS scores nearly four times that of the low PMT group. On subscales of the CSQ, the high PMT group had significantly higher scores on the Catastrophizing subscale ($p < .001$).

Table 10
ANOVA of Ischemic Arm Task Pain Ratings

Source	df	F
Between Subjects		
Group (G)	1	32.96**
Error	58	(22.65)
Within Subjects		
Time	1.73	34.84**
Time X Group	1.73	3.89
Error	100.20	(3.30)

Note. Values in parentheses represent mean squared error. Geisser-Greenhouse correction was applied. **$p < .001$

Figure 6.
Pain ratings on ischemia arm task over time by group.

Mean Ischemic Arm Pain Ratings by Group
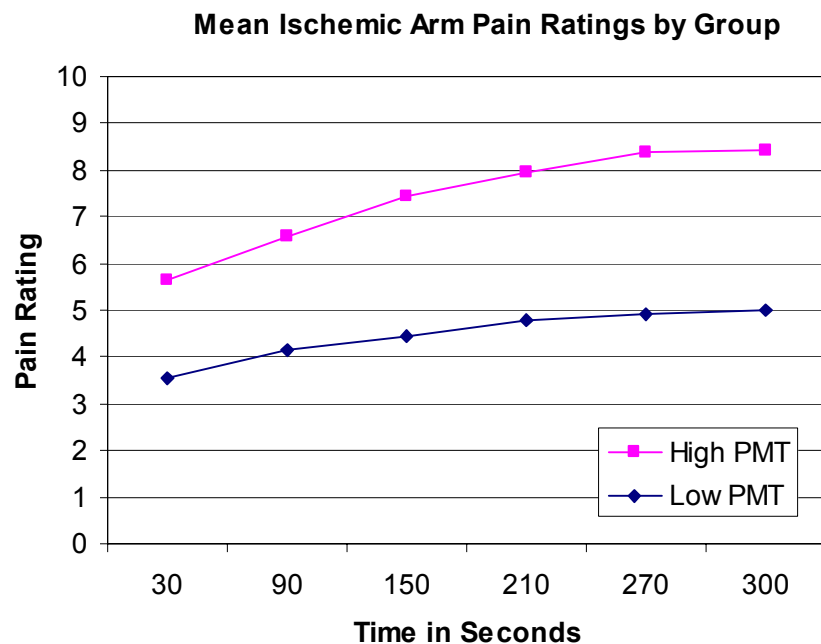
Table 11

Post-ischemic arm task measures by group

	Session 2 Participants		
	High PMT	Low PMT	*t(df)*
McGill Pain Questionnaire—SF	19.35 (7.58)**	10.28 (7.99)	$t(58) = 4.40$
Pain Catastrophizing Scale	24.04 (10.90)**	6.42 (8.16)	$t(39.73)^1 = 6.76$
Coping Strategies Scale			
Diverting Attention	8.92 (6.26)	7.69 (8.13)	$t(58) = .62$
Reinterpreting Pain	11.21 (7.50)	8.47 (7.69)	$t(58) = 1.36$
Coping Self-Statements	21.0 (7.96)	15.69 (8.46)	$t(58) = 2.44$
Ignoring Pain	11.92 (6.42)	13.72 (8.81)	$t(57.48)^i = -.86$
Praying or Hoping	8.96 (8.87)	3.67 (5.18)	$t(33.51)^i = 2.64$
Catastrophizing	12.67 (9.09)**	2.56 (5.40)	$t(33.85)^i = 4.91$

Note. ** Indicates significantly different from low PMT Group, *p* < .001.

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[1] Equal variances not assumed.

Discussion

The goal of this research was to explore the possible psychosocial correlates of sensitization as measured by pericranial muscle tenderness to manual palpation and to provide a starting point from which future studies and hypothesis can be generated. This study utilized a two-part design by which participants were recruited for an initial session during which psychological data was collected, a clinical diagnostic interview was completed, and pericranial muscle tenderness and pressure pain thresholds were assessed. Participants were asked to return for additional physiological assessment based on pericranial muscle tenderness data collected during the first session. Data collected allowed for further exploration of the distribution of pericranial muscle tenderness (PMT) and pressure pain thresholds (PPT) in a sample of undergraduate females, assessment of the stability of PMT and PPT scores over time, and examination of the relationship among PMT, PPT, and psychosocial variables collected in this study. Generally, it was found that individuals with high PMT differed from those with low PMT on a wide range of variables including physiological measures of experimental pain sensitivity and pain thresholds as well as on measures of subjective stress, affect, family history of pain disorders, pain coping, and presence of a psychiatric diagnosis. Additionally, there was limited evidence to indicate that high levels of PMT were associated with an ongoing pain or headache problem, though accurate headache diagnosis was not possible given the use of self-report data in the current study. Thus, the present research suggests PMT is not an isolated characteristic but rather correlated with both measures of pain sensitivity and psychosocial variables. Though elevated levels of PMT were found to be associated with the presence of both allodynia and hyperalgesia, they were not

necessarily associated with report of an ongoing clinical pain or headache disorder. As such, it is possible that this cluster of characteristics evident in those with high PMT may precede the appearance of a pain disorder, and better understanding of the development of and interrelationships among these variables may help to increase understanding of vulnerability to developing a pain disorder. To clarify the present findings, the following discussion will first evaluate the current results in light of previous research. Then, the discussion will move to synthesize the results with a focus on how the current study suggests new directions for chronic pain and sensitization research.

Psychophysiological Measurements & Sensitization

Total tenderness scores (TTS) measuring pericranial muscle tenderness (PMT) were found to be stable across the one-week assessment period for participants in both the low and high PMT group. As hypothesized, TTS were found to be significantly associated with reduced pressure pain thresholds (PPT), a measure of widespread muscle tenderness, and elevated pain ratings during an ischemic pain arm task.

Total tenderness scores (TTS) were found to be inversely associated with pressure pain thresholds (PPT) taken at both the finger and temporalis in the larger sample of all study participants. Thus, higher pericranial TTS were significantly associated with lower PPT at both cephalic and extracephalic sites. This relationship remained significant when the two smaller experimental groups were examined for similar differences such that high PMT participants exhibited significantly lower finger and temporalis PPT than low PMT participants. These group differences were significant both at session one and session two. Though both measures of TTS and PPT have been frequently used in literature on headache, no previously published study has examined whether these measures are stable

within individuals over even short periods of time. The current research suggests that these measures may be stable within individuals across assessments taken within approximately one week of another. Further research will need to be conducted to determine the stability of pericranial TTS and PPT over longer periods of time.

The current study has replicated some previous findings and expanded upon earlier work examining the relationship between PMT and PPT. However the current study takes a different approach than previous studies by using pericranial TTS as an independent variable and examining possible psychosocial and pain sensitivity correlates of pericranial TTS. Typically, previous studies examining pericranial TTS and finger and temporalis PPT have found evidence for an inverse relationship between tenderness and mechanical pain thresholds in tension-type headache patients. These findings have led researchers to hypothesize that sensitization, as measured by TTS and PPT, underlies a headache or pain problem. Similar conclusions have been drawn from research using measures of mechanical pain sensitivity with fibromyalgia and TMD populations. In accordance with several previous studies, the current research found a high correlation between pericranial TTS and PPT (in both the finger and temporalis). Previous research has typically examined the relationship between pericranial TTS and PPT in groups of participants drawn from headache clinics with diagnoses of episodic or chronic tension type headache. For example, Langemark et al. (1989) found a significant inverse relationship between TTS and PPT and several previous studies (Jensen et al., 1998; Bendtsen et al., 1996) have found pericranial TTS and PPT at both the temporalis and the finger were correlated for patients diagnosed with chronic tension-type headache (CTTH) with correlations ranging from -.36 to -.41 at the finger and -.53 to -.61 at the temporalis.

Thus, a significant inverse relationship between pericranial TTS and PPT is not an unexpected finding. What is of note in the current study is the relationship between elevated TTS and reduced PPT exists in a non-clinic sample and in the absence of ongoing pain. The current research demonstrates a significant inverse relationship exists between TTS and PPT in a non-clinic sample of undergraduate females. No previously published study has demonstrated this relationship. Additionally, the unique design of the current study also demonstrated that elevated pericranial TTS scores and reduced finger and temporalis PPT scores were not necessarily limited to individuals with a headache or pain problem. This finding suggests that central sensitization, believed to be indexed by TTS and PPT, alone may not be uniquely related to pain problems as previously hypothesized. Indeed, other variables such as the psychosocial measures discussed in the following section also appear to be related to sensitization (or at least to pericranial TTS which is believed to index sensitization).

In the current study, PPT at the finger and temporalis were found to be positively correlated. Previous research has found similar significant correlations between finger PPT and temporalis PPT in CTTH patients (Bendtsen et al., 1996). Again, the current research suggests that the relationship between PPT at the finger and at the temporalis may not be specific to a headache problem, a finding that has not been reported by previously published studies. In the current study, this relationship between finger and temporalis PPT was found to be significant regardless of headache symptoms in a non-clinic sample. Lowered pain thresholds were not observed only locally at the temporalis, but rather appeared to be diffuse such that individuals who were tender in the pericranial region tended to demonstrate extracephalic tenderness as measured by finger PPT and

widespread tenderness as measured by the MPTS. However, this widespread tenderness was not clearly associated with report of an ongoing pain problem. In comparison to their low PMT counterparts, high PMT participants demonstrated widespread muscle tenderness as measured by the manual tender point survey (MTPS) conducted during session two. A significant relationship was found between group membership and widespread tenderness such that high PMT group participants had MTPS scores nearly seven times that of their counterparts in the low PMT group. Thus, the present research suggests that individuals who demonstrate high levels of tenderness in the pericranial area also demonstrate widespread extracephalic tenderness. While previously published research has found a relationship between a diagnosis of fibromyalgia and the presence of a headache disorder (Lautenbacher et al., 1994; Okifuji et al., 1999), no previously published study has examined the relationship between the physiological assessments of tenderness frequently used in research with these populations (i.e., PMT in headache and MTPS in fibromyalgia). The results from the current study suggest that individuals who exhibit high levels of pericranial TTS to manual palpation also exhibit high levels of tenderness throughout the body. However, though high pericranial TTS was associated with widespread tenderness, it was not significantly related to report of ongoing pain complaints. This suggests PMT as a measure of sensitization may not be invariably related to chronic pain even though it appears to be related to widespread tenderness. And, it additionally suggests that differences observed between low and high PMT groups may reflect differences in central pain modulation rather than sensitization of the peripheral nerves, as peripheral sensitization would be localized and not widespread. Thus, in the current study differences in central pain modulation as indexed by

membership in high or low PMT groups were found without report of ongoing pain. This finding is unexpected as previous research suggests that differences in central pain modulation (as indexed by experimental measures of hyperalgesia and allodynia) are correlated with the presence of ongoing pain.

Finally, significant group differences existed on pain ratings taken during an ischemic arm pain task conducted during the second session. Participants in the high PMT group were found to have significantly higher pain ratings on this ischemic arm task than those in the low PMT group. Previous research using a version of this pain task has found that, compared with healthy controls, participants with a chronic pain disorder report earlier pain onset and lowered pain tolerance in response to the task (Maixner et al., 1995). Similarly, individuals diagnosed with minor depression have been found to have higher overall pain ratings and lower pain tolerances compared to control participants on this task (Pinerua-Shuhaibar et al., 1999). However, in the current research the high PMT participants did not report significantly more ongoing pain than the low PMT participants, even though the high PMT participants did have a significantly greater likelihood of having a PrimeMD diagnosis. Current results suggest that differences noted found in pain ratings from an ischemic arm pain task may be related to differences in TTS. No previously published research has examined participant's pain responses to such a task by using experimental groups formed according to muscle tenderness ratings. Typically, previous research has compared individuals with a psychological (e.g., depression) or medical (e.g., fibromyalgia) diagnosis to healthy control participants on pain ratings taken during the ischemic arm pain task. The present study suggests that PMT is associated with elevated pain sensitivity in the forearm, and

provides additional evidence that pericranial tenderness is associated with widespread tenderness evident on diverse measures of experimental pain sensitivity.

Psychophysiological Measurements & Sensitization: Summary

As hypothesized, total tenderness scores (TTS) of pericranial muscle tenderness (PMT) were found to be significantly associated with pressure pain thresholds (PPT), measures of widespread tenderness, and pain ratings taken during an ischemic arm task. A significant inverse relationship between pericranial TTS and PPT was found in a large sample of undergraduate females. Most notably, individuals with high levels of pericranial muscle tenderness were found to be significantly different from those with low levels of tenderness on each physiological measure included in this study. This study provides evidence that individuals with high PMT demonstrate both increased tenderness and decreased pressure pain thresholds suggestive of a state of allodynia. These differences in tenderness and pain detection occurred across the body at both cephalic and extracephalic locations. Additionally, high PMT participants demonstrated a hypersensitivity to painful stimuli suggestive of a state of hyperalgesia, Thus, high PMT participants exhibited widespread hyperalgesia and allodynia relative to participants in the low PMT group. Despite demonstrating hyperalgesia and allodynia relative to their low PMT peers, high PMT did not necessarily report ongoing pain. This was an unexpected finding as previous studies have found significant differences between healthy controls and chronic pain patients (including headache, TMD, and fibromyalgia) on measures of tenderness such as PMT that are believed to index sensitization and, from these results, hypothesized that this sensitization is uniquely correlated with chronic pain. While, sensitization is likely correlated with chronic pain, the current study suggests that

sensitivity as measured by PMT may exist in non-clinic samples apart from the presence of ongoing pain.

If the tenderness and pain sensitivity found in high PMT participants is not uniquely associated with ongoing pain, then the question remains to what this tenderness is related. The widespread nature of the tenderness and pain sensitivity evidenced by participants in this study with high PMT suggests that sensitization of peripheral myofascial nociceptors as the sole mechanism of this tenderness seems unlikely. However, it is possible that sensitization at the peripheral level could interact with other factors—such as sensitization of second order neurons at the spinal/trigeminal level or impaired central modulation of the nociceptive activity—to result in such widespread tenderness and pain sensitivity. The widespread tenderness found in the high PMT group could suggest a disturbance in the manner by which the central nervous system processes pain, a central misinterpretation of incoming peripheral stimuli that could account for the significant and widespread differences in pain sensitivity between these groups. However, since high PMT was not significantly associated with report of ongoing pain, this would suggest central deficits in pain processing (previously believed to be indexed by sensitization and related to the presence of a chronic pain disorder) could exist apart from a report of ongoing pain in some cases and that other factors—such as the psychosocial variables to be discussed in the following section—could be related to sensitization. While the current research suggests PMT may index an important dysfunction in central pain modulation, PMT was also found to be related to a constellation of other findings that appear related to but distinct from chronic pain. The

following section will discuss the relationship found between PMT and the psychological measures taken in this study.

Psychosocial Measurements & Sensitization

As outlined above, in the current study high levels of pericranial muscle tenderness (PMT) were found to be associated with widespread allodynia and hyperalgesia. However, not only did high PMT participants demonstrate abnormalities in pain regulation as evidenced by the physiological measures discussed in the previous section, they also were significantly different than their low PMT peers on psychosocial measures included in the present research. As originally hypothesized, participants with high PMT were found to have significantly higher scores on self-report measures of depression, anxiety, and subjective stress when compared with those in the low PMT group. High PMT participants were significantly more likely than low PMT participants to be diagnosed with an anxiety or mood disorder according to DSM-IV criteria. Group differences were also found on measures of pain coping administered during the initial assessment and following an ischemic arm pain task. Finally, significant differences existed between high and low PMT groups on family history of chronic pain. Thus, high PMT participants—who also exhibited widespread alterations in pain sensitivity— demonstrated significant differences in affect regulation, pain coping, and family history of chronic pain disorders.

The current research found an association between pain and affective dysregulation such that individuals with increased pain sensitivity demonstrated increased symptoms of both depression and anxiety and were more likely to receive a diagnosis of a mood or anxiety disorder. Previous research examining the relationship

between depression and pain sensitivity typically has focused on comparisons between

groups of depressed individuals versus groups of healthy controls on experimental pain

tasks. Generally, the results of these findings have been mixed with some studies

supporting reduced pain thresholds (Merskey, 1965) and pain tolerances (Willoughby et

al., 2002; Zelman et al., 1991) while others support increased pain thresholds (Bezzi et

al., 1981; Dworkin et al., 1995; Hall & Stride, 1954; Lautenbacher & Kreig, 1994) in

response to experimental pain in depressed individuals compared to healthy controls.

Research examining the relationship between anxiety and experimental pain has found

similar results with anxious individuals demonstrating reduced thresholds to experimental

pain when compared to healthy control subjects in some studies (Haslam, 1966; Dougher,

1979; Dougher, Goldstein, & Leight, 1987; Rhudy & Meagher, 2000) and demonstrating

analgesia in response to experimental pain in others (Malow, 1981; Pitman, van der Kolk,

Orr, & Greenberg, 1990; Janssen & Arntz, 1996). The current study uses a different

paradigm where individuals were divided into experimental groups based upon PMT.

These high and low tender groups were subsequently compared for differences on

measures of depression and anxiety, with findings that individuals with high PMT also

report more symptoms of depression and anxiety and are more likely to have a diagnosis

of a mood or anxiety disorder than low PMT individuals. In comparison to their low PMT

peers, the high PMT group—who reported significantly greater symptoms of depression

and anxiety—demonstrated widespread tenderness to both brief mechanical pressure as

well as sustained ischemic pain. However, the question remains as to how much

symptoms such as depression and anxiety interact with central processing of nociceptive

stimulation or the emotional and motivational state of the participant to report on pain,

and as a result impact upon participant's report of tenderness to experimental pain. Also, other factors such as poor pain coping, increased subjective stress, and family history of chronic pain found to be significantly associated with high PMT in the present study may also interact with these variables to alter response to experimental pain.

The current research also replicated previous findings of a relationship between pain coping and increased tenderness. Previous studies have found that fewer positive coping thoughts are associated with increases in participant's pain ratings in response to experimental pain (Heyneman, Fremouw, Gano, Kirkland, & Heiden, 1990; Sullivan, Bishop, & Pivik, 1995). Ratings on catastrophizing measures obtained from undergraduate subjects as much as 10 weeks prior to assessment with a cold pressor task have been found to predict pain ratings during the task (Sullivan et al., 1995). Investigators have suggested that attention and thought control may be important factors that mediate the relationship between coping and reported pain intensity (Heyneman et al., 1990; Spanos et al., 1979; Sullivan et al., 1995; Sullivan et al, 1997). Coping, in particular catastrophizing, has been found to be associated with pain related disability in chronic back pain patients (Rosenstiel & Keefe, 1983; Turner & Clancy, 1986), even independent of depression and anxiety, and has been found to contribute to the prediction of disability above the variance accounted for by pain intensity in individuals with soft-tissue injuries (Sullivan et al., 1998). Much of the previous research examining coping and catastrophizing in pain has focused on chronic pain populations recruited from specialty clinics. The current study, utilizing an undergraduate population, suggests that individuals with high PMT demonstrate reduced pain coping as evidenced by increased catastrophizing in comparison to their low PMT peers.

Finely, the current research also found a relationship between family history of chronic pain and PMT such that individuals in the high PMT group reported a greater incidence of chronic pain in first-degree relatives than those in the low PMT group. Little previous research has been done examining the influence of family history, in particular a history of chronic pain, on response to experimental pain. Fillingim, Edwards, and Powell (2000) found healthy females (but not males) with a positive family history of chronic pain reported significantly increased pain sensitivity to thermal stimuli compared to females without a family history. A similar study found lower pressure pain thresholds among female but not male relatives of fibromyalgia patients compared to controls (Neumann & Buskila, 1997). The nature of the relationship between family history and experimental pain sensitivity is still unclear and in need of further research, however Fillingim et al. (2000) speculate that the relationship is likely related to both environmental, social learning factors as well as genetic effects. Of note, at least one animal study also supports a relationship between genetics and pain sensitivity (Mogli, 1999). In this study, 11 different inbred mouse strains demonstrated significant heritability for all nociceptive measures utilized in the study. Additionally, a recent study of pressure pain thresholds in mono- and dizygotic twins demonstrated strong correlations between pain thresholds within twin pairs with monozygotic twins demonstrating slightly higher correlations than dizygotic twins (Macgregor, Griffiths, Baker, & Spector, 1997). Thus, though further research is needed to clarify this relationship, currently available evidence and the findings of the present study support the likelihood of a relationship between family history and response to experimental pain.

Psychosocial Measures & Sensitization: Summary

Total tenderness scores (TTS) of pericranial muscle tenderness (PMT) were found to be associated with both abnormalities in pain regulation (as evidenced by significant differences on physiological measures) and psychosocial measures including indices of affect regulation, subjective stress, pain coping/catastrophizing, and family history of chronic pain. Thus, the constellation of variables associated with high PMT found in the present study includes altered response to experimental pain, decreased pain coping as evidenced by increase catastrophizing, greater likelihood of a family history of chronic pain, and affective dysregulation. However, in the present research, though high PMT participants were significantly different from low PMT participants on a constellation of variables, these differences did not include participant's report of ongoing pain. Further research is needed to clarify the relationship between pain sensitivity and these psychosocial variables, in particular to determine the role, if any, of central sensitization and the interrelationship of these variables—affect, pain sensitivity, pain coping, family history, and central sensitization—to the presence of chronic pain problems. It is possible that each of these variables present a risk factor for developing chronic pain such that an individual's risk increases as the number of risk factors increases. For example, an individual with a diagnosis of depression, increased pain sensitivity, and a family history of chronic pain may be at greater risk for developing a chronic pain disorder than someone with a diagnosis of depression alone. Or, there might be certain pathways by which these variables interact to lead to chronic pain disorders. For example, the experience of increased pain sensitivity—which could be influenced by family history— might lead to catastrophizing and symptoms of depression and anxiety that over time and

in the presence of subjective stress, lead to an increased vulnerability for a chronic pain disorder. Or, there might be a third variable that accounts for all these factors. Overall, the present research suggests that high PMT is related to a broad range of psychosocial and physiological variables, but not uniquely correlated with ongoing pain.

Headache Ratings, Ongoing Pain, & Sensitization

The present research found no significant relationship between participant's report of either headache or ongoing pain based upon level of pain sensitivity as measured by PMT. Thus, the high PMT group did not significantly differ from their low PMT peers on their report of ongoing pain problems. This finding—particularly considering the comparatively strong relationship found between psychosocial variables and pain sensitivity—was somewhat unexpected given previous findings of a significant relationship between PMT and tension-type headache.

Contrary to the original hypothesis, participants in the high PMT group did not demonstrate significantly different headache frequency compared to their low PMT peers. When self-report data was used to examine group differences in headache diagnosis, the high PMT group did not report symptoms of chronic or episodic tension-type headaches according to IHS criteria[1]. Not only is this a rate not significantly different from the low PMT group, it is notably lower than the rate that tension-type headaches exist in the general population. However, as diagnosis was based upon self-report data and not clinical assessment, these findings should be interpreted with caution. And, while there were no group differences on headache frequency or diagnosis, the high

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[1] In most cases, headache frequency was enough to meet HIS criteria for diagnosis. Rather, it was the participant's unclear/inconsistent report of associated features (such as presence of nausea, photophobia, or phonophobia) that made diagnosis impossible with current data.

PMT group did report significantly greater mean headache intensity than those in the low PMT group. Finally, though there were no significant group differences in mean headache frequency and contrary to the original hypothesis, participants in the high PMT group did not report significantly more ongoing pain than those in the low PMT group.

The finding of no significant group differences on headache frequency is contrary to what would be expected given the previous literature. In these studies (Hatch et al., 1992; Jensen, 1995; Jensen et al., 1993; Langemark and Olesen, 1987; Lipchik et al., 1996; Lipchik et al., 2000; Lipchik et al., 1997; Lous and Olesen, 1982) participants who are prone to tension type headaches demonstrated higher levels of pericranial muscle tenderness than individuals with no significant headache problems who demonstrated few signs of tenderness. The present study drawn from a population of female undergraduates and not headache sufferers found somewhat different results, that the presence of muscle tenderness was not clearly related to differences in headache characteristics as might have been expected from previous research.

There could be several reasons for the differences between current and previous findings. First, the current design is methodologically different than these previous studies. The previous studies examined differences in PMT comparing individuals with a headache diagnosis to healthy control participants, and other correlates of PMT beyond headache have not been previously well investigated. The current study provides the first evidence that other factors—such as the psychosocial variables discussed in the previous section—are related to PMT. Second, while the current study did collect information on headache symptoms via a self-report symptom questionnaire, no clinical assessment was conducted to confirm the symptoms reported on this measure. Thus, headache symptoms

and headache diagnosis in this study are based entirely upon participants' self-report and should be interpreted with caution.

While the current study found no significant group differences on reported headache frequency, the groups also did not significantly differ on report of ongoing pain. Thus, individuals in the high PMT group were not significantly more likely to report ongoing pain in at least one body site when compared to those in the low PMT group. No previously published study has examined the relationship between PMT and individual's report of widespread pain at extra-cephalic sites. Given the lack of previously published data on this relationship and the presumed relationship between pericranial TTS and ongoing headache pain, it is notable that no significant relationship was found to exist between PMT and ongoing pain in the current study. Though this lack of significance should be interpreted with caution as differences (thought not significant at the .01 level) did exist between the two groups, less equivocal results would be expected given previous research. If, as previous research suggests, pericranial muscle tenderness (PMT) is an index of pain processing and related to a process of central sensitization, then one might expect individuals who have elevated levels of PMT to report increased frequency of ongoing pain. In the current study, more than half the individuals who had high PMT did not report ongoing pain or a headache diagnosis— only 38% of high PMT participants reported ongoing pain compared to 20% of the low PMT participants. One might hypothesize that these highly tender individuals, who demonstrated abnormal pain and affect regulation but are not reporting the presence of ongoing pain, may be vulnerable to developing a pain problem later in life. Thus, abnormal regulation of these systems may precede development of a pain disorder in

certain individuals. However, further research is needed to clarify the relationship among these variables and the role they play in development of either a chronic pain or affect regulation disorder.

Synthesis and Future Directions

While the current study shares some common findings with previous research, it breaks from traditionally used experimental designs to explore a novel paradigm that suggests important new directions for research in this area. The current findings have generally replicated previous work establishing correlations among physiological variables such as those utilized in this study. However, previous studies have focused on using pericranial muscle tenderness (PMT) as a measure of sensitization such that aberrant PMT was believed to be associated primarily with disorders of the pericranial tissue, such as headache and TMD. In these studies, PMT was utilized as a measure of central pain modulation such that high levels of PMT were believed to index dysfunction of these pain control systems. The current research suggests that while PMT may index dysfunction in central systems, it is related to, yet also distinct from, the presence of a chronic pain disorder. While previous research has hypothesized that the sensitization indexed by PMT underlies a chronic pain problem, the present findings indicate other psychosocial variables may also influence PMT. Thus, by examining PMT outside the context of a chronic pain paradigm, the current research has found PMT to be strongly related to a constellation of variables. Previous research would have suggested that by identifying individuals with high levels of PMT we would also identify those individuals who have conditions—such as headache and TMD—associated with pericranial tenderness. In contrast, the current study found high levels of PMT identified individuals

who demonstrated pervasive pain sensitivity, deregulated affect, increased subjective stress, poor pain coping, and a family history of chronic pain. And yet, contrary to what would be expected given previous research, many of these individuals with high PMT did not report the presence of ongoing pain.

The current findings of an association between pericranial muscle tenderness (PMT), reduced pressure pain thresholds (PPT), psychosocial variables (including poor pain coping and symptoms of anxiety and depression, and family history of chronic pain) could suggest that a single deficit may underlie all these. Previous research would suggest that this deficit could be related to a central misinterpretation or dysfunction of the pain processing system—perhaps impaired central modulation of nociceptive activity—such that central pain systems become "rewired" and central sensitization results with the accompanying hyperalgesia and allodynia. However, exactly how such central dysfunction could also be related to variables such as pain coping, depression and anxiety, and family history, how it could exist in the absence of ongoing pain, and what role each of these plays in the development of a central deficit such as that believed to be indexed by PMT is unclear. The question also remains how such a central deficit and the psychosocial variables the current study suggests may be related to indices of this deficit could be related to the development of a chronic pain complaint. Previous research has assumed that central sensitization indexed by significant muscle tenderness underlies pain problems such as tension-type headache, fibromyalgia, and TMD and is directly related to an individual's chronic pain problem. The current findings suggest that, assuming PMT is a somewhat direct measure of central sensitization, a straightforward relationship does not necessarily exist between chronic pain and central sensitization. Rather, a

constellation of other physiological factors (such as lowered pain thresholds) and psychological factors (such as the presence of a mood or anxiety disorder, increased subjective stress, poor pain coping, and a family history of chronic pain) appear to be influencing this relationship. It still remains unclear whether these other factors influence sensitization directly due to central processing changes associated with these factors, for example the central changes believed to occur with a diagnosis of depression or anxiety. Or, whether these variables influence sensitization indirectly, for example by changing one's attention or motivation to report on pain sensitivity. Or, even both these factors exist concurrently influencing each other.

If a central deficit underlies the current findings of an association between allodynia, hyperalgesia, and the psychosocial variables measured in the current study, it raises the question as to how these variables in combination relate to chronic pain problems. In the current study, findings of pain sensitivity were significantly related to several psychosocial variables but not to report of ongoing pain, even though approximately one-third of the high PMT group reported ongoing pain. However, all but one of the high PMT participants who reported ongoing pain also qualified for a PrimeMD diagnosis. Taken together, the current results suggest two possible hypotheses. First, the possibility that pain sensitivity such as that indexed by PMT is not related to ongoing pain problems. Or, rather that it is related to pain problems only in the presence of other variables, such as presence of affective dysregulation or poor pain coping. A second, and perhaps more likely, possibility is that PMT indexes a deficit in central processing that may precede development of a chronic pain complaint.

The current study, because of the young age of its female participants, may be uniquely designed to capture a "snapshot" of the early development of chronic pain. Though the high PMT participants in this study were significantly different from their low PMT peers on many psychosocial variables, differences between the two groups on report of ongoing pain were less striking. When subgroups of participants with and without ongoing pain were examined, subjective stress and the presence of a PrimeMD disorder stood out as variables that might differentiate high PMT subjects with and without ongoing pain. Even though the sample sizes of these subgroups were small, the fact that nearly 90% of high PMT participants who had ongoing pain also had a PrimeMD disorder is somewhat striking. One could conjecture that the presence of high PMT leads to a vulnerability, perhaps due to the environmental and/or genetic influence of a family history of chronic pain disorders, to developing affect and pain dysregulation. These individuals may, in part due to this vulnerability of increased pain sensitivity, be predisposed to mood or anxiety disorders and increased catastrophizing that could contribute to the eventual development of a chronic pain complaint.

Taken together, the current results suggest several avenues for future research to increase understanding of the relationships among pain sensitivity, chronic pain disorders, affective dysregulation, poor pain coping, and family history of chronic pain complaints. First, though the present study demonstrated PMT to be stable across a brief period of time, it would be useful to track individuals over time to examine possible long-term fluctuations in PMT and what correlates are associated with these fluctuations. For example, it would be interesting to know whether individuals' PMT levels are stable over longer periods of time and whether ongoing presence of high PMT—especially in the

presence of ongoing stress and poor coping—would eventually lead to the development of chronic pain or affective disorders. If high PMT turns out to be a risk factor for developing pain and affective complaints, from the perspective of intervention it would be useful to examine how PMT might be manipulated through treatments—either psychological or medical—that could help prevent the development of further problems. For example, by examining whether stress management training and teaching positive coping skills could help inoculate high PMT individuals from developing pain problems. Conversely, it would be interesting to examine exactly how high PMT individuals respond to stress. The current findings suggest that high PMT individuals report increased levels of subjective stress and are significantly more likely to catastrophize in response to pain than their low PMT peers. It would be interesting to replicate this finding using a laboratory stress task—such as a math stress task—and to examine post-task report of pain and fluctuations in PMT and coping in response to the stressor.. Additionally, as a relationship was found between high PMT and family history of chronic pain, it would be interesting to examine more closely this relationship by collecting data on PMT in family members and more thoroughly and directly assessing for the presence of chronic pain complaints rather than relying on the self-report data of one member as was done in the current study. Finally, it would be of importance to examine in greater detail the biological basis of high PMT by examining other measures such as cortisol and serotonin believed to be associated with stress and pain and affective dysregulation. Furthering this research, being open to new paradigms with which to examine PMT, and strengthening the connections between the biological and

psychological sciences may help discover important information about the connections among and interventions for pain and affective disorders.

Limitations of Current Research

Several limitations of the current study require mention. First, to eliminate the confounding effects of gender only females were studied. Results thus cannot be generalized to males. Also, though females were recruited from a wide range of ages the current sample was drawn from a university and not a community population. Thus, results should be generalized to a community population with caution.

While confirmatory clinical assessments were used when possible, it was necessary to rely solely upon self-report data for some of the information collected during this study. Most notably, both the headache data and data regarding ongoing pain were collected entirely on self-report. Also, data of family history was not collected through direct interview of family members but rather though the report of the participant alone. Second, the scale used to collect information on muscle tenderness assessed by the PMT assessment and the MTPS assessment was a zero to ten scale. Previous assessments of PMT utilize a zero to three scale, while previous assessments similar to the MTPS included in this study have utilized a zero to three scale, a zero to five scale, and a zero to ten scale (though the zero to ten scale is most commonly used). The discrepancies in scales utilized to assess muscle tenderness limits the cross study comparisons that can be made with ease as not all studies are utilizing a standardized, common scale. Third, previous studies in this area have also attempted to insure blindness of the examiner such that experimenters conducting physiological assessments would be unaware of the individual's headache diagnosis and vice versa. Ideally, the examiner conducting the

physiological assessments in this study would have been blind to information about the individual's headache symptoms, pain symptoms, family history, symptoms of psychological distress, and PrimeMD diagnosis. Though every attempt was made to limit examiner's knowledge of participant's responses by restricting access to session one data for the examiner conducting the second session, complete blindness was not possible due to the number of measures (i.e., the same examiner often completed the PrimeMD and PMT assessment in the first session and the physiological assessments in the second session). Finally, though formal corrections for the number of tests were not conducted, to control for error a p-value of .01 rather than .05 was utilized throughout the study.

Conclusions

Despite the limitations, this study is the first to systematically examine correlates of PMT. The goal of the current research was to provide data to lay the foundation to generate future hypothesis and research examining psychosocial correlates of sensitization. The current study found that individuals with high PMT were significantly different than those with low PMT on both physiological assessments of allodynia and hyperalgesia as well as psychosocial measures including assessments of affect, pain coping, and family history; however, highly tender individuals were not found to be significantly different from their less tender peers on measures of ongoing pain and headache diagnosis. As abnormal pain and affect regulation was found to be present without the report of a current pain problem in some individuals, it is possible that this constellation of characteristics precedes the development of a chronic pain disorder in certain vulnerable individuals. Further research is needed to clarify the association between pain sensitivity and these psychosocial variables, in particular to determine the

role, if any, central sensitization plays in the relationship of psychosocial and

physiological variables to the development of chronic pain complaints.

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Appendix A: Psychosocial Questionnaires

Possible Prime-MD Diagnoses

Mood

    Major Depressive Disorder

    Partial Remission of Major Depressive Disorder

Dysthymia

    Minor Depressive Disorder

    R/O Bipolar Disorder

Anxiety

    Panic Disorder

    Generalized Anxiety Disorder

    Anxiety Disorder NOS

Alcohol

    Probable Alcohol Abuse/Dependence

Eating

    Binge Eating Disorder

    Bulimia Nervosa, Purging Type

    Bulimia Nervosa, Non-purging Type

McGill Pain Questionnaire—Short Form

Instructions: Please read the following list of words. Rate the extent to which each word describes your physical feelings or sensations AT THIS MOMENT **from none (not experiencing the feeling/sensation at all) to severe (worst possible experience of the sensation) by putting an X next to the appropriate value.**

	None	**Mild**	**Moderate**	**Severe**
Throbbing	0) _____	1) _____	2) _____	3) _____
Shooting	0) _____	1) _____	2) _____	3) _____
Stabbing	0) _____	1) _____	2) _____	3) _____
Sharp	0) _____	1) _____	2) _____	3) _____
Cramping	0) _____	1) _____	2) _____	3) _____
Gnawing	0) _____	1) _____	2) _____	3) _____
Hot-Burning	0) _____	1) _____	2) _____	3) _____
Aching	0) _____	1) _____	2) _____	3) _____
Heavy	0) _____	1) _____	2) _____	3) _____
Tender	0) _____	1) _____	2) _____	3) _____
Splitting	0) _____	1) _____	2) _____	3) _____
Tiring-Exhausting	0) _____	1) _____	2) _____	3) _____
Sickening	0) _____	1) _____	2) _____	3) _____
Fearful	0) _____	1) _____	2) _____	3) _____
Punishing-Cruel	0) _____	1) _____	2) _____	3) _____

Please indicate your overall experience of pain intensity **AT THIS MOMENT** using the following scale:

No Pain ●--● Worst Possible Pain

0	No Pain	_____
1	Mild	_____
2	Discomforting	_____
3	Distressing	_____
4	Horrible	_____
5	Excruciating	_____

Headache & Symptoms Questionnaire

Instructions: Please read the following questions and mark one answer per question that best describes your headache experience. **Think about the headache(s) you experience most frequently/typically and answer these questions based on your experience of these headaches. DO NOT include headaches due to substance abuse or withdrawal** (i.e., hangovers, caffeine, medications, etc.).

1.   How often do you get headaches—i.e., how many times a week, month, or year do you experience a headache?

2.   Where (on your head/neck) do you most often experience your headaches?

___ Forehead   ___ Neck   ___ Back of head   ___ Top of head   ___ Side of head

3.   Do you experience the pain from your most typical headache on one side of your head or on both sides of your head?
_____ One side   _____ Both sides

4.   Please circle one of the word pairs below that best describes your most typical headache pain:
   • Pressing/Tightening   • Dull ache   • Pulsating   • Sharp/Piercing

5.   On a scale of 0 to 10—with 0 being no pain and 10 being the most intense pain you can imagine—how would you rate the pain of your most typical headache?
_____

6.   Are your headaches frequent and/or severe enough to stop you from performing your daily activities (i.e., so bad that you can't do anything but lay down)?
_____ Yes   _____ No

7.   On average, how long does your most typical headache last if you **do not take any pain medication**?
_____

8.   Does routine physical activity (NOT exercise or sports), such as walking up one flight of stairs, worsen your headache pain?
_____ Yes   _____ No

9.   Would typical room light, such as the light in this room, worsen your headache pain?
_____ Yes   _____ No

10. Would sound, such as the sound of a person speaking at a regular volume, worsen your headache pain?

_____ Yes   _____ No

11. Do you experience any visual disturbances (such as spots or lights) during your typical headache?

_____ Yes   _____ No

12. Do you often feel sick to your stomach during your typical headache?

_____ Yes   _____ No

13. Do you often experience vomiting/throw up during your typical headache?

_____ Yes   _____ No

14. Do you experience any additional symptoms during your typical headache that we have not asked included here? If so, please describe these symptoms below.

_____
_____
_____

15. What do you believe causes your headaches? PLEASE RANK YOUR RESPONSES 1, 2, & 3.

_____Stress	_____ Allergies	_____ Menstruation	_____ Alcohol
_____Foods	_____ Caffeine	_____ Weather	_____ Head injury/trauma
_____Odors	_____Not eating	_____Dehydration	_____ Other

16. How long have you experienced these headaches with the symptoms you described above (i.e., how long has it been since you remember first getting these headaches)?

_____

17. Does anyone in your immediate family (parents/siblings) experience headaches severe enough to interfere with their daily activities?

_____ Yes   _____ No

18. If you answered yes to the above question, please describe further by indicating the family member who experiences headaches and the kinds of headaches they experience below.

_____
_____
_____

19. Have you ever seen a medical specialist (physician, nurse practitioner, chiropractor, etc.) about your headaches?

_____ Yes   _____ No

20.   If so, who did you see and what did they tell you about your headaches (include diagnosis, treatment, etc.)?

_____
_____
_____
_____

The following questions will ask you about some of your sleep habits. When answering these questions, please think about your habits from the past two weeks.

1. An average, how many hours of sleep per night have you gotten during the past two weeks? _____

2. During the past two weeks, have you frequently experienced difficulty falling asleep—i.e., does it often take you more than 20 minutes to fall asleep on more than half the days in the past two weeks?
   _____ Yes   _____ No

3. During the past two weeks, have you frequently had difficulty remaining asleep—i.e., do you often find yourself waking up several times a night on more than half the days in the past two weeks?
   _____ Yes   _____ No

4. Have you felt refreshed and rested when you wake up on more than half the days during the past two weeks?
   _____ Yes   _____ No

The following questions will ask you about your medical history, your immediate family's medical history, and your current general health. Please answer carefully to the best of your ability.

1. What is the typical length of your entire menstrual cycle—i.e., how many days between the first day of one menstrual period and the first day of your next period?
   _____ Days

2. How many days has it been since the first day of your last menstrual period (your first day of menstruation)?
   _____ Days

3. Are you taking any contraceptives?
   _____ Yes _____ No

4. If so, what
    brand/kind?_____

5. Please list any medications, and/or dietary supplements (i.e. herbs, vitamins, etc.)
    you take now and how often you take them. Please list everything--prescription
    AND over-the-counter medications:
    _____
    _____
    _____

6. Have you recently experienced any sort of acute injury severe enough for you to
    seek medical treatment? Examples of acute injuries could include a broken bone,
    muscle strain or sprain, injuries from a car accident, etc.
    _____ Yes   _____ No

7. If you answered yes to the above question, please describe your condition, its
    treatment, and how long ago it occurred in detail here:
    _____
    _____

8. Have you ever been diagnosed with any sort of chronic medical condition?
    Consider a chronic condition any physical difficulty you experience (or have
    experienced) on a regular basis and for which your have sought treatment. These
    could include back pain, headaches, heart conditions, allergies, diabetes, cancer,
    etc.
    _____ Yes   _____ No

9. If you answered yes to the above question, please describe your condition, its
    treatment, and when you were diagnosed with it in detail here:
    _____
    _____

10. Have you sought professional help for depression (i.e., physician, psychologist,
    counselor, pastor, etc.)?
    _____ Yes   _____ No

11. Have you ever sought professional help for anxiety (i.e., physician, psychologist,
    counselor, pastor, etc.)?
    _____ Yes   _____ No

12. Have you ever sought professional help for any other psychological disorder (i.e.,
    physician, psychologist, counselor, pastor, etc.)?
    _____ Yes   _____ No

13. If you answered yes to any of the previous three questions, please briefly describe your difficulty/diagnosis, its treatment, AND WHEN TREATMENT BEGAN & ENDED here.

_____
_____

14. Has anyone in your immediate family (parents/siblings) ever been diagnosed with any sort of chronic medical condition? Consider a chronic condition any physical difficulty they experience (or have experienced) on a regular basis and for which they have sought treatment. These could include back pain, headaches, heart conditions, allergies, diabetes, cancer, etc.

_____ Yes   _____ No

15. If you answered yes to the above question, please briefly describe what you know about your family member's condition/diagnosis and its treatment here:

_____
_____
_____

16. Does anyone in your immediate family (parents/siblings) currently experience persistent and/or frequent pain (such as headaches, back pain, or other aches)?

_____ Yes   _____ No

17. If you answered yes to the above question, please briefly describe what you know about your family member's condition/diagnosis and its treatment here:

_____
_____
_____

18. Is there a history of depression, anxiety, or any other psychological diagnosis in your immediate family (parents/siblings)?

_____ Yes   _____ No

19. If you answered yes to the previous question, please briefly describe your family member's history and its treatment here (which family member, their diagnosis, treatment, etc.).

_____
_____
_____

20. Do you <u>currently</u> experience persistent and/or frequent pain (a pain you experience every day or nearly every day that interferes with your daily activities) in any of the following areas?

Head   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Neck   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Shoulders   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
 IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Upper Back   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Lower Back   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Chest   yes_____ no _____
IF YES, where is your pain located? Right Side _____   Left Side _____   Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Stomach   yes_____ no _____
IF YES, where is your pain located? Right Side _____   Left Side _____   Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Hips   yes_____ no _____
IF YES, where is your pain located? Right Side _____   Left Side _____   Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Arms   yes_____ no _____
IF YES, where is your pain located? Right Side _____   Left Side _____   Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Elbows   yes_____ no _____
IF YES, where is your pain located? Right Side _____   Left Side _____   Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with 0 being no pain and 10 the worst pain you can imagine?

_____

Wrists   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Hands   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Fingers   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Legs   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Knees   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Ankles   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

Feet & Toes   yes_____ no _____
IF YES, where is your pain located? Right Side _____ Left Side _____ Both Sides _____
IF YES, how long have you experienced this pain
(months/years)?_____
IF YES, how you would you rate the average intensity of this pain on a scale of 0-10 with
0 being no pain and 10 the worst pain you can imagine?

_____

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PCS

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – Not at all   1 – To a slight degree   2 – To a moderate degree   3 – To a great degree   4 – All the time

When I'm in pain…

1. I worry all the time about whether the pain will end.	0	1	2	3	4
2. I feel I can't go on.	0	1	2	3	4
3. It's terrible and I think it's never going to get any better.	0	1	2	3	4
4. It's awful and I feel that it overwhelms me.	0	1	2	3	4
5. I feel I can't stand it anymore.	0	1	2	3	4
6. I become afraid that the pain will get worse.	0	1	2	3	4
7. I keep thinking of other painful events.	0	1	2	3	4
8. I anxiously want the pain to go away.	0	1	2	3	4
9. I can't seem to keep it out of my mind.	0	1	2	3	4
10. I keep thinking about how much it hurts.	0	1	2	3	4
11. I keep thinking about how badly I want the pain to stop.	0	1	2	3	4
12. There's nothing I can do to reduce the intensity of the pain.	0	1	2	3	4
13. I wonder whether something serious may happen.	0	1	2	3	4

CSQ

When individuals experience pain they often use different ways of coping, or "dealing," with their pain. These include saying things to themselves when they experience pain, or engaging in different activities. Below are a list of things that people have reported doing when they feel pain. For each activity, I want you to indicate, using the scale outlined below, how much you engage in that particular activity when you feel pain. A 0 indicates you never do that particular activity when you experience pain and a 6 indicates you always do that when you experience pain. *Please write the numbers you choose in the blanks beside the activities.* Remember, you can use any point along the scale.

0	1	2	3	4	5	6
Never do that			Sometimes do that			Always do that

When I feel pain…

_____ 1. I try to feel distant from the pain, almost as if the pain was is somebody else's body.
_____ 2. I leave the house and do something, such as going to the movies or shopping.
_____ 3. I try to think of something pleasant.
_____ 4. I don't think of it as pain but rather as a dull or warm feeling.
_____ 5. It is terrible and I feel it's never going to get any better.
_____ 6. I tell myself to be brave and carry on despite the pain.
_____ 7. I read.
_____ 8. I tell myself that I can overcome the pain.
_____ 9. I take my medication.
_____ 10. I count numbers in my head or run a song through my mind.
_____ 11. I just think of it as some other sensation, such as numbness.
_____ 12. It is awful and I feel that it overwhelms me.
_____ 13. I play mental games with myself to keep my mind off the pain.
_____ 14. I feel my life isn't worth living.
_____ 15. I know someday someone will be here to help me and it will go away for awhile.
_____ 16. I walk a lot.
_____ 17. I pray to God it won't last long.
_____ 18. I try not to think of it as my body, but rather as something separate from me.
_____ 19. I relax.
_____ 20. I don't think about the pain.
_____ 21. I try to think years ahead, what everything will be like after I've gotten rid of the pain.
_____ 22. I tell myself it doesn't hurt.
_____ 23. I tell myself I can't let the pain stand in the way of what I have to do.
_____ 24. I don't pay any attention to the pain.
_____ 25. I have faith in doctors that someday there will be a cure for my pain.
_____ 26. No matter how bad it gets, I know I can handle it.
_____ 27. I pretend it's not there.
_____ 28. I worry all the time about whether it will end.
_____ 29. I lie down.
_____ 30. I replay in my mind pleasant experiences in the past.
_____ 31. I think of people I enjoy doing things with.

0	1	2	3	4	5	6
Never do that			Sometimes do that			Always do that

When I feel pain…

_____ 32. I pray for the pain to stop.
_____ 33. I take a shower or bath.
_____ 34. I imagine that the pain is outside of my body.
_____ 35. I just go on as if nothing happened.
_____ 36. I see it as a challenge and don't let it bother me.
_____ 37. Although it hurts, I just keep on going.
_____ 38. I feel I can't stand it anymore.
_____ 39. I try to be around other people.
_____ 40. I ignore it.
_____ 41. I rely on my faith in God.
_____ 42. I feel like I can't go on.
_____ 43. I think of things I enjoy doing.
_____ 44. I do anything to get my mind off the pain.
_____ 45. I do something I enjoy, such as watching TV or listening to music.
_____ 46. I pretend it's not a part of me.
_____ 47. I do something active, like household chores or projects.
_____ 48. I use a heating pad.

Based on all the things you do to cope or deal with pain that you experience, on an average day how much control do you feel you have over any pain you experience? Please circle the appropriate number. Remember, you can circle any number along the scale.

0	1	2	3	4	5	6
No control			Some control			Complete control

Based on all the things you do to cope or deal with pain that you experience, on an average day how much are you able to decrease any pain you experience? Please circle the appropriate number. Remember, you can circle any number along the scale.

0	1	2	3	4	5	6
Can't decrease it at all			Can decrease it somewhat			Can decrease it completely

USQ

Below are listed a variety of events that may be viewed as stressful or unpleasant. Read each item carefully and decide whether or not that event has happened to you during this **PAST WEEK**. If the event did not happen this week, circle the 0 to the right of that item. If the event did happen to you this past week, show the amount of stress that it caused you by circling a number from 1 to 5 to the right of that item (see scale below).

0	1	2	3	4	5
Did not happen	Happened, not stressful	Slightly stressful	Moderately stressful	Very stressful	Extremely stressful

1. Had a class presentation.	0	1	2	3	4	5
2. Had a lot of tests.	0	1	2	3	4	5
3. Preparation for finals.	0	1	2	3	4	5
4. Applying to graduate school.	0	1	2	3	4	5
5. Working while in school.	0	1	2	3	4	5
6. Assignments in all classes due the same day.	0	1	2	3	4	5
7. Crammed for a test.	0	1	2	3	4	5
8. Trying to decide on a major.	0	1	2	3	4	5
9. Parents controlling with money.	0	1	2	3	4	5
10. Couldn't find a parking space.	0	1	2	3	4	5
11. You have a hard upcoming week.	0	1	2	3	4	5
12. Went into a test unprepared	0	1	2	3	4	5
13. Noise disturbed you while trying to study.	0	1	2	3	4	5
14. Had to ask for money.	0	1	2	3	4	5
15. Did worse than expected on test.	0	1	2	3	4	5
16. Ran out of typewriter/printer ribbon while typing/printing.	0	1	2	3	4	5
17. Had projects, research papers due	0	1	2	3	4	5
18. Did badly on a test.	0	1	2	3	4	5
19. Can't understand your professor.	0	1	2	3	4	5
20. Trying to get into your major or college.	0	1	2	3	4	5
21. Having roommate conflicts.	0	1	2	3	4	5
22. Registration for classes.	0	1	2	3	4	5
23. Stayed up late writing a paper.	0	1	2	3	4	5
24. No time to eat.	0	1	2	3	4	5
25. Problems with your computer.	0	1	2	3	4	5
26. Talked with a professor.	0	1	2	3	4	5
27. Got to class late.	0	1	2	3	4	5
28. Dealt with incompetence at the Registrar's office.	0	1	2	3	4	5
29. Thought about unfinished work.	0	1	2	3	4	5
30. No sleep.	0	1	2	3	4	5

31. Sat through a boring class.	0	1	2	3	4	5
32. Favorite sporting team lost.	0	1	2	3	4	5
33. Applying for a job.	0	1	2	3	4	5
34. Fought with boy-/girlfriend.	0	1	2	3	4	5
35. Victim of a crime.	0	1	2	3	4	5
36. Arguments, conflicts of values with friends.	0	1	2	3	4	5
37. Bothered by having no social support of family.	0	1	2	3	4	5
38. Performed poorly at a task.	0	1	2	3	4	5
39. Can't finish everything you needed to do.	0	1	2	3	4	5
40. Heard bad news.	0	1	2	3	4	5
41. Had confrontation with an authority figure.	0	1	2	3	4	5
42. Maintaining a long-distance boy-/girlfriend.	0	1	2	3	4	5
43. Breaking up with boy-/girlfriend.	0	1	2	3	4	5
44. Feel unorganized.	0	1	2	3	4	5
45. Found out boy-/girlfriend cheated on you.	0	1	2	3	4	5
46. Feel isolated.	0	1	2	3	4	5
47. Lots of deadlines to meet.	0	1	2	3	4	5
48. Property stolen.	0	1	2	3	4	5
49. Lost something (like your wallet).	0	1	2	3	4	5
50. Someone borrowed something without permission.	0	1	2	3	4	5
51. Death of a pet.	0	1	2	3	4	5
52. Had an interview.	0	1	2	3	4	5
53. Erratic schedule.	0	1	2	3	4	5
54. Parents getting divorced.	0	1	2	3	4	5
55. Dependent on other people.	0	1	2	3	4	5
56. Car/bike broke down, flat tire, etc.	0	1	2	3	4	5
57. Got a traffic ticket.	0	1	2	3	4	5
58. Someone you expected to call did not.	0	1	2	3	4	5
59. Someone broke a promise.	0	1	2	3	4	5
60. Can't concentrate.	0	1	2	3	4	5
61. Someone did a "pet peeve" of yours.	0	1	2	3	4	5
62. Living with boy-/girlfriend.	0	1	2	3	4	5
63. Felt need for transportation.	0	1	2	3	4	5
64. Bad haircut today.	0	1	2	3	4	5
65. Job requirements changed.	0	1	2	3	4	5
66. Missed your period and waiting.	0	1	2	3	4	5
67. Felt some peer pressure.	0	1	2	3	4	5
68. You have a hangover.	0	1	2	3	4	5
69. Coping with addictions.	0	1	2	3	4	5
70. Problem getting home from bar when drunk.	0	1	2	3	4	5
71. Used a fake ID.	0	1	2	3	4	5
72. No sex in a while.	0	1	2	3	4	5
73. Someone cut ahead of you in line.	0	1	2	3	4	5

74. Checkbook didn't balance.	0	1	2	3	4	5
75. Visit from a relative and entertaining them.	0	1	2	3	4	5
76. Decision to have sex on your mind.	0	1	2	3	4	5
77. Thoughts about future.	0	1	2	3	4	5
78. Change of environment (new doctor, dentist, etc.)	0	1	2	3	4	5
79. Exposed to upsetting TV show, book, or movie.	0	1	2	3	4	5
80. Lack of money.	0	1	2	3	4	5
81. Holiday.	0	1	2	3	4	5
82. Sick, injury.	0	1	2	3	4	5
83. Death (family member **or** friend).	0	1	2	3	4	5

Others (List below):

84.	0	1	2	3	4	5
85.	0	1	2	3	4	5

86. How much stress or pressure are you under this week?

much less than usual   less than usual   about the usual level of stress

more than usual   much more than usual

Appendix B: Supplemental Tables & Graphs

Table B1

Participant characteristics: Frequency of TTS

	Frequency	Percent	Cumulative Percent
Total Tenderness Scores (0 – 100)			
0	**71**	**23.5**	**24.5**
1	36	11.9	36.9
2	27	8.9	46.2
3	**20**	**6.6**	**53.1**
4	19	6.3	59.7
5	15	5.0	64.8
6	16	5.3	70.3
7	4	1.3	71.7
8	**10**	**3.3**	**75.2**
9	7	2.3	77.6
10	10	3.3	81.0
11	4	1.3	82.4
12	5	1.7	64.1
13	6	2.0	86.2
14	5	1.7	87.9
15	4	1.3	89.3
16	3	1.0	90.3
17	3	1.0	91.4
18	3	1.0	92.4
19	2	.7	93.1
20	2	.7	93.8
22	3	1.0	94.8
23	2	.7	95.5
25	2	.7	96.2
26	1	.3	96.6
28	1	.3	96.9
35	1	.3	97.2
37	1	.3	97.6
40	1	.3	97.9
43	2	.7	98.6
44	1	.3	99.0
45	1	.3	99.3
54	1	.3	99.7
73	**1**	**.3**	**100**
Total	290	96.00	100.00

Note. Approximate quartiles are indicated in bold.

Table B2
Participant characteristics: PrimeMD diagnosis by group

	Session 1 (N = 295)	Session 2	
		High PMT (N = 24)	Low PMT (N = 36)
Mood Disorder			
Major Depressive Disorder	12 (4.1%)	2 (8.3%)	-
Partial Remission of Major Depressive Disorder	6 (2.0%)	1 (4.2%)	-
Dysthymia	4 (1.4%)	2 (8.3%)	-
Minor Depressive Disorder	12 (4.1%)	5 (20.8%)	1 (2.8%)
R/O Bipolar Disorder	3 (1.0%)	-	-
Anxiety Disorder			
Panic Disorder	5 (1.7%)	1 (4.2%)	1 (2.8%)
Generalized Anxiety Disorder	5 (1.7%)	3 (12.5%)	-
Anxiety Disorder NOS	17 (5.6%)	3 (12.5%)	1 (2.8%)
Alcohol Disorder			
Probable Alcohol Abuse/Dependence	8 (2.7%)	3 (12.5%)	1 (2.8%)
Eating Disorder			
Binge Eating Disorder	1 (0.3%)	-	-
Bulimia Nervosa, Purging Type	-	-	-
Bulimia Nervosa, Nonpurging Type	-	-	-

Table B3
Headache diagnosis by group

	Session 1 Participants (N = 299)	Session 2 Participants	
		High PMT (N = 24)	Low PMT (N = 36)
Headache Diagnosis			
Migraine	23	5	2
Infrequent Episodic Tension Type	16	0	6
Frequent Episodic Tension Type	3	0	1
Chronic Tension Type	10	0	0

Note. Not every participant who reported headache activity qualified for a headache diagnosis according to IHS criteria. In many cases, symptoms reported did not allow for clear classification according to HIS criteria.

Appendix C: Supplemental Analyses

In order to determine whether the observed differences between high and low PMT groups on measures of experimental pain and affect could be attributed to the presence of persistent pain, an independent samples T-test was conducted to examine differences between high PMT individuals with ongoing pain and high PMT individuals without ongoing pain on these measures (including PPT, MTPS, BDI, BAI, USQ, PCS, MPQ, family history, and presence of PrimeMD disorder). Though the group N's were small (high PMT with ongoing pain N = 9, high PMT without ongoing pain N = 15), differences approaching significance were found between the two groups on total USQ score (Ongoing pain mean score = 9.87, Without ongoing pain mean score = 6.65; p = .03) and total MPQ (Ongoing pain mean score = 1.87; Without ongoing pain mean score = 1.07; p = .005). A chi-square analysis was conducted to determine any differences between high PMT participants with and without ongoing pain on presence of a PrimeMD disorder, presence of family chronic pain disorder, or presence of family psychiatric disorder. The only difference approaching significance between the two groups was on presence of a PrimeMD disorder (X2 = 4.00, p = .046). Approximately 89% of high PMT participants with ongoing pain were also diagnosed with a PrimeMD disorder, while only 33% of those without ongoing pain in the high PMT group were diagnosed with a PrimeMD disorder.

Similar analyses were conducted to examine significant group differences between participants in the high PMT group who did not report ongoing pain (N = 15) and low PMT participants who did not report ongoing pain (N = 29). Differences at or approaching significance between the two subgroups were found on finger PPT (high PMT mean = 2.73, low PMT mean = 4.49; p = .001), temporalis PPT (high PMT mean =

4.50, low PMT mean = 6.21; p = .012), BAI total scores (high PMT mean = 8.67, low

PMT mean = 4.96; p .026), MPQ total scores (high PMT mean = 4.73, low PMT mean =

1.34; p = .008), and MTPS total scores (high PMT mean = 94.33; low PMT mean =

16.25; p < .001). A chi-square analysis was conducted to determine any differences

between high PMT without ongoing pain and low PMT participants without ongoing pain

on presence of a PrimeMD disorder, presence of family chronic pain disorder, or

presence of family psychiatric disorder. Differences approaching significance were found

between the two groups on family history of a chronic pain disorder (X^2 = 4.86, p = .028).

Approximately 53% of high PMT subjects without ongoing pain reported a family history

of a chronic pain disorder, while only 21% of those in the low PMT group without

ongoing pain reported a similar family history.