The effect of vaginal and cervical self-stimulation on pain thresholds and intensity in women with chronic pain

by

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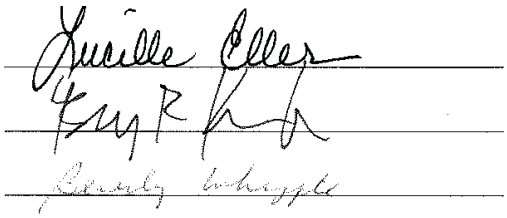

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ABSTRACT

The effect of vaginal and cervical self-stimulation on pain thresholds and intensity in women with chronic pain

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The purpose of this study was to determine the effect of vaginal self-stimulation (VS-S) and cervical self-stimulation (CS-S) on: chronic pain intensity (CPI), pain detection threshold (PDT), and pain tolerance threshold (PTT); the time course of the induced analgesia; the duration of the effect; whether there was a difference between VS-S and CS-S on the dependent variables; and determine the relationship of other independent variables and the effect of VS-S and CS-S.

It was hypothesized that in women with chronic pelvic, abdominal, or low back pain: VS-S and CS-S would decrease CPI and increase PDT and PTT during stimulation; CS-S would have a significantly greater effect than VS-S; and the effect would outlast stimulation.

Subjects were screened for exclusion criteria prior to being randomly assigned to either VS-S or CS-S for the first experimental session; the alternate method was applied in a second experimental session within two weeks of the first session. The Multidimensional Pain Inventory (MPI), a background data sheet, the Pain-o-Meter (POM), and the Ugo Basile Analgesy meter were used to collect information about CPI, PDT, and PTT. A curved stimulator apparatus was used to self-stimulate the anterior

vaginal wall and a straight stimulator was used to self-stimulate the cervix. Subjects continued to record their CPI following each experimental session.

There was no statistically significant CPI change during VS-S or CS-S. In women with visceral pain, CPI increased and PDT and PTT decreased during VS-S. There were significant changes in PDT and PTT during VS-S and CS-S two subjects with somatic pain. There were differences in the response to self-stimulation by the type of somatic pain, inflammatory or non-inflammatory. Although not statistically significant, the effect of VS-S was greater than CS-S on CPI, PDT, and PTT. The effect of both VS-S and CS-S outlasted stimulation.

Although the results must be viewed cautiously based on the small sample size, this study is the first human study to demonstrate a difference in the effect of neurostimulation on analgesia and pain thresholds based on the type of pain, visceral, somatic, inflammatory, or non-inflammatory. Additional research is needed to substantiate this finding.

Preface

Acknowledgements

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Chapter 1

"Pleasure and pain destroy one another…" Benjamin Franklin

Discussion of the problem

Neuroanatomy and Physiology of Pain

Acute Pain

The experience of pain is the result of a complex series of physiological, biochemical, and psychological activities. Pain can be categorized into acute and chronic pain. Acute pain serves as a warning of actual or potential injury to the organism following noxious stimulation. In acute pain conditions, a noxious stimulus is transduced through thermal, mechanical, or chemical receptor cells, causing an impulse that activates the peripheral afferent neurons (Devor, 1999). At the synapse of the peripheral afferent neuron and the central nervous system neuron, the painful neural impulse triggers the release of neurotransmitters, neuromediators, and neuromodulators that have excitatory or inhibitory effects on transmission through the dorsal horn (Moore, K. A., Baba, & Woolf, 2000; Pleuvry & Lauretti, 1996; Terman & Bonica, 2001). From the dorsal horn the impulse is transmitted via the spinothalamic tract, the spinoreticular tract, the spinomesencephalic tract, or the dorsal column tract to the brain where it is detected and interpreted as pain (Heavner & Willis, 2000; Markenson, 1996; Willis, 1985).

Chronic pain

In chronic pain, there is often no identifiable noxious stimulus or pathology to account for the experience of pain. According to the International Association for the Study of Pain (IASP) definition (Merskey & Bogduk, 1994) "many people report pain in the absence of tissue damage or any likely pathophysiological cause; usually this happens

for psychological reasons" (p.210). However, over the last decade this psychological explanation of chronic pain has been questioned (Gamsa, 1990; Gupta, 1986) with psychological symptoms of chronic pain now viewed as consequences of chronic pain not antecedent to chronic pain and pathophysiological explanations now predominate (Breen, 2002).

Although the exact pathophysiological mechanism of chronic pain remains unknown, it appears that there are both peripheral and central mechanisms involved. It is unclear at what level or in what order this pathophysiological process occurs. Peripherally, there is evidence that there is an inflammatory cascade of events that results in increases in potassium, bradykinin, prostaglandins, 5-hydroxytryptamine (5-HT; serotonin), histamine, and cytokines all of which increase cell permeability causing plasma extravasation and directly or indirectly hypersensitize the peripheral afferent nerves (DeLeo & Yezierski, 2001; Devor, 1999; Sutherland, Cook, & McCleskey, 2000). Inflammatory activity also increases neurotrophic activity, releasing nerve growth factor (NGF), which stimulates the development of nerve sprouts that reportedly more readily transmit and amplify painful and innocuous stimuli (Dray, 1996). As a result of either neural injury or large amounts of glutamate activating DL-α-amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid (AMPA) receptors over a long period of time, the n-methyl-D-aspartate (NMDA) ionotropic receptor channels on afferent nerve terminals that are normally silent are activated allowing less peripheral stimulation, including non-noxious stimuli, to initiate a painful response (Basbaum, Bautista, Scherrer, & Julius, 2009; Brookoff, 2000). Ultimately peripheral neuronal plasticity, changes in neuronal cell function and structure, can perpetuate pain in the absence of stimulation (Zimmermann &

Herdegen, 1996). Centrally there are altered gating responses of sodium and calcium ion channels (Basbaum et al., 2009; Cummins, Dib-Hajj, Black, & Waxman, 2000) and specific receptor channels, such as N-methyl-D-aspartate (NMDA), γ-Aminobutyric acid (GABA) and tachykinin receptors (Baranauskas & Nistri, 1998; Black et al., 2001). Altered gating results in action potential windup, allowing wide dynamic range (WDR) neurons, that do not normally conduct painful stimuli, to conduct noxious stimuli in addition to the conduction by nociceptive specific neurons thus changing the normal transmission through the dorsal horn (Moore, K. A. et al., 2000; Pockett, 1995; Roberts, Beyer, & Komisaruk, 1986; Terman & Bonica, 2001). Furthermore, activation of receptor channels alters the release of neuropeptides, monoamines, amino acids, and other neurochemicals that serve as neurotransmitters, neuromediators, and neuromodulators, including cholecystokinin (CCK), calcitonin gene related peptide (CGRP) prostanoids (PGE2), protein kinase C (PKC), 5-hydroxytryptamine (5-HT, serotonin), substance P (SP) that activates neurokinin-1 (NK-1) receptors, vasoactive intestinal peptide (VIP), enkephalin, γ-Aminobutyric acid (GABA), glycine, norepinephrine, and orphanin FQ/nociceptin (OFQ) (Abbadie, Brown, Mantyh, & Basbaum, 1996; Christensen & Hulsebosch, 1997; Delander, Schott, Brodin, & Fredholm, 1997b; Dray, 1996; Malmberg, 2000). Altered transmission, mediation, and modulation of pain may lead to long-term potentiation or long-term depression that may be responsible for peripheral and central sensitization (Basbaum et al., 2009; Moore, K. A. et al., 2000; Sandkuhler, Benrath, Brechtel, Ruscheweyh, & Heinke, 2000). Abnormal patterns of neuroactive chemicals in the dorsolateral prefrontal cortex of individuals with chronic pain compared with healthy controls indicate central neurotransmitter neuroplasticity (Grachev,

Fredrickson, & Apkarian, 2000). Long-term changes in the somatosensory pathways alter gene expression. Although the duration and chronology of immediate early gene (IEG) expression in animal models of chronic pain resembles immediate early gene (IEG) expression in acute pain, in chronic pain models c-jun, a neuropeptide that regulates the expression of other genes that stimulate second and third messenger ribonucleic acid (mRNA), remains elevated and may be related to plastic changes in the spinal cord (Delander, Schott, Brodin, & Fredholm, 1997a; Delander et al., 1997b; Devor, 1999). As a consequence of these biochemical and genetic changes, neuroinflammation, nerve sprouting, neuronal plasticity, and central reorganization develop, resulting in peripheral and central sensitization that may perpetuate chronic pain (Goff, Burkey, Goff, & Jasmin, 1998; Sandkuhler et al., 2000; Zimmermann & Herdegen, 1996).

Treatment of chronic pain has focused on the mechanisms apparently involved in chronic pain. These include blocking neuroreceptor channels with drugs such as opiate agonists that bind to and activate endogenous opioid receptors (McCaffery & Pasero, 1999; Vaccarino & Kastin, 2001) and Gabapentin (Neurontin), an n-methyl-D-aspartate (NMDA) receptor channel blocker (Gu & Huang, 2001; Parsons, 2001). Other pharmacological treatment is aimed at reducing the inflammatory process, using nonsteroidal anti-inflammatory drugs (NSAIDs). Still other treatments are aimed at centrally increasing the level of serotonin, using drugs such as tramadol hydrochloride (Ultram), that inhibits the reuptake of serotonin, Finally, neurotransmitters can be blocked or depleted, for example, Capsaicin depletes substance P (SP) from the primary afferent terminals in the dorsal horn (Pleuvry & Lauretti, 1996). Although some pharmacological interventions have been shown to be effective, there are significant

problems with the pharmacological management of chronic pain. For example, long term opiate therapy not only is associated with tolerance, dependence, and the significant stigma of addiction (Haddox et al., 1996; McQuay, 1997), but there is evidence that indicates that it can result in hyperalgesia and allodynia through an interaction with n-methyl-D-aspartate (NMDA) receptors (Mao, 1999; Vaccarino & Kastin, 2001), alteration of spinal glutamate transporters (Mao, Sung, Ji, & Lim, 2002a), or increased neuronal apoptosis (Mao, Sung, Ji, & Lim, 2002b). In addition, the complexity of chronic pain often makes it difficult to know which drug to order, the dose needed to reduce pain often results in significant side effects, and it is rare for any drug to eliminate the pain (Cervero & Laird, 1996; Ferrell, McCaffery, & Rhiner, 1992; Parsons, 2001; Pleuvry & Lauretti, 1996). Non-pharmacological measures in the management of chronic pain have focused on stimulation of both the peripheral and central nervous systems (Stanton-Hicks & Salamon, 1997).

The long-term effectiveness of peripheral stimulation using transcutaneous electrical nerve stimulation (TENS) units to manage chronic pain is inconclusive and may be related to the type, distribution, and intractability of pain (Lampl, Kreczi, & Klingler, 1998; Moore, C. D., McQuay, Fairman, Tramer, & Leijon, 2002). Additionally, there is evidence that for chronic pain, acupuncture may not be more effective than placebo or no treatment (Ezzo et al., 2000). Finally, spinal cord stimulation (SCS) is not effective for all types of pain, the effectiveness is reduced over long-term therapy, and concomitant drug therapy is often needed to bolster its effectiveness (De La Porte & Van de Kelft, 1993; Doerr, Krainick, & Thoden, 1978; Kemler et al., 2001; Meilman, Leibrock, & Leong, 1989; Meyerson & Linderoth, 2000; North, Kidd, Wimberly, & Edwin, 1996).

Prevalence of Chronic Pain in Women

In international, epidemiological studies chronic pain prevalence is reported to range from 2% to 40% with point prevalence of 14% to 21.5% (Gureje, Von Korff, Simon, & Gater, 1998; Verhaak, Kerssens, Dekker, Sorbi, & Bensing, 1998). In a review of 105 epidemiological studies Unruh (1996) reported that chronic pain is more prevalent, more severe, and of longer duration in women than in men. Subsequent studies have supported the finding that chronic pain is significantly over-represented in women (Gureje et al., 1998; Verhaak et al., 1998).

Influence of Reproductive System on Pain Detection and Pain Tolerance Thresholds

Berkley (1997) deductively reasoned that the female reproductive structure, with direct vaginal and cervical access to visceral organs, might increase vulnerability to infection and painful diseases and that reproductive function including large variation in hormone cycles, monthly and over time, during the onset of menses, pregnancy and menopause, may act as a noxious stimulus or may condition women over time to experience pain in the absence of a stimulus. Brody (1997) argued against Berkley's premise stating that the vagina is not only resistant to pathogens that may cause painful disease but there is evidence that vaginal stimulation is a source of intense pleasure and analgesia (Crowley, Jacobs, Volpe, Rodriguez-Sierra, & Komisaruk, 1976; Whipple & Komisaruk, 1985; , 1988), accentuated by orgasm (Whipple & Komisaruk, 1988).

Endogenous Descending Inhibitory System

According to the gate control theory (Melzack & Wall, 1965) "the presence or absence of pain is determined by the balance between the sensory and central inputs to the gate control system" (p.977). There is evidence that pain is modulated through an

endogenous, descending, inhibitory system (Melzack, 1999a; Melzack & Wall, 1965). Once a critical level of nociception (Basbaum & Fields, 1978; Willis, 1985) is reached, afferent impulses activate the central control system, stimulating cells of the dorsal column that activate a descending inhibitory control mechanism that modulates input to the transmission cells through the gate. The descending system controls pain by limiting at the gate the amount of ascending nociceptive information reaching the brain through activation of the GABAergic inhibitory interneurons (Basbaum et al., 2009) and alterations in the production and release of neurotransmitters. This antinociceptive system controls pain through endogenous opioid and nonopioid mechanisms. The endogenous opioid mechanism modulates pain at the brainstem level through endogenous opioid peptides and opioid receptors found in the periaqueductal gray (PAG) and sensory relay nuclei such as the solitary tract nucleus (nTS) in the caudal medulla and at the spinal cord dorsal horn (Basbaum & Fields, 1978; Pertovaara, 2000). Endogenous opioids decrease activation of the receptors that amplify pain signals (Moore, K. A. et al., 2000). The nonopioid antinociceptive mechanism involves both noradrenergic and serotonergic systems. 5-Hydroxytryptamine (5-HT, serotonin), released by the locus coeruleus (LC) and the nucleus raphe magnus (NRM) of the medulla, has been linked to pain control with increased serotoninergic neurotransmission increasing pain thresholds (Basbaum & Fields, 1978; Bonica, 1977; Singewald & Philippu, 1998; Zimmermann & Herdegen, 1996).

In chronic pain, there may be diminished pain modulation by the endogenous descending inhibitory system mechanism. It has been suggested that either the magnitude, frequency, and duration of noxious stimulation in chronic pain overwhelms

the descending antinociceptive system or an impairment in the endogenous system is related to increased pain sensitivity and the development of chronic painful conditions (Bruehl, McCubbin, & Harden, 1999; Maixner, Fillingim, Sigurdsson, Kincaid, & Silva, 1998). There may be pathophysiological dysfunction in the production of serotonin and endogenous opioids in chronic pain conditions (Sundblom et al., 1997; Zimmermann & Herdegen, 1996). Furthermore neuropathic injury may reduce the number of pre-synaptic C-fiber opioid receptors available for pain reduction (Cervero & Laird, 1991; , 1996; Dickenson, 1996). These changes in the opioid and nonopioid endogenous descending inhibitory system may result in changes in effective synaptic transmission (Baranauskas & Nistri, 1998). Decreased inhibitory control of pain may ultimately lead to hyperexcitability that can produce central structural reorganization (Zimmermann & Herdegen, 1996).

Stimulation-Produced Analgesia

The term "stimulation produced analgesia" (p.1353) was coined by Mayer, Wolfle, Akil, Carder and Liebeskind (1971) who identified specific areas of the brain, including the dorsal and ventral tegmentum, the dorsal and medial thalamus, and the juncture of the ventral tegmentum and posterior hypothalamus, which when stimulated resulted in analgesia that outlasted stimulation. Melzack (1977) proposed that intense peripheral stimulation also produces analgesia. Various pain interventions have been predicated on sensory stimulation of A fibers, theorizing that "intense stimulation is potentially capable of inhibiting pain signals and may represent an important clinical approach to the modulation of pain" (Melzack, 1977, p. 81) by inhibiting wide dynamic range neuron response to noxious input (Devor, 1999). Peripheral stimulation is most

effective when it is applied close to the painful body site and produces analgesia by stimulating the same somatotopic area of the midbrain, releasing endogenous opiates, and activating the descending inhibitory system (Soper & Melzack, 1982). Increasing sensory input, from simple stimulation such as rubbing, or massage, to more complex stimulation through electrical counter stimulation, can increase both pain detection threshold and pain tolerance threshold (Anand & Craig, 1996; Maspes & Pagni, 1974; Melzack, 1977; Sternbach, 1970).

Vaginal-cervical stimulation (VCS) is a form of peripheral stimulation-produced analgesia. VCS in animals (Komisaruk & Larsson, 1971; Komisaruk & Wallman, 1977) and VS-S in women (Whipple, 1986; Whipple & Komisaruk, 1985) have been shown to produce analgesia. This analgesic effect might be the result of increasing A-δ fiber activity closing the gate by presynaptic stimulation of the Lamina 5 cells, thought to be the transmission cells of the gate (Henry, 1983; Komisaruk & Wallman, 1977). VS-S has also been found to effectively raise pain detection threshold and pain tolerance threshold to experimentally induced pain in women, including four women with chronic pain (Komisaruk & Whipple, 1986; Whipple, 1986).

Statement of the Problem

Based upon the above findings, the following questions are raised. Primarily, what is the effect of vaginal-cervical self-stimulation (VCS-S) on chronic pain intensity, pain detection threshold, and pain tolerance threshold in women with chronic pelvic, abdominal, or low back pain? Sub questions include: 1) What is the time course of the effect of VCS-S on chronic pain intensity, pain detection threshold, and pain tolerance threshold? 2) Does the effect of cervical self-stimulation (CS-S) on these measures differ

from that of vaginal self-stimulation (VS-S)? 3) What is the duration of the VS-S and CS-S effect on chronic pain intensity, pain detection threshold, and pain tolerance threshold? Finally, 4) What effect does the force used in stimulation, menstrual cycle, reproductive stage, opiate drugs used to manage chronic pain, the duration of chronic pain, and pain classification have on the effect of VS-S and CS-S in women with chronic pelvic, abdominal, or low back pain?

Definition of terms

Chronic Pain Intensity

For this study, chronic pain intensity was defined as the amount of chronic pelvic, abdominal, or low back pain. Chronic abdominal or pelvic pain is a form of chronic visceral pain attributed to endometriosis, dysmenorrhea, urethral syndrome, interstitial cystitis, irritable bowel syndrome, and unknown etiology that may result in abdominal, thigh and low back pain, although back pain is often cited as the most frequent (47.8%) symptom of all forms of chronic pelvic pain (Banerjee, Farrell, & Lembo, 2001; Cervero & Laird, 1999; Collett, 2001; Gambone et al., 2002; Gurel & Atar Gurel, 1999; McMahon, 1997; O'Leary, Sant, Fowler Jr, Whitmore, & Spolarich-Kroll, 1997; Wesselmann & Czakanski, 2001; Wesselmann & Lai, 1997). Chronic low back pain may be referred pelvic pain or attributed to musculoskeletal disorders, arthritis, or unknown etiology. Chronic pain intensity in this study was operationalized as the subject's self-reported chronic pain intensity measured as the number of centimeters on the 10 cm visual analog scale of the Pain-o-Meter (POM-VAS) and the summed physical and emotional intensity scores determined using the verbal rating scale of the Pain-o-Meter (POM-WDS) (Gaston-Johansson, 1996; Gaston-Johansson, Franco, & Zimmerman,

1992; Hofgren, Karlson, Gaston-Johansson, & Herlitz, 1994; Sittner, Hudson, Grossman, & Gaston-Johansson, 1998). Chronic pain intensity can only be measured indirectly, all measures of pain are subjectively reported, and there is no absolute standard against which to measure reported pain. The sensory and affective components of pain may act independently or together to create an intensity response. For naturally occurring pain the sensory, affective, and evaluative aspects of pain can be measured (Melzack, 1983; Melzack & Casey, 1968).

Vaginal Self-Stimulation (VS-S) and Cervical Self-Stimulation (CS-S)

VS-S and CS-S are forms of peripheral nerve stimulation performed by the woman herself. The hypogastric and pelvic nerves are stimulated during vaginal stimulation and additionally the vagus nerve is stimulated during cervical stimulation (Berkley, Guilbaud, Benoist, & Gautron, 1993; Cueva-Rolon et al., 1996; Cunningham, Steinman, Whipple, Mayer, & Komisaruk, 1991; Komisaruk, Adler, & Hutchison, 1972; Komisaruk et al., 1996; Peters, L. C., Kristal, & Komisaruk, 1987). VS-S was operationalized as pressure of less than 10 lb/in^2 applied by the subject in a way that feels pleasurable to the anterior vaginal wall for 10 to 12 minutes (Komisaruk, Gerdes, & Whipple, 1997). CS-S was operationalized as pressure of less than 10 lb/in^2 applied for 10 to 12 minutes by the subject in a way that feels pleasurable to the cervix of the uterus that is protected by a diaphragm (Komisaruk et al., 1997).

Pain Detection Threshold (PDT)

Pain detection was defined in this study as the moment a subject first perceives the gradually increasing intensity of experimentally-induced pressure to be pain. It was operationalized as the amount of force in grams at which the woman says “pain,”

averaged over the four fingers of the woman's non-dominant hand, applied using the Ugo Basile Analgesy-Meter (Stoelting Co., Wood Dale, IL). The Analgesy-Meter was used to both create experimental pain and to measure pain detection threshold.

Pain Tolerance Threshold (PTT)

Pain tolerance threshold was defined in this study as the point at which experimentally-induced pressure pain becomes too uncomfortable for the subject to continue to bear. It was operationalized as the amount of force in grams, at which the woman says "stop" and the pressure increase is stopped, averaged over the four fingers of the woman's non-dominant hand, applied by the Ugo Basile Analgesy-Meter (Stoelting Co., Wood Dale, IL).

Delimitations

Only women were the subjects in this study because the study used vaginal and cervical self-stimulation. The women included in the study were over the age of 18, in any menstrual phase or reproductive stage, who had a steady state of chronic pelvic, abdominal, or low back pain, who were on a steady dose and frequency of pain medication. Only subjects over the age of 18 were included in the study to avoid any concerns related to testing children using VS-S and CS-S. Only women who spoke and were able to read English and were cognitively intact were included because verbal communication with the PI who only speaks English was necessary during testing and subjects had to read, understand, and answer questions on the Multidimensional Pain Inventory (MPI). Excluded from the study were women who were pregnant or had any physical or gynecological condition that her health care provider deemed to be a risk. Women with a history of sexual abuse, active substance abuse, active suicidal ideation, or

psychosis were excluded from the study.

Significance

The findings of this study will add to our understanding of VS-S and CS-S under conditions in which the technique has not been used. The effect of VS-S and CS-S in the presence of chronic pain in an area close to stimulation and with women using medication to control chronic pain is unknown. If VS-S and CS-S activate the descending inhibitory control system and that system is dysfunctional, will there be the same effect? Therefore, finding that VS-S or CS-S has no effect or only a partial analgesic effect in the presence of chronic pain will add to our understanding of this mechanism. Finding that VS-S or CS-S has an analgesic effect will confirm previous findings and extend our understanding of this mechanism. The findings of this study will add to our understanding of chronic pelvic, abdominal, and low back pain, which has been particularly difficult to treat, and chronic pain control.

Chapter 2

Introduction

This chapter begins by examining the theoretical support for vaginal-cervical stimulation (VCS) as a form of stimulation-produced analgesia (SPA). Then empirical evidence of the effect of vaginal self-stimulation (VS-S) and cervical self-stimulation (CS-S) will be described followed by evidence that suggests that the effect of VCS may outlast the period of stimulation. Next, the theoretical support of the relationship between SPA, chronic pain intensity, pain detection threshold (PDT), and pain tolerance threshold (PTT) will be described. Finally, based on the evidence presented, it will be hypothesized that both VS-S and CS-S will modulate chronic pain intensity, PDT, and PTT to experimentally induced mechanical pressure pain that outlasts the period of stimulation and that CS-S will have a greater effect.

Independent Variables

Stimulation Produced Analgesia

Theoretical Support for Stimulation Produced Analgesia

According to the gate control theory (Melzack & Wall, 1965) "the presence or absence of pain is determined by the balance between the sensory and central inputs to the gate control system" (p.977). Afferent impulses arriving at the substantia gelatinosa (SG) over large A fibers close the gate, preventing impulses from reaching the transmission cells of the dorsal horn. Afferent impulses that arrive at the substantia gelatinosa (SG), located in laminae II and III, over small C fibers open the gate allowing painful impulses to reach the transmission cells. Once a critical level is reached, the transmission cells stimulate pathways that project to the brain (Melzack & Casey, 1968).

In addition, afferent impulses stimulate cells of the dorsal column activating an endogenous descending inhibitory control system that pre- and post-synaptically modulates input to the transmission cells (Melzack, 1977). Various treatment modalities have been based on the concept of descending inhibitory control over the gate theorizing that "intense stimulation is potentially capable of inhibiting pain signals and may represent an important clinical approach to the modulation of pain" (Melzack, 1977, p.81). The resulting pain modulation has been called stimulation-produced analgesia (Mayer et al., 1971).

Vaginal-cervical stimulation produced analgesia

In an early study with rats, Komisaruk and Larsson (1971) found that either stimulating the lower vaginal tract or stimulating the cervix suppressed both leg withdrawal reflex and vibrissa retraction to noxious pinch. In a subsequent study, Komisaruk, Adler and Hutchinson (1972) reported that stimulation of the vaginal wall and cervix activated the pelvic nerve. Subsequently researchers (Cunningham et al., 1991) demonstrated that the analgesic effect of VCS on tail flick latency (TFL) was almost abolished by transection of both the pelvic and hypogastric nerves but not by transection of either the pelvic or the hypogastric nerve leaving the other nerve intact. The analgesic effect of vaginal stimulation on vocalization threshold (Voc-T) to electrical shock to the tail was abolished by bilateral transection of both the hypogastric and pelvic nerves and reduced by bilateral transection of the hypogastric nerves although bilateral transection of the pelvic nerves had no effect on vocalization threshold (Voc-T) (Cunningham et al., 1991). However, pelvic neurectomy significantly reduced ($\underline{p} < 0.05$) while hypogastric neurectomy significantly increased ($p < 0.05$) the analgesic response to

VCS, as measured by tail flick latency (TFL), compared with controls (Gintzler & Komisaruk, 1991). "These findings suggest that the pelvic and hypogastric nerves activate separate pain-inhibitory systems that utilize distinct neurotransmitters / neuromodulators, thereby differentially affecting the TFL and Voc-T responses" (Cunningham et al., 1991, p.342).

There is evidence that in cats VCS evokes responses in wide dynamic range (WDR) and nociceptive-specific (NS) neurons (Price, Bushnell, & Iadarola, 1981). Stimulation of afferent fibers of the hypogastric nerve convey input to dorsal horn neurons located in T13 through L1 and afferent fibers of the pelvic nerve convey input to the neurons located in L6 through S2 (Berkley, Hubscher, & Wall, 1993). “C-fos-protein-like immunoreactivity in the nuclei of postsynaptic neurons of the dorsal horn of the spinal cord” (Hunt, Pini, & Evan, 1987, p. 632) has been used to localize the effect of VCS in the spinal cord. Significantly more c-fos cells ($p < 0.05$) have been found in laminae I, IV, V-VI, and X of L5-S1 following VCS than in control animals indicating that these laminae may be related to stimulation of the endogenous descending nonopioid inhibitory system (Chinapen, Swann, Steinman, & Komisaruk, 1992).

There is evidence to suggest that VCS continues to have an analgesic effect even when the spinal cord is transected. For example, in an early study with rats, Komisaruk and Larsson (1971) reported that cervical probing continued to suppress leg withdrawal to noxious stimulation even after a complete mid-thoracic transection of the spinal cord, above the level at which both pelvic and hypogastric nerves enter the spinal cord. Similarly, VCS continued to produce a significant increase ($p < 0.05$) in tail flick latency (TFL) following spinal transection at T2 (Watkins, Faris, Komisaruk, & Mayer, 1984).

Furthermore, although bilateral pelvic and hypogastric neurectomy abolished motor responses to VCS, the analgesic response persisted, supporting the contention that VCS evokes non-spinal, vagal nerve stimulation (Cueva-Rolon et al., 1996; Cueva-Rolon et al., 1991). Hubscher and Berkley (1995) subsequently reported that responses of neurons of the solitary tract nucleus (nTS) to mechanical stimulation of the vagina and cervix were eliminated or reduced following vagotomy and complete spinal transection above L1 following vagotomy eliminated all response to vaginal and cervical stimulation. In yet another study (Komisaruk et al., 1996) rats with spinal cords transected at T7 (T7X) or L5 (L5X) continued to have a significant increase ($p < 0.002$) in vocalization threshold (Voc-T) in response to VCS compared with pre-stimulation. Following vagotomy, there was no response to VCS in the T7X group. These findings indicate "that in the female rat, vagus nerves provide a functional afferent extramedullary pathway from the female genital tract directly to the brainstem, thus bypassing the spinal cord" (Komisaruk et al., 1996, p. 133).

In women with spinal cord injuries at T10 or higher, VS-S significantly increased PDT (91.6%, $p < 0.01$) and PTT (46.1%, $p < 0.01$) and CS-S significantly increased PDT (72.7%, $p < 0.05$) and PTT (36.5%, $p < 0.01$) over the control conditions (Komisaruk et al., 1997). The researchers concluded that "in light of positive evidence of a functional vagal afferent pathway in rats, we postulate a genital sensory role for the vagus nerves in humans" (Komisaruk et al., 1997, p.1519). Furthermore, in recent studies of women with spinal cord injury (SCI) and one uninjured woman using positron emission tomography (PET) scans and magnetic resonance imaging (MRI) (Komisaruk et al., 2002; Whipple & Komisaruk, 2002) response to vaginocervical stimulation in the solitary tract nucleus

(nTS) the sensory nucleus of the vagus led researchers to conclude "that the Vagus nerves provide a spinal cord-bypass pathway for vaginal– cervical sensibility in women with complete spinal cord injury above the level of entry into spinal cord of the known genitospinal nerves" (Komisaruk et al., 2004, p. 77).

Investigators have reported that neurons located in the midbrain, the caudal brainstem (Rose, 1975), the medulla, the pons (Hornby & Rose, 1976), the brain stem reticular formation, midbrain central gray, deep tectum, and a small number in the posterior diencephalon (Rose, 1979) responded to VCS. Komisaruk and Wallman (1977) found that cervical stimulation suppressed thalamic neuron response to noxious stimulation in rats. Finally, vaginal stimulation (VS) continued to have a significant analgesic effect in rats despite mid-collicular decerebration ($p < 0.001$), spinal transection at T2 ($p < 0.05$) and bilateral destruction of the dorsolateral funiculus (DLF) ($p < 0.001$) (Watkins et al., 1984). These results suggest that the endogenous inhibitory pathway arises below the mid-collicular level from the caudal brainstem and "projects to the spinal cord through the DLF" (Watkins et al., 1984, p.62).

Activation of the endogenous opioid mechanism

Is the analgesic effect of vaginal stimulation due to stimulation of an endogenous opioid mechanism? Researchers (Crowley, Rodriguez-Sierra, & Komisaruk, 1977a) found that administration of the morphine antagonist naloxone did not change the analgesic response to noxious stimulation and that vaginal stimulation significantly increased ($p < 0.01$) vocalization threshold (Voc-T) in rats made tolerant to morphine, rats naïve to morphine but given 5mg/kg prior to testing, and rats given a saline injection prior to testing. The researchers concluded that using vocalization threshold as the

analgesic measure, VCS is not a morphine sensitive mechanism. However, Hill and Ayliffe (1981) found that naloxone significantly reduced ($p < 0.01$) the effect of VCS on tail flick latency (TFL) to nociceptive heat stimulation indicating that VCS activates an endogenous opiate mechanism and tail flick latency (TFL) may be an effective measure of endogenous opioid stimulated analgesia while vocalization threshold (Voc-T) may be a measure of endogenous nonopioid stimulated analgesia.

Activation of the endogenous nonopioid mechanism

Crowley, Rodriguez-Sierra and Komisaruk (1977b) tested the effect of norepinephrine (NE), dopamine (DA), and 5-hydroxytryptamine (5-HT, serotonin) on the antinociceptive effect of VCS to determine if VCS activated a nonopioid mechanism of the descending inhibitory system. In a series of experiments with rats, researchers demonstrated that the antinociceptive effect (Voc-T) of VCS is increased by an increase in central and peripheral norepinephrine (NE), blocking dopamine (DA) receptors, and depletion of serotonin. The authors concluded that VCS may "activate a descending noradrenergic system that serves to inhibit further the transmission of pain input in the spinal cord, thereby elevating vocalization thresholds" (Crowley et al., 1977b, p.81). Further evidence that VCS activates this nonopioid mechanism was provided when administration of a high dose of a norepinephrine (NE) antagonist abolished the antinociceptive effect of VCS as measured by vocalization threshold (Voc-T), but not tail flick latency (TFL); administration of a 5-hydroxytryptamine (5-HT, serotonin) antagonist significantly attenuated ($p < 0.001$) the antinociceptive effect of VCS on tail flick latency (TFL), but not vocalization threshold (Voc-T); and spinal fluid levels of norepinephrine (NE) and 5-hydroxytryptamine (5-HT, serotonin) were significantly

increased ($p < 0.01$) over pre-VCS and post-VCS levels (Steinman, J.L., Komisaruk, Yaksh, & Tyce, 1983). Together these findings support the hypothesis that VCS activates a nonopioid (norepinephrine, 5-hydroxytryptamine) mechanism of the endogenous descending inhibitory system.

Effect on neurotransmitters, neuromediators, and neuromodulators

The antinociceptive effect of VCS may also be related to an effect on other neurotransmitters, neuromediators, and neuromodulators. Vasoactive intestinal peptide (VIP) produces analgesia when administered directly to the spinal cord and VIP is released during vaginal stimulation in rats (Komisaruk et al., 1988); therefore the analgesic effect of VCS might be related to (VIP). Studies have indicated that glycine administration resulted in hyperalgesia and that VCS was mediated by glycine, as post-synaptic glycine antagonism produced hyperalgesia (Beyer, Roberts, & Komisaruk, 1985). Subsequently, studies demonstrated that blocking NMDA receptors decreased post-synaptic excitation and enhanced the analgesic effect of glycine released in the spinal cord in response to VCS (Beyer, Komisaruk, Lopez-Colome, & Caba, 1992; Caba, Komisaruk, & Beyer, 1998).

Masters, Jordan, Beyer and Komisaruk (1993) collected spinal fluid from rat spinal cords T12 through S2, the area at which both the hypogastric and pelvic nerves enter the spinal cord, and measured amino acids released in response to VCS and nociceptive stimulation. VCS: significantly increased ($\underline{p} < 0.05$) alanine, arginine, glutamine, phenylalanine and threonine release compared with pre-stimulation levels; significantly increased ($p < 0.01$) the release of taurine over pre-stimulation levels; and significantly increased ($p < 0.005$) the amount of aspartate, glutamate, lysine, and glycine

levels released compared with pre-stimulation levels. Researchers (Steinman, J. L., Hoffman, Banas, & Komisaruk, 1994) similarly found that substance P released into spinal fluid in rats significantly decreased in absolute concentration following VCS alone ($p < 0.004$) or in combination with noxious foot shock ($p < 0.01$) suggesting that "it is possible that the ability of VS to reduce the concentration of substance P released into spinal cord superfusates underlies, at least in part, the analgesia produced by VS" (Steinman, J. L. et al., 1994, p. 207).

Other factors

There are consistent indications throughout the literature cited that reproductive hormones and reproductive stage have an influence on the effect of VCS in animals. In a study (Crowley et al., 1976) in which rats received estradiol benzoate (EB), progesterone, a combination of estradiol benzoate (EB) and progesterone, or no hormones, researchers demonstrated that hormones had no effect on pain thresholds prior to cervical probing but that "EB significantly enhanced the analgesic effects of cervical probing" (p.485) and that progesterone alone had no effect. In another study (Rothfeld, Gross, & Watkins, 1985), 5 µg estradiol significantly increased ($p < 0.05$) tail flick latency (TFL) response to 100 g of cervical pressure and vocalization threshold (Voc-T) response to 200g of force. In animals with ovaries intact, VCS altered the release of noradrenalin and γ-Aminobutyric acid (GABA) in the pre-estrous but not the met-estrous stage, with estrous stage determined by vaginal smear (Guevara-Guzman et al., 2001). The number of c-fos neurons found in the dorsal horn following VCS also varies as a function of the estrous stage with significantly more c-fos neurons in the estrous stage ($p < 0.05$) than in the diestrous stage and significantly more in the diestrous stage ($p < 0.05$) than in the

proestrous stage (Ghanima, Bennis, & Rampin, 2002). These studies indicate that reproductive hormones influence the neuronal, analgesic, and neurochemical response to VCS. However, this influence has not been demonstrated in human studies. Although Whipple (1986) classified women in her study according to their menstrual phase on the day they participated in the VS-S experiment she found "no significant difference in elevation in pain thresholds under various control and experimental conditions among any of the phases of the menstrual cycle (ANOVA, $p > .05$)" (p.64).

Cervical stimulation

Is there a difference between vaginal and cervical stimulation? Komisaruk and Larsson (1971) ligated the vagina to avoid direct contact with the cervix and reported that vaginal stimulation alone and cervical stimulation alone suppressed nociceptive responses. Komisaruk, Adler and Hutchison (1972) attempted to stimulate the cervix without stimulating the vaginal wall by first inserting a glass tube into the vagina pressing against the cervix, waiting for the response to subside, then scraping the surface of the cervix with a wire inserted into the glass tube. However, by inserting the tube into the vagina and pressing against the cervix, both the vaginal wall and the cervix were stimulated. Furthermore, with the glass tube remaining in the vagina during cervical scraping, vaginal distention could have caused additional vaginal stimulation. Therefore, it is unlikely that cervical stimulation was isolated. Although researchers (Berkley, Guilbaud et al., 1993) have differentiated responses of neurons to vaginal stimulus and cervical stimulus, it is more likely that these neurons were responsive to simultaneous vaginal and cervical stimulation. As Erskine (1995) pointed out, in most cases cervical stimulation also stimulates the vaginal wall which results in convergence and summation

of visceral and somatic stimulation (Komisaruk, 1974).

In a study with rats, Gintzler and Komisaruk (1991) used an implanted silastic disc in the uterus with a silk thread attached protruding through the cervix and vagina to apply pressure to the uterine side of the cervix without vaginal stimulation. In this study uterine cervical pressure at 150 g of force significantly increased ($p < 0.03$) tail flick latency (TFL) in six out of 7 rats and at 100 g of force there was a 76 to 100% increase in 3 rats. However, in 4 rats there was a 3 to 21% decrease in tail flick latency (TFL). Furthermore, uterine cervical pressure applied following both pelvic and hypogastric neurectomy significantly decreased ($p < 0.05$) tail flick latency (TFL). Interestingly, this study found that cervical stimulation does not always induce analgesia. Similarly, researchers (Komisaruk et al., 1996) were surprised to find that stimulation of the cervix, following transection of the spinal cord at T7 with the pelvic, hypogastric, and vagus nerves intact, significantly decreased ($p < 0.05$) vocalization threshold (Voc-T). These studies indicate that stimulation of the cervix can either increase or decrease nociceptive response.

Effect may outlast stimulation

Several studies provide evidence that the analgesic response to VCS outlasts stimulation. In rats, the analgesic effect of VS was reported to last for several minutes after probing, gradually diminishing over a period of four to 6.5 minutes (Komisaruk & Wallman, 1977). In yet another study, researchers (Cueva-Rolon, Gomez, Komisaruk, & Munoz-Martinez, 1995) found that at frequencies of 20-80 Hz electrical stimulation of the Aδ fibers of the vicerocutaneous branch of the pelvic nerve completely inhibited leg withdrawal to nociceptive foot pinch that persisted beyond the period of stimulation.

Longer trains of electrical stimulation produced long-lasting inhibition of the response to noxious stimulation persisting for up to 20 minutes after the termination of the stimulation. Finally, Whipple (1986) reported that in one human subject with chronic pain the analgesic effect of VS-S lasted eight minutes beyond stimulation during which time she had total pain relief.

Critical analysis

Although a great deal of research has been conducted on the effects of VCS, there are gaps in the research. First, this method of stimulation-produced analgesia has not been well-tested in humans with various forms of chronic pain. Whipple (1986) conducted a pilot study with four subjects who had chronic pain. According to Whipple (personal communication, March 21, 2003) subjects who had neck pain, low back pain, rheumatoid arthritis, and chest wall pain were asked not to take medication prior to testing. There is no indication of chronic pain intensity or the type or dose of medications subjects may have been using to manage their pain. Moreover, no specific information has been reported regarding the effect of VS-S on pain detection or pain tolerance thresholds or chronic pain intensity except that "their chronic pain decreased on all 4 scales of the McGill Pain Questionnaire during the two VS experimental conditions" (Whipple, 1986, p.142). Whipple has suggested that this is an area for future research.

Although there is abundant evidence in the literature that reproductive hormones affect pain thresholds, Whipple (1986) reported no effect of menstrual cycle on pain thresholds before or during VS-S. However, subsequent human studies have not accounted for this effect. Because menstrual cycle effect on pain thresholds and nonpharmacological methods of pain control remains unclear, especially in women with

chronic pain, studies of chronic pain in women should control for menstrual cycle and reproductive stage.

There have been differences in methods of stimulation, particularly between anterior wall and cervical stimulation, cited in the literature. However, there are few studies comparing the effects of each. In addition, too little time between the applications of various experimental conditions may have confounded the results in some studies. Although the analgesic effect may not significantly outlast stimulation in animals (Gomora, Beyer, Gonzalez-Mariscal, & Komisaruk, 1994; Lee & Erskine, 2000), other neuroendocrine effects may outlast stimulation by four days (Kornberg & Erskine, 1994). Many of the human studies reviewed did not report the duration of effect.

In summary, the studies cited indicate that VCS is a form of intense peripheral stimulation that modulates pain. VCS in animals and humans is a form of stimulation-produced analgesia that stimulates the pelvic and hypogastric nerves, increasing A-fiber stimulation of the wide dynamic range and nociceptive specific neurons of the ventral and dorsal horn of spinal cord segments T13 through S2. VCS also stimulates the vagus nerve, an extraspinal nerve that terminates in the solitary tract nucleus (nTS). VCS activates neurons of the thalamus, amygdala, brainstem, and midbrain, areas that have also been shown to produce analgesia when directly stimulated (Mayer & Liebeskind, 1974; Mayer et al., 1971; Reynolds, 1969). Endogenous inhibitory response arises from the reticular formation and central gray neurons of the brainstem and midbrain and project to the spinal cord via the dorsolateral funiculus (DLF). VCS significantly increases nociceptive responses in animals and VS-S and CS-S increases pain detection and pain tolerance thresholds to experimental pain in humans. The analgesic effect of

VCS might be the result of modulation at interneurons of laminae I through VI, and/or activation of the endogenous descending inhibitory system thereby presynaptically and postsynaptically inhibiting pain transmission. VCS activates both an opioid mechanism and a nonopioid noradrenergic mechanism of the endogenous descending inhibitory system. The antinociceptive effect of VCS may be related to the production or release of other neurotransmitters, neuromediators, and neuromodulators including vasoactive intestinal peptide (VIP), glycine, excitatory and inhibitory amino acids, substance P, and oxytocin in the spinal cord and supraspinally. Reproductive hormones and reproductive stage have an influence on the effect of VCS in animals. Estrogen enhances the analgesic effect of VCS, the response of neurons of the brain and spinal cord to VCS, and alters VCS stimulated release of neurochemicals. However, in humans menstrual cycle phase has had no effect on pain thresholds under various control or VS-S experimental conditions. The effects of VCS on inhibitory neuronal responses in the brain and spinal cord and the analgesic effects outlast stimulation in animals and it was reported that the analgesic effect of VS-S lasted eight minutes after VS-S in one human subject with chronic pain.

There is a glaring absence of research of VCS using visceral and somatic chronic pain animal models. Additional study of VS-S and CS-S in humans with chronic pain is needed. All human studies of VS-S and CS-S should control for menstrual cycle and reproductive stage. Studies in which VS-S and CS-S are used should compare the results to determine if there are differences in the effect. Finally, a longer time period between VS-S and CS-S testing sessions is needed to allow alterations in neurotransmitters, neuromediators, neuromodulators, and neuroendocrines to return to baseline levels.

Dependent Variables

Chronic pain intensity

Theoretical concepts

According to the gate control theory (Melzack & Wall, 1965) "any lesion that impairs the normal downflow of impulses to the gate control system would open the gate" (p.977) and "any central nervous system condition that increases the flow of descending impulses would tend to close the gate" (p.977). Thus, chronic pain conditions may open the gate and conditions of intense stimulation close the gate. "The presence or absence of pain is determined by the balances between the sensory and central inputs to the gate control system" (Melzack & Wall, 1965, p.977).

Pain intensity processing in the human brain occurs bilaterally in the thalamus, somatosensory cortex, the anterior cingulate cortex, motor cortex, and the insula (Bushnell et al., 1999; Coghill, Sang, Maisog, & Iadarola, 1999; Davis, Kwan, Crawley, & Mikulis, 1998). With increasing stimulus intensity more areas of the brain are activated (Derbyshire et al., 1997). In individuals with chronic low back pain the present pain intensity index of the McGill Pain Questionnaire (MPQ) was significantly correlated ($F = 13.51$, $p < 0.0003$) with the abnormal patterns of glutamine, lactate, scyllo-inositol complex, glucose, γ-Aminobutyric acid (GABA), choline, N-acetyl aspartate predominant in the dorsolateral prefrontal cortex and the cingulate cortex (Grachev et al., 2000).

Stimulation-produced analgesia and chronic pain intensity

Several forms of stimulation have been used to relieve chronic pain intensity including direct stimulation of the brain (Duncan et al., 1998; Schvarcz, 1980),

stimulation of the dorsal column (Lindblom & Meyerson, 1975; Shealy, Mortimer, & Reswick, 1967; Shealy, Taslitz, Mortimer, & Becker, 1967), spinal cord (De La Porte & Van de Kelft, 1993; Doerr et al., 1978; Meyerson & Linderoth, 2000), and peripheral stimulation using transcutaneous electrical nerve stimulation (TENS) (Cheing & Hui-Chan, 1999; Jeans, 1979; Melzack, 1975b; Moore, C. D. et al., 2002; Sjolund & Eriksson, 1979; Wall & Sweet, 1967). These stimulation methods produce analgesia by directly stimulating brain areas that have been associated with analgesia, by inhibiting nociceptive input at the spinal cord level, stimulating the opioid and nonopioid mechanisms of the descending inhibitory pain system, and altering neurotransmitters, neuromediators, or neuromodulators in the central nervous system. There are equivocal reports of the effectiveness of these stimulation methods in reducing chronic pain.

VS-S and chronic pain intensity

VS-S is a specialized form of peripheral stimulation that has been reported to effectively reduce chronic pain intensity. Whipple (1986) conducted a pilot study with four women who had chronic pain. She reported a decrease in chronic pain intensity as measured by four scales of the McGill Pain Questionnaire. In addition, one subject reported total relief that lasted for eight minutes. These examples of stimulation-produced analgesia are consistent with the gate control theory (Melzack & Wall, 1965) concept that intense stimulation modulates pain. There are no human studies testing the effect of CS-S on chronic pain

Pain detection and pain tolerance thresholds

Theoretical concepts

According to the gate control theory (Melzack & Wall, 1965) intense peripheral

stimulation inhibits noxious transmission at the substantia gelatinosa (SG) of the dorsal horn and activates an endogenous descending inhibitory pain control system. Based on this theory there is evidence that increasing sensory input can increase both pain detection threshold and pain tolerance threshold (Anand & Craig, 1996; Maspes & Pagni, 1974; Melzack, 1977; Sternbach, 1970).

Influence of chronic pain on pain detection and tolerance thresholds

There is conflicting evidence concerning pain thresholds in chronic pain. Seventeen studies, published between 1952 and 1999, of pain detection threshold and pain tolerance threshold were reviewed. Eight of the studies used pressure as the experimental pain stimulus. In two of these studies (Lautenbacher, Rollman, & McCain, 1994; Ohrbach & Gale, 1989), pain detection thresholds were lower in subjects with chronic pain than in healthy controls without pain. In four of the studies (Bendtsen, Jensen, & Olesen, 1996; Clauw et al., 1999; McDermid, Rollman, & McCain, 1996; Vatine, Tsenter, & Nirel, 1998), both pain detection and pain tolerance thresholds were found to be lower in subjects with chronic pain than in pain-free controls. In the two remaining studies, one (Peters, M. L. & Schmidt, 1992) found no difference in pain detection thresholds between subjects and controls and the other (Jensen, R., Rasmussen, Pedersen, & Olesen, 1993) found no difference in pain detection threshold or pain tolerance threshold between subjects and controls. Differences in pain detection threshold and tolerance threshold found in these studies may be related to the chronic pain diagnosis, or an interaction of the stimulus and diagnosis.

Influence of VCS on pain detection and tolerance thresholds

Applying animal VCS research to humans, Whipple and Komisaruk (1986, 1985) compared the change in tactile detection to calibrated vonFrey fibers, PDT, and PTT to mechanical pressure pain applied to a finger during anterior wall VS-S, posterior wall VS-S, tactile stimulation, pressure applied to a knee, and contraction of pelvic floor muscles. For anterior wall stimulation, pre-VS-S PDT (384 g +/-36.4 SEM) was significantly greater than (10.3%, $p < 0.05$) post-VS-S PDT (348 g +/-31.6 SEM) and during-VS-S PDT (493.2 g +/-61.6 SEM) was significantly greater than (41.7.3%, $p < 0.05$) post-VS-S PDT (348 g +/-31.6 SEM); PTT during-VS-S (656 g+/-49.2 SEM) was significantly increased (30.2%, $p < 0.05$) over post-VS-S PTT (504 g+/-37.2 SEM). Changes in PDT or PTT in response to posterior wall VS-S, tactile stimulation with vonFrey fibers, pressure on the knee, or contraction of pelvic floor muscles was not significant. VS-S applied in a pleasurable way, significantly increased ($p < 0.05$) PDT 53% and PTT 36.8% and in women, who reached orgasm, PDT increased 106.7% and PTT increased 74.6% over post-VS-S control thresholds respectively. In another experiment to determine whether genital stimulation was site-specific (Whipple, 1986; Whipple & Komisaruk, 1988), researchers demonstrated that anterior wall VS-S increased PDT (48.8%) significantly more ($p < 0.05$) than posterior wall VS-S (28.4%), clitoral pressure (19.1%), or distraction (24.9%) over the post-VS-S PDT. Similarly, anterior wall VS-S increased PTT (26.8%) significantly more ($p < 0.05$) than posterior wall VS-S (20.8%), clitoral pressure (12.2%), or distraction (16.8%) over the control condition. Once again, applying VS-S in a pleasurable way produced a greater increase in both PDT (48.8%) and PTT (36.6%) over the control condition. These human studies demonstrate that “the sensory input produced by vaginal stimulation produces a powerful

pain-blocking (analgesic) effect" (Komisaruk & Whipple, 1995, p.163). However, the effect is not anesthetic because there was no effect on tactile detection nor is it merely distracting, as other forms of distraction had no significant effect on pain thresholds. Furthermore, the most significant effects occurred in women who experienced VS-S as pleasurable or who reached orgasm during the procedure indicating that there is a dose-related response with greater force, application of VS-S in a pleasurable way or to orgasm, resulting in a greater antinociceptive response. In women without spinal cord injuries and women with spinal cord injuries below and above T10, researchers (Komisaruk et al., 1997) first demonstrated that not only VS-S but also CS-S significantly increased PDT and PTT compared with resting control conditions. VS-S was found to have to have a similar effect on pain detection and tolerance thresholds in women with chronic pain as in women without chronic pain in a previously cited pilot study (Whipple, 1986).

In summary, studies of individuals with chronic pain using noxious mechanical pressure had equivocal findings with PDT and PTT no different than healthy controls or PDT and PTT lower than healthy controls. In the presence of chronic pain, intense stimulation is reported to have mixed effects on chronic pain intensity, PDT, and PTT. However, VS-S increased both PDT and PTT to noxious mechanical pressure pain in healthy women and four women with chronic pain. A dose-related response was demonstrated with a greater antinociceptive effect when women experienced orgasm. Finally, VS-S was not simply a form of distraction as other forms of distraction did not have an antinociceptive effect.

Hypotheses

This study is interested in determining if there is an effect of VS-S and CS-S on chronic pain intensity, PDT, and PTT in the presence of chronic pelvic pain in women.

Hypothesis 1: Chronic pain intensity will decrease and pain detection threshold and pain tolerance threshold will increase during VS-S at four, eight, and 12 minutes in women with chronic pelvic, abdominal, or low back pain.

Hypothesis 2: Chronic pain intensity will decrease and pain detection threshold and pain tolerance threshold will increase during CS-S at four, eight, and 12 minutes in women with chronic pelvic, abdominal, or low back pain.

Hypothesis 3: CS-S will have a significantly greater effect on chronic pain intensity, pain detection threshold, and pain tolerance threshold than VS-S in women with chronic pelvic, abdominal, or low back pain.

Hypothesis 4: The effect of VS-S on chronic pain intensity, pain detection threshold, and pain tolerance threshold will outlast stimulation.

Hypothesis 5: The effect of CS-S on chronic pain intensity, pain detection threshold, and pain tolerance threshold will outlast stimulation.

Chapter 3

Introduction

This was a repeated measures experimental design in which the experimental procedure, either vaginal self-stimulation (VS-S) or cervical self-stimulation (CS-S) was randomly assigned and each woman served as her own control. The subjects included in the study, sampling method, random assignment, and power analysis will be described in this chapter. The conceptual foundation, reliability, and validity of the Multidimensional Pain Inventory (MPI), and the Pain-o-meter (POM) will be described. The Ugo Basile Analgesy-Meter used to experimentally apply mechanical pressure pain and measure pain detection threshold (PDT) and pain tolerance threshold (PTT) will be described. Both the VS-S stimulator that was used to apply stimulation to the anterior wall of the vagina and the CS-S stimulator that was used to apply stimulation to the vaginal cervix will be described. Finally, the experimental protocol and measures taken to protect subjects from potential harm will be described.

Research setting

This experimental study was conducted at a pain management center (PMC) of a university medical center in New Jersey, the Rutgers University College of Nursing laboratory, and a community hospital in central New Jersey. The PMC is a tertiary care pain center providing medical and psychological evaluation, invasive and noninvasive medical treatment, and behavioral treatment for chronic and treatment resistant pain. The PMC agreed to allow recruitment of its patients and provided space at its facility to conduct this study. Additionally, subjects were referred by independent physicians and advanced practice nurse practitioners who practice at a community hospital in central

New Jersey. For subjects unable to travel to central New Jersey, the Rutgers University College of Nursing laboratory was used for testing.

Sample

A convenience sample of women who met the eligibility criteria was recruited. The subjects included in the study were English-speaking women, over the age of 18, who had chronic pelvic, abdominal, or low back pain. Only women were the subjects in this study because the study used vaginal and cervical self-stimulation. The subjects were 18 years or older to avoid any ethical concerns related to conducting vaginal and cervical self-stimulation in children. Because communication between the subject and the nurse investigator, who does not speak any foreign languages, was required during the course of the experiment, only English-speaking subjects were included. Subjects had to be cognitively intact, be able to read English, to be able to choose words indicated on the POM-WDS (POM verbal rating scale), and mark a response to complete the MPI. Subjects experiencing a steady-state level of pain and on a steady dosage and frequency of medication for at least two weeks before the experiment were included in the study. Subjects in any menstrual phase and reproductive stage were eligible to participate in the study. Excluded from the study were women who were pregnant or who had any physical or gynecological condition deemed by her health care provider to be a risk. Also excluded from the study were women who had a history of sexual abuse, active substance abuse, active suicidal ideation, or psychosis as determined through evaluation by a psychologist recommended by the New York Psychiatric Institute and trained in using the Structured Clinical Interview for DSM-IV Research Version (SCID) (First, Spitzer, Gibbon, & William, 2001).

Three web-based statistical power calculators were used to determine the proposed sample size of 10 subjects (Lenth, 2001; Schoenfeld, 1995; Statistics, 2002). Historical data were used to plan a sample size appropriate to achieve a power greater than .80 at a 5% significance level. Based on the average PDT effect size of .58 and the average PTT effect size of .44 reported in response to anterior wall VS-S (Whipple & Komisaruk, 1985) and the average PDT effect size of .54 and an average PTT effect size of .344 reported in response to CS-S (Komisaruk et al., 1997) if 10 subjects are enrolled in the study there is a ≥98% probability ($p < 0.05$, 2-tailed) that the study will detect a relationship between the independent variables and the dependent variables. Calculating the sample size for a study, in which the effects of two treatments VS-S and CS-S are compared in the same subjects if 10 subjects are enrolled there is between an 85% and 99% probability ($p < 0.05$, 2-tailed) that the study will detect a treatment difference (Schoenfeld, 1995).

Instruments and Devices

Instruments

The Multidimensional Pain Inventory (MPI)

The MPI (See Appendix A), previously known as the West Haven Yale Multidimensional Pain Inventory (WHYMPI) (Kerns, Turk, & Rudy, 1985; Turk & Rudy, 1988), was developed to assess the cognitive-behavioral dimension of chronic pain. The MPI is based on cognitive-behavioral theory (Fordyce, 1989; Turk, Meichenbaum, & Genest, 1983) and the gate control theory conceptualization of pain as a multidimensional, sensory-discriminative, affective-motivational, and cognitive-evaluative process (Melzack & Casey, 1968; Melzack & Wall, 1965). The tool is

comprised of three sections of 13 scales containing 61 items all rated on a 0 (lowest score) to 6 (highest score). Section I includes 28 questions in five scales related to pain severity (PS), interference (I), life control (LC), affective distress (AD), and support (S). Section II contains three scales with 14 questions related to punishing responses (PR), solicitous responses (SR), and distracting response (DR). Section III contains 19 questions in four scales related to chores, outdoor work, activities away from home, and social activities that are summed in one general activity level scale (GA). The time perspective of the MPI includes the present and recent past with demonstrated stability over a two-week period. Turk and Rudy (1987) created a multiaxial assessment of pain (MAP) in which physical, psychosocial, and behavioral responses to chronic pain measured by the MPI were integrated and used to differentiate and create an empirical taxonomy of chronic pain patients. The MPI scores on all three sections converted to T scores ($10z + 50 = T$) were analyzed using a k-means clustering approach. Using a multivariate generalized squared distance model and Bayesian posterior probabilities, three profiles were identified. The first profile, labeled dysfunctional (DYS), consisted of individuals reporting severe pain that interferes with their life causing high psychological distress, a low sense of control, and low activity. The second profile, labeled interpersonally distressed (ID), consisted of individuals who feel that their families and significant others are not supportive of them causing great interpersonal distress. The third profile, labeled adaptive copers (AC), consisted of individuals who have lower pain severity, distress, and sense that pain interferes with their lives and have high activity and sense of control over their lives. Statistical analysis indicated that “the MPI scales made 95% fewer errors in cluster classification than would be expected by random assignment”

(Turk & Rudy, 1987, p.245). Following initial studies, a computer program (Rudy, 1989b), to classify patients using the MAP-MPI, was developed that reports raw scores, T-scores for each axis, a chi-square and p-value based on the generalized squared distance of a subject's MPI profile from the MPI prototype profile centroid, and the Bayesian posterior probabilities. To eliminate missing responses, individuals who were not married and living alone were asked to designate as significant other, a person with whom they felt the closest and indicate if they lived with this person.

The MPI is norm referenced. The norm reference group for pelvic pain consisted of 34 women (Rudy, 1989a). The MPI was initially developed and tested with 120 patients (18.5% women), 50.8 years of age (*SD* = 14.5), with chronic pain (36.4%), for an average of 10.2 years (6 months – 40.6 years), who previously had pain-related surgery (55.8%), and were taking analgesic medication (67.4%) (Kerns et al., 1985). Internal consistency, based on the Cronbach alpha method, of 0.70 to 0.90 was adequate. Two weeks after the first administration of the MPI, it was administered a second time to 60 patients. Pearson product moment correlation coefficients of .62-.91 indicated stability over this period. Construct validity was established by correlating the results with similar scales of six questionnaires with established reliability and validity: McGill Pain Questionnaire (MPQ) (Melzack, 1975a), Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), Depression Adjective Checklist (DACL) (Lubin, 1965), State-Trait Inventory – State form (STAI-S) (Speilberger, Gorsuch, & Lushene, 1970), Multidimensional Health Locus of Control (MHLC) (Wallston, Wallston, & DeVellis, 1978), and the Marital Adjustment Scale (MAS) (Locke & Wallace, 1959). Factor analysis of the correlation matrix demonstrated internal as well as external

construct validity (Kerns et al., 1985). A study of the MAP (Turk & Rudy, 1988) was conducted with 122 patients (20.5% women), age 49.2 years (*SD* = 13.2), with chronic pain (36.5%), for an average of 10.6 years (*SD* = 11.7), who had previous pain-related surgery (56.7%), and were taking analgesic medications (67.4%). The MAP analysis resulted in three distinct profiles. To validate these profiles, the clusters were compared with scores of the same six questionnaires that had been used to establish validity of the MPI. Turk and Rudy (1988) found that they could correctly profile 97.5% of the 122 cases studied (κ =.975, z = 15.14, $p < 0.00001$). A second experiment in this study (Turk & Rudy, 1988) of 100 patients (62.2% women), age 42.2 years (*SD* = 14.9), with chronic pain for 7.98 years (*SD* = 10.1), who had previous pain-related surgery (39.4%), and were taking analgesic medications (58.4%), coded the primary pain site according to the International Association for the Study of Pain (IASP) guidelines following physical examination and determination of a summed medial pathology score. Statistical tests revealed no significant differences ($\underline{p} < 0.18$) between profile groups in the first and second studies based on age, gender, site, duration of pain, or the medical pathology (Turk & Rudy, 1988).

Pain-o-meter (POM)

The POM, a multidimensional pain assessment tool developed by a nurse, was used to measure present pain in this study. Although Gaston-Johansson never explicitly linked the POM with the gate control theory, there is evidence of this connection. Gaston-Johansson described “two major dimensions – sensory-cognitive and affective – of the pain experience” (Gaston-Johansson & Allwood, 1988, p.89). She specified the sensory-cognitive dimension using temporal, dynamic, spatial, intensity, and thermal

characteristics and the affective dimension with physiological, emotional, and evaluative reactions. Translating the concepts of the gate control theory into semantics, Gaston-Johansson (Gaston-Johansson & Allwood, 1988) suggests that words used to describe fast and localized pain "may be carried by A-delta fibers and the neo-spino-thalamic tract" (p. 89) and words used to modify ache indicate "sensory information carried by C-fibers and the medially located paleo-spinothalamic tract involving slow, dull, less specifically localized pain experiences"(p. 89). The instrument subjectively measures four dimensions of pain: intensity, duration, quality, and location. Intensity is measured by means of a visual analog scale (VAS). On the front side of the tool the subject moves a plastic slide with an arrow along a vertical 10 cm line anchored on the bottom by the words "no pain" and at the top by the words "worst possible pain" to indicate the amount of her current pain. On the reverse side a numerical scale with 0.2 cm markings for easy scoring can be seen through a small window. The duration of pain, that is whether it comes and goes or is continuous, marked at the bottom on the front side of the instrument, is then documented on a form that accompanies the tool. The POM-WDS is composed of a sensory (or physical) scale (POM-WDSP), consisting of 14 words, and an emotional scale, consisting of 11 words (POM-WDSE). The intensity of the sensory and emotional words, ranked between 1 (the lowest score) and 5 (the highest score) are summed to create a pain index. The total summed sensory scale is 47 and the total summed emotional scale is 37. Scoring reported in an earlier study (Gaston-Johansson et al., 1992) reflect an earlier version of the Pain-o-meter (F. Gaston-Johansson, personal communication February 23, 1999). A body outline chart, divided into numbered

segments from 1 to 79, and located inside a pocket of the tool is used to identify the location of pain.

One of the strengths of the tool is its utilization of a VAS that has been shown to be reliable and valid in measures of experimental and chronic pain in previous studies (Jensen, M. P., Karoly, & Braver, 1986; Ohnhaus & Adler, 1975; Price, McGrath, Rafii, & Buckingham, 1983; Wewers & Lowe, 1990) and highly correlated with verbal rating scales (VRS) (Ohnhaus & Adler, 1975). Two of the scales of the POM, the POM-VAS and POM-WDS, are norm-referenced. On the POM-VAS, the norm is each individual's previous score, also called ipsative comparisons (Waltz, Strickland, & Lenz, 1991; Wewers & Lowe, 1990). The lowest possible score on the POM-VAS is 0 and the highest score is 10. Three initial studies were conducted with chronic pain patients and professional content experts to establish content validity and norm reference of the POM (Gaston-Johansson, 1984; Gaston-Johansson & Allwood, 1988; Gaston-Johansson & Asklund-Gustafsson, 1985). Gaston-Johansson conducted a major correlational and comparative, two-part study to determine reliability and validity of the POM (Gaston-Johansson, 1996). The sample consisted of 279 subjects: 90 with chronic pain, 98 with acute post-op pain, and 91 with labor pain. For chronic pain patients significant test-retest using the POM-VAS (.88, $p < 0.001$) and significant test-retest using the POM-WDS (.68, $p < 0.001$ to .73, $p < 0.001$) were found. Although stability (test-retest) was measured, the whole idea of test-retest may be invalid for a dynamic concept such as pain that can change in quality and intensity from moment to moment. Furthermore, it is impossible to know if the score, the absolute zero, or the intensity intervals mean the same thing to every subject. As predicted there was a significant decrease in pain

intensity over the post-operative period measured on the POM-VAS ($F_{(1,29)} = 7.5$, $p < 0.05$) and analgesic medication use ($F_{(1,29)} = 3.73$, $p < 0.001$) appropriately supporting construct validity through a hypothesis testing approach. Concurrent validity was demonstrated between the POM-WDS and the McGill Pain Questionnaire (MPQ) for chronic pain patients: (.69, $p < 0.001$). Significant criterion validity comparing the POM-VAS with POM-WDS sensory (.78, $p < 0.011$) and affective (.80, $p < 0.011$) and the combined scores of the POM-WDS with the McGill Pain Questionnaire (MPQ) (.69, $p < 0.011$) has also been reported.

Devices

Analgesy-Meter Ugo Basile (Milan, Italy; Stoelting Company, Wood Dale, IL)

The Analgesy-Meter was used to create and quantify PDT and PTT in grams of mechanical force. The Analgesy-Meter (Figure 1) is manufactured by the Ugo Basile company of Camerio, Italy (Ugo Basile) and distributed exclusively through the Stoelting Co., (Wood Dale, IL) in the U.S. and Canada. The Ugo Basile Company holds an ISO 9100 certification to design, manufacture, sell, and service biological research equipment. The moving parts and motor are made to operate without lubrication or maintenance. The Analgesy-Meter was designed as a paw pressure analgesia meter. However, it has been modified to use with humans by mounting the pusher on the base and the plinth on a bracket fixed to the arm. The plinth and pusher are separated by a one- to two-millimeter gap. This is so that the pad of the subject's finger can rest on the point of the cone-shaped pusher. A rotating weight displacing screw with a pitch of 16 mm and driven by a motor at a speed of 60 RPM moves a slide along a linear scale (1 to 25) calibrated in 10-gram steps at a constant speed of 10 grams per second. Additional weighted discs have been

added to the slide increasing the weight at 1 gram on the scale to 60 grams so that the first measurement can be read in the lower third of the scale to avoid tolerance thresholds beyond the 25-millimeter mark. A foot pedal is used to start and stop the motor. The arm can be balanced by adjusting a weight near the motor. Maintaining the arm slightly off-balance will exert a slight initial force on the finger to keep it in place and will result in a slight, but constant, error in the actual force compared with the scale measure. As the slide moves along the scale, the flat surface of the plinth pushes down on the fingernail, decreasing the distance between the plinth and the pusher and increasing the pressure on the pusher.

Ugo Basile Analgesy-Meter

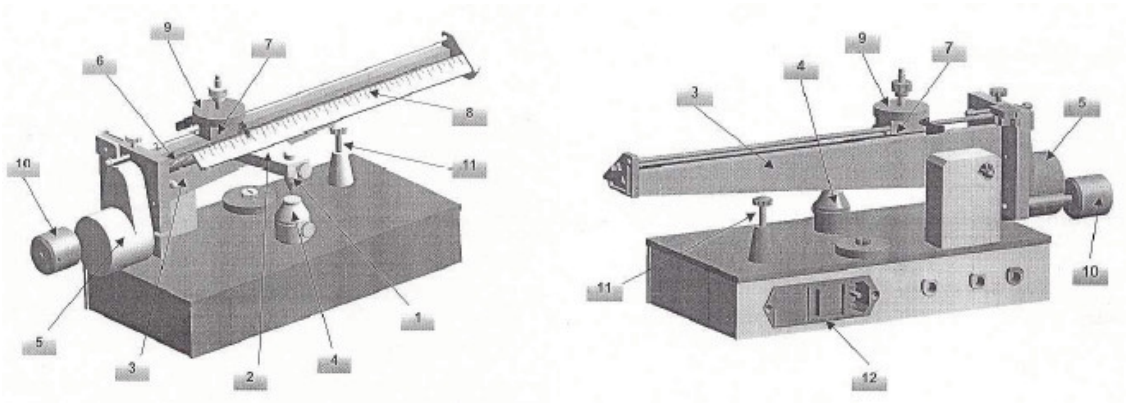


Figure 1. Analgesy-Meter (Ugo Basile) (Reproduced with permission, Stoelting Co.)

1 Pusher	4 Plinth	7 Slide	10 Calibration weight
2 Bracket	5 Motor	8 Scale	11 Travel limit column
3 Arm	6 Weight displacing Screw	9 Weighted discs	12 Power module

Studies using the Analgesy-Meter have been shown it to be sensitive enough to discriminate hyperalgesic or analgesic effects under different conditions. It has been used to discriminate analgesic effects among different classes of drugs (Hayes, Sheehan, &

Tyers, 1987; Randall & Selitto, 1957; Stein, Millan, Shippenberg, Peter, & Herz, 1989; White & Cousins, 1998). It has also been used to discriminate the effect of various agents on injury-induced hyperalgesia (Carey, Haworth, & Whalley, 1988; Ohkubo, Shibata, Takahashi, & Inoki, 1990; White, 2000; White & Cousins, 1998). Finally, it has been used in human studies to discriminate changes in PDT and PTT in response to VS-S and CS-S (Martinez-Gomez, Whipple, Oliva-Zarate, Pacheco, & Komisaruk, 1988; Whipple, 1986; Whipple & Komisaruk, 1985; , 1988; Whipple, Martinez-Gomez, Oliva-Zarate, & Komisaruk, 1989). Therefore, to increase comparability with these studies, the same method of applying experimental pain was used in this study.

VS-S stimulator

The stimulator that was used for VS-S, stimulating the anterior wall of the vagina, consists of a disposable, curved plastic rod that is connected to the stimulator handle and is inserted into a disposable tampon that has a cushioned tip as had been used in previously published human studies conducted by Komisaruk and Whipple (Komisaruk et al., 1997; Whipple, Gerdes, & Komisaruk, 1996; Whipple & Komisaruk, 2002). The stimulator handle contains a mechanism connected to a readout meter so the amount of force used during VS-S and CS-S can be monitored.

Figure 2. Positioning of VS-S Stimulator

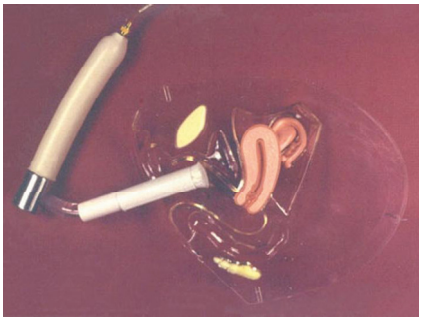
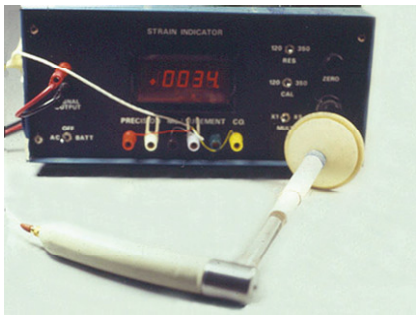


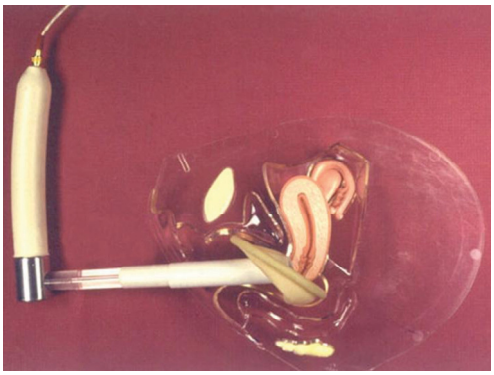
Figure 3. Readout meter



CS-S stimulator

The stimulator used for CS-S is the same as that used in previously published human studies conducted by Komisaruk and Whipple (Komisaruk et al., 1997; Whipple et al., 1996). It consists of a disposable, straight plastic rod attached to the stimulator handle and inserted into a disposable tampon with a Velcro tip that will attach to a matching Velcro® fabric disk attached to a diaphragm. Attaching the Velcro® tip of the tampon to the Velcro® disc on the diaphragm maintains the position of the area of self-stimulation directly over the cervix and will protect it from abrasion.

Figure 4. Positioning of the CS-S Stimulator



Procedures for data collection

Methods

Testing was conducted at a pain management center (PMC) of a university medical center in New Jersey, the Rutgers University College of Nursing laboratory, and a community hospital in central New Jersey. Women agreeing to participate were asked to sign a consent form. Each woman was psychologically screened using the SCID-IV I/NP (First et al., 2001) (see Appendix B) to assess cognitive status and screen for active drug or alcohol abuse, active suicidal thoughts, psychoses, a history of sexual abuse, or any other condition that the psychologist determined should exclude her from the study.

A letter describing the study protocol, a release form, and a stamped self-addressed envelope was given to the woman to give to her healthcare provider. The woman's healthcare provider then conducted a gynecological examination to rule out conditions that would contraindicate participation, fit her for a diaphragm, and signed a release form approving her participation in the study. Following the examination the woman mailed the prescription for the diaphragm and the release approving her participation in the study to the investigator. The investigator obtained the diaphragm and modified it, by fastening a Velcro disc to it for use in the experiment. Once the release and the diaphragm prescription were received and within six months of her healthcare examination, the woman was given appointments for the experimental sessions. The first and second experimental sessions, with VS-S or CS-S randomly assigned to the first session, were scheduled within two weeks of each other. Subjects were asked to avoid treatment changes between experimental sessions. Subjects were reminded to continue taking pain medication and using non-drug treatments as ordered to maintain a steady state of medication and treatment during the two-week intervals before and between the first and second experimental sessions. (See Timeline in Appendix C) A copy of the MPI was mailed to the subject before the first scheduled experimental session. Subjects were asked to complete the MPI on the day before the first experimental session. Instructions were provided in a written cover letter mailed with the MPI in advance of the first experiment date ensuring that every subject received the same instructions. As with many self-report measures, the MPI is sensitive to response bias. To control response bias, the instructions included a brief statement that the woman herself should complete the MPI on the day before the first experimental session, that a significant other, selected before beginning

the MPI should be the reference for the questions in Section II, and that the information gathered would be used as background data. Subjects were told that the purpose of the study was to determine if there is any relation between pain and vaginal/cervical self-stimulation. All subjects were blind to the hypotheses.

Upon arrival at the testing site, each subject met with the nurse investigator who collected the MPI (see Appendix A) that had been completed, reviewed the study procedures, instruments, and the previously signed consent (see Appendix D). For subjects capable of being pregnant, before beginning the experimental session, a pregnancy test was used to determine if the subject was pregnant. If the subject was not pregnant and agreed to proceed, the nurse investigator collected background data including demographic data, the date of the onset of chronic pain, diagnosis, other health problems, reproductive stage, and the date of the last menstrual period (see Appendix F). The subject used the Pain-o-meter to rate her chronic pain intensity using the VAS, describe the pain duration, describe the physical and emotional pain, and locate the pain using the body chart. The nurse investigator documented this information on an adaptation of the POM pain sheet (Appendix G). Following the initial data collection use of the tampon stimulator with digital force readout was explained to the subject. The subject was asked to relax on an examination table or bed in the laboratory after emptying her bladder. The subject inserted the diaphragm with the assistance of the nurse investigator to assure correct placement of the diaphragm directly over the cervix.

To create experimental pain, each of the fingers of the non-dominant hand, excluding the thumb, was placed over the 1mm blunt point pusher of the Ugo Basile Analgesy meter (see Figure 1). Over the next 26 seconds, an increasing force was applied

to each finger, pressing the subject's finger down on the point. At the moment the subject first perceived experimentally induced pain (pain detection threshold) she was instructed to say "pain" and at the point that it was too uncomfortable to continue (pain tolerance threshold) she was instructed to say "stop" and the pressure-applying device was immediately lifted off the finger. To avoid reactivity bias to the experience of experimentally applied pressure pain, the mean of three PDT measures and the mean of three PTT readings taken at beginning of testing were used to establish baseline thresholds. This allowed subjects to become familiar with the process. Subjects were asked not to look at the scale of the Analgesy-Meter to avoid the potential reactivity bias of seeing the slide move up the scale as the pressure increases. Following the collection of this base-line data, there was a four-minute rest period.

Following the rest period the subject applied self-stimulation, either to the anterior vaginal wall or to the cervix, as randomly assigned, for 10 to 12 minutes. During stimulation the amount of force used with the vaginal or cervical stimulator was monitored continuously by the nurse investigator and was recorded every 30 seconds on an experimental data collection sheet (see Appendix H). The maximum pressure permitted was 10 lb/in^2 approximately that required to lift a 1-gallon plastic container of water with two fingers. No subject exceeded the 10-lb/in^2 pressure. Experimental PDT and PTT, and chronic pain intensity were measured at four minutes and eight minutes after the beginning of VS-S or CS-S. Self-stimulation ceased at 10 to 12 minutes and post-stimulation PDT, PTT, and chronic pain intensity was measured immediately following the termination of self-stimulation and every four minutes until PDT or PTT returned approximately to the subject's baseline level.

Each laboratory test session lasted for approximately 90 minutes including the pre-experiment data collection. Following the completion of the laboratory experiment, subjects took home a representation of the POM used during testing and continued to measure their chronic pain intensity using the POM-VAS, POM-WDS, and body chart. Subjects were asked to measure their chronic pain intensity every 30 minutes during waking hours and to document each pain score on a POM Pain Sheet provided to them. They were told to stop measuring their chronic pain intensity and location after the POM-VAS has returned to the pre-test baseline measure noted on the form, on two successive 30-minute intervals. The POM Pain Sheet were returned to the investigator at the second session and following the second session using a stamped, self-addressed envelope provided to them.

Rights of human subjects protected

An application and all attachments were submitted to Institutional Review Boards (IRBs) for full board review. The research protocol, informed consent, and data collection tools as outlined above were initially approved by Rutgers University IRB on November 29, 1999 and by the university medical center IRB on November 22, 2000. (See Appendix E) A minor revision to allow a letter of recruitment to be mailed to patients was subsequently approved on February 15, 2002. Minor revisions to the protocol and consent were submitted to both IRBs in April, 2003. The study was approved by the community hospital IRB on March 15, 2004. Continuation applications have been filed and approved by IRBs yearly thereafter. There was minimal risk or discomfort from the experimental mechanically induced pain. It was explained to each subject that she was in control of the amount of experimental pain she would tolerate and

that she was free to terminate the test at any time. Subjects did not report emotional distress during or following the experimental procedures. Subjects were given the opportunity to discuss the experience with the principal investigator following the initial experimental session and there was a complete debriefing at the end of the final testing session. Although the results of this study may provide some direct benefit to the subjects by identifying a non-pharmacological method of reducing chronic pain intensity this eventuality was not presented to the subjects prior to the testing session to avoid biasing the experimental findings. The subjects were told that the purpose of the research was to ascertain whether there is any relation between pain and response to VS-S or CS-S. Questionnaires used to collect sensitive data were identified with code numbers, not names. Each subject was assigned a code number used as identification during the study. A master list of study participants' code numbers, maintained in a secure computer file available only to the principal investigator, will be destroyed following the completion of the study. Paper copies of releases to participate, consent forms, and data collection forms will be kept in a locked file cabinet in a home office by the nurse investigator for five years following the completion of the study at which time they will be destroyed.

Chapter 4

Introduction

The purpose of this study was to determine the effect of vaginal self-stimulation (VS-S) and cervical self-stimulation (CS-S) on the dependent variables: chronic pain intensity (CPI), pain detection threshold (PDT), and pain tolerance threshold (PTT); the time course of the onset and cessation of induced analgesia; the duration of the effect on the dependent variables; and whether there was a difference between the effect of VS-S and CS-S on the dependent variables. Additionally, this study sought to determine the effect of the force used in stimulation, menstrual cycle, reproductive stage, opiate drugs used to manage chronic pain, the duration of chronic pain, and pain classification on the effect of VS-S and CS-S. Data were collected on five women between the ages of 20 and 46, who had chronic pelvic, abdominal, or low back pain. The Multidimensional Pain Inventory (MPI) was used to collect data on pain severity, the support of a significant other, and how much pain interfered with activities. The Multiaxial Assessment of Pain (MAP) was used to classify each woman into one of four descriptive categories based on MPI data. The Pain-o-Meter (POM) was used to collect information on present pain, including pain intensity, the physical and emotional modifiers used to describe pain, the frequency (intermittent or continuous), and the location of pain. The Analgesy-Meter was used to both create experimental pain, and to measure the PDT and PTT in grams of mechanical force. Data were analyzed using paired sample t-tests, univariate and repeated measure ANOVAs, and multiple regression in SPSS, (Release 12.0.1, SPSS Inc., Chicago, IL).

Sample

The study was discussed with 43 women who met eligibility criteria. Twenty-eight (28) of these women agreed to review the consent in an effort to decide whether or not they wished to participate in the study. The most common reasons women cited for nonparticipation were that their pain was too severe or had subsided and they did not want to risk an exacerbation that the procedure might cause. Only women with mild to moderate pain agreed to be in the study. Ten women verbally agreed to be in the study; four did not sign the informed consent. Of the four women who did not sign the consent: one woman could not be fitted with a diaphragm; one woman did not want to participate after she had a hypogastric nerve block that relieved her pain; one woman got married and moved from the area; and contact was lost with one woman when she stopped attending the pain management center (PMC). One woman who had interstitial cystitis, signed the consent, was psychologically and physically screened, but had surgery unrelated to interstitial cystitis prior to participation; she died of post-operative complications. Five women ultimately participated in the study. (See Table 1)

The average age of the subjects tested was 33.4 years (range 20-46). Diagnoses were coded using the International Association for the Study of Pain (IASP) codes. Subject 1 and Subject 2 were diagnosed with interstitial cystitis. Subject 1 also had fibromyalgia with continuous chronic low back pain, low abdominal pain, and perineal pain for 48 months. Subject 2 also had endometriosis and irritable bowel syndrome with continuous chronic low back pain, pelvic pain, and pain in the sacrum and coccyx for 54 months. Subject 3 had Complex Regional Pain Syndrome Type I, also known as reflex sympathetic dystrophy, with continuous chronic burning pain in her left ankle, left leg, left lower abdomen, left rib cage, left upper back, left upper arm, and left wrist for 115

months. Subject 4 had osteoarthritis of the spine with intermittent chronic pain located in her low back, lumbar spine, sacral, and coccyx for 38 months. Subject 5 had idiopathic low back pain. She had continuous chronic low back pain and sciatica for 63 months. The average duration of the subjects' chronic pain was 63.6 months.

Subjects 3 and 5 were post-menopausal. Subject 3 reported her last menstrual period to be one year prior to testing in June 2003. Subject 5 described herself as post-menopausal but did not remember the date of her last menstrual period. Three women, subjects 1, 2 and 4, were pre-menopausal. Subject 2 who had endometriosis was pharmacologically rendered amenorrheal; her menstrual cycle day was coded as 0. Two of the women, subjects 1 and 4, had normal menses. Subject 1 was tested on day 9 of her menstrual cycle using VS-S; this subject was not tested using CS-S. Subject 4 was tested using VS-S on day 22 of her menstrual cycle and CS-S on day 7 of her menstrual cycle. For subjects capable of being pregnant, a pregnancy test was used to determine if the subject was pregnant; no subjects were pregnant at the time of testing.

Three of the women, subjects 1, 2, and 3, took opiate medication to manage their chronic pain with daily morphine equivalent dosages of 75 mg, 375 mg, and 930 mg respectively. Only two of these women, subjects 2 and 3, were reportedly taking medication at the time of testing. Subject 4 and subject 5 did not take any medication to manage their chronic pain. All of the women used non-pharmacological pain management techniques including the application of heat or cold, nerve stimulation, exercise, physical therapy, massage, relaxation, music, distraction, guided imagery, and biofeedback. None of these non-pharmacological methods were reportedly being used at the time of testing.

Table 1: Subject data

Subj			Age	Dur	24-hr opiate dose	Pre-Test		Post-Test		Pre-VS-S				Post-VS-S				Pre-CS-S				Post-CS-S			
						MPI	MAP	MPI	MAP	POM VAS	POM WDS	PDT	PTT	POM VAS	POM WDS	PDT	PTT	POM VAS	POM WDS	PDT	PTT	POM VAS	POM WDS	PDT	PTT
1	Diagnosis	Interstitial cystitis, Fibromyalgia	20	48	75 mg	531	3			3.8	9	668	1080	6.2	9	593	938								
	Pain type	Visceral																							
	Location	Perineum, abd, low back																							
	Frequency	Continuous																							
	Rep.	Premenopausal																							
2	Diagnosis	Interstitial cystitis, Endometriosis	27	54	375 mg	631	1			6	50	473	671	6.5	22	345	566								
	Pain type	Visceral																							
	Location	Pelvis, Low back Sacrum, coccyx																							
	Frequency	Continuous																							
	Rep.	Premenopausal ammenorrheal																							
3	Diagnosis	Complex Regional Pain Syndrome I	44	115	930 mg	675	2	717	4	3.5	35	893	1178	3.23	35	1080	1298	3.88	34	926	1084	3	19	1020	1253
	Pain type	Inflammatory																							
	Location	Left upper arm & back, Left rib cage, Left lower abdomen & leg																							
	Frequency	Continuous																							
	Rep.	Postmenopausal																							
4	Diagnosis	Osteoarthritis	30	38	0	617	2	606	2	3.5	8	510	1078	0	0	555	953	0.06	0	530	854	0	0	548	881
	Pain type	Inflammatory																							
	Location	Low back Lumbar spine, Sacrum, coccyx																							
	Frequency	Intermittent																							
	Rep.	Premenopausal																							
5	Diagnosis	Chronic low back pain	46	63	0	580	4	566	3	3	4	570	833	1	0	1095	1500	3.5	4	690	1120	1	0	1470	1440
	Pain type	Idiopathic																							
	Location	Low back, Sciatica																							
	Frequency	Continuous																							
	Rep.	Postmenopausal																							

Frequency: Pain Frequency **MPI :** Multidimensional Pain Inventory **POM:** Pain-O-Meter **VS-S:** Vaginal Self-Stimulation **PDT:** Pain Detection Threshold
Rep.: Reproductive Stage **MAP:** Multiaxial Assessment of Pain **VAS:** Visual Analogue Scale **CS-S:** Cervical Self-Stimulation **PTT:** Pain Tolerance Threshold
Dur: Pain Duration **WDS:** Words

Statistical Description of the Variables

Multidimensional Pain Inventory (MPI)

The pre-study MPI mean score was 606.69 (*SD* = 54.17) and the post-study mean was 629.77 (*SD* = 78.18) (See Table 1). There were no significant differences in pre-study MPI scores by reproductive stage, cycle day, or pain frequency, intermittent or continuous (see Table 2). There was a significant difference in pre-study MPI scores by age ($F = 17.08$, $df = 4$, $p = .02$, $\eta^2 = .958$) with lowest scores in subject 1, who was the youngest subject ($M = 531.33$). There was a significant difference in MPI scores by pain duration ($F = 17.08$, $df = 4$, $p = .02$, $\eta^2 = .958$); the longer the pain duration the higher the scores ($M = 695.92$). There was a significant difference in MPI scores by pain location ($F = 29.48$, $df = 3$, $p = .003$, $\eta^2 = .957$); higher scores were reported with upper back pain ($M = 767.68$). There was a significant difference in MPI scores by the 24-hour opiate drug dose ($F = 29.48$, $df = 3$, $p = .003$, $\eta^2 = .957$); the greater the 24-hour opiate drug dose the higher the MPI score ($M = 767.68$). Finally, there was a significant difference in MPI scores by the type of pain, visceral or somatic ($F = 6.59$, $df = 1$, $p = .042$, $\eta^2 = .523$); higher MPI scores ($M = 401.70$) were reported with somatic pain. The data from the MPI were entered into the MAP-MPI computer program (Rudy, 1989b) developed to classify patients into one of four categories. The following data were entered for each subject: the subject identification code, the date of the MPI assessment, the gender code (1 = male, 2 = female), the age of the subject in years, the duration of the pain in months, the primary pain site using the IASP taxonomy codes, and the responses to the 61 questions on the MPI. A report for each subject was generated that included raw scores, T-scores for each section, profile centroid distance chi square and *p*-values, and Bayesian posterior

probabilities indicating the classification of the subject to a profile (see Appendix A). Before testing subject 2 was classified as dysfunctional (cluster assignment code 1). This profile indicates higher scores on the pain scale, higher scores on the interference scale, lower scores on the life control scale, higher affective distress scale scores, and lower scores on the general activity scale. Two women, subjects 3 and 4, were classified as interpersonally distressed (cluster assignment code 2). This profile is the result of lower scores on perceived social support scale, higher scores on the perceived punishing responses scale, lower scores on the perceived solicitous responses scale, and lower scores on the perceived distracting responses scale. Subject 1 was identified as an adaptive coper (cluster assignment code 3). This profile indicates lower levels of pain severity, lower levels of interference, higher levels of life control, lower levels of affective distress, and higher levels of general activity. Subject 5 was classified as a hybrid of interpersonally distressed and adaptive coper (cluster assignment code 4). This profile is a combination of both the interpersonally distressed and adaptive coper clusters. Following testing the MAP classification was different for two of the women. Subject 3 classified prior to testing as interpersonally distressed was classified after testing as a hybrid of interpersonally distressed and an adaptive coper (cluster assignment code 4). Subject 5 classified as a hybrid of interpersonally distressed and adaptive coper prior to testing was classified as an adaptive coper (cluster assignment code 3) after testing. The MAP classification categories were entered into the data spreadsheet. Only the pre-testing MAP-MPI classification was used in the post hoc statistical evaluations of study data because the post-test MPI was returned by only three of the five subjects.

Table 2: MPI pre- and post-test results

Pre-test (n=5)	Mean	Median	Range	SD
MPI	606.69	616.93	143.35	54.17
Post-test (n=3)				
MPI	629.77	605.73	150.72	78.18

Table 3: ANOVA Pre-study MPI scores

Variable	F	df	p
Age	17.08	4	= .02
Reproductive stage	.793	4	=.41
Cycle day	.732	4	=.59
Intermittent / continuous	.855	4	=.39
Pain duration	17.08	4	=.02
Location	29.48	3	=.003
Opiate 24-hr dose	29.48	3	=.003
Visceral / somatic	6.59	1	=.042

POM results

The pre-study POM values including VAS, WDS (the sum of physical and emotional scores), pain duration and location documented on the POM Pain Sheet were entered into the spreadsheet as the chronic pain intensity (CPI) (See Table 4). Subjects 3, 4, and 5 reported POM VAS of 3.5, subject 1 reported a score of 3.8 and subject 2 reported a score of 6 prior to VS-S testing. The average POM VAS score was 4.21 (range 3 - 6) on a scale of 0 (no pain) to 10 (worst possible pain) prior to VS-S testing. The average POM WDS score was 18 (range 4-35). Prior to CS-S testing subject 4 reported a POM VAS score of zero, except her pain score was 0.6 when she walked. Subject 5 reported a POM VAS score of 3.5 and subject 3 reported a score of 3.88 prior to CS-S testing. The average POM VAS score prior to CS-S testing was 2.53 (range 0.6 – 3.5) on a scale of 0 (no pain) to 10 (worst possible pain) and the average POM WDS score was 12.33 (range 0-33). There were no significant differences in pre-study POM VAS scores by age, reproductive stage, cycle day, pain frequency (intermittent or continuous), pain

duration, location, or 24-hour opiate drug dose, MPI-MAP classification, or pain type (visceral or somatic) (See Table 4). There were no significant differences in POM WDS scores by reproductive stage, cycle day, pain frequency (intermittent or continuous), MPI-MAP classification, or pain type (visceral or somatic) (See Table 5).There was a significant difference in POM-WDS scores by age ($F = 35.23$, $df = 4$, $p = .007$, $\eta^2 = .979$) with lower scores in subject 4 ($M = 4$) and subject 5 ($M = 4$). There was a significant difference in POM-WDS scores by pain duration ($F = 35.23$, $df = 4$, $p = .007$, $\eta^2 = .979$); the longer the pain duration the higher the averaged scores ($M = 25.40$). There was a significant difference POM-WDS scores ($n = 5$) by the location of pain ($F = 62.62$, $df = 3$, $p = .001$, $\eta^2 = .979$); the lowest scores were reported with low back pain ($M = 4$). There was also a significant difference POM-WDS scores by the 24-hour opiate drug dose ($F = 62.62$, $df = 3$, $p = .001$, $\eta^2 = .979$); the greater the 24-hour opiate drug dose the higher the score ($M = 34$). The POM-VAS percent change scores allowed comparisons of the average variability with thresholds measured during self-stimulation at four and eight minutes, within subjects and between subjects. Pre-stimulation, during stimulation, and post-stimulation results were entered into a spreadsheet and difference scores were calculated for POM-VAS (Appendix I).

Table 4: Pre-study POM scores

Test 1	Mean	Median	Range	SD
POM-VAS	4.06	3.50	2.50	1.09
POM-WDS	21.0	9.0	46.0	20.07
Test 2				
POM-VAS	2.66	3.50	3.28	1.79
POM-WDS	13.0	4.0	35.0	19.16

Table 5: ANOVA Pre-study POM scores

	POM-VAS			POM-WDS		
Variable	F	df	p	F	df	p

Age	1.67	4	.351	35.23	4	= .007
Reproductive stage	.033	1	.862	.302	1	=.603
Cycle day	2.37	3	.212	.676	3	=.610
Intermittent/	3.66	1	.104	1.80	1	=.228
Pain duration	1.67	4	.351	35.23	4	=.007
Location	2.03	3	.253	62.62	3	=.001
Opiate 24 hr dose	2.03	3	.253	62.62	3	=.001
MPI-MAP Class	1.00	3	.477	.520	3	=.691
Visceral/somatic	2.34	1	.177	.327	1	=.588

Force

The self-stimulation force for each subject noted every thirty seconds during each experimental condition was recorded, averaged, and entered into the data spreadsheet. The average self-stimulation force used during VS-S was 59.89 grams of pressure (range 16.94-133.46). The average force used during CS-S was 27.06 grams (range 4.25-53.53). There was a significant difference in the amount of force used during VS-S and CS-S ($F_{df1} = 6.69$, $p = .017$). The mean force used during VS-S (59.89 grams) and the mean force used during CS-S (27.06 grams); and the averaged force measured every thirty seconds prior to four (4) minutes (VS-S 63.58 *SEM* ± 19.10 grams; CS-S 24.78 *SEM* ± 10.44 grams), eight (8) minutes (VS-S 56.37 *SEM* ± 16.48 grams; CS-S 33.44 *SEM* ± 12.83 grams), and twelve (12) minutes (VS-S 59.72 *SEM* ± 15.60 grams; CS-S 22.96 *SEM* ± 7.93 grams) were used in post hoc analysis of study data. There was no significant difference in the amount of force used by the type of pain (visceral or somatic), by whether the pain was continuous or intermittent, by the MAP classification of pain, or the duration of self-stimulation. There was a significant difference in the average amount of force used in self-stimulation by age ($F_{df4} = 3.32$, $p = .032$); the older subjects used greater force. There was a significant difference in the amount of force used by reproductive stage ($F_{df2} = 3.74$, $p = .041$); menopausal women used greater force. There

was a significant difference in the amount of force used by the opiate drug dose (F_{df3} = 4.22, p = .018); the greater the 24-hour opiate drug dose the greater the force used. There was a significant difference in the amount of force used by pain duration (F_{df4} = 3.32, p = .032); the longer the duration of pain the greater the force used. There was a significant difference in force used by the location of pain (F_{df3} = 4.22, p = .018); the further away the location of pain from the self-stimulation the greater the force used.

Pain detection results

There were no significant differences in average baseline PDT by reproductive stage, cycle day, pain frequency (intermittent or continuous), MPI-MAP classification, or pain type (visceral or somatic) (See Table 6). There was a significant difference in average baseline PDT by age (F = 18.91, df = 4, p = .018, η^2 = .962); subject 3 had the highest baseline average PDT (M = 15.16). There was a significant difference in baseline average PDT by pain duration (F = 18.91, df = 4, p = .018, η^2 = .962); the longer the pain duration the higher the baseline average PDT (M = 15.16). There was a significant difference in average baseline PDT by the location of pain (F = 12.52, df = 3, p = .017, η^2 = .904); the highest baseline average PDT were found with upper back pain (M = 16.16). There was also a significant difference in average baseline PDT by the 24-hour opiate drug dose (F = 15.52, df = 3, p = .017, η^2 = .904); the greater the 24-hour opiate drug dose the higher the baseline average PDT (M = 15.16). Table 7 lists the PDT percent change during VS-S testing and Table 8 lists the PDT percent change during CS-S testing. The PDT percent change scores allowed comparisons of the average variability with thresholds measured during self-stimulation at four and eight minutes, within subjects and between subjects. The PDT pre-stimulation, during stimulation, and post-

stimulation results were entered into a spreadsheet and difference scores were calculated for PDT (See Appendix J).

Table 6: ANOVA Average baseline PDT

Variable	F	df	p
Age	18.91	4	=.018
Reproductive stage	5.63	1	=.055
Cycle day	.44	3	=.734
Intermittent / continuous	1.91	1	=.216
Pain duration	18.91	4	=.018
Location	12.52	3	=.017
Opiate 24-hr dose	15.52	3	=.017
MPI-MAP Classification	.37	3	=.780
Visceral / somatic	.65	1	=.453

Table 7: PDT results during VS-S

Subject	% change during 4 min	% change during 8 min	Average variability %
1	7.87	-8.4	-11.24
2	-15.87	-21.4	-26.98
3	32.77	38.66	21.01
4	5.88	7.35	8.82
5	47.37	78.95	92.11
Average	7.512	13.324	14.566

Table 8: PDT results during CS-S

Subject	% change during 4 min	% change during 8 min	Average variability %
3	-7.69	10.12	10.12
4	-5.19	-6.60	3.30
5	13.04	65.22	113.04
Average	13.54	32.43	45.78

Pain tolerance results

There were no significant differences in average baseline PTT by age, reproductive stage, cycle day, pain frequency (intermittent or continuous), pain duration, pain location, MPI-MAP classification, or pain type (visceral or somatic) (See Table 9). Table 10 lists the PTT percent change during VS-S testing and Table 11 lists the PTT percent change during CS-S testing. The PTT percent change scores allowed comparisons

of the average variability with thresholds measured during self-stimulation at four and eight minutes, within subjects and between subjects. The PTT pre-stimulation, during, and post-stimulation results were entered into a spreadsheet and percent change scores were calculated (See Appendix J).

Table 9: ANOVA Average baseline PTT

Variable	F	df	p
Age	1.60	4	= .365
Reproductive stage	1.14	1	=.327
Cycle day	.25	3	=.857
Intermittent / continuous	.03	1	=.861
Pain duration	1.60	4	=.365
Location	2.83	3	=.170
Opiate 24-hr dose	13.94	3	=.170
MPI-MAP Classification	1.51	3	=.340
Visceral / somatic	1.06	1	=.340

Table 10: PTT results during VS-S

Subject	% change during 4 min	% change during 8 min	Average variability %
1	3.47	-4.83	-13.19
2	-15.08	-15.35	-15.64
3	19.75	19.75	19.75
4	-2.2	-9.86	-9.86
5	51.35	69.37	80.18
Average	7.024	10.564	11.412

Table 11: PTT results during CS-S

Subject	% change during 4 min	% change during 8 min	Average variability %
3	-2.42	13.49	15.57
4	6.73	2.78	2.78
5	19.87	20.54	28.57
Average	15.45	14.36	17.03

Psychometric and Biometric Properties of the Instruments Used

Instruments

Multidimensional Pain Inventory (MPI)

Cronbach's alpha for the MPI pre-study and post-study were .70 and .93 respectively, indicating acceptable internal consistency. This is similar to the Cronbach's alpha found in studies conducted in the development of the MPI. In those studies Cronbach's alpha was .70 to .90. According to Nunnally and Bernstein (Nunnally & Bernstein, 1994) a coefficient alpha of .70 is adequate. The MPI was self-administered again after the study was completed approximately one to two weeks after the pre-study test. Three women, subjects 3, 4, and 5, returned the post-study MPI. Pearson product moment correlation of MPI pre-study and post-study scores (r = .989) indicated stability over this time period.

Pain-o-meter (POM)

Cronbach's alpha for the POM is inappropriate. Criterion validity of the POM was supported by observed correlations between the POM VAS and POM WDS (r = .782, p = .022), POM WDS and POM WDSP (r = .870, p = .005), and POM WDS and POM WDSE (r = .799, p = .017). As expected, due to the dynamic nature of pain, stability (test-retest) of the POM-VAS (.63, p = .564) and POM-WDS (.974, p = .144) was not significant. Additionally post-hoc construct validity was conducted comparing the POM-VAS, POM-WDSP, POM-WDSE, and the combined POM-WDS with the MPI total score and the scores of the three scales of the MPI. Concurrent validity was demonstrated between POM-WDSP and the MPI total score (.84, p = 0.01) and the MPI Scale I (.89, p = 0.003). Concurrent validity was demonstrated between POM-WDSE and the MPI Scale II (.72, p = 0.04). Finally, concurrent validity was demonstrated between

combined POM-WDS, the MPI Scale I (.91, $p = 0.002$), and the MPI Scale II (.82, $p = 0.013$).

Devices

Ugo Basile Analgesy Meter

The moving parts and motor of the Ugo Basile Analgesy Meter (Ugo Basile, Stoelting Co., Wood Dale, IL) are made to operate without lubrication or maintenance. The Analgesy Meter was calibrated manually by moving the weight displacing screw to the one millimeter mark on the linear scale. The meter that indicated the amount of force used was manually set to zero prior to each test period.

Results of Hypotheses

The data from the spreadsheet were entered into a statistical program and inspected for outliers, missing data, and irregularities. Data were analyzed using SPSS (Release 12.0.1, Chicago, IL). The first three hypotheses were tested using two-tailed, paired sample t-tests. In a test of the first two hypotheses the average variability of the POM-VAS, PDT and PTT were compared with percent differences during self-stimulation at four and eight minutes in both experimental conditions. In a test of the third hypothesis, the VS-S average variability of the POM-VAS, PDT, and PTT were compared with the CS-S average variability of the POM-VAS, PDT, and PTT. Paired sample t-tests rather than independent t-tests were used because the experimental and control groups are dependent groups with each woman serving as her own control. Pre-self-stimulation, post-self-stimulation, and during self-stimulation at four and eight minutes difference scores were from the same individual in both experimental conditions. The paired sample t-test was appropriate to test the first three research hypotheses

comparing differences between the experimental and control conditions. The dependent variables (PDT, PTT, POM-VAS) were measured on ratio scales, random assignment to the order of experimental procedure satisfies the assumption of random assignment in a repeated measures design, and homogeneity of variance is assured because the same individuals make up the experimental and control groups. Finally, the variables were tested to determine that they were normally distributed. Although the t-test is robust with regard to normality, tests for normal distribution were conducted before other statistical measures. Data not normally distributed were transformed using log transformation. Although subjects were randomly assigned to experimental order, the comparison of the VS-S and CS-S effect was additionally tested using Wilcoxon-signed ranks test, a nonparametric test similar to the paired t-test. This test treated the VS-S and CS-S average variability as ordinal data to test whether there was a significant difference between VS-S and CS-S. The level of significance was set at $p \leq .05$ for all tests. For hypotheses 4 and 5, the duration of the effect was reported as a simple mean. A t-test was used to test the hypotheses that the effect of VS-S and CS-S lasted beyond the termination of self-stimulation at 12 minutes. A paired t-test was not necessary here because there is no comparison with the control condition.

Hypothesis 1

It was hypothesized that chronic pain intensity would decrease and pain detection threshold and pain tolerance threshold would increase during VS-S at four, eight, and 12 minutes in women with chronic pelvic or low back pain.

Chronic pain intensity during VS-S (See Figure 2)

Prior to testing, subjects' baseline chronic pain scores ranged from 3.5 to 6 on a visual analog scale (VAS) anchored by 0 no pain and 10 the worst possible pain. Subjects 3, 4, and 5 reported their pain score to be 3.5, subject 1 reported her pain score to be 3.8, and subject 2 reported her pain score to be 6. Subjects used words such as "aching" (n = 5), "dull" (n = 4), "pressing," "burning," "sore," "hurt," and "sharp" to describe the physical effect of their pain. Subjects used words such as "nagging" (n = 5), "troublesome" (n = 3), "annoying" (n = 3), "tiring" (n = 3), and "miserable" (n = 2) to describe the emotional effect of their pain. The average variability of chronic pain intensity assuming that post stimulation was 12 minutes was -32.18% (range -100% to +63.16%, *SD* 66.42%). The mean percent change in the chronic pain intensity during self-stimulation at four (4) minutes measured with the POM was -25.49% (range -100% to +36.84%, *SD* 57.09%). The mean percent change in the chronic pain intensity at eight (8) minutes was -17.02% (range -100% to +50%, *SD* 55.95%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability and the percent change at four (4) minutes ($t_{df4} = .715$, $p = .514$). Similarly, there was no significant difference between the average variability and the percent change at eight (8) minutes ($t_{df4} = 1.426$, $p = .227$). Subjects 1 and 2 experienced an increase in chronic pain intensity that lasted throughout and beyond the testing period. Subject 2 continued to experience chronic pain intensity greater than the baseline for 20 minutes; subject 1 continued to experience increased chronic pain intensity for three hours beyond the testing period. Because the chronic pain intensity

response lasted beyond twelve minutes, the percent change was analyzed at sixteen (16) minutes and at twenty (20) minutes. The average variability of chronic pain intensity at sixteen (16) minutes was -34.54% (range -100% to +31.58%, *SD* 56.35%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability, using sixteen (16) minutes to calculate the average variability, and the percent change at four (4) minutes ($t_{df4} = 1.11$, $p = .328$) or the percent change at eight (8) minutes ($t_{df4} = 1.91$, $p = .129$). The average variability of chronic pain intensity at twenty (20) minutes was -43.40% (range -100% to +31.58%, *SD* 59.03%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability, using twenty (20) minutes to calculate the average variability, and the percent change at four (4) minutes ($t_{df4} = 2.16$, $p = .097$) or the percent change at eight (8) minutes ($t_{df4} = 1.87$, $p = .136$).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the change in CPI during VS-S attributable to other independent variables (see Table 11). Statistically significant differences in the change in CPI was found by the pain type (visceral or somatic); CPI increased during VS-S in subjects who had visceral pain and decreased in subjects with somatic pain. This statistically significant difference in CPI change accounts for the significant changes seen in several other variables including age, MPI-MAP classification, menstrual cycle day, pain duration, the location of pain, and force of stimulation. There were also significant differences in the CPI change by pain frequency (intermittent or continuous) and the 24-hour opiate drug dose; women who took no opiate drugs and who had continuous pain had the greatest change in CPI.

Figure 2: Percent change in CPI during VS-S

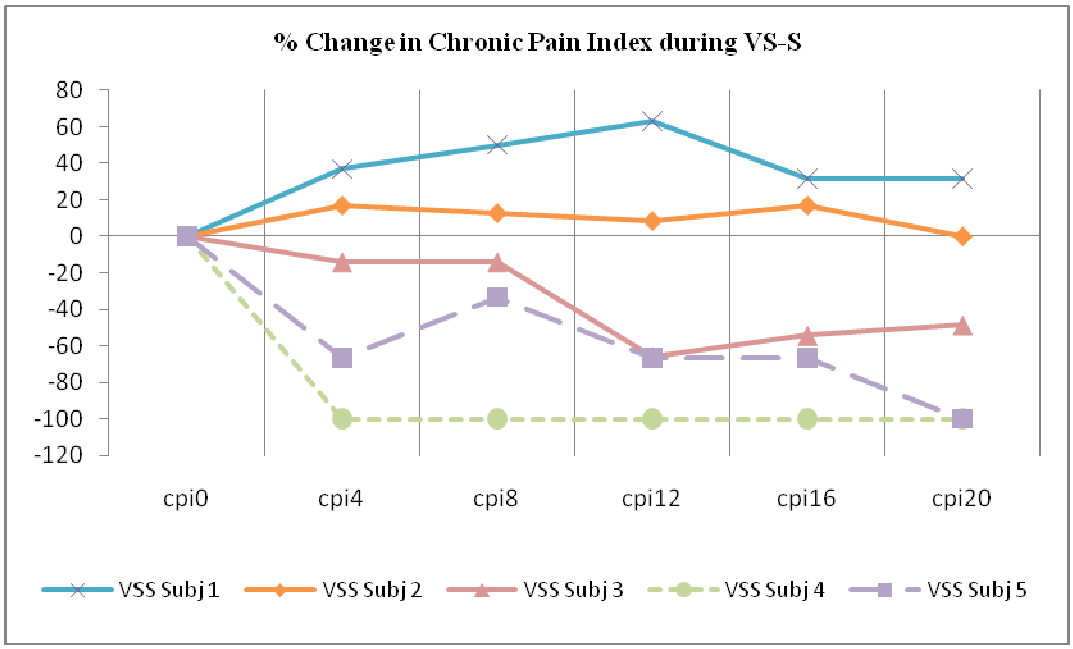


Table 12: CPI differences during VS-S

Variable	F	df	p
Age	35.44	4	<.001
MPI-MAP	12.49	3	<.001
Reproductive stage	1.00	2	= .396
Cycle day	20.19	2	<.001
Intermittent /	12.15	1	=.004
Pain duration	35.44	4	<.001
Location	23.78	3	<.001
Opiate 24-hr dose	23.78	3	<.001
Visceral / somatic	33.45	1	<.001
Force	35.44	4	<.001
Time (4, 8 or 12 minutes)	.08	2	= .924

Pain detection threshold during VS-S (See Figure 3)

Prior to VS-S pain detection threshold (PDT) was measured three times using the Analgesy-Meter. The averaged PDT prior to stimulation ranged from a low of 510 grams of pressure to a high of 926.25 grams of pressure. The average variability of pain detection, assuming that post stimulation was 12 minutes, was 16.74% (range -26.98% to +92.11%, *SD* 45.98%). The mean percent change in PDT during self-stimulation at four

(4) minutes measured with the Analgesy-Meter was 15.60% (range -15.87% to +47.37%, *SD* 24.74%). The mean percent change in PDT at eight (8) minutes was 19.03% (range -21.4% to +78.95%, *SD* 40.31%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT and the percent change at four (4) minutes (t_{df4} = .128, p = .904) or the percent change at eight (8) minutes (t_{df4} = .691, p = .528). Subject 2 experienced a decrease in PDT at four (4) minutes and in subjects 1 and 2 PDT was below the baseline threshold at eight (8) minutes and twelve (12) minutes. In subject 1 PDT returned to baseline in sixteen (16) minutes; in subject 2 PDT was still below threshold at twenty (20) minutes. Because the effect of VS-S on PDT lasted beyond the end of stimulation, the percent change was analyzed at sixteen (16) minutes and at twenty (20) minutes. The average variability in PDT at sixteen (16) minutes was 3.79% (range -25.4% to +51.23%, *SD* 28.97%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT, using sixteen (16) minutes to calculate the average variability, and the percent change at four (4) minutes (t_{df4} = 2.22, p = .091) or at eight (8) minutes (t_{df4} = 1.77, p = .151). The average variability in PDT at twenty (20) minutes was -1.92% (range -7.94% to 2.57%, *SD* 4.72%). A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT, using twenty (20) minutes to calculate the average variability, and the percent change at four (4) minutes (t_{df4} = 1.58, p = .190) or at eight (8) minutes (t_{df4} = 1.09, p = .336).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the change in PDT during VS-S attributable to other independent variables (see Table 13). Statistically significant differences in the change in PDT was found by the pain type (visceral or somatic); PDT increased during VS-S in subjects 3, 4 and 5 who had somatic pain and decreased in subjects 1 and 2 who had visceral pain.

As a result of these heterogeneous results additional statistical tests were conducted for descriptive purposes. The PDT raw data in grams of force measured on all four fingers of the non-dominant hand before testing, at four (4) minutes, eight (8) minutes, and 12 minutes separately for each subject were analyzed using repeated measures ANOVA. For significant departures from the assumption of sphericity the degrees of freedom were corrected using Greenhouse-Geisser for epsilon less than 0.75 or Huynh-Feldt for epsilon greater than 0.75. The change in PDT over time was not statistically significant in subject 1 ($F_{df1.132} = .550$, $p = .528$), subject 2 ($F_{df1.302} = 1.58$, $p = .294$), or subject 4 ($F_{df4} = .907$, $p = .491$). However, there were significant differences in PDT over time in subject 3 ($F_{df5} = 10.351$, $p < .001$), and subject 5 ($F_{df1.19} = 42.607$, $p = .004$). Subsequent paired comparisons were tested for subjects with statistically significant repeated measure ANOVA results. Subsequent paired comparisons for subject 3 indicated that there were significant differences between pre-stimulation PDT and PDT at four (4) minutes ($p = .036$), eight (8) minutes ($p = .005$), and 12 minutes ($p=.042$). Subsequent paired comparisons for subject 5 found significant differences between pre-stimulation PDT and PDT at four (4) minutes ($p = .004$), eight (8) minutes ($p = .001$), 12 minutes ($p =.010$), and 16 minutes ($p = .005$).

The statistically significant difference in PDT change by pain type accounts for the significant changes seen in several other variables including age, pain duration, location of pain, and force of stimulation. There were also significant differences in the PDT change by the MPI-MAP Classification and the 24-hour opiate drug dose. Finally, there were significant differences between subjects 3, 4, and 5 in PDT raw data in grams of force measured on all four fingers of the non-dominant hand before testing.

Figure 3: Percent change in PDT during VS-S

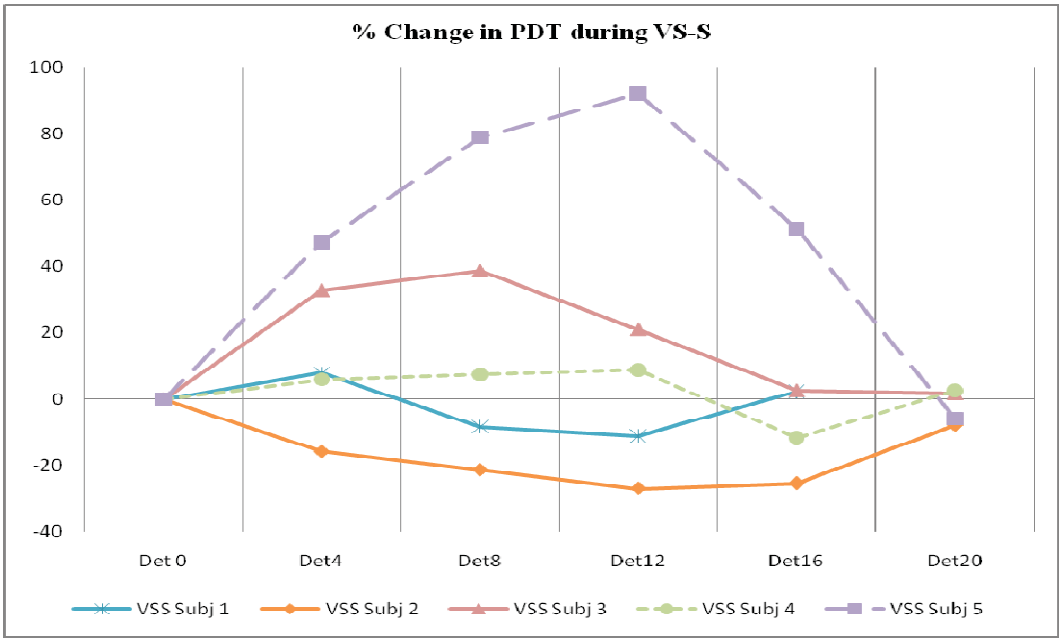


Table 13: PDT differences during VS-S

Variable	F	df	p
Age	26.60	4	< .001
MPI-MAP	23.85	3	<.001
Reproductive stage	18.14	2	< .001
Cycle day	1.04	2	= .385
Intermittent / continuous	.273	1	= .610
Pain duration	26.60	4	< .001
Location	4.40	3	= .029
Opiate 24-hr dose	4.40	3	= .029
Visceral / somatic	13.49	1	= .003
Force	26.60	4	< .001
Time (4, 8 or 12 minutes)	.01	2	= .990

Pain tolerance threshold during VS-S (See Figure 4)

Prior to VS-S pain tolerance threshold (PTT) was measured three times using the Analgesy-Meter. The averaged pain tolerance threshold prior to stimulation ranged from a low of 671.25 grams of pressure to a high of 1083.75 grams of pressure. The average variability of PTT assuming that post stimulation was 12 minutes was 12.25% (range -15.64% to +80.18%, *SD* 40.57%). The mean percent change in PTT during self-stimulation at four (4) minutes measured with the Analgesy-Meter was 11.46% (range -15.08% to +51.35%, *SD* 25.57%). The mean percent change in PTT at eight (8) minutes was 11.82% (range -15.35% to +69.37%, *SD* 34.86%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PTT and the percent change at four (4) minutes (t_{df4} = .121, p = .910) or at eight (8) minutes (t_{df4} = .088, p = .934). Subjects 2 and 4 experienced a decrease below the baseline PTT threshold at four (4) minutes that remained below the baseline threshold at twenty (20) minutes. Subject 1 initially had an increase in PTT above the baseline threshold at four (4) minutes but dropped below the baseline PTT at eight (8) minutes and remained below the baseline threshold twenty minutes (20) after the beginning of stimulation. Because the effect of VS-S on PTT lasted beyond the end of stimulation, the average variability was analyzed at sixteen (16) minutes and at twenty (20) minutes. The average variability in PTT at sixteen (16) minutes was -2.45% (range -19.61% to +36.04%, *SD* 21.98%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PTT at sixteen (16) minutes and the percent change at four (4) minutes (t_{df4} = 2.60, p = .060)

or the percent change at eight (8) minutes (t_{df4} = 2.10, p = .104). The mean percent change in PTT at twenty (20) minutes was -7.99% (range -11.17% to -3.82%, *SD* 3.17%). A paired t-test of the log transformed data indicated that there was no significant difference between the average variability, using twenty (20) minutes to calculate the average variability of PTT, and the percent change at four (4) minutes (t_{df4} = 1.796, p = .147) or at eight (8) minutes (t_{df4} = 1.296, p = .265).

Independent variables were analyzed using ANOVA to determine if there were statistically significant differences in the change in PTT during VS-S attributable to other independent variables (see Table 14). There was a significant increase in the PTT change by age, MPI-MAP Classification, duration of pain, reproductive stage, and force of stimulation. There were significant differences between subjects in pre-study PTT raw data in grams of force measured on all four fingers of the non-dominant hand. Statistically significant differences in the change in PTT was also found by the pain type (visceral or somatic); PTT increased during VS-S in subjects 3, 4, and 5 who had somatic pain and decreased in subjects 1 and 2 who had visceral pain.

Again, as a result of these heterogeneous results, additional statistical tests were conducted for descriptive purposes. The PTT raw data in grams of force measured on all four fingers of the non-dominant hand before testing, at four (4) minutes, eight (8) minutes, and 12 minutes separately for each subject were analyzed using repeated measures ANOVA. The degrees of freedom were corrected for repeated measures ANOVA results violating the assumption of sphericity using Greenhouse-Geisser for epsilon less than 0.75 or Huynh-Feldt for epsilon greater than 0.75. The change in PTT over time was not statistically significant in subject 1($F_{df3.95}$ = 1.933, p = .171), subject 2

($F_{df1.244}$ = 1.7278, p = .275), or subject 4 ($F_{df1.5}$ = 3.041, p = .148). However, there were significant differences in PTT over time in subject 3 ($F_{df1.679}$ = 14.856, p = .009) and subject 5 (F_{df5} = 62.619, p < .001). Paired comparisons of pre-stimulation PTT with during stimulation were conducted for significant results. Subsequent paired comparisons for subject 3 found significant differences between pre-stimulation PTT and PTT at four (4) minutes (p = .007), eight (8) minutes (p = .007), and at 12 minutes (p=.007). Subsequent paired comparisons for subject 5 found significant differences between pre-stimulation PTT and PTT at four (4) minutes (p = .002), eight (8) minutes (p < .001), and at 12 minutes (p <.001).

Figure 4: Percent change in PTT during VS-S

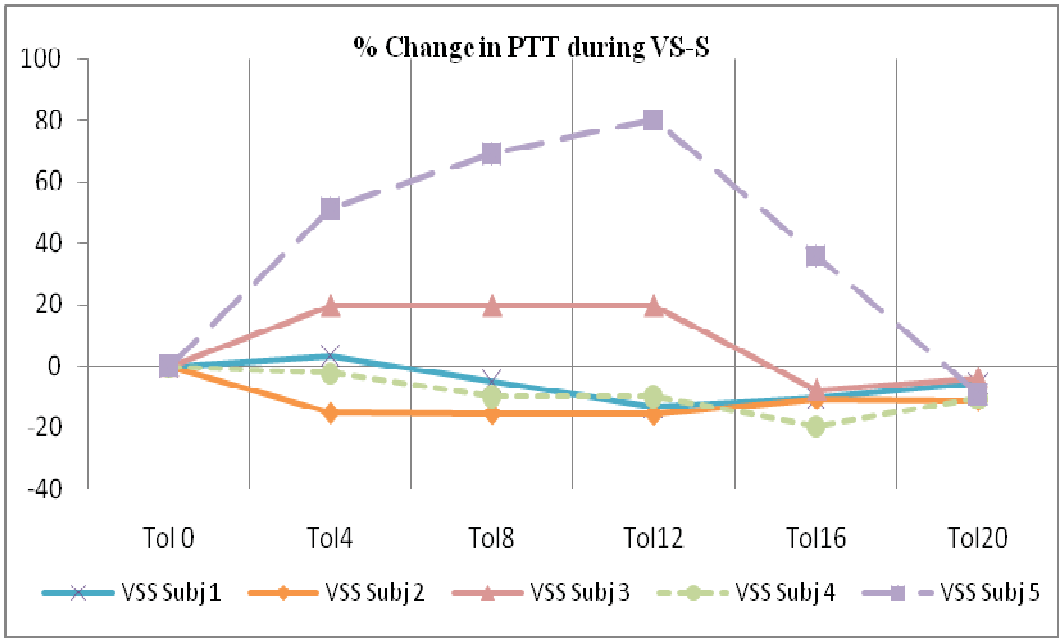


Table 14: PTT differences during VS-S

Variable	F	df	p
Age	55.87	4	< .001
MPI-MAP	26.66	3	<.001
Reproductive stage	15.33	2	< .001
Cycle day	1.78	2	= .210
Intermittent / continuous	1.41	1	= .256
Pain duration	55.87	4	< .001

Location	2.14	3	= .153
Opiate 24-hr dose	2.14	3	= .153
Visceral / somatic	6.77	1	= .022
Force	55.87	4	< .001
Time (4, 8 or 12 minutes)	.001	2	= .999

Hypothesis 2

It was hypothesized that chronic pain intensity would decrease and pain detection threshold and pain tolerance threshold would increase during CS-S in women with chronic pelvic or low back pain. Subjects 3, 4, and 5 were tested using CS-S. A table of random numbers generated at the beginning of the study was used to assign either VS-S or CS-S as the first experimental session. Subject 1 and subject 2 were assigned to VS-S for the first experimental session. Once VS-S increased their chronic pain, they refused further participation. Therefore, subjects 1 and 2 who had visceral pain did not participate in the CS-S experimental session.

Chronic pain intensity during CS-S (See Figure 5)

Prior to testing, subjects' baseline chronic pain intensity scores ranged from 0.6 to 3.5 on a visual analog scale (VAS) anchored by 0 no pain and 10 the worst possible pain. Subject 4 reported that she had no pain at rest but her pain score was 0.6 when walking. Subject 3 reported a pain score that was site specific varying from 3 to 3.75 and subject 4 reported her intermittent pain to be 3.5. Subjects used words such as "aching" (n = 2), "dull" (n = 2), "pressing" (n = 1), "burning" (n = 1), "sore" (n = 1), "hurt" (n = 1), and "sharp" (n = 1), to describe the physical effect of their pain. Subjects used words such as "annoying" (n = 2), "nagging" (n = 1), "troublesome" (n = 1), and "tiring" (n = 1) to describe the emotional effect of their pain. The average variability of chronic pain intensity assuming that post stimulation was 12 minutes was -62.41% (range -100% to

15.79%, *SD* 42.82%). The mean percent change in chronic pain intensity during self-stimulation at four (4) minutes, measured with the POM, was -42.36% (range -100% to 15.79%, *SD* 57.90%). The mean percent change in chronic pain intensity at eight (8) minutes was -49.37% (range -100% to -5.26%, *SD* 47.70%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between the average variability and the percent change at four (4) minutes ($t_{df2} = 1.959$, $p = .189$) or the percent change at eight (8) minutes ($t_{df2} = 1.64$, $p = .234$). Because the chronic pain intensity response lasted beyond twelve minutes, the percent change was analyzed at sixteen (16) minutes and at twenty (20) minutes. The mean percent change in the chronic pain intensity at sixteen (16) minutes was -62.41% (range -100% to -15.79%, *SD* 24.72%). A paired t-test of the log transformed data indicated that there was no significant difference between the average variability, using sixteen (16) minutes to calculate the average variability, and the percent change at four (4) minutes ($t_{df2} = 1.959$, $p = .189$) or the percent change at eight (8) minutes ($t_{df2} = 1.64$, $p = .234$). The mean percent change in the chronic pain intensity at twenty (20) minutes was –71.93% (range -100% to -15.79%, *SD* 28.079%). A paired t-test of the log transformed data indicated that there was no significant difference between the average variability, using twenty (20) minutes to calculate the average variability, and the percent change at four (4) minutes ($t_{df2} = 1.536$, $p = .264$) or the percent change at eight (8) minutes ($t_{df2} = 1.316$, $p = .319$).

Significant differences in the change in CPI during CS-S (see Table 15) were found by age, MPI-MAP Classification, menstrual cycle day, reproductive stage, pain duration, the frequency of pain (continuous or intermittent), and the force used during

self-stimulation. All significant differences in the change in CPI were accounted for by subject 4 who had a 100% decrease in CPI during CS-S. This woman was the youngest subject tested using CS-S, the only pre-menopausal woman and tested on day 7 of her menstrual cycle. She had intermittent chronic pain for the shortest duration, was not taking opiate drugs and used the least force during CS-S.

Figure 5: Percent change in CPI during CS-S

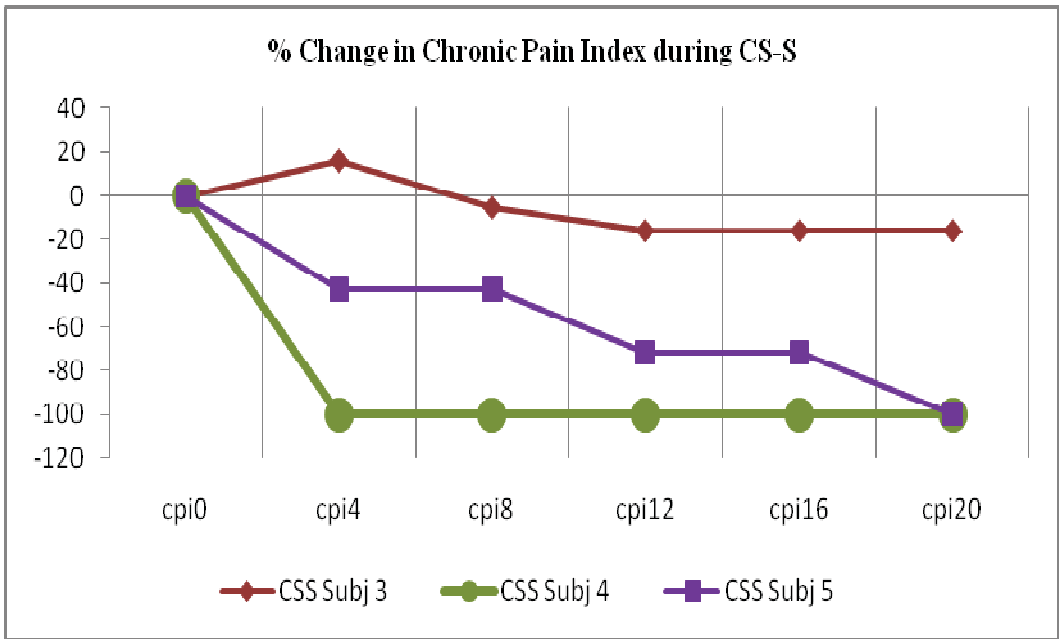


Table 15: CPI differences during CS-S

Variable	F	df	p
Age	31.44	2	=.001
MPI-MAP	31.44	1	=.001
Reproductive stage	15.65	1	=.005
Cycle day	15.18	1	=.006
Intermittent / continuous	15.65	1	=.005
Pain duration	14.76	1	=.006
Location	14.76	1	=.006
Opiate 24-hr dose	14.76	1	=.006
Force	40.94	2	<.001
Time (4, 8, 12 minutes)	.125	2	=.885

Pain detection threshold during CS-S (See Figure 6)

Prior to CS-S pain detection threshold (PDT) was measured three times using the Analgesy-Meter. The averaged PDT prior to stimulation ranged from a low of 530 grams of pressure to a high of 892.5 grams of pressure. The average variability of PDT, assuming that post stimulation was 12 minutes, was 42.15% (range 3.3% to 113.4%, *SD* 61.48%). The mean percent change in PDT during self-stimulation at four (4) minutes measured with the Analgesy-Meter was .053% (range -7.69% to +13.04%, *SD* 11.32%). The mean percent change in PDT at eight (8) minutes was 22.91% (range -6.6% to +65.22%, *SD* 37.58%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT and the percent change at four (4) minutes (t_{df2} = -1.604, p = .250) or at eight (8) minutes (t_{df2} = -1.463, p = .281). Subjects 3 and 4 experienced a decrease in PDT at four (4) minutes. In subject 4 the PDT remained below baseline threshold at eight (8) minutes but increased to 3.3% above the baseline at twelve (12) minutes; her PDT was 0.47% above baseline twenty minutes (20) after the beginning of stimulation. PDT was 21.01% above the baseline average in subject 3 and in subject 5 it was 113.04% above baseline. Because the effect of VS-S on PDT lasted beyond the end of stimulation in all of the subjects, the percent change was analyzed at sixteen (16) minutes and at twenty (20) minutes. The average variability in PDT at sixteen (16) minutes was 41.61% (range 4.72% to 101.09%, *SD* 52.00%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT, using sixteen (16) minutes to calculate the average variability, and the percent change at four (4) minutes (t_{df2} = -1.982, p = .186) or at eight (8) minutes (t_{df2} = -2.856, p = .104). The average

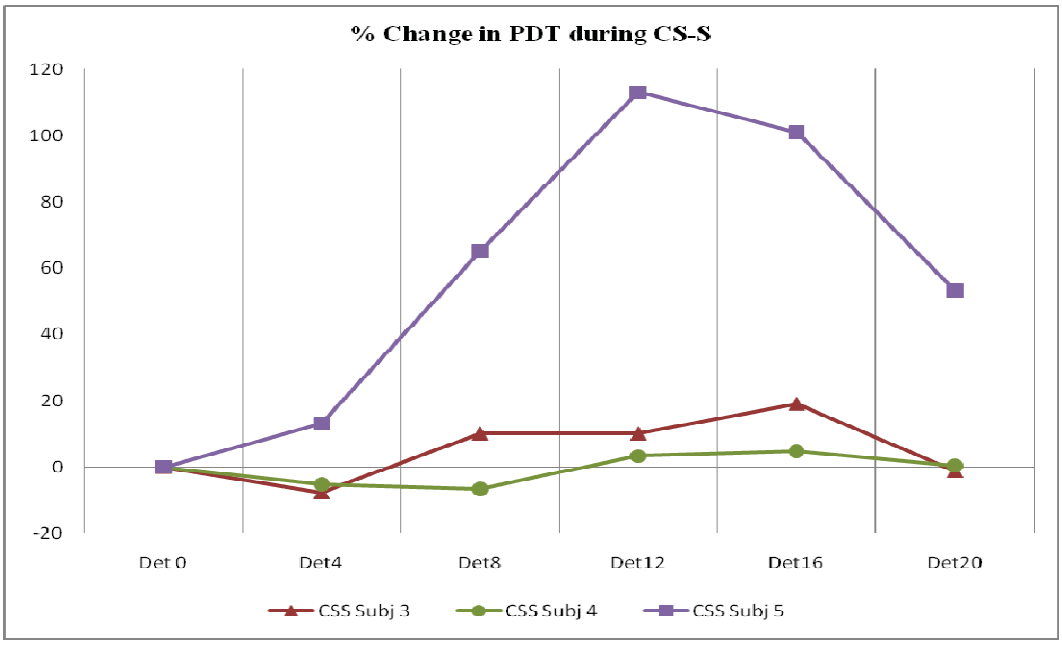
variability of PDT at twenty (20) minutes was 17.51% (range -1.21% to 53.26%, *SD* 30.97%). A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT, using twenty (20) minutes to calculate the average variability, and the percent change at four (4) minutes (t_{df2} = -1.651, p = .241). Similarly, there was no significant difference between the average variability at twenty (20) minutes and the percent change at eight (8) minutes (t_{df2} = .758, p = .527).

The PDT raw data in grams of force measured on all four fingers of the non-dominant hand before testing, at four (4) minutes, eight (8) minutes, and 12 minutes were analyzed using repeated measures ANOVA. Corrections were made to the degrees of freedom using Greenhouse-Geisser if epsilon was less than 0.75 or Huynh-Feldt if epsilon was greater than 0.75 for results violating the assumption of sphericity. The decrease in PDT was not statistically significant in subject 3 (F_{df5} = 1.811, p = .171) or subject 4 (F_{df5} = .779, p = .580). However, the difference in PDT over time was statistically significant in subject 5 ($F_{df1.25}$ = 45.290, p = .003). Paired comparisons between pre-stimulation PDT and other time periods were only conducted for statistically significant results of the repeated measures ANOVA. Subsequent paired comparisons for subject 5 found significant differences between pre-stimulation PDT and PDT at eight (8) minutes (p = .010), 12 minutes (p <.001), and 16 minutes (p = .001).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the change in PDT during CS-S attributable to other independent variables. There were no significant differences in PDT by age, reproductive stage, menstrual cycle day, pain frequency, duration, location, 24-hour opiate drug dose,

force used during CS-S, or the time period. There was a significant difference in PDT by MPI-MAP Classification (F_{df1} = 10.42, p = .014). Finally, there were significant differences between subjects in pre-study PDT raw data in grams of force measured on all four fingers of the non-dominant hand.

Figure 6: Percent change in PDT during CS-S



Pain tolerance threshold during CS-S (See Figure 7)

Prior to CS-S pain tolerance threshold (PTT) was measured three times using the Analgesy-Meter. The averaged PTT prior to stimulation ranged from a low of 853.75 grams of pressure to a high of 1177.5 grams of pressure. The average variability of PTT assuming that post stimulation was measured at 12 minutes was 15.64% (range 2.78% to 28.57%, *SD* 12.90%). The mean percent change in PTT during cervical self-stimulation at four (4) minutes measured with the Analgesy-Meter was 8.06% (range -2.42% to 19.87%, *SD* 11.20%). The mean percent change in PTT at eight (8) minutes was 12.27% (range 2.78% to 20.54%, *SD* 8.94%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired sample t-test of the log

transformed data indicated that there was no significant difference between the average variability of PTT and the percent change at four (4) minutes (t_{df2} = -1.153, p = .368) or at eight (8) minutes (t_{df2} = -1.419, p = .292). In subjects 3 and 4 the PTT was above baseline after twelve (12) minutes of stimulation but had returned to baseline sixteen (16) to 20 (20) minutes after the beginning of self-stimulation. The PTT in subject 5 remained 14.51% above baseline at twenty (20) minutes after the beginning of stimulation. Because the effect of VS-S on PTT lasted beyond the end of stimulation, the average variability was analyzed at sixteen (16) minutes and at twenty (20) minutes. The average variability in PTT at sixteen (16) minutes was 15.51% (range 2.49% to +27.9%, *SD* 15.95%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PTT at sixteen (16) minutes and the percent change at four (4) minutes (t_{df2} = -.750, p = .532) or the percent change at eight (8) minutes (t_{df2} = -.689, p = .562). The average variability in PTT at twenty (20) minutes was 4.75% (range -1.73% to 14.51%, *SD* 8.60%). A paired sample t-test of the log transformed data indicated that there was no significant difference between the average variability of PTT, using twenty (20) minutes to calculate the average variability, and the percent change at four (4) minutes (t_{df2} = 1.618, p = .247) or the percent change at eight (8) minutes (t_{df2} = 1.812, p = .212).

The PTT raw data in grams of force measured on all four fingers of the non-dominant hand before testing, at four (4) minutes, eight (8) minutes, and 12 minutes were analyzed using repeated measures ANOVA. The degrees of freedom were corrected for results violating the assumption of sphericity using Greenhouse-Geisser for epsilon less than 0.75 or Huynh-Feldt for epsilon greater than 0.75. The change in PTT over time was

not statistically significant in subject 4 ($F_{df1.214}$ = .341, p = .634). However, there were significant differences in PTT over time in subject 3 ($F_{df1.653}$ = 6.283, p = .047) and subject 5 ($F_{df1.612}$ = 17.037, p = .007). Paired comparisons of pre-stimulation PTT with during stimulation were conducted for significant results. Subsequent paired comparisons for subject 3 found significant differences between pre-stimulation PTT and PTT at 12 minutes ($p < .001$) and 16 minutes (p = .014). Subsequent paired comparisons for subject 5 found significant differences between pre-stimulation PTT and PTT at four (4) minutes (p = .001), eight (8) minutes ($p < .001$), 12 minutes (p = .006), 16 minutes (p = .008), and 20 minutes (p = .022).Statistically significant differences in the change in PTT during CS-S (see Table 16) were found by age, MPI-MAP Classification, pain duration, and force used during CS-S. All significant differences in the change in PTT were accounted for by subject 4 who had the least percent increase in PTT during CS-S. This woman was the youngest subject tested using CS-S, the only pre-menopausal woman, and tested on day 7 of her menstrual cycle. She had intermittent chronic pain for the shortest duration, was not taking opiate drugs, and used the least force during CS-S. Additionally, there were significant differences in PTT raw data in grams of force measured on all four fingers of the non-dominant hand before testing between subjects 3, 4, and 5.

Figure 7: Percent change in PTT during CS-S

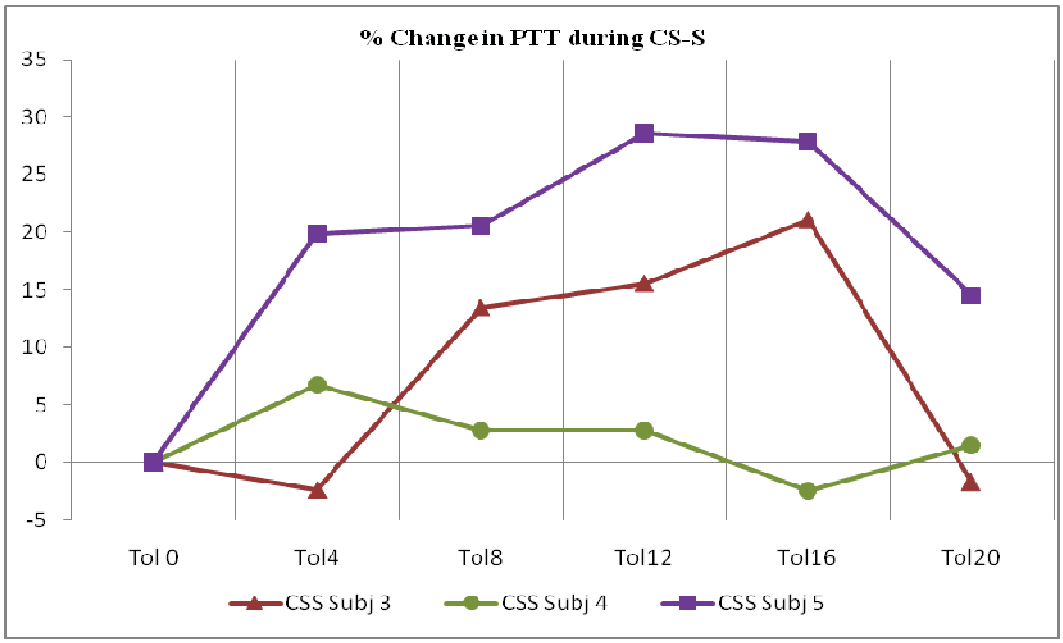


Table 16: PTT differences during CS-S

Variable	F	df	p
Age	6.92	2	=.028
MPI-MAP	13.37	1	=.008
Reproductive stage	3.57	1	=.101
Cycle day	3.57	1	=.101
Intermittent / continuous	3.57	1	=.101
Pain duration	6.92	2	=.028
Location	.387	1	=.553
Opiate 24-hr dose	.387	1	=.553
Force	6.92	2	=.028
Time (4, 8, 12 minutes)	.349	2	=.719

Hypothesis 3

It was hypothesized that CS-S would have a significantly greater effect on chronic pain intensity, pain detection threshold, and pain tolerance threshold than VS-S in women with chronic pelvic or low back pain. Only the women who were tested during VS-S and CS-S (Subjects 3, 4, and 5) were included in these analyses. There were no significant differences in age, cycle day, reproductive stage, pain duration, the 24-hour opiate drug dose, or force used by VS-S or CS-S between subjects.

Chronic pain intensity during CS-S compared with VS-S (See Figure 8)

The mean percent change in the chronic pain intensity during VS-S at four (4) minutes measured with the POM was -60.32% (range -100% to -14.29%, *SD* 43.21%). The mean percent change in chronic pain intensity during CS-S at four (4) minutes, measured with the POM, was -42.36% (range -100% to 15.79%, *SD* 57.90%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between chronic pain intensity at four (4) minutes during VS-S and chronic pain intensity at four (4) minutes during CS-S (t_{df2} = .614, p = .602).

The mean percent change in the chronic pain intensity during VS-S at eight (8) minutes was -49.21% (range -100% to -14.29%, *SD* 45.00%). The mean percent change in chronic pain intensity during CS-S at eight (8) minutes was -53.68% (range -100% to -18.18%, *SD* 41.97%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between chronic pain intensity at eight (8) minutes during VS-S and chronic pain intensity at eight (8) minutes during CS-S (t_{df2} = 1.634, p = .244).

The average variability of chronic pain intensity during VS-S at twelve (12) minutes, was -77.46% (range -100% to -65.71%, *SD* 19.53%). The average variability of chronic pain intensity during CS-S at twelve (12) minutes, was -62.41% (range -100% to -15.79%, *SD* 42.82%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of

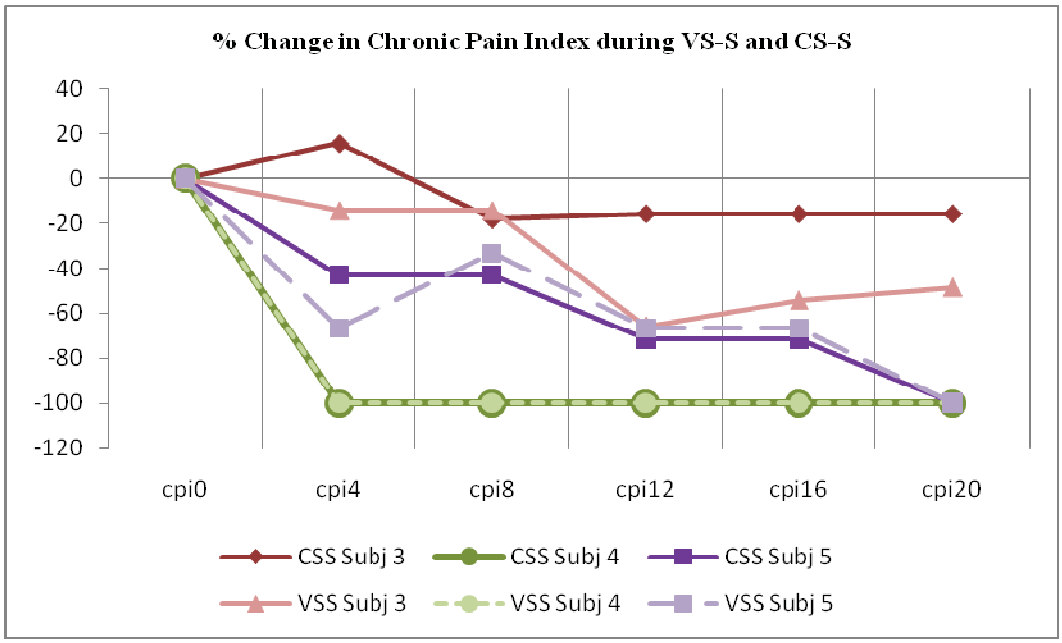
chronic pain intensity at twelve (12) minutes during VS-S and during CS-S (t_{df2} = -.842, p = .488).

The average variability of chronic pain intensity during VS-S at sixteen (16) minutes was -73.65% (range -100% to -54.29%, *SD* 23.64%). The average variability of chronic pain intensity during CS-S at sixteen (16) minutes was -62.41% (range -100% to -15.79%, *SD* 42.82%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of chronic pain intensity at sixteen (16) minutes during VS-S and during CS-S (t_{df2} = -.778, p = .518).

The average variability of chronic pain intensity during VS-S at twenty (20) minutes was -82.86% (range -100% to -48.57%%, *SD* 29.69%). The average variability of chronic pain intensity during CS-S at twenty (20) minutes was –71.93% (range -100% to -15.79%, *SD* 48.62%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of chronic pain intensity at twenty (20) minutes during VS-S and during CS-S (t_{df2} = -1.000, p = .423).

There was no significant difference in the mean percent change in CPI during VS-S (-62.33%) compared with CS-S (-51.38%) (F = .341, df = 1, p = .567, η^2 = .021). There was a significant difference in force used during VS-S (79.54 grams) compared with CS-S (27.06 grams) (F_{df1} = 19.22, p < .001).

Figure 8: Percent change in CPI during VS-S and CS-S



Pain detection thresholds during CS-S compared with VS-S (See Figure 9)

The mean percent change in pain detection threshold (PDT) during VS-S at four (4) minutes measured with the Analgesy-Meter was 28.67% (range 5.88% to +47.37%, *SD* 21.05%). The mean percent change in PDT during CS-S at four (4) minutes measured with the Analgesy-Meter was .053% (range -7.69% to +13.04%, *SD* 11.32%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PDT at four (4) minutes during VS-S and pain detection at four (4) minutes during CS-S ($t_{df2} = 3.29$, $p = .081$).

The mean percent change in PDT during VS-S at eight (8) minutes was 41.65% (range 7.35% to +78.95%, *SD* 35.89%). The mean percent change in PDT during CS-S at eight (8) minutes was 22.91% (range -6.6% to +65.22%, *SD* 37.58%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant

difference between PDT at eight (8) minutes during VS-S and PDT at eight (8) minutes during CS-S (t_{df2} = 3.57, p = .070).

The average variability of PDT during VS-S at twelve (12) minutes, was 40.65% (range 8.82% to +92.11%, *SD* 44.98%). The average variability of PDT during CS-S at twelve (12) minutes was 42.15% (range 3.3% to 113.4%, *SD* 61.48%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between the average variability of PDT at twelve (12) minutes during VS-S and the average variability of PDT at twelve (12) minutes during CS-S (t_{df2} = .074, p = .948).

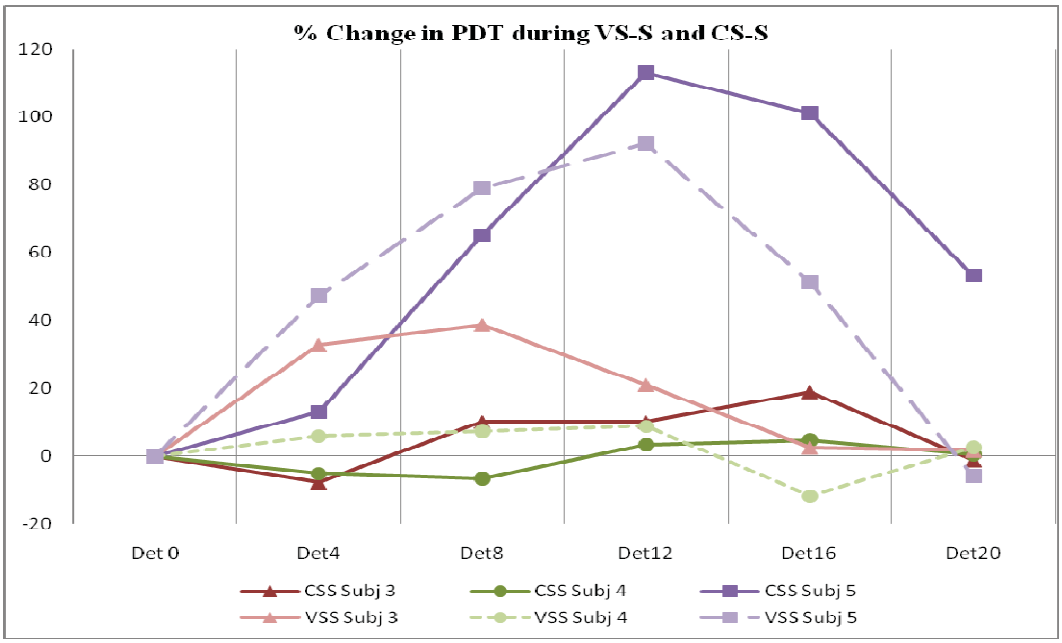
The average variability of PDT during VS-S at sixteen (16) minutes was 14.03% (range -11.76% to +51.32%, *SD* 33.08%). The average variability of PDT during CS-S at sixteen (16) minutes was 41.61% (range 4.72% to 101.09%, *SD* 52 %). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between pain detection at sixteen (16) minutes during VS-S and pain detection at sixteen (16) minutes during CS-S (t_{df2} = 3.44, p = .075).

The average variability of PDT during VS-S at twenty (20) minutes was -.556% (range -5.92% to 2.57%, *SD* 4.67%). The average variability of PDT during CS-S at twenty (20) minutes was 17.51% (range -1.21% to 53.26%, *SD* 30.97%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant

difference between pain detection at twenty (20) minutes during VS-S and pain detection at twenty (20) minutes during CS-S (t_{df2} = -.866, p = .478).

There was no significant difference in the mean percent change in PDT during VS-S (17.13%) compared with CS-S (21.71%) (F = .084, df = 1, p = .774, η^2 = .004).

Figure 9: Percent change in PDT during VS-S and CS-S



Pain tolerance thresholds during CS-S compared with VS-S (See Figure 10)

The mean percent change in pain tolerance threshold (PTT) during VS-S at four (4) minutes measured with the Analgesy-Meter was 22.97% (range -2.20% to +51.35%, *SD* 26.92%). The mean percent change in PTT during CS-S at four (4) minutes measured with the Analgesy-Meter was 8.06% (range -2.42% to 19.87%, *SD* 11.20%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PTT at four (4) minutes during VS-S and PTT at four (4) minutes during CS-S (t_{df2} = 1.81, p = .359).

The mean percent change in PTT during VS-S at eight (8) minutes was 26.42% (range -9.86% to +69.37%, *SD* 40.03%). The mean percent change in PTT during CS-S at eight (8) minutes was 12.27% (range 2.78% to 20.54%, *SD* 8.94%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PTT at eight (8) minutes during VS-S and PTT at eight (8) minutes during CS-S (t_{df2} = .709, p = .552).

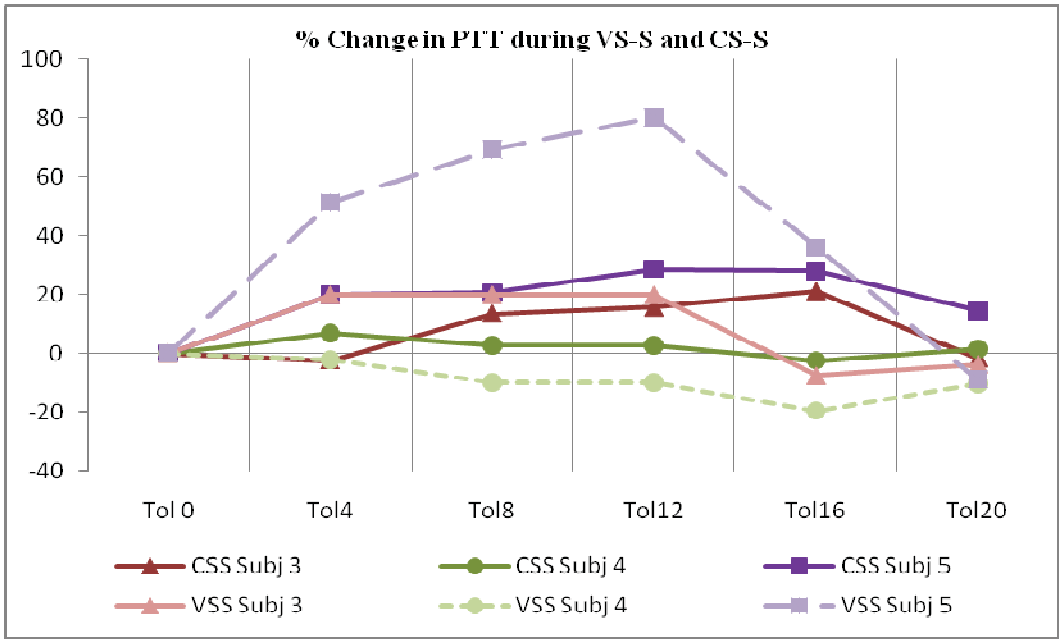
The average variability of PTT during VS-S at twelve (12) minutes was 30.02% (range -9.86% to +80.18%, *SD* 45.89%). The average variability of PTT during CS-S at twelve (12) minutes was 15.64% (range 2.78% to 28.57%, *SD* 12.90%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PTT at twelve (12) minutes during VS-S and PTT at twelve (12) minutes during CS-S (t_{df2} = .667, p = .573).

The average variability of PTT during VS-S at sixteen (16) minutes was 2.93% (range -19.61% to +36.04%, *SD* 29.29%). The average variability of PTT during CS-S at sixteen (16) minutes was 15.51% (range -2.49% to +27.9%, *SD* 15.95%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PTT at sixteen (16) minutes during VS-S and PTT at sixteen (16) minutes during CS-S (t_{df2} = -1.250, p = .338).

The average variability of PTT during VS-S at twenty (20) minutes was -10.81% (range -19.61% to -3.82%, *SD* 8.05%). The average variability of PTT during CS-S at

twenty (20) minutes was 4.75% (range -1.73% to 14.51%, *SD* 8.60%). Because the data were not normally distributed a log transformation was used prior to statistical analysis. A paired t-test of the log transformed data indicated that there was no significant difference between PTT at twenty (20) minutes during VS-S and PTT at twenty (20) minutes during CS-S (t_{df2} = -2.051, p = .177). There was no significant difference in the mean percent change in PTT during VS-S (11.84%) compared with CS-S (11.99%) (F = .000, df = 1, p = .989, η^2 = .000).

Figure 10: Percent change in PTT during VS-S and CS-S



Hypothesis 4

It was hypothesized that the effect of VS-S on chronic pain intensity, pain detection threshold, and pain tolerance threshold would outlast stimulation. Subjects 4 and 5 reportedly did not take pain medication before, during, or following the experimental session. Subject 1 had taken pain medication in the past but reported that at this time she was not taking medication because she did not like the way it made her feel. Subjects had been told to continue taking pain medication as ordered to maintain a steady

state of medication during the two-week intervals before and between the first and second experimental sessions. Subjects 2 and 3 were taking opiate medications that had been ordered. Although they did not take pain medication during the testing session, it is likely that they took pain medication as prescribed following the testing session because subjects were told not to change pain management throughout the test period. This could have had an effect on the duration of the effect of VS-S on their CPI, PDT, and PTT.

Effect of VS-S on chronic pain intensity duration

The mean duration of the effect of VS-S on chronic pain intensity was determined to be the number of minutes that it took for the chronic pain intensity to return to the baseline measure. When there was more than one pain location, the pain site that was most effected by VS-S was used to identify the duration of effect. Extreme outliers were entered into the statistical program for analysis as sixty (60) minutes. The mean duration of the effect of VS-S on chronic pain intensity was 52 minutes (range 20 minutes to 60 minutes, *SD* 17.89). The effect of VS-S on chronic pain intensity significantly outlasted stimulation ($t_{df4} = 5.00$, $p = .007$).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of VS-S on CPI attributable to other independent variables. Statistically significant differences in the change in CPI was found by the pain type (visceral or somatic) ($F = 58.52$, $df = 1$, $p < .001$, $\eta^2 = .818$); the duration of the effect of VS-S on CPI was longest in subjects 3, 4 and 5 who had somatic pain. This statistically significant difference in the duration of CPI by the type of pain accounts for the significantly longer duration by the location of pain ($F = 32.16$, $df = 1$, $p < .001$,

η^2 = .898), reproductive stage (F = 9.26, df = 1, p = .004, η^2 = .607), and 24-hour opiate drug dose (F = 32.16, df = 1, p < .001, η^2 = .898).

Effect of VS-S on pain detection threshold duration

The mean duration of the effect of VS-S on the PDT was determined to be the number of minutes that it took for the PDT to return to the baseline measure. The mean duration of the effect of VS-S on pain detection threshold was 18.4 minutes (range 16 minutes to 20 minutes, *SD* 2.19). The effect of VS-S on pain detection threshold significantly outlasted stimulation (t_{df4} = 6.53, p = .003).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of VS-S on PDT attributable to other independent variables. There was no statistically significant differences in the change in PDT by the pain type (visceral or somatic) (F = .371, df = 1, p = .553, η^2 = .028). Statistically significant differences in the duration of the effect of VS-S on PDT was by the frequency of pain (continuous or intermittent) (F = 7.80, df = 1, p = .015, η^2 = .375), location (F = 5.13, df = 1, p = .018, η^2 = .583) and by the 24-hour opiate drug dose (F = 5.13, df = 1, p = .018, η^2 = .583).

Effect of VS-S on pain tolerance threshold duration

The mean duration of the effect of VS-S on the pain tolerance threshold was determined to be the number of minutes that it took for the pain tolerance threshold to return to the baseline measure. The mean duration of the effect of VS-S on pain tolerance threshold was 17.6 minutes (range 14 minutes to 20 minutes, *SD* 2.61). The effect of VS-S on pain tolerance threshold significantly outlasted stimulation (t_{df4} = 4.802, p = .009).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of VS-S on PTT attributable to other independent variables. There was a statistically significant differences in the change in PTT by the pain type (visceral or somatic) ($F = 31.20$, $df = 1$, $p < .001$, $\eta^2 = .706$); pain frequency (continuous or intermittent) ($F = 19.15$, $df = 1$, $p = .001$, $\eta^2 = .596$), location ($F = 8.8$, $df = 3$, $p = .003$, $\eta^2 = .706$), and the 24-hour opiate drug dose ($F = 8.8$, $df = 3$, $p = .003$, $\eta^2 = .706$).

Hypothesis 5

It was hypothesized that the effect of CS-S on chronic pain intensity, pain detection threshold, and pain tolerance threshold would outlast stimulation. Subjects 4 and 5 reported that they did not take pain medication to manage their pain. Subject 3 was taking opiate medications as prescribed. However, since subjects had been told to continue taking pain medication as ordered during the two-week intervals before and between the first and second experimental sessions a steady state of medication should have been maintained. Although this subject did not take pain medication during the testing session, it is likely that she took pain medication following the testing session. This could have had an effect on the duration of the effect of CS-S on her CPI, PDT, and PTT.

Effect of CS-S on chronic pain intensity duration

The mean duration of the effect of CS-S on chronic pain intensity was determined to be the number of minutes that it took for the chronic pain intensity to return to the baseline measure. When there was more than one pain location, the pain site that was most effected by CS-S was used to identify the duration of effect. The mean duration of

the effect of CS-S on chronic pain intensity was 123.3 minutes (range 60 minutes to 180 minutes, *SD* 60.28). The effect of CS-S on chronic pain intensity did not significantly outlast stimulation (t_{df2} = 3.20, p = .085).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of CS-S on CPI attributable to other independent variables. There were no statistically significant differences in the duration of the effect of CS-S on CPI attributable to other independent variables.

Effect of CS-S on pain detection threshold duration

The mean duration of the effect of CS-S on the pain detection threshold was determined to be the number of minutes that it took for the pain detection threshold to return to the baseline measure. The mean duration of the effect of CS-S on pain detection threshold was 21.3 minutes (range 20 minutes to 24 minutes, *SD* 2.31). The effect of CS-S on pain detection threshold significantly outlasted stimulation (t_{df2} = 7.00, p = .020).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of CS-S on PDT attributable to other independent variables. There were no statistically significant differences in the duration of the effect of CS-S on PDT attributable to other independent variables.

Effect of CS-S on pain tolerance threshold duration

The mean duration of the effect of CS-S on the pain tolerance threshold was determined to be the number of minutes that it took for the pain tolerance threshold to return to the baseline measure. The mean duration of the effect of CS-S on pain tolerance threshold was 20 minutes (range 16 minutes to 24 minutes, *SD* 4.00). The effect of CS-S on pain tolerance threshold did not significantly outlast stimulation (t_{df2} = 3.46, p = .074).

Variables were analyzed using ANOVA to determine if there were statistically significant differences in the duration of the effect of CS-S on PTT attributable to other independent variables. There were no statistically significant differences in the duration of the effect of CS-S on PTT attributable to other independent variables.

Analysis of additional findings

Post hoc multiple regression analysis was used to test if there was a relationship between force used during self-stimulation, the day of the woman's menstrual cycle, reproductive stage, opiate analgesic 24-hour dose, pain duration, MAP-MPI classification, location, frequency, and pain type and the effect of self-stimulation on CPI, PDT, and PTT. The percent difference scores at four minutes, eight minutes, and the average variability for each experimental condition, VS-S and CS-S, were included in the model to provide enough degrees of freedom to conduct the regression analysis using eight independent variables. Variables were entered into the equation in the order listed above based on the empirical evidence that supports a relationship. The order in which variables are entered into the equation may influence the amount of variance accounted for by it. Significance tests of the slopes for the model and their intercepts were conducted. Backward elimination was used to produce the most efficient model to explain the findings.

The independent variables were regressed on the percent change in the chronic pain intensity. The variables that accounted for 93.3% of variance ($F_{df6} = 39.19$, $p < .001$) included pain type, menstrual cycle day, MPI-MAP Classification, the force used during self-stimulation, pain duration, and pain frequency. Backward elimination removed non-significant variables and resulted in a more efficient model that accounted

for 92.1% of the variance ($F_{df4} = 55.65$, $p < .001$). The pain type (β = -116.722, $p < .001$) was the most important variable followed by the MAP-MPI Classification score (β = 12.13, $p = .003$), the pain duration (β = 1.251, $p < .001$), and the force used during self-stimulation (β = -.251, $p = .067$). The menstrual cycle day (β = .995, $p = .331$) and pain frequency (β = -3.04, $p = .942$) did not reach significance and were excluded from the model.

The independent variables were regressed on the percent change in pain detection threshold. The variables that accounted for 73.5% of variance in the change in pain detection threshold which was significant ($F_{df6} = 7.842$, $p < .001$) included pain type, menstrual cycle day, MPI-MAP Classification, the force used during self-stimulation, pain duration, and pain frequency. Backward elimination removed non-significant variables and resulted in a more efficient model that accounted for 67.1% of the variance ($F_{df3} = 13.59$, $p < .001$). The pain type (β = -30.627, $p = .03$) was the most important variable followed by pain frequency (β = 21.224, $p = .002$), and MAP-MPI Classification score (β = 17.151, $p = .002$). The pain duration (β = -.934, $p = .364$), menstrual cycle day (β = -.337, $p = .764$), and the force used during self-stimulation (β = -.296, $p = .126$) did not reach significance and were excluded from the model.

The independent variables were regressed on the percent change in pain tolerance threshold. The variables that accounted for 79.3% of variance in the change in pain tolerance threshold, which was significant ($F_{df6} = 10.827$, $p < .001$) included pain type, menstrual cycle day, MPI-MAP Classification, the force used during self-stimulation, pain duration, and pain frequency. Backward elimination removed non-significant variables and resulted in a more efficient model that accounted for 76.6% of the variance

(F_{df4} = 15.58, p < .001). The pain type (β = 15.24, p = .042), MAP-MPI Classification score (β = 15.24, p < .001), menstrual cycle day (β = -.987, p = .021), and the force used during self-stimulation (β = .168, p = .086) were included in the final model. Pain duration (β = -.171, p = .612) and pain frequency (β = -8.22, p = .816) did not reach significance and were excluded from the model.

Chapter 5

The purpose of this study was to determine the effect of vaginal-cervical self-stimulation (VCS-S) on chronic pain intensity (CPI), pain detection threshold (PDT), and pain tolerance threshold (PTT); the time course of the onset and cessation of induced analgesia; whether there was a difference between the effect of vaginal self-stimulation (VS-S) and cervical self-stimulation (CS-S); and the duration of the effect. This study also sought to determine the separate and collective effects of the force used in self-stimulation, menstrual cycle, reproductive stage, opiate drugs used to manage chronic pain, the duration of chronic pain, and pain classification on the effects of vaginal and cervical self-stimulation.

According to the gate control theory (Melzack & Wall, 1965) "the presence or absence of pain is determined by the balance between the sensory and central inputs to the gate control system" (p.977) with intense peripheral stimulation of A fibers inhibiting noxious transmission at the substantia gelatinosa (SG) of the dorsal horn and activating an endogenous descending inhibitory pain control system. Based on this theory there is evidence that increasing sensory input can increase both the pain detection threshold and pain tolerance threshold (Anand & Craig, 1996; Maspes & Pagni, 1974; Melzack, 1977; Sternbach, 1970). The resulting pain modulation has been called stimulation-produced analgesia (Mayer et al., 1971). Vaginal-cervical stimulation (VCS) is a form of peripheral stimulation-produced analgesia. VCS activates both the nonopioid and opioid descending pain blocking systems (Komisaruk, 1982). VCS has been shown to produce analgesia in animals (Komisaruk & Larsson, 1971; Komisaruk & Wallman, 1977) and VS-S has been found to effectively raise pain detection and pain tolerance thresholds to experimentally

induced pain in women, including four women with chronic pain (Komisaruk & Whipple, 1986; Whipple, 1986). Studies with rats found that it is stimulation of the hypogastric, pelvic, and vagus nerves that produces analgesia in response to VCS (Cueva-Rolon et al., 1996; Cueva-Rolon et al., 1991; Cunningham et al., 1991; Guevara-Guzman et al., 2001; Komisaruk et al., 1996). In rats the analgesic effect of VCS was reported to last for several minutes after probing, gradually diminishing over a period of four minutes (Komisaruk & Wallman, 1977). In a pilot study of four women with chronic pain (Whipple, 1986), one subject reported that the analgesic effect of VS-S lasted eight minutes, during which time she had total pain relief.

Hypothesis 1

It was hypothesized that CPI would decrease and PDT and PTT increase during VS-S at four (4), eight (8), and twelve (12) minutes in women with chronic pelvic, abdominal, or low back pain. This hypothesis was partially supported by the data. A surprising finding was that there was a statistically significant difference in the percent change in CPI, PDT, and PTT by whether the pain was visceral or somatic in origin. In women with visceral pain (Subjects 1 and 2), there was a completely opposite, statistically non-significant response than responses previously reported in animal studies and women. That is, CPI increased and PDT and PTT decreased as a result of self-stimulation. In two of the subjects with somatic pain, there was a statistically significant difference between pre-stimulation pain thresholds and thresholds measured during self-stimulation.

Chronic pain intensity during VS-S

There was no significant difference between the percent change in CPI at four (4) minutes or the percent change in CPI at eight (8) minutes and the average variability whether calculated at twelve (12) minutes, sixteen (16) minutes, or twenty (20) minutes. The mean percent change in CPI increased 27% during VS-S in subjects 1 and 2 who had visceral pain and decreased 69% in subjects 3, 4, and 5 who had somatic pain. There was a greater increase in the percent change in CPI in the youngest subjects and subjects who had low abdominal or pelvic pain who were also the subjects with visceral pain. The two subjects with visceral pain experienced an increase in chronic pain intensity throughout the testing period. In subject 2 the greatest increase in CPI was 17% above baseline at four (4) minutes of self-stimulation. Her CPI returned to baseline eight (8) minutes following the end of self-stimulation. But in subject 1, the greatest increase in the CPI that she reported was 63% above baseline after twelve minutes of self-stimulation. At twenty (20) minutes it was 32% above baseline and remained above the baseline for three hours. Subject 3 who had somatic pain, diagnosed as Complex Regional Pain Syndrome Type I, previously known as Reflex Sympathetic Dystrophy, had multiple painful sites prior to the beginning of VS-S including her left wrist, left hip, and left ankle. She reported an average 39% decrease in CPI in her left ankle during self-stimulation that did not return to baseline for 27 hours after the end of self-stimulation. Greater decreases in the percent change in CPI was found in the women who had continuous, somatic pain, took no opiate drugs, and used the greater force in self-stimulation than in other subjects.

Pain detection threshold during VS-S

There was no significant difference between the average variability of PDT whether calculated at twelve (12) minutes, sixteen (16) minutes, or twenty (20) minutes and the percent change in PDT at four (4) minutes or at eight (8) minutes. There were statistically significant differences in the percent change in PDT by whether the pain was visceral or somatic; PDT increased an average of 25% during VS-S in subjects who had somatic pain and decreased and average of 11% in subjects with visceral pain. Subject 5 who had idiopathic low back pain reported a 92% increase in PDT after twelve (12) minutes of self-stimulation. Subject 2 experienced a 16% decrease below PDT baseline at four (4) minutes that decreased further to 27% below baseline and did not return to baseline for eight (8) minutes after self-stimulation ended. Subject 1 who had visceral pain experienced an initial increase in PDT 8% above baseline threshold at four (4) minutes but her PDT dropped 8% below baseline at eight (8) minutes, decreased further to 11% below baseline at twelve (12) minutes; PDT returned to baseline at sixteen (16) minutes.

As a result of these heterogeneous results additional statistical tests were conducted for descriptive purposes only. The PDT raw data in grams of force measured on all four fingers of the non-dominant hand before testing, at four (4) minutes, eight (8) minutes, and 12 minutes separately for each subject were analyzed using repeated measures ANOVA with subsequent pre-stimulation and during stimulation paired comparisons for significant results. The change in PDT over time was statistically significant in subjects 3 and 5. Additionally, there were greater increases in the percent change in PDT in women who took no opiate drugs and used the greatest force in self-

stimulation. There were also significant differences in pre-study PDT between the subjects.

Pain tolerance threshold during VS-S

There was no significant difference between the average variability of PTT whether calculated at twelve (12) minutes, sixteen (16) minutes, or twenty (20) minutes and the percent change at four (4) minutes or at eight (8) minutes. Statistically significant differences in the percent change in PTT was found by the pain type (visceral or somatic); PTT increased an average of 15% during VS-S in subjects 3, 4 and 5, who had somatic pain, and decreased an average of 10% in subjects 1 and 2 who had visceral pain. Subjects 1, 2, and 4 experienced a decrease in the percent change in PTT. Surprisingly PTT decreased below baseline PTT and remained below baseline PTT for eight (8) minutes after the end of self-stimulation in one woman with somatic pain resulting from osteoarthritis, an inflammatory pain syndrome. One of the women with visceral pain related to endometriosis (subject 2), experienced a decrease in PTT throughout self-stimulation that did not return to baseline for eight (8) minutes after the end of self-stimulation. In subject 1, PTT initially increased 3.5% above baseline at four (4) minutes but PTT decreased to 4.8% below baseline by eight (8) minutes and 13.2% below baseline at twelve (12) minutes. Her PTT remained 5.6% below baseline at twenty (20) minutes. Once again, as a result of these heterogeneous responses, repeated measures ANOVA with subsequent pre-stimulation and during stimulation paired comparisons for significant results were conducted separately for each subject for descriptive purposes. The change in PTT grams of force measured on all four fingers of the non-dominant hand over time was not statistically significant in subjects 1, 2, or 4. However in two of the

subjects with somatic pain, subjects 3 and 5, the difference in PTT over time was statistically significant. Paired comparisons of pre-stimulation with during stimulation measures revealed significant differences at four (4), eight (8), and 12 minutes in both of these subjects. The greatest increases in PTT during VS-S was in menopausal women, who were the oldest subjects, who had pain for the longest time, who took no opiate drugs, and who used the greatest force in self-stimulation. There were also significant differences in pre-study PTT between the subjects.

The finding that there was not a significant decrease in CPI and no significant increase in PDT or in PTT in three of the five subjects is inconsistent with the gate control theory and not concordant with the results of previous studies (Komisaruk & Whipple, 1986; Whipple, 1986). According to the gate control theory (Melzack & Wall, 1965) although chronic pain conditions open the gate, intense stimulation should close the gate, inhibiting noxious transmission at the substantia gelatinosa (SG) of the dorsal horn, and activating an endogenous descending inhibitory pain control system that can increase both pain detection threshold and pain tolerance threshold (Anand & Craig, 1996; Maspes & Pagni, 1974; Melzack, 1977; Sternbach, 1970). Therefore VS-S, as a form of intense peripheral stimulation, should have decreased CPI and increased both PDT and PTT in all of the subjects. In fact, in a pilot study of four women with chronic pain Whipple (1986) reported that "the intensity of their chronic pain decreased" (p.142) during VS-S and there was a similar increase in PDT and PTT as had been found in healthy women. According to Whipple (personal communication, March 21, 2003) subjects had neck pain, low back pain, rheumatoid arthritis, and chest wall pain, all forms of somatic pain. Women with abdominal, pelvic, or low back pain were chosen as

subjects in this study because there is evidence that peripheral stimulation is most effective when it is applied close to the painful body site and produces analgesia by stimulating the same somatotopic area of the midbrain, releasing endogenous opiates, and activating the descending inhibitory system (Soper & Melzack, 1982). In the current study, CPI decreased and the PDT and PTT increased during self-stimulation as hypothesized in women with somatic pain, located in the lower back, hip, lower limb, although it was statistically significant in only two of the subjects. However, contrary to previous studies, VS-S had an opposite effect on CPI, PDT, and PTT in the women in this study who had visceral pain due to endometriosis and interstitial cystitis, although the effect was not statistically significant. This appears to indicate that not only are somatic pain and visceral pain not the same but there may also be idiosyncratic responses in women with different types of somatic pain.

Animal models of endometriosis and interstitial cystitis were created in rats by implanting uterine horn tissue in surrounding organs that subsequently grew into endometriotic cysts (Berkley, Cason, Jacobs, Bradshaw, & Wood, 2001; Giamberardino et al., 2002; Vernon & Wilson, 1985). This resulted in symptoms similar to those seen in women with endometriosis and interstitial cystitis including pain, decreased bladder capacity, and hyperalgesia that varied with the estrous cycle (Berkley, Rapkin, & Papka, 2005; Cason, Samuelsen, & Berkley, 2003; Giamberardino et al., 2002). Inflammatory substances including plasma cells, polymorphonuclear cells, leukocytes, cytokines including nerve growth factor (NGF), prostaglandins, lymphocytes, and macrophages were found both inside and outside of these endometriotic cysts (Berkley, Dmitrieva, Curtis, & Papka, 2004; Cason et al., 2003; Giamberardino et al., 2002; Odagiri et al.,

2009). Inflammation, that has been shown to stimulate the development of nerve sprouts (Cervero & Laird, 1991), could explain the sympathetic and sensory C- and Aδ-fibers found in endometriotic cysts in rats and in layers of the endometrium and endometriotic lesions in women (Berkley et al., 2005; Tokushige, Markham, Russell, & Fraser, 2006; Tokushige, Markham, Russell, & Fraser, 2007; Zhang, Dmitrieva, Liu, McGinty, & Berkley, 2008). The adrenergic and C-fibers that innervate endometriotic lesions and directly connect with the spinal cord and brain via the pelvic, splanchnic, and vagus nerves (Berkley et al., 2004; Nagabukuro & Berkley, 2007) most likely explain the abdominal, vaginal, and sensory nerve hyperalgesia reported in endometriosis (Berkley, McAllister, Accius, & Winnard, 2007; Giamberardino et al., 2002; Odagiri et al., 2009). In a study of an animal model of cystitis, researchers (Bielefeldt, Lamb, & Gebhart, 2006) found evidence of viscerovisceral, viscerosomatic, and somatovisceral convergence with NGF related to the development of hyperalgesia. Inflammation and stimulation of sensitized nerves entering the spinal cord at many divergent areas results not only in viscero-visceral-somatic convergence but also in central sensitization (Berkley et al., 2005; Cason et al., 2003; Giamberardino et al., 2002). Finally, in the presence of chronic neuropathic and inflammatory pain descending controls can be either antinociceptive or pronociceptive depending on the stimulus modality, the level of cord segment involved, and whether the noxious stimulus arises from tissue of primary or secondary hyperalgesia (Pertovaara, 2000; Sawynok & Reid, 1996). Therefore, it is possible that CPI increased and PDT and PTT decreased in the subjects with visceral pain in this study as a result of somatic hyperalgesia, viscera-visceral-somatic convergence, and central sensitization (Bajaj, Bajaj, Madsen, & Arendt-Nielsen, 2003; Berkley et al.,

2004; Berkley et al., 2007; Berkley et al., 2005). The failure to support the hypothesis that CPI would decrease and PDT and PTT would increase during VS-S in subjects with visceral pain is likely related to the fact that stimulation during VS-S occurred close to the location of visceral pain and stimulated the same sensitized nerves associated with visceral pain.

Why was there not a significant decrease in CPI and significant increases in PDT and PTT in every women with somatic pain? VS-S might not have the same effect in women with different types of chronic abdominal, pelvic, or low back pain or as in animals, in healthy women, and women with pain sites distant to the stimulation site because of alterations in the endogenous pain control system. There is conflicting evidence concerning pain thresholds in subjects with chronic pain. In two studies (Lautenbacher et al., 1994; Ohrbach & Gale, 1989) that used pressure as the experimental pain stimulus, pain detection thresholds were lower in subjects with chronic pain than in healthy controls without pain. In four studies (Bendtsen et al., 1996; Clauw et al., 1999; McDermid et al., 1996; Vatine et al., 1998) that used pressure as the experimental pain stimulus, both pain detection and pain tolerance thresholds were found to be lower in subjects with chronic pain than in pain-free controls. In two other studies that used pressure as the experimental pain stimulus, one (Peters, M. L. & Schmidt, 1992) found no difference in pain detection thresholds between subjects and controls and the other (Jensen, R. et al., 1993) found no difference in pain detection threshold or pain tolerance threshold between subjects and controls. In a more recent study researchers (Giesecke et al., 2004) found significantly lower pain thresholds to pressure applied to the thumb and altered central nervous system pain processing in patients with idiopathic pain compared

with healthy controls. The persistent inflammation of arthritis creates hyperalgesia, peripheral hypersensitivity, and central sensitization that results in decreased pressure pain thresholds (Abramson, 2008; Imamura et al., 2008). In the chronic phase of CRPS I there is no longer inflammation but there may be changes in the central nervous system that result in changes in pain thresholds to cold, heat, and mechanical stimulation (Gradl et al., 2006; Huge et al., 2008; Kemler et al., 2001; Schinkel et al., 2006). There were significant differences in pre-study PDT and PTT among the subjects with somatic pain. Therefore, pre-stimulation differences in PDT and PTT in the women with chronic idiopathic low back pain, arthritis, and CRPS I may account for the variable effect of VS-S on PDT and PTT in this study.

Taken together the studies above indicate that there may be differential endogenous pain modulation in the presence of different chronic pain conditions. It has been suggested that either the magnitude, frequency, and duration of noxious stimulation in chronic pain overwhelms the descending antinociceptive system or an impairment in the endogenous system is related to increased pain sensitivity and the development of chronic painful conditions (Basbaum et al., 2009; Bruehl et al., 1999; Maixner et al., 1998). Porreca (2002) reported that persistent noxious input from peripheral inflammatory conditions results in increased descending facilitation of pain via the RVM rather than inhibition. This was supported by a study in which researchers (Kosek & Ordeberg, 2000) found that reduced descending noxious inhibitory control (DNIC) response to pressure pain in patients with chronic osteoarthritic pain was restored following surgery that eliminated their pain. This indicates that the endogenous descending pain system was dysfunctional in the presence of chronic pain but functioned

normally once the chronic pain was relieved. There is evidence that "in chronic CRPS, symptoms of inflammation disappear while neurological signs of small nerve fiber degeneration prevail" (Huge et al., 2008, p.e2742). In addition, contralateral sensory changes point to central nervous system involvement. Subjects with idiopathic back pain may have thresholds similar to healthy controls. In a study of spatial summation using cold water as the noxious stimulus, found that in chronic low back patients DNIC response was the same as healthy controls. This "suggests that chronic low back pain is not related to a lack of inhibitory influences…but rather to peripheral nociceptive activity and/or central sensitization" (Julien, Goffaux, Arsenault, & Marchand, 2005, p. 299). These pathophysiological differences might explain the idiosyncratic responses of statistically non-significant changes over time in PDT and PTT during VS-S in subject 4 diagnosed with osteoarthritis, an inflammatory condition, but statistically significant changes over time in 3 and subject 5, who did not have inflammatory conditions.

Hypothesis 2

It was hypothesized that CPI would decrease and PDT and PTT would increase at four (4), eight (8), and twelve (12) minutes during CS-S in women with chronic pelvic, abdominal, or low back pain. However, the data only partially supported this hypothesis. There was no statistically significant decrease CPI. However there was a statistically significant increase in PDT across time but only in subject 5 and a statistically significant increase in PTT during CS-S but only in subject 3 and subject 5. There were also significant differences in pre-study PDT and PTT among the subjects with somatic pain. Women with visceral pain did not complete this part of the study; only three women with somatic pain, subjects 3, 4, and 5 conducted CS-S.

Chronic pain intensity during CS-S

There was no significant difference between the average variability, whether calculated at twelve (12), sixteen (16), or twenty (20) minutes, and the percent change in CPI at four (4) minutes and the percent change at eight (8) minutes. The average change in CPI over baseline measurement during CS-S was 58%. The reported CPI increased 16% over baseline after four (4) minutes of self-stimulation in subject 3 diagnosed with Complex Regional Pain Syndrome Type I. After eight (8) minutes of self-stimulation she reported her CPI had decreased 5% below baseline and after twelve (12) minutes her CPI was 16% below baseline. Her CPI returned to baseline sixty (60) minutes after the beginning of CS-S. The other two women who participated in CS-S reported greater changes in CPI. Subject 5, with idiopathic low back pain, reported a 71% decrease in CPI after twelve (12) minutes of self-stimulation and a 100% decrease after twenty (20) minutes. She stopped recording her CPI after 180 minutes at which time it remained 100% below baseline. It is not known when it returned to baseline. Prior to testing that subject had reported continuous pain of 3.5 on a 0 to 10 scale. Subject 4 diagnosed with osteoarthritic low back pain, who prior to testing reported intermittent pain of 0.6 on a 0 to 10 scale, reported a 100% change in CPI over baseline after only four (4) minutes of self-stimulation. Her CPI returned to baseline after 130 minutes. Although she reported a 100% change in CPI during self-stimulation she said that it was difficult to accurately report the change in her back pain because she was aware of it mostly when walking. However, she confirmed that it was completely gone when she got up and walked after testing. This woman was the youngest subject, pre-menopausal, tested on day 7 of her menstrual cycle, had intermittent chronic pain for the shortest duration, was not taking

opiate drugs, and used the least force during CS-S. Significant differences in the change in CPI during CS-S by age, reproductive stage, menstrual cycle day, the frequency of pain (continuous or intermittent), pain duration, and the force used during self-stimulation were accounted for by this subject.

Pain detection threshold during CS-S

There was no statistically significant difference between the average variability of the PDT calculated at twelve (12), sixteen (16), or twenty (20) minutes and the percent change in PDT at four (4) minutes and the percent change at eight (8) minutes. The average variability of PDT at twelve (12) minutes was 42.15% (range 3.3% to 116.4%) above the baseline average. Subject 4 experienced a 5% decrease in PDT at four (4) minutes and a 6.6% decrease at eight (8) minutes; her PDT increased to 3.3% above the baseline at twelve (12) minutes; her PDT was 0.47% above baseline twenty (20) minutes after the beginning of stimulation. In subject 3, PDT decreased 8% below the pre-stimulation average after four (4) minutes of self-stimulation but increased to 10% above the pre-stimulation average after eight (8) minutes of self-stimulation and returned to baseline between sixteen (16) and twenty (20) minutes. Subject 5 diagnosed with idiopathic back pain was the only subject to have a statistically significant change in PDT over time during CS-S. Additionally, there were statistically significant differences between subjects in the pre-study PDT raw data in grams of force measured on all four fingers of the non-dominant hand.

Pain tolerance threshold during CS-S

There was no statistically significant difference between the average variability of the PTT calculated at twelve (12), sixteen (16) or twenty (20) minutes and the percent

change at four (4) minutes or at eight (8) minutes. PTT in subject 3, diagnosed with Complex Regional Pain Syndrome Type I, dropped 2% below the pre-stimulation average PTT after four (4) minutes of self-stimulation but after eight (8) minutes PTT was 14% above the pre-stimulation average and returned to baseline between sixteen (16) and twenty (20) minutes. The subject with osteoarthritic low back pain (subject 4) had minimal percent increases in PTT over the pre-stimulation average throughout self-stimulation, with the greatest increase (7%) after four (4) minutes of self-stimulation. Her average percent change in PTT throughout CS-S was 2%. The increase in PTT in subject 5 remained 14.51% above baseline at twenty (20) minutes after the beginning of stimulation. Repeated measures ANOVA of the raw PTT in grams of force revealed that there was a significant change in PTT over time in subject 3 and in subject 5. Additionally, there were statistically significant differences between subject 4 and subjects 3 and 5 in the pre-study PDT raw data in grams of force measured on all four fingers of the non-dominant hand before testing.

According to the gate control theory the endogenous descending inhibitory system controls pain by limiting at the gate the amount of ascending nociceptive information reaching the brain through alterations in the production and release of neurotransmitters (Basbaum et al., 2009). Centrally the principle structures involved in this descending system are the locus coeruleus (LC) and periaqueductal gray (PAG) of the midbrain, the raphe magnus (nRM) nucleus, and reticular formation of the medulla, and the dorsal horn of the spinal cord (Basbaum & Fields, 1978; Derbyshire, 2000; Hudson, 2000; Singewald & Philippu, 1998; Yelle, Oshiro, Kraft, & Coghill, 2009). It was believed for some time that vagal stimulation activated afferent neurons that terminate in the solitary tract

nucleus (nTS) and relay input primarily to the nucleus raphe magnus, and the locus coeruleus (LC) stimulating the endogenous descending inhibitory opiate, noradrenergic, and serotonergic systems (Hubscher & Berkley, 1994; Randich & Gebhart, 1992). Researchers (Komisaruk et al., 2002; Whipple & Komisaruk, 2002) demonstrated in studies of women with spinal cord injury (SCI) and one uninjured woman using positron emission tomography (PET) scans and magnetic resonance imaging (MRI) that response to vaginocervical stimulation occurred in the solitary tract nucleus (nTS). This was confirmed by evidence, using functional magnetic resonance imaging (fMRI), that in women with complete spinal cord injury, VS-S and CS-S activated the nucleus of the solitary tract, i.e., the vagal sensory nucleus in the medulla oblongata (Komisaruk, et al, 2004). There is evidence that stimulating the vagus nerve decreases pain. Stimulation of cervical or thoracic vagal afferents has been found to modulate response to noxious stimulation (Ness, Fillingim, Randich, Backensto, & Faught, 2000; Randich & Gebhart, 1992; Ren, Randich, & Gebhart, 1988). Furthermore, in women with spinal cord injuries at T10 or higher, VS-S significantly increased PDT (91.6%, $p < 0.01$) and PTT (46.1%, $p < 0.01$) and CS-S significantly increased PDT (72.7%, $p < 0.05$) and PTT (36.5%, $p < 0.01$) over the control conditions (Komisaruk et al., 1997). Therefore it was surprising that a statistically significant decrease in CPI over pre-stimulation averages was not found in this study and that statistically significant increases in PDT and PTT over time were not found in all subjects in this study.

However, there is empirical evidence that even direct stimulation of the brain does not always decrease chronic pain. For example, Schvarcz (1980) reported that even with direct stimulation of the thalamus two of six individuals with chronic pain failed to

obtain relief, two had a 50-70% pain reduction, and only two had greater than a 75% pain reduction. Furthermore, stimulation had no effect on experimentally induced pain. Direct low frequency stimulation of the somatosensory thalamus in five individuals with chronic neuropathic pain located in the face (3), low back and leg (1), and hand (1) resulted in a 60% long term reduction in chronic pain with repeated stimulation, although during stimulation pain intensity increased in two of the five subjects (Duncan et al., 1998). In a study with rats, Gintzler and Komisaruk (1991) used an implanted silastic disc in the uterus with a silk thread attached protruding through the cervix and vagina to apply pressure to the uterine side of the cervix without vaginal stimulation. In this study uterine cervical pressure at 150 g of force significantly increased ($p < 0.03$) tail flick latency (TFL) in six out of seven rats and at 100 g of force there was a 76 to 100% increase in three rats. However, in four rats there was a 3% to 21% decrease in tail flick latency (TFL). Furthermore, uterine cervical pressure applied following both pelvic and hypogastric neurectomy significantly decreased ($p < 0.05$) tail flick latency (TFL). Interestingly, this study found that cervical stimulation does not always induce analgesia. Similarly, researchers (Komisaruk et al., 1996) were surprised to find that stimulation of the cervix, following transection of the spinal cord at T7 with the pelvic, hypogastric, and vagus nerves intact, significantly decreased ($p < 0.05$) vocalization threshold (Voc-T). These studies of rats indicate that stimulation of the cervix can either increase or decrease nociceptive response.

There may be changes in brain function and structure in patients with chronic pain that account for the differential response to CS-S seen in this study. Imaging studies of subjects with chronic back pain (Flor, Braun, Elbert, & Birbaumer, 1997) found increased

cortical reactivity in the chronic pain subjects compared with healthy controls indicating an extension of the cortical representation of the painful area and functional reorganization of the primary somatosensory cortex (SI). In a review of studies of individuals with neuropathic pain, Peyron, Laurent and Garcia-Larrea (2000) reported decreased thalamic regional cerebral blood flow (rCBF), abnormal stimulus amplification in the thalamus, insula, SII, and posterior parietal cortex in response to acute pain stimulation of painful areas, and abnormal response in the anterior cingulate cortex (ACC) of either increased or decreased activity. Grachev, Fredrickson and Apkarian (2000) compared the concentrations of neurochemicals including glutamate, glutamine, γ-Aminobutyric acid (GABA), myo- and scyllo-inositol complex, glucose, and lactate, in three areas of the brain, the dorsolateral prefrontal cortex, cingulate cortex, and hypothalamus, between nine individuals with chronic pain and eleven controls without pain. Individuals with chronic back pain had significantly less total neurochemical concentration ($p < 0.0005$) in the dorsolateral prefrontal cortex and significant differences ($p < 0.02$) in the chemical interrelationships within and across brain regions related to diagnosis. There were significant ($p < 0.03$) enough differences in chemical connectivity patterns in the dorsolateral prefrontal cortex to differentiate between back pain subjects and controls. In addition, researchers found a significant effect ($p < 0.0007$) between perceptual measures of pain, including present pain intensity, duration, sensory, and affective components, and regional chemicals. The researchers concluded that these "results provide direct evidence of abnormal brain chemistry and chemical network in chronic back pain, which may be a consequence of long-term neurotransmitter changes in chronic pain sufferers" (p.16). Aberrations both peripherally and centrally with

concomitant changes in some of these same neurotransmitters have been implicated as the cause of chronic pain (Cervero & Laird, 1996; Dray, 1996; Kumazawa, Kruger, & Mizumura, 1996; Mense, Hoheisel, & Reinert, 1996; Nemeroff, 1988). Furthermore, VCS mediates many of these same neurotransmitters (Beyer et al., 1985; Komisaruk et al., 1988; Masters et al., 1993; Steinman, J. L. et al., 1994). More recently, using voxel-based morphometry (VBM) on structural MRI scans, studies of patients with chronic low back pain have shown structural loss of gray matter in the somatosensory cortex, dorsolateral prefrontal cortx, temporal lobe, and brainstem and significant increases in gray matter of the thalamus correlated with the intensity of pain (Schmidt-Wilcke et al., 2006) and with the duration of pain (Valet et al., 2009). These differences in brain function and structure may be related to changes in pain processing and explain why there were pre-study differences in PDT and PTT and why CS-S did not significantly decrease CPI and increase pain thresholds in all of the subjects with somatic pain conditions.

There is evidence that probing the vaginal cervix stimulates the vagus nerve and changes pain thresholds (Cueva-Rolon et al., 1996; Cueva-Rolon et al., 1991; Guevara-Guzman et al., 2001; Komisaruk et al., 1996). It is believed that vagal stimulation activates the endogenous descending inhibitory opiate, noradrenergic, and serotonergic systems (Randich & Gebhart, 1992). Studies with rats have demonstrated that VCS increases the release of endogenous serotonin and norepinephrine both of which are involved in the endogenous nonopioid descending inhibitory system (Crowley, Rodriguez-Sierra, & Komisaruk, 1977; Steinman & Komisaruk, 1981; Steinman, Komisaruk, Yaksh, & Tyce, 1983). Other studies have indicated that VCS stimulates an

endogenous opioid mechanism (Hill & Ayliffe, 1981; Rothfeld et al., 1985; Steinman, Roberts, & Komisaruk, 1982). Additionally, there is evidence that VCS alters the release of neurotransmitters, which activates both the nonopioid and opioid descending pain blocking systems (Komisaruk, 1982) that originates in the brain and descends through the dorsolateral funiculus (DLF) of the spinal cord (Watkins, Faris, Komisaruk, & Mayer, 1984). The rostral ventromedial medulla (RVM) is the main site of DLF projections (Fields, Malick, & Burstein, 1995). Direct stimulation of the RVM elicits responses similar to vagal stimulation. The RVM relays descending modulation of pain that is intensity dependent; that is, at low intensity stimulation it facilitates nociceptive transmission and at greater intensity it inhibits noceptive transmission at the spinal dorsal horn from noxious and non-noxious stimulation (Gebhart, 2004). It is possible that the stimulation used during CS-S in this study was not intense enough to have a significant inhibitory effect to experimental pain to result in a significant increases in pain thresholds in all subjects with somatic pain. Therefore in the subjects with somatic pain, PDT increased significantly only in subject 5 and PTT only increased significantly in subject 3 and subject 5.

There is equivocal evidence of the effectiveness of stimulation produced analgesia in subjects with chronic pain. Sweet and Wepsic (1968) applied electrical stimulation transcutaneously to several subjects but with mixed success. Two subjects experienced a decrease in chronic pain intensity by stimulating periodically. However, another subject reported that the chronic pain intensity was unrelieved after seven weeks of treatment. Jeans (1979) applied brief, intense TENS over painful areas, over distant trigger points, over distant nonrelevant points, and sham stimulation in a study of individuals with low

back pain, musculoskeletal pain, phantom limb pain, neuralgia, and causalgia. Only stimulation over painful areas showed significant improvement in chronic pain intensity as measured by the MPQ, Present Pain Intensity scale; the duration of pain relief, and the responses varied among subjects. Cheing and Hui-Chan (1999) reported a greater reduction in chronic pain intensity the longer that TENS was maintained (Spearman r = -.783, p = 0.013) on subjects with chronic low back pain. Therefore, it is possible that a longer period of CS-S may have been needed for the effect to be significant. In fact, CS-S continued to decrease CPI during the twelve (12) minutes of stimulation and in the subject with idiopathic pain a 100% decrease in the change in CPI was not reached for eight (8) minutes following the end of stimulation. Additionally, there was only a significant increase in PDT over pre-stimulation PDT in subject 5 after eight (8) minutes of self-stimulation. It took 12 minutes of self-stimulation to reach a significant increase in PTT in subject 3. However, all of the subjects reported that self-stimulation for twelve (12) minutes was tiring. Therefore, although a longer period of stimulation may have improved the effect on CPI, PDT, and PTT, it is unlikely that self-stimulation could have been maintained for longer than twelve (12) minutes.

Hypothesis 3

It was hypothesized that CS-S would have a significantly greater effect on chronic pain intensity, pain detection threshold, and pain tolerance threshold than VS-S in women with chronic pelvic or low back pain. Only the women with somatic pain were tested during both VS-S and CS-S (n=3). None of the subjects included in this analysis had visceral pain.

Chronic pain intensity during CS-S compared with VS-S

The findings, although not statistically significant, were opposite of what was hypothesized. Although the difference between the percent change in CPI at four (4) minutes during VS-S and the percent change in CPI at four (4) minutes during CS-S was not statistically significant, negative percent change in CPI was greater during VS-S than during CS-S. There was also no statistically significant difference between the percent change in CPI at eight (8) minutes during VS-S and the percent change in CPI at eight (8) minutes during CS-S; after eight minutes of self-stimulation CPI was slightly less (0.16%) during CS-S than during VS-S. Finally, there was also no statistically significant difference in the average variability of CPI at twelve (12) minutes, at sixteen (16) minutes, or at twenty (20) minutes during VS-S and the average variability of CPI at twelve (12) minutes, at sixteen (16) minutes, or at twenty (20) minutes during CS-S. However, the percent change in CPI following VS-S was consistently lower than the percent change in CPI following CS-S. Additionally, although there was not a statistically significant difference in the mean change in CPI during VS-S (-62.33) compared with the mean change in CPI during CS-S (-51.38), the percent change in CPI was greater during VS-S than it was during CS-S.

Pain detection thresholds during CS-S compared with VS-S

There was no statistically significant difference between the percent change in PDT at four (4) minutes or at eight (8) minutes during VS-S and the percent change in PDT at four (4) minutes or at eight (8) minutes during CS-S. However, at four (4) minutes and at eight (8) minutes PDT was higher during VS-S than during CS-S. There was not a statistically significant difference in the average variability of the PDT at

twelve (12) minutes, at sixteen (16) minutes, or at twenty (20) minutes during VS-S and the average variability of PDT at twelve (12) , at sixteen (16) minutes, or at twenty (20) minutes during CS-S. The average variability of PDT at twelve (12) minutes, at sixteen (16) minutes, and at twenty (20) minutes was higher during CS-S than during VS-S. Peak PDT during VS-S occurred at eight (8) minutes, while peak PDT during CS-S occurred at 12 minutes.

Pain tolerance thresholds during CS-S compared with VS-S

Although there was no statistically significant difference between the percent change in PTT at four (4) minutes or at eight (8) minutes during VS-S and the percent change in PTT at four (4) minutes or at eight (8) minutes during CS-S, PTT was higher during VS-S than during CS-S. There was no statistically significant difference between the average variability of PTT at twelve (12) minutes and the average variability of PTT at twelve (12) minutes during CS-S although the average variability of PTT was higher during VS-S than during CS-S. Similarly, there was no statistically significant difference in the average variability at sixteen (16) minutes or at twenty (20) minutes during VS-S and the average variability of PTT at sixteen (16) minutes or at twenty (20) minutes during CS-S. However, the PTT was higher during CS-S than during VS-S at sixteen (16) minutes and at twenty (20) minutes. Peak PTT occurred at 12 minutes during both VS-S and CS-S.

It was hypothesized that CS-S would have a significantly greater effect on CPI, PDT, and PTT than VS-S in women with chronic pelvic or low back pain because animal studies demonstrated greater response when the uterine cervix was stimulated (Berkley, Guilbaud et al., 1993; Rose, 1979) most likely because cervical stimulation also

stimulates the vaginal wall (Erskine, 1995). This results in convergence and summation of somatic and visceral stimulation (Komisaruk, 1974). Surprisingly, the findings of this study did not support this hypothesis. In fact, although not statistically significant, VS-S, rather than CS-S, had a greater effect on CPI throughout the testing session. Additionally, VS-S, rather than CS-S, had a greater effect on PDT and PTT during stimulation at four (4) and eight (8) minutes.

A simple explanation might be based on a dose-related response. In rats, VCS significantly increased Voc-T to electrical stimulation of the tail at forces of 100g ($\underline{p} < 0.05$), 200g ($\underline{p} < 0.05$), 400g ($\underline{p} < 0.05$), and 800g ($\underline{p} < 0.01$). Voc-T was increased 95% above pre-probe baselines at 100g, 104% above pre-probe baselines at 400g, and 256% above pre-probe baselines at 800g during the first minute of probing (Crowley et al., 1976). These findings demonstrate a dose-related response with greater force eliciting higher thresholds. In human studies, women who applied VS-S in a pleasurable way and women who achieved orgasm also demonstrated a greater analgesic response (Whipple, 1986; Whipple & Komisaruk, 1985; , 1988) and a greater increase in both PDT (48.8% to 146.8%) and PTT (36.6% to 114.3%) over the control condition (Whipple, 1986; Whipple & Komisaruk, 1988). Women who reportedly stimulated in a way that was not uncomfortable or pleasurable had the lowest PDT and PTT. These findings demonstrate a dose-related response with greater force, application of self-stimulation in a pleasurable way, or to orgasm resulting in a greater antinociceptive response. In the current study all of the women reported CS-S to be uncomfortable; one subject reported an increase in CPI at four minutes. Consequently, the women who participated in both VS-S and CS-S used significantly less force during CS-S (27.06 grams) than during VS-S (79.54 grams) (F_{df1}

= 19.22, $p < .001$). Subject 4, who used the least amount of force, had the smallest percent change in both PDT and PTT during CS-S. None of the women in this study experienced orgasm.

However, neither VS-S nor CS-S produced statistically significant responses in CPI, PDT, or PTT at four (4) minutes or at eight (8) minutes compared with the average variability of CPI, PDT, or PTT. Therefore, neither VS-S nor CS-S had the same effect as seen in previous animal or human studies. According to the gate control theory (Melzack & Wall, 1965) VS-S and CS-S, as forms of intense peripheral stimulation, should have activated an endogenous descending inhibitory pain control system through both an opioid (Crowley et al., 1977a; , 1977b) and nonopioid (noradrenergic) (Rodriguez-Sierra, Crowley, & Komisaruk, 1976; Steinman, J.L. et al., 1983) mechanism and inhibited noxious transmission of both chronic pain and experimentally induced pain at the SG of the dorsal horn. However, the gate control theory might not provide an adequate explanation of chronic pain. Although the gate control theory attempted to explain aspects of chronic pain, such as hyperalgesia, referred, and spontaneous pain, in terms of changes in the peripheral nervous system, this peripheral explanation failed to explain the development of chronic pain, in which there often is no known noxious stimulus. Chronic pain is neurophysiologically different from acute pain in more ways than simply the duration (Breen, 2002). As a result, interventions appropriate to acute pain may not be appropriate or effective in chronic pain (Pleuvry & Lauretti, 1996; Stubhaug & Breivik, 1997).

Finally, several studies have found structural loss of gray matter in the somatosensory cortex, dorsolateral prefrontal cortex, temporal lobe, and brainstem

(Schmidt-Wilcke et al., 2006; Valet et al., 2009). Coincidentally, these areas are also associated with the endogenous inhibitory system. “A decrease of gray matter in a brain region that is highly associated with pain suppression could certainly lead to a loss of effective antinociception”(Schmidt-Wilcke et al., 2006, p. 94). It is possible that different chronic pain conditions resulted in variation in the structural loss of gray matter and changes in the endogenous pain control system that resulted in differential pain modulation during both experimental conditions. This could explain why there were no significant decreases in CPI and idiosyncratic PDT and PTT responses in both experimental conditions as well as no significant difference between VS-S and CS-S in this study.

Hypothesis 4

It was hypothesized that the effect of VS-S on CPI, PDT, and PTT would outlast stimulation. The data from this study supported this hypothesis.

Effect of VS-S on chronic pain intensity duration

The decrease in CPI following VS-S lasted for an average of thirty-seven hours. The predicted duration of effect was 12 minutes. The effect of VS-S on chronic pain intensity, measured in minutes, lasted 11218% longer than predicted. The effect of VS-S on CPI in subjects with visceral pain was shorter than in subjects with somatic pain. CPI increased in subjects with visceral pain. The subject with interstitial cystitis (subject 1) reported that the increase in her CPI lasted for three (3) hours after testing. The subject with endometriosis (subject 2) also experienced an increase in CPI that lasted for eight minutes following the termination of VS-S. The subjects with somatic pain experienced a decrease in CPI that lasted from 23 hours to 51 hours following the termination of VS-S.

In addition to statistically significant differences in the change in CPI found by the pain type (visceral or somatic), and by the location of pain, statistically significant differences were also found by reproductive stage, and 24-hour opiate drug dose. The duration of the effect of VS-S on CPI was longest in subjects who had low back pain, were menopausal, and who took no opiate drugs.

Effect of VS-S on pain detection threshold duration

Subjects 1 and 2 experienced a decreased pain detection threshold that lasted for sixteen (16) minutes in subject 1 and for twenty (20) minutes in subject 2. In subject 3, the pain detection threshold was decreased at four (4) minutes but by eight (8) minutes was above the baseline measure and the increase in the pain detection threshold lasted for twenty (20) minutes. The pain detection thresholds returned to baseline twenty (20) minutes in all of the subjects. The mean duration of the effect of VS-S on pain detection threshold was 18.4 minutes (range 16 minutes to 20 minutes, *SD* 2.19). The effect of VS-S on PDT was predicted to be 12 minutes. The effect lasted 53% longer than predicted. There were no statistically significant differences in the change in PDT by the pain type (visceral or somatic). The duration of the effect of VS-S on PDT was significantly shorter in subjects who had continuous, low abdominal pain. The duration of the effect of VS-S on PDT was significantly longer the larger the 24-hour opiate drug dose.

Effect of VS-S on pain tolerance threshold duration

Subjects 2 and 4 experienced a decreased pain tolerance threshold that lasted for twenty (20) minutes. In subject 1, the pain tolerance threshold was increased at four (4) minutes but by eight (8) minutes was below the baseline measure and the decrease in the

pain detection threshold lasted for twenty (20) minutes. Subjects 3 and 5 had higher pain tolerance thresholds during VS-S; the effect on their pain detection thresholds lasted for fourteen (14) minutes in subject 3 and for eighteen (18) minutes in the subject 5. The mean duration of the effect of VS-S on pain tolerance threshold was 17.6 minutes (range 14 minutes to 20 minutes, *SD* 2.61). The effect of VS-S on PTT was predicted to be 12 minutes. The effect lasted 47% longer than predicted. Additionally, statistically significant differences in the change in PTT were found by the pain type (visceral or somatic); the duration of the effect of VS-S on PTT was shortest in subjects with somatic pain. The duration of the effect of VS-S on PTT was significantly shorter in subjects who had continuous, back pain, and who took no opiate drugs.

Hypothesis 5

It was hypothesized that the effect of CS-S on CPI, PDT, and PTT would outlast stimulation. In all cases the predicted duration of the effect was twelve (12) minutes. The effect of CS-S on chronic pain intensity lasted 928% longer than predicted. The effect of CS-S on PDT lasted 78% longer than predicted. The effect of CS-S on PTT lasted 68% longer than predicted.

Effect of CS-S on chronic pain intensity duration

Subject 5 stopped measuring at 180 minutes at which time the CPI had not returned to baseline. In subject 4 the chronic pain intensity score did not return to baseline for 130 minutes and in subject 3 the score did not return to baseline. The decrease in CPI following CS-S lasted for an average of two hours. The mean duration of the effect of CS-S on chronic pain intensity was 123.33 minutes (range 60 minutes to 180 minutes, *SD* 60.28). The predicted duration of effect was 12 minutes. The effect of CS-S

on chronic pain intensity lasted 928% longer than predicted. There were no statistically significant differences in the duration of the effect of CS-S on CPI attributable to other independent variables. In both experimental conditions, the effect outlasted the testing session.

Effect of CS-S on pain detection threshold duration

Subject 4 experienced a decreased pain detection threshold that lasted for eight (8) minutes but was above the baseline threshold by twelve (12) minutes and remained above the baseline for twenty (20) minutes. Subject 3 experienced a decreased pain detection threshold at four (4) minutes that was above the baseline at eight (8) minutes and lasted for twenty (20) minutes. In subject 5 PDT was above the baseline and remained that way for twenty-four (24) minutes. The mean duration of the effect of CS-S on pain detection threshold was 21.33 minutes (range 20 minutes to 24 minutes, *SD* 2.31). The effect of CS-S on PDT was predicted to be 12 minutes. The effect lasted 78% longer than predicted. There were no statistically significant differences in the duration of the effect of CS-S on PDT attributable to other independent variables.

Effect of CS-S on pain tolerance threshold duration

The pain tolerance threshold was increased in all of the subjects with the effect of CS-S on pain detection threshold lasting for sixteen (16) minutes in subject 4, for 20 minutes in subject 3, and for twenty-four (24) minutes in the subject 5. The mean duration of the effect of CS-S on pain tolerance threshold was 20 minutes (range 16 minutes to 24 minutes, *SD* 2.31). The effect of CS-S on PTT was predicted to be 12 minutes. The effect lasted 68% longer than predicted. There were no statistically

significant differences in the duration of the effect of CS-S on PTT attributable to other independent variables.

As was hypothesized the effect of VS-S and CS-S on CPI, PDT, and PTT outlasted stimulation. There is theoretical evidence to support this hypothesis. Wall and Sweet (Wall & Sweet, 1967) reported that the application of electrical stimulation over peripheral afferent nerves of seven subjects with various forms of neuropathic pain reduced the perception of pain that outlasted the period of stimulation for variable periods. The authors concluded analgesia outlasted stimulation because "once the gate is closed by an artificially generated heavy barrage of nerve impulses in the remaining large axons, the low level spontaneous activity in the smaller axons takes time to reopen the gate" (Wall & Sweet, 1967, p.109). Furthermore there is empirical evidence to support the hypothesis that the effect of VS-S on pain thresholds would outlast stimulation. In cats, (Rose, 1975), rats (Komisaruk & Wallman, 1977), and monkeys (Rose, 1979) neuronal response outlasted stimulation for up to five minutes. Price and others (Price et al., 1981) reported that WDR neuronal response outlasted rhythmic stimulation by 28-56 seconds extended the administration of estrogen. In another study, researchers (Berkley, Hubscher et al., 1993) observed that only inhibitory responses outlasted stimulation.

Several studies provide evidence that the analgesic response to VCS outlasts stimulation. In rats, the analgesic effect of VS was reported to last for several minutes after probing, gradually diminishing over a period of four to 6.5 minutes (Komisaruk & Wallman, 1977). In yet another study, researchers (Cueva-Rolon et al., 1995) found that at frequencies of 20-80 Hz electrical stimulation of the Aδ fibers of the vicerocutaneous branch of the pelvic nerve completely inhibited leg withdrawal to nociceptive foot pinch

that persisted beyond the period of stimulation. Longer trains of electrical stimulation produced long-lasting inhibition of the response to noxious stimulation persisting for up to 20 minutes after the termination of the stimulation. Following natural copulation, analgesia as measured by vocalizations outlasted stimulation by only 15 seconds (Gomora et al., 1994) and analgesia as measured by TFL outlasted copulatory stimulation no longer than 60 seconds and was related to the mating stimulus used (Lee & Erskine, 2000). However, Kornberg and Erskine (1994) reported that following natural copulation reproductively intact female rats displayed prolactin surges and progesterone levels that increased over a period of four days related to mating treatment. Finally, Whipple (1986) reported that in one human subject with chronic pain the analgesic effect of VS-S lasted eight minutes beyond stimulation during which time she had total pain relief.

Analysis of additional findings

The results of the regression analysis clarify what was found in the analysis of the variables using ANOVA already reported for each hypothesis. Statistically significant differences of the percent change in CPI during VS-S and CS-S were found by pain type (visceral or somatic), MPI-MAP classification, menstrual cycle day, frequency (intermittent or continuous), pain duration, location, the 24-hour opiate drug dose, and force used during self-stimulation. Multiple regression analysis allows the collective and separate analysis of all of these variables simultaneously. Regression analysis of CPI resulted in a model that includes pain type, higher MAP-MPI classification, duration of pain, and the force used during self-stimulation to account for the percent changes in CPI throughout VS-S and CS-S.

Statistically significant differences of the percent change in PDT during VS-S included age, pain type (visceral or somatic), MPI-MAP classification, pain duration, location, the 24-hour opiate drug dose, reproductive stage, and force used during self-stimulation. The only statistically significant difference in the percent change in PDT during CS-S was the MPI-MAP Classification. Once again, multiple regression analysis allowed the collective and separate analysis of all of these variables simultaneously. Regression analysis of PDT resulted in a model that includes pain type, pain frequency, and the MAP-MPI Classification score to account for the percent change in PDT during VS-S and CS-S.

Statistically significant differences of the percent change in PTT during VS-S included pain type, MPI-MAP Classification, reproductive stage, pain duration, and force. Statistically significant differences in the percent change in PDT during CS-S included age, MPI-MAP Classification, pain duration, and force. Statistically significant difference in the percent change in PDT during CS-S included the pain type, MPI-MAP Classification, pain duration, and the force used during self-stimulation. Again multiple regression analysis allowed the collective and separate analysis of all of these variables simultaneously. Regression analysis of PTT resulted in a model that included the pain type, the MAP-MPI Classification score, menstrual cycle day, and the force used during self-stimulation to account for the percent change in PDT during VS-S and CS-S.

Study Limitations

The greatest limitation of this study is the small sample size. During the early years of this study the investigator worked at a pain management center and had contact with many potential subjects. Even then it was difficult to obtain subjects for this study

primarily because women with chronic abdominal, pelvic, and low back pain were reluctant to participate for fear that stimulation would increase their chronic pain if they currently had pain or that it would cause their pain to return if they currently were pain-free. However, once the pain management center closed, it became even more difficult to find subjects. Primary care physicians regarded this study skeptically. The greatest source of referral was advanced practice nurses who worked with physicians in gastrointestinal and gynecological practices.

Additionally, there was an unbalanced sample. Three (3) subjects had somatic pain but only two (2) subjects had visceral pain. Statistically significant differences in CPI by the type of pain were found; subjects with visceral pain had an increase in CPI during stimulation and subjects with somatic pain experienced a decrease in CPI. Unfortunately the women with visceral pain were randomized to use VS-S first. Once their pain increased they were unwilling to participate in the second session using CS-S. Therefore, only three (3) women participated in the CS-S test, making this sample even smaller. Therefore, the sample is too small to generalize this finding.

It took longer during VS-S and CS-S to collect PDT, PTT, and CPI data than the one minute that was planned. Therefore, the reporting time periods varied slightly. For purposes of analysis, they were all analyzed as four (4), eight (8), twelve (12), sixteen (16), and twenty (20) minutes, although these times may have varied slightly. It is unknown if this affected the results of the study. Some women paused in self-stimulation as they tired. This pause may have had an effect on the PDT and PTT measures. The women in the CS-S condition of this study reported that CS-S was uncomfortable. Consequently less force was used during CS-S than during VS-S. This could have

resulted in lower percent changes in CPI, PDT, and PTT than might have occurred if greater force had been used.

The duration of effect on CPI beyond the VS-S and CS-S testing period was surprising. However, this too must be regarded with caution because subjects reported post-test CPI erratically. Some subjects reported only when they noticed a change in CPI, others forgot to document their CPI. This resulted in uneven time periods of analysis. Finally the women who took opiate drugs reported that they were not taking these medications at the time of testing. Subjects had been told to continue taking pain medication and using non-drug treatments as ordered to maintain a steady state of medication and treatment during the two-week intervals before and between the first and second experimental sessions. However, no blood levels were tested so the level of medication is unknown. Therefore, the effect of these opiates on the study findings, including the duration of the effect, is unknown. Finally, subjects reportedly did not use non-pharmacological methods of pain control during the study period, but there was no way to confirm that.

Chapter 6

The purpose of this study was to determine the time course and the duration of the effect of vaginal self-stimulation (VS-S) and cervical self-stimulation (CS-S) on the dependent variables chronic pain intensity (CPI), pain detection threshold (PDT), and pain tolerance threshold (PTT) and whether there was a difference between the effect of VS-S and CS-S on the dependent variables. Additionally, this study sought to determine the influence of the force used in stimulation, menstrual cycle, reproductive stage, opiate drugs used to manage chronic pain, the duration of chronic pain, and pain classification on the effect of VS-S and CS-S.

It was theorized that the chronic pain conditions experienced by the subjects of this study would open the gate and that the intense stimulation of VS-S and CS-S, forms of stimulation produced analgesia, would inhibit noxious transmission at the substantia gelatinosa (SG) of the dorsal horn, close the gate, and activate an opioid and nonopioid mechanism of the endogenous descending inhibitory pain control system (Melzack, 1977; Melzack & Wall, 1965). However, the findings of this study call into question the adequacy of this explanation in the presence of chronic pelvic, abdominal, and low back pain and specifically visceral pain.

It was hypothesized that CPI would decrease and PDT and PTT would increase during VS-S and CS-S at four (4), eight (8), and twelve (12) minutes in women with chronic pelvic, abdominal, or low back pain. It was also hypothesized that CS-S would have a significantly greater effect on CPI, PDT, and PTT than VS-S in women with chronic pelvic, abdominal, or low back pain. It was further hypothesized that the effect of VS-S and CS-S on CPI, PDT, and PTT would outlast stimulation.

Data were collected on five women between the ages of 20 and 46. Two of the women (subject 1 and 2) had chronic pelvic, abdominal, and low back visceral pain related to interstitial cystitis; subject 2 also had endometriosis. Three subjects had somatic low back pain that was idiopathic (subject 5), related to osteoarthritis (OA) (subject 4), and related to Chronic Regional Pain Syndrome Type I (CRPS I) (subject 3). The average duration of the subjects' chronic pain was 63.6 months. Subjects 3 and 5 were post-menopausal; subjects 1, 2, and 4 were pre-menopausal, although subject 2 was pharmacologically rendered amenorrheal. Although opiate medications were used by subjects 1, 2, and 3 and non-pharmacological pain management techniques were used by all of the subjects to manage their chronic pain reportedly none of the subjects used either at the time of testing.

The Multidimensional Pain Inventory (MPI) was used to collect data on pain severity, the support of a significant other, and how much pain interfered with activities. A computerized Multiaxial Assessment of Pain (MAP) was used to classify each woman into one of four descriptive categories based on MPI data. The Pain-o-Meter (POM) was used to collect information on present pain, including pain intensity, the physical and emotional modifiers used to describe pain, the frequency (intermittent or continuous), and the location of pain. The Analgesy-Meter was used to both create experimental pain, and to measure the PDT and PTT in grams of mechanical force. The stimulator handle used for both VS-S and CS-S was connected to a meter to monitor the amount of pressure used during stimulation. The stimulator used for VS-S consisted of a disposable, curved plastic rod inserted into a disposable tampon with a cushioned tip on one end the other end was inserted into the stimulator handle. The stimulator used for CS-S consisted of a

disposable, straight plastic rod attached to the stimulator handle and inserted into a disposable tampon with a Velcro® tip attached to a matching Velcro® fabric disk attached to a diaphragm to maintain the area of self-stimulation directly over the cervix and protect it from abrasion.

Data were analyzed using paired sample t-tests, multiple regression, and univariate and repeated measure ANOVAs, with subsequent paired comparisons of significant results using SPSS (Release 12.0.1, Chicago, IL: SPSS Inc.).

The hypothesis that CPI would decrease and PDT and PTT would increase during VS-S at four, eight, and 12 minutes in women with chronic pelvic, abdominal, or low back pain was partially supported by the data. In women with somatic pain, VS-S resulted in a decrease in CPI and an increase in PDT and PTT that was significant over time in two of the subjects. However, surprisingly in the subjects with visceral pain, CPI increased and PDT and PTT decreased during and following VS-S, although the change was not statistically significant. It was hypothesized that CPI would decrease and PDT and PTT would increase during CS-S in women with chronic pelvic, abdominal, or low back pain. There was no statistically significant decrease in CPI. There was however a statistically significant change in PDT over time in subject 5 and a statistically significant change in PTT over time in subject 3 and 5 during CS-S in this study. Although it was hypothesized that CS-S would have a significantly greater effect on CPI, PDT, and PTT than VS-S in women with chronic pelvic, abdominal, or low back pain the opposite was found; that is VS-S had a greater effect than CS-S, although it was not significant. The hypothesis that the effect of VS-S would outlast stimulation was supported by the data. In women with somatic pain VS-S decreased CPI for 23 to 51 hours after stimulation. In

women with visceral pain, VS-S increased CPI for 8 minutes and 3 hours following the end of stimulation. The effect of VS-S, either an increase or decrease in the PDT, lasted for four (4) to eight (8) minutes following the end of stimulation. The effect of VS-S on PTT, either an increase or decrease, lasted for two (2) to eight (8) minutes following the end of stimulation. The hypothesis that the effect of CS-S would outlast stimulation was supported by the data. CPI decreased and did not return to baseline measures for one to three hours following stimulation. The effect on PDT lasted for eight (8) to twelve (12) minutes following the end of stimulation. Similarly the effect of CS-S on PTT lasted for four (4) to twelve (12) minutes following the end of stimulation.

Conclusions

Although the results of this study must be viewed with caution based on the small sample size, it appears that this is the first human study to demonstrate a difference in the effect of neurostimulation on analgesia and pain thresholds. The results of this study indicate that not all chronic pain, even when located in the same area of the body, is the same.

At least in the sample in this study there was a significant difference in the effect of VS-S and CS-S on chronic pain intensity and pain detection and pain tolerance by the type of pain, visceral or somatic, and the type of somatic pain, that is inflammatory or non-inflammatory. The idiosyncratic responses of subjects in this study may explain the responses seen by other researchers when different stimulation methods were used. For example, other studies have found that stimulation of visceral organs produced excitation, inhibition, or both excitation and inhibition in central nervous system neurons (Berkley, Guilbaud et al., 1993; Berkley, Hubscher et al., 1993; Berkley, Wood, Scofield, & Little,

1995; Hornby & Rose, 1976). Stimulation of visceral organs by distention could have created visceral pain similar the condition experienced by the subjects in this study. It is possible that viscero-visceral-somatic convergence resulted in excitation of central nervous system neurons and increased CPI and decreased PDT and PTT not found in earlier animal or human studies using VS-S (Komisaruk & Whipple, 1986; , 1995; Whipple & Komisaruk, 1985; , 1988).

Many women who have chronic pelvic, abdominal, or low back pain complain of pain during intercourse (Huntington & Gilmour, 2005). In fact this causes sexual dysfunction in many chronic pain patients (Ambler, Williams, Hill, Gunary, & Cratchley, 2001). One subject in this study had not resumed sexual relations with her husband following the birth of their last child nine months before, because it was too painful for her to have intercourse. Therefore, it is not surprising that the women in this study used significantly less force and none of the women in this study experienced orgasm. It is possible that the force of stimulation in this sample was not intense enough to have a significant inhibitory effect on PDT and PTT to experimentally induced pain. Indeed studies have found that mechanical stimulation of the vaginal canal at different intensities depressed dorsal horn neurons (Henry, 1983). Additionally, studies have shown that VCS activates the descending pain blocking system (Komisaruk, 1982) that descends through the rostral ventromedial medulla (RVM) (Fields et al., 1995). The RVM relays descending modulation that at low intensity stimulation facilitates nociceptive transmission and at greater intensity inhibits noceptive transmission at the spinal dorsal horn from noxious and non-noxious stimulation (Gebhart, 2004). Furthermore, previous studies have found a dose-related effect of VS-S and CS-S (Komisaruk et al., 1997;

Whipple, 1986). Therefore, the failure to find a significant decrease in CPI and increase in PDT and PTT in all of the subjects may be related to the minimal force used in self-stimulation. It seems that the greatest effect of VS-S and CS-S was on CPI. From the patient perspective this is the most important concern. The change in PDT and PTT is of no importance to women suffering from chronic pain. Interestingly, the woman mentioned above did experience relief of chronic pain following VS-S for several days. She subsequently showed her husband this technique and as a result successfully resumed sexual intercourse.

Recent technological advances have enabled identification of central nervous system changes in structure and in pain processing in the brain (Schmidt-Wilcke et al., 2006; Valet et al., 2009). It is possible that VS-S or CS-S did not significantly decrease CPI and increase PDT and PTT in all of the subjects as a result of these structural and processing changes in the central nervous system. Central nervous system changes may have created dysfunction of the endogenous descending inhibitory pain control system. Or it may be that visceral pain conditions and inflammatory somatic pain conditions alter the normal physiologic response of the endogenous descending inhibitory pain control system.

There remain many unanswered questions. For example, is it chronic pain that results in central nervous system changes that causes dysfunction of the endogenous descending inhibitory pain system or is it dysfunction of the descending inhibitory pain system that enhances the transmission of nociceptive messages that leads to the development of chronic pain? Answers to these questions may help to understand the

responses of the subjects in this study to VS-S and CS-S and understand the complexity of chronic pain conditions.

Implications for Nursing

As a result of this study it is apparent that pain processing does not occur in the same way under different conditions of chronic pain, even when it appears that the pain is from the same location. It is important for nurses to realize that not all pain is the same and that not all pain interventions work the same way for everyone. This study demonstrated the need for targeted therapies for the management of chronic pain. If targeted therapies can be developed, perhaps we will have better pain control. With better pain control, there may be less medication misuse patients with chronic pain (Barry, Beitel, Joshi, & Schottenfeld, 2009; Savage, 2009).

Obviously mechanical VS-S and CS-S as tested in this study is impractical as a pain control treatment. Although VCS may not have the same effect in all subjects with chronic pain, it may be an effective method of pain control for some subjects. Anecdotally, subject 4 had not resumed sexual relations with her husband following the birth of her last child. However, when VS-S reduced her CPI she showed her husband the technique. This technique provided pain relief such that they were able to resume normal sexual relations once again. Therefore, VS-S might used to decrease CPI with specific chronic pain conditions. Manual self-stimulation might be difficult to use on a day to day basis. It might be possible to apply VS-S using a temporary, removable, tampon-like, electrical stimulator or an implanted electrical stimulator for long-term control. One of the things found in this study was that there was a delayed response to stimulation. The

use of an electrical stimulator would allow for longer periods of stimulation. However, additional study is needed before moving on to this step.

Recommendations

As a result of the findings of this study it is apparent that more research is needed to differentiate the effect of stimulation-produced analgesia on various types of chronic pain. Researchers will need to explicate the mechanisms that explain the responses to VS-S and CS-S in this study. To completely understand the mechanics, work must be done with animal models of somatic and visceral chronic pain. The objective of this research will be to more completely understand the pathophysiological conditions that account for the effect of VS-S and CS-S seen in this study.

Additional nursing research is needed to understand the relationship between chronic pain conditions and various treatment modalities. Nurses' traditional focus on biomedical approaches to treatment of patients with pain may be helpful in this regard. Nurses could be at the forefront of identifying the responses of patients with chronic pain to various treatment modalities. Nursing research should focus on effective treatments of chronic pain differentiated by the type of pain, location, frequency, reproductive stage, all variables found to be significantly related to CPI, PDT, and PTT in this study. The documentation of the responses to treatment needs to be more detailed for chronic pain than for acute pain. Nurses tend to treat all types of pain the same, as if it is acute. McCaffrey and Pasero's (1999) observation that chronic pain does not manifest the same signs and symptoms as acute pain is truer than they may have realized. New nursing information may lead to more informed decisions related to treatment of chronic pain. We are a long way from understanding of chronic pain and chronic pain management.

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Appendices

APPENDIX A

MPI

MPI Single User License Agreement

Dr. Rudy and the University of Pittsburgh provide the program called MPI (hereafter "the program") and license its use. You assume full responsibility for the selection of the program to achieve your intended results, and the installation, use and results obtained from the program.

License

You may (a) use the program on a single machine at one time, and (b) copy the program into any machine readable or printed form for backup purposes. You must reproduce and include the copyright notice on any copy made.

You may not (a) use, copy, modify or transfer the program, or any copy in whole or part without the expressed written permission of Dr. Rudy of the Pain Evaluation and Treatment Institute, and (b) copy the documentation (manual) for the program.

Limited Warranty

The program is provided "AS IS" without warranty of any kind, either expressed or implied, including, but not limited to, the implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the quality and performance of the program is with you. Should the program prove defective, you (and not Dr. Rudy or the University of Pittsburgh) assume the entire cost of all necessary servicing, repair, or correction. Further, neither Dr. Rudy nor the University of Pittsburgh warrants, guarantees or makes any representation regarding the use of, or the results of the use of, the program in terms of correctness, accuracy, reliability, currentness, or otherwise. You rely on the program and results solely at your own risk.

Neither Dr. Rudy nor the University of Pittsburgh warrants that the functions contained in the program will meet your requirements or that the operation of the program will be uninterrupted or error free. Neither Dr. Rudy, the University of Pittsburgh, its faculty, staff, employees, or agents, nor anyone else who has been involved in the creation, production, or delivery of this program shall be liable for any direct, indirect, consequential, or incidental damages arising out of the use, the results of use, or inability to use this program even if Dr. Rudy and/or the University of Pittsburgh has been advised of the possibility of such damages, or for any claim by any other party.

Dr. Rudy and the University of Pittsburgh do warrant that the diskette on which the program is furnished to be free from defects in materials and workmanship under normal use for a period of thirty (30) days from the date of delivery.

General

You may not sublicense, assign or transfer the license or the program to any other individual or organization. By installing the enclosed software, you acknowledge that you have read this agreement, understand it and agree to be legally bound by its terms and conditions.

SCORING PROCEDURES

SECTION I - MPI Version 1

```
Scale 1: Pain Severity      = (Q1+Q7+Q12) / 3[a]
Scale 2: Interference       = (Q2+Q3+Q4+Q8+Q9+Q13+Q14+Q17+Q19) / 9
Scale 3: Life Control       = (Q11+Q16) / 2
Scale 4: Affective Distress = ((6-Q6)+Q18+Q20) / 3
Scale 5: Support            = (Q5+Q10+Q15) / 3
```

SECTION I - MPI Version 2

```
Scale 1: Pain Severity      = (Q1+Q8+Q16) / 3[a]
Scale 2: Interference       = (Q2+Q3+Q4+Q10+Q11+Q12+Q18+Q19+Q23+Q25+Q27) / 11
Scale 3: Life Control       = (Q14+Q21+Q22+Q24) / 4
Scale 4: Affective Distress = ((6-Q6)+Q26+Q28) / 3
Scale 5: Support            = (Q5+Q13+Q20) / 3
```

SECTION II

```
Scale 6: Punishing Responses   = (Q1+Q4+Q7+Q10) / 4
Scale 7: Solicitious Responses = (Q2+Q5+Q8+Q11+Q13+Q14) / 6
Scale 8: Distracting Responses = (Q3+Q6+Q9+Q12) / 4
```

SECTION III

```
Scale 9:  Household Chores           = (Q1+Q5+Q9+Q13+Q17) / 5
Scale 10: Outdoor Work               = (Q2+Q6+Q10+Q14+Q18) / 5
Scale 11: Activities Away From Home  = (Q3+Q7+Q11+Q15) / 4
Scale 12: Social Activities          = (Q4+Q8+Q12+Q16) / 4
Scale 13: General Activity Level     = (Scale9+Scale10+Scale11+Scale12) / 4
```

[a] This scoring procedure calculates a mean score for each scale. The denominator, which reflects the number of items in that scale, will need to be adjusted if there are missing values for the summed items in a particular scale (i.e., the numerator). For example, if a patient indicated that question 1 in Section I was not applicable or left this question blank, then the denominator of scale 1 would be 2 rather than 3 and only 2 items would be summed to form the numerator. This type of adjustment should be made for each scale that contains missing values so that a patient's score can be compared to scale norms as well as compared back to the original unit of measurement, the item ratings, on which scale scores are based.

NORMATIVE INFORMATION

Heterogeneous Chronic Pain Sample (N = 300)

	Mean	Std. Dev.
Scale 1: Pain Severity	4.521	1.038
Scale 2: Interference	4.606	1.163
Scale 3: Life Control	3.189	1.615
Scale 4: Affective Distress	3.775	1.279
Scale 5: Support	4.627	1.421
Scale 6: Punishing Responses	1.853	1.658
Scale 7: Solicitious Responses	3.568	1.581
Scale 8: Distracting Responses	2.416	1.463
Scale 9: Household Chores	2.871	1.728
Scale 10: Outdoor Work	1.037	1.201
Scale 11: Activities Away From Home	2.247	1.214
Scale 12: Social Activities	2.026	1.233
Scale 13: General Activity Level	2.047	0.985

IASP Primary Pain Site 7: Pelvic region (N = 34, all women)

	Mean	Std. Dev.
Scale 1: Pain Severity	3.92	1.47
Scale 2: Interference	3.28	1.68
Scale 3: Life Control	3.58	1.72
Scale 4: Affective Distress	3.74	1.48
Scale 5: Support	4.24	1.58
Scale 6: Punishing Responses	1.94	1.77
Scale 7: Solicitious Responses	3.28	1.77
Scale 8: Distracting Responses	2.04	1.34
Scale 9: Household Chores	4.87	0.99
Scale 10: Outdoor Work	1.64	1.31
Scale 11: Activities Away From Home	3.03	1.22
Scale 12: Social Activities	2.63	1.01
Scale 13: General Activity Level	3.04	0.88

IASP Primary Pain Site 5: Lower back, lumbar spine, sacrum, & coccyx (N = 150)

	Mean	Std. Dev.
Scale 1: Pain Severity	4.640	1.001
Scale 2: Interference	4.794	0.981
Scale 3: Life Control	3.093	1.526
Scale 4: Affective Distress	3.848	1.290
Scale 5: Support	4.599	1.431
Scale 6: Punishing Responses	1.725	1.624
Scale 7: Solicitious Responses	3.605	1.551
Scale 8: Distracting Responses	2.466	1.462
Scale 9: Household Chores	2.746	1.601
Scale 10: Outdoor Work	0.863	1.049
Scale 11: Activities Away From Home	2.186	1.069
Scale 12: Social Activities	2.048	1.158
Scale 13: General Activity Level	1.964	0.913

IASP Primary Pain Site 6: Lower limbs (N = 30)

	Mean	Std. Dev.
Scale 1: Pain Severity	4.533	1.058
Scale 2: Interference	4.464	1.356
Scale 3: Life Control	3.280	1.932
Scale 4: Affective Distress	3.760	1.393
Scale 5: Support	4.957	1.138
Scale 6: Punishing Responses	1.920	1.722
Scale 7: Solicitious Responses	3.932	1.645
Scale 8: Distracting Responses	3.080	1.489
Scale 9: Household Chores	2.632	1.673
Scale 10: Outdoor Work	0.860	1.173
Scale 11: Activities Away From Home	2.497	1.463
Scale 12: Social Activities	2.443	1.407
Scale 13: General Activity Level	2.108	0.925

IASP Primary Pain Site 2: Upper Shoulder & Upper Limbs (N = 20)

	Mean	Std. Dev.
Scale 1: Pain Severity	4.549	0.807
Scale 2: Interference	4.675	0.981
Scale 3: Life Control	3.000	1.591
Scale 4: Affective Distress	3.471	1.214
Scale 5: Support	4.479	1.615
Scale 6: Punishing Responses	2.500	1.541
Scale 7: Solicitious Responses	3.052	1.410
Scale 8: Distracting Responses	2.406	1.384
Scale 9: Household Chores	2.894	1.706
Scale 10: Outdoor Work	0.895	1.269
Scale 11: Activities Away From Home	2.196	1.558
Scale 12: Social Activities	1.608	1.501
Scale 13: General Activity Level	1.898	1.042

MAP Classification Sheet

Subject #: Name: Age:
Test Date: Pain Duration: months
IASP Location of pain:

Test Results for Axis II: Psychosocial

	Raw Score	T-Score
Scale 1. Pain Severity		
Scale 2. Interference		
Scale 3. Life Control1		
Scale 4. Affective Distress		
Scale 5. Support		

Test Results for Axis III: Behavioral

Scale 6. Punishing Responses		
Scale 7. Solicitous Responses		
Scale 8. Distracting Responses		
Scale 9. Household Chores		
Scale 10. Outdoor Work		
Scale 11. Activities Away from Home		
Scale 12. Social Activities		
Scale 13. General Activity Level		

Profile Centroid Distance Tests

	Chi-Square	p-value
Profile 1. Dysfunctional		
Profile 2. Interpersonnaly Distressed		
Profile 3. Adaptive Coper		

Bayesian Posterior Probabilities from Patient Profiles

Profile 1. Dysfunctional	
Profile 2. Interpersonnaly Distressed	
Profile 3. Adaptive Coper	

Cluster assignment code:

MPI version #:

APPENDIX B

Structured Clinical Interview for DSM IV Non-patient Research Version

Permission to Make Copies of Research Version
SCID Central
Biometrics Research Department
New York State Psychiatric Institute
1051 Riverside Drive - Unit 60
New York, NY 10032
Telephone: 212-543-5524
FAX: 212-543-5525
e-mail: mbf2@columbia.edu
Michael B. First, MD (Editor, SCID Web page)
Miriam Gibbon, MSW (Co-editor, SCID Web page)
Robert L. Spitzer, MD (Director, Biometrics Research)
Janet B.W. Williams, DSW (Deputy Director, Biometrics Research)
Noah Spitzer-Williams (Webmaster)
Phone: 212-543-5524
EMAIL: mbf2@columbia.edu
FAX: 212-543-5525

Memorandum

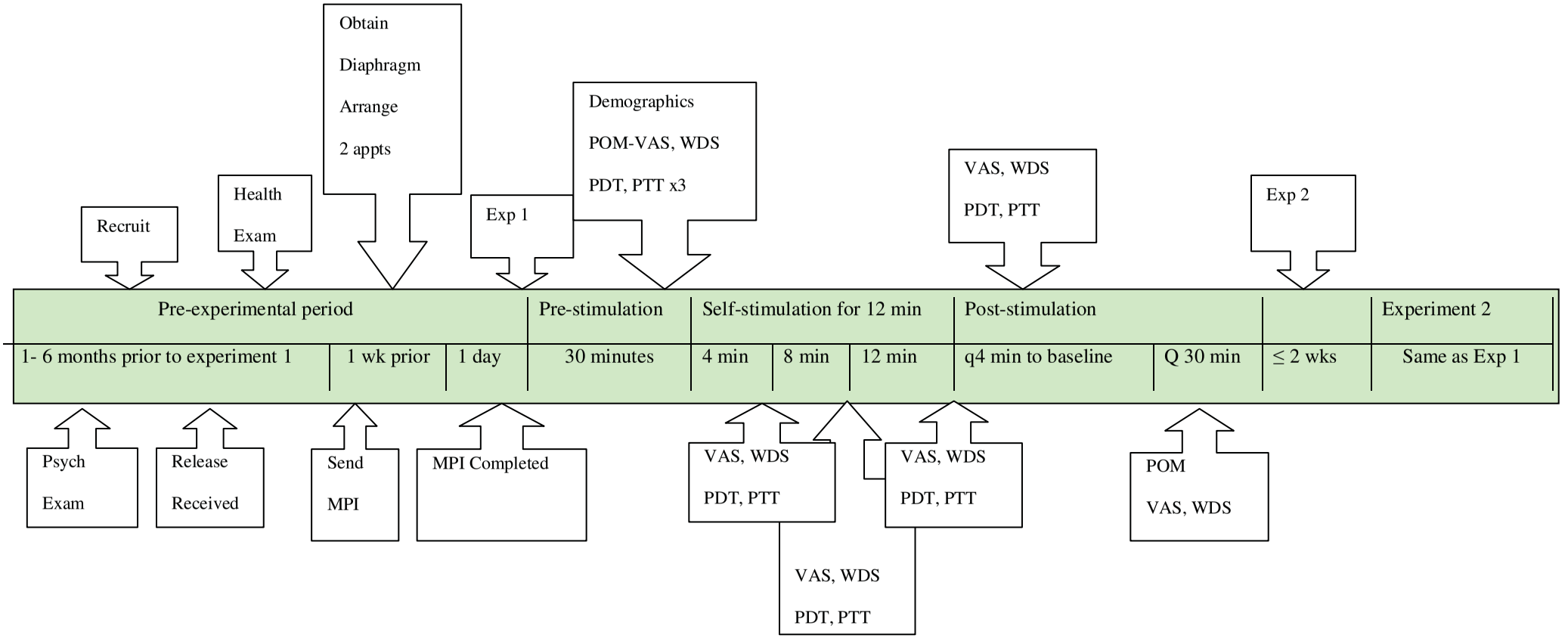
DATE: May 28, 1998
TO: Users of Research Version of SCID-I
FROM: Biometrics Research Department of New York State Psychiatric Institute
RE: Permission to make photocopies of the SCID.

The Research Version of the SCID is distributed as a single-sided master copy. The Biometrics Research Department of New York State Psychiatric Institute, the developer of the SCID, hereby grants permission to any investigator doing research funded by non-for-profit institutions (e.g., NIMH, NARSAD, Veteran's Administration) to make as many photocopies as they need--of the entire document or of any modules.

For research conducted by or funded by commercial enterprises (e.g. pharmaceutical companies), there is a licensing fee for the use of the SCID, depending upon the number of subjects to be entered in a study. Please contact Biometrics Research (212-543-5524) for additional information.

APPENDIX C

VS-S and CS-S Experiment Timeline



APPENDIX D

Informed Consent

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

TITLE OF STUDY:

The effect of vaginal/cervical self-stimulation in women with chronic pain

RESEARCH STUDY:

I, _____, have been asked to participate in a research study under the direction of Janice Breen and Dr(s) Komisaruk and Whipple. Other professional persons who work with them as study staff may assist or act for them.

PURPOSE:

The purpose of this research study is to determine if there is any relation between pain and vaginal/cervical self-stimulation. This study will extend the findings of previous studies conducted by two of the investigators.

DURATION:

My participation in this study will require about 90 minutes on two occasions in the University of Medicine and Dentistry-New Jersey Medical School (UMDNJ-NJMS), a nursing laboratory in the College of Nursing, Rutgers, The State University of New Jersey or CentraState Medical Center. In addition, I may take home the pain measurement instrument, the Pain-o-meter (see descriptive literature attached), used during testing and be asked to continue to measure my chronic pain intensity every 30 minutes while I am awake. I will document each chronic pain intensity score on a form that will be provided to me. I will stop measuring my chronic pain intensity when it returns to my pre-test baseline measure.

PROCEDURES:

I have been told that during the course of this study, the following will occur:

If I agree to participate, I will be asked to be interviewed by phone to make sure that I do not have any psychological problems such as psychosis, active substance abuse, active suicidal thoughts or a history of sexual abuse; if I do I will be excluded from participation in the study. It will take approximately one hour to complete the phone interview. Following the psychological evaluation interview, I will be asked to make an appointment with my primary care physician, gynecologist or nurse practitioner to determine that there are no conditions that would prohibit me from participating. If my healthcare provider agrees that I may participate I should be fitted for a diaphragm. Once I receive the prescription for the diaphragm from my healthcare provider I should mail it to the principal investigator along with a release from my physician approving my participation in the study. The principal investigators will obtain the diaphragm and modify it, by attaching a Velcro disc to it, for use in the experiment. After the principal investigators receive the prescription they will call me to arrange an appointment for testing. At that time I will be instructed continue to take pain medication exactly as prescribed both in dosage and frequency for two weeks before my appointment. The West Haven-Yale Multidimensional Pain Inventory will be mailed to me and I will be asked to complete it the day before testing and to bring the completed form with me on the day of testing. Other testing will take place at the UMDNJ-NJMS in Newark, NJ, a nursing laboratory in the College of Nursing, Rutgers, The State University of New Jersey or CentraState Medical Center in Freehold, NJ.

When I arrive at the testing center, I will meet with the female nurse investigator, Janice Breen, who will review the study procedures, instruments, and this consent form with me. If I am capable of being pregnant, before beginning the experimental session, a pregnancy test will be used to determine if I am pregnant. If I am pregnant, I will be withdrawn from the study. If I am not

pregnant and agree to participate in the study, the nurse investigator will collect background data including demographic data, the date of the beginning of my last menstrual period, medications that I may be taking and a short health history. I will then be asked to rate my chronic pain intensity and point out the location(s) of pain using a pain measurement scale that is called a Painometer. The Painometer is simply used to describe pain; it does not produce any pain. All of this information is needed for the study and will only be used for the study. No information that would directly link me with the study will be used in any report of the results of the study.

Following this initial collection of information, the stimulators that will be used for vaginal/cervical self-stimulation will be explained to me. This type of stimulator has been used in previously published studies conducted by two of the investigators. The stimulator handle contains a mechanism connected to readout meter so the amount of pressure that I use during vaginal/cervical self-stimulation can be monitored to ensure that it does not exceed 10 lb/in2, about the pressure that would be felt by using two fingers to lift a one-gallon plastic container of water. The stimulator that will be used for self-stimulation of the anterior wall of the vagina consists of a disposable, curved plastic rod that is connected to the stimulator handle and is inserted into a disposable tampon that has a cushioned tip. For cervical self-stimulation a disposable, straight rod also attached to the stimulator handle is inserted into a disposable tampon with a Velcro tip that will attach to a matching Velcro fabric disk attached to the diaphragm. Attaching the Velcro tip of the tampon to the Velcro disc on the diaphragm will maintain the position of the area of self-stimulation directly over the cervix and will protect it from abrasion. The Velcro disk is attached to the diaphragm by flexible, non-toxic dental adhesive as in our prior published studies.

After the stimulators are described, I will be asked to empty my bladder. I will then be asked to relax on an examination table in the office. I will insert the diaphragm with the help of the nurse investigator. One of the measures that will be evaluated is my pain detection threshold. To create experimental pain, each of the four fingers of my non-dominant hand will be placed one at a time over the

1mm diameter blunt point of a Ugo Basile analgesy meter. This instrument will be shown to me before the testing procedure. Over 26 seconds, a gradually increasing force will be applied to my finger, pressing it down on the point. At the moment I first perceive this pressure to be painful I will be instructed to say "pain." The force will continue increasing gradually until it becomes too uncomfortable to continue. At this point, I will be instructed to say "stop." As soon as I say "stop," the pressure will be lifted off my finger. Following the collection of this baseline data, there will be a four-minute rest period. These procedures measure your pain detection threshold and your pain tolerance threshold.

Following the rest period I will be asked to apply self-stimulation, either to the anterior vaginal wall or cervix for 12 minutes. During self-stimulation, the amount of force that I use comfortably with the stimulator will be monitored and the investigators will measure my pain detection threshold, pain tolerance threshold, and chronic pain intensity using the same method used before I started the self-stimulation. Measurements will be recorded at 4 minutes, 8 minutes and 12 minutes during my application of vaginal or cervical self-stimulation. After I end self-stimulation, my experimental pain detection threshold, pain tolerance threshold, and chronic pain intensity will be measured every 4 minutes until pain detection and pain tolerance thresholds return to the base-line levels. At this point the first part of the experiment will be completed. It is expected that this first testing session will last approximately 90 minutes, including the pre-test collection of information.

I will then arrange an appointment to conduct the alternate form of self-stimulation, that is, if I applied vaginal stimulation during the first experiment, I will apply cervical stimulation during the second experiment; if I applied cervical stimulation during the first experiment, I will apply vaginal stimulation during the second experiment. If I am capable of being pregnant, before beginning the second experimental session, a pregnancy test will be used to determine if I am pregnant. If I am pregnant, I will be withdrawn from the study. If I am not pregnant, I will be asked to apply either cervical or vaginal self-stimulation using

the same procedure outlined above. My pain detection threshold, pain tolerance threshold, and chronic pain intensity will be measured in the same way as in the previous test.

To minimize any embarrassment I may feel, during all vaginal/cervical self-stimulation periods of testing, only the nurse investigator will have access to the laboratory room. No one outside the room can see into the room. Every attempt will be made to minimize intrusion, except for the recording of experimental measurements, during vaginal/cervical self-stimulation. Every attempt will be made to address concerns that I may have.

Following the completion of each testing procedure, I may take home the Painometer, which is the measuring card that I used to rate my chronic pain intensity during the experiment. I will be asked to rate my chronic pain intensity every 30 minutes during waking hours and write down the results on a form that will be provided for me. My chronic pain score before the testing session will be written on the form. I will stop rating my chronic pain intensity when it returns to what it was before the testing two times in a row.

SUBJECTS:

I will be one of up to 10 women, all over the age of 18 to participate in this trial. I have one of the following types of pain: low back pain; pelvic pain such as bladder pain, pain from pelvic adhesions or endometriosis; perineal pain such as rectal pain, peri-anal pain, anal pain, or coccydynia. I have experienced chronic pain for at least 3 months. I have been experiencing continuous pain and have been on a steady dosage and frequency of medication for at least two weeks before the testing. I agree to continue a steady dosage and frequency of medication in the period between experiments.

EXCLUSIONS:

I should not participate in this study if:

I am pregnant, have a cystocele, cervical dysplasia or any other condition that my healthcare provider believes would contraindicate my participation in this

study or if I am abusing drugs or alcohol, have psychosis, active suicidal thoughts or have a history of sexual abuse.

RISKS/DISCOMFORTS:

I have been told that the study described above may involve the following risks and/or discomforts:

The investigators believe that this study poses little or no risk to me. There may be minimal discomfort from the experimental pain; however, I am in control of the amount of experimental pain I will tolerate and I am free to terminate the test at any time. I may feel some embarrassment during self-stimulation. A member of the research team will be available to me following the testing procedure to discuss my feelings. In the event that additional counseling is needed I will be referred for counseling and my insurance carrier will be billed. The amount of pressure used in vaginal/cervical self-stimulation will be monitored by the investigators at all times to ensure that the pressure I use remains within previously established safe limits. The amount of pressure required in previous experiments to produce an effect was minimal and produced no ill effects in the study participants. If I do experience any ill effects as a result of my participation in this study I will be referred to a healthcare provider as necessary for appropriate care. If I should require medical care or additional counseling, the cost of services will be charged to my insurer. No guarantee can be made that my health insurance, UMDNJ, Rutgers, The State University of New Jersey or CentraState Medical Center, will pay for these medical services or provide other compensation.

I have been instructed that I should not become pregnant between my visit with my physician clearing me for participation in this study and the dates of my participation. If I do become pregnant during the period of time preceding or during this study, I should notify the principal investigator of this fact as soon as possible since the risks to me or the fetus are unknown.

I understand that despite all precautions, there may exist unknown risks or unknown side effects related to this research project. I understand that I may experience mild anxiety or embarrassment during this study and that I will given

an opportunity to discuss my feelings and concerns and the purpose of the study with a member of the research team following the completion of the study.

BENEFITS:

The investigators do not know yet whether the proposed research will affect my chronic pain. However by participating in this research project I will have the satisfaction of knowing that I am contributing to a scientific study that may contribute to the understanding of and treatment of chronic pain.

ALTERNATIVES:

This is a research project, not a treatment. The alternative to participating in this study is not to participate.

NEW FINDINGS:

During the course of the study, I will be told about any new information that may affect my willingness to remain in the study.

WHO WILL HAVE ACCESS TO MY RESEARCH RECORDS FROM THIS STUDY:

By participating in this study, I should understand that the study collects demographic data and data on my health. The researchers will analyze the data in order to gain information obtained as part of this study as well as, for general health research. The Institutional Review Board (a committee that reviews research studies), Officials of the University of Medicine and Dentistry of New Jersey-New Jersey Medical School, University Hospital, the researchers from Rutgers, the State University of New Jersey and Officials of CentraState Medical Center IRB, will be allowed to inspect sections of my medical and research records related to this study and will keep the data as long as the subject is under study. My data may be used in scientific publications. If the findings from the study are published, I will not be identified by name. My personal identity, that is my name, address, and other identifiers, will remain confidential (will have a code number and my actual name will not be used). Only the study researchers will be able to link the code number to my name and will keep this

information for 1 year following the completion of the study. My identity will remain confidential. The exception to this rule will be when there is a court order or when a law exists requiring the study doctor to report communicable diseases. In this case, I will be informed of the intent to disclose this information to the state agency. Such a law exists in New Jersey for diseases such as cancer, infectious diseases such as hepatitis, HIV, viruses and many others.

The investigators will be allowed to examine the data in order to analyze the information obtained from this study, and for general health research.

If I do not sign this approval form, I will not be able to take part in this research study.

I can change my mind and revoke this approval at any time. If I change my mind, I must revoke my approval in writing. Beginning on the date that I revoke my approval, no new personal health information will be used for research. However, the study doctor/investigator may continue to use the health information that was provided before I withdrew my approval.

I have the right to look at my study data at my study doctor's office and to ask for corrections of any of my data that is wrong.

FINANCIAL COSTS TO THE SUBJECT:

I understand that my participation in this study may involve cost to me for medical care or counseling. I understand that should I require medical care or additional counseling, the cost of services will be charged to my insurer. Some of these costs may be covered by my health insurance provider however, I understand that no guarantee can be made that my health insurance, UMDNJ, Rutgers, The State University of New Jersey or CentraState Medical Center, will pay for these medical services or provide other compensation.

PAYMENT FOR PARTICIPATION:

I understand that upon completion of the experimental procedures, I will receive a check for $50 to cover my participation. Upon presentation of paid receipts I will receive additional reimbursement for my travel expenses and the cost of my pre-study medical examination and pregnancy test. I will be

compensated fully even if I decide to terminate my participation after arriving at the laboratory or terminate my participation in the study at any time prior to completing it.

MEDICAL THERAPY FOR INJURY

If I participate in this study, I may be exposed to certain risks of injury in addition to those connected with standard forms of treatment although the researchers believe that this study poses little or no risk to me. I understand that there may be minimal discomfort from the experimental pain; however, I realize that I am in control of the amount of experimental pain I will tolerate and I understand that I am free to terminate the test at any time. I understand that I may feel some embarrassment during self-stimulation and that a member of the research team will be available to me following the testing procedure to discuss my feelings. I understand that the amount of pressure used in vaginal/cervical self-stimulation will be monitored by the investigators at all times to ensure that the pressure I use remains within previously established safe limits. The amount of pressure required in previous experiments to produce an effect was minimal and produced no ill effects in the study participants.

It is possible that in the course of these studies, new adverse effects of this intervention that result in physical injury may be discovered. Medical treatment will be arranged by UMDNJ or CentraState Medical Center for participants who sustain physical injuries or illnesses as a direct consequence of participation in this research. My health insurance carrier or other third party payor will be billed for the cost of this treatment. No additional financial compensation is available.

RIGHT TO REFUSE OR WITHDRAW:

I understand that my participation is voluntary and I may refuse to participate, or may discontinue my participation at any time, without penalty or loss of benefits to which I am otherwise entitled. I also understand that the investigator has the right to withdraw me from the study at any time. I will be

compensated fully even if I decide to terminate my participation after arriving at the laboratory or if I terminate my participation in the study prior to completion.

INDIVIDUAL(S) TO CONTACT:

If I have any questions about my treatment in this study, I can contact:

Janice Breen MSN, APRN BC 77 Barberry Drive Tel/Fax: 732-530-9705
Ph.D. candidate Ocean, NJ 07712 Cell: 908-313-2425
email: jbreen@careplus-consulting.com

Barry Komisaruk, Ph.D. Rutgers University Tel: 973-353-5834
Professor II Psychology Cell: 973-462-0178
Hill Hall, Suite 401
360 Dr. Martin Luther King Blvd
Newark, NJ 07102 email: BRK@psychology.rutgers.edu

Beverly Whipple, Ph.D. Rutgers University
Professor Emeritus College of Nursing
87 Matlack Drive Tel/Fax: 856-309-1510
Voorhees, NJ 08043 email: bwhipple@pics.com

If I have any questions about my rights as a research subject, I can contact:

Rutgers University Institutional Review Board for the Protection of Human Subjects

Office of Research and Sponsored Programs

3 Rutgers Plaza

New Brunswick, NJ 08901-8559

Tel: 732-932-0150 ext. 2104

Email: humansubjects@orsp.rutgers.edu

I will receive a copy of this consent form if I agree to participate in this research study.

SIGNATURE OF SUBJECT

I have read this entire form, or it has been read to me, and I understand it completely. All of my questions regarding this form or this study have been answered to my complete satisfaction. I agree to participate in this research study.

Subject: Name: _____ Signature: _____

Witness: Name: _____

Signature:_____

Date: _____

SIGNATURE OF INVESTIGATOR OR RESPONSIBLE INDIVIDUAL

To the best of my knowledge the subject, _____, has assimilated the entire content of the above consent form, and understands the study and its risks well. The subject's questions have been accurately answered to her complete satisfaction.

Investigator: Name: _____ Signature: _____

Witness: Name: _____ Signature: _____

DATE: _____

APPENDIX E

IRB approval letters

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

October 27, 2009

P.I. Name: Breen
Protocol #: 00-131M05x

Janice Breen
77 Barberry Drive
Ocean Grove NJ 07712

Dear Janice Breen:

(Initial / Amendment / Continuation / Continuation w/ Amendment)

Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date:	9/17/2009	**Expiration Date:**	9/16/2010	**Expedited Category:**	8c
Approved # of Subject(s):	10	**Currently Enrolled:**	5		

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- **This Approval**-The research will be conducted according to the most recent version of the protocol that was submitted. **This approval is valid ONLY for the dates listed above;**
- **Reporting**-ORSP must be immediately informed of any injuries to subjects that occur and/or problems that arise, in the course of your research;
- **Modifications**-Any proposed changes MUST be submitted to the IRB as an amendment for review and approval prior to implementation;
- **Consent Form(s)**-Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research. The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research;
- **Continuing Review**-You should receive a courtesy e-mail renewal notice for a Request for Continuing Review before the expiration of this project's approval. However, it is your responsibility to ensure that an application for continuing review has been submitted to the IRB for review and approval prior to the expiration date to extend the approval period;

Additional Notes: **- Expedited Continuation Approval per 45 CFR 46.110**
- **IRB Approval has been provided for data analysis only. PI is to contact the IRB prior to the recruitment of additional subjects or further interactions/interventions with subjects.**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Sheryl Goldberg
Director of Office of Research and Sponsored Programs
graser@orsp.rutgers.edu

cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

November 6, 2008

P.I. Name: Breen
Protocol #00-131M05

Janice Breen
77 Barberry Drive
Ocean Grove NJ 07712

Dear Janice Breen:

✓
(Initial / Amendment / Continuation / Continuation w/ Amendment)

Protocol # 00-131M05
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date:	10/25/2008	**Expiration Date:**	10/24/2009
Expedited Category(s):	4		
Approved # of Subject(s):	10	**Currently Enrolled:**	5

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Notes: **Continuation Expedited Approval per 45 CFR 46.110**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,
Michelle Gabel
acting for
Sheryl Goldberg
Director of Office of Research and Sponsored Programs
graser@orsp.rutgers.edu

cc: Dr. Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

December 17, 2007

P.I. Name: Breen
Protocol #00-131M05

Janice Breen
77 Barberry Drive
Ocean Grove NJ 07712

Dear Janice Breen:

✓
(Initial / Amendment / Continuation / Continuation w/ Amendment)

Protocol # 00-131M05
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 11/19/2007 **Expiration Date:** 11/18/2008
Expedited Category(s): 4

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Notes: **Continuation Expedited Approval per 45 CFR 46.110**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Karen M. Janes 12/17/07

Karen M. Janes
Associate Director, Research Integrity and Compliance
janes@orsp.rutgers.edu

cc: Dr. Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

January 19, 2007

P.I. Name: Breen
Protocol #00-131M05

Janice Breen
77 Barberry Drive
Ocean Grove NJ 07712

Dear Janice Breen:

(Initial / Revised / Continuation)

Protocol # 00-131M05
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 1/4/2007 **Expiration Date:** 1/3/2008
Expedited Category(s): 4

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Notes: **Expedited Continuation Approval per 45 CFR 46.110, Category 4**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

James Cavazzoni, Ph.D.
Sponsored Programs Administrator
cavazzoni@orsp.rutgers.edu

cc: Dr. Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

March 2, 2006

P.I. Name: Breen
Protocol #00-131M05

Janice Breen
School of Nursing - Newark
37 Broadway
Ocean Grove NJ 07756

Dear Janice Breen:

(Initial / Revised / Continuation)

Protocol # 00-131M05
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 2/28/2006 **Expiration Date:** 1/31/2007
Expedited Category(s): 4

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Notes:
- Expedited Continuation Approval per 45 CFR 46.110, Category 4
- This protocol has been reassessed and determined to involve minimal risk to subjects
- Expedited Amendment Approval per 45 CFR 46.110(b)(2) for Modification to Informed Consent, and Change in Research Site

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

László Szabó, CIP
Sponsored Programs Administrator
cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

February 16, 2005

P.I. Name: Breen
Protocol #00-131R05

Janice Breen
School of Nursing - Newark
37 Broadway
Ocean Grove NJ 07756

Dear Janice Breen:

(Initial / Revised / Continuation)

Protocol # 00-131R05
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 2/2/2005 **Expiration Date:** 2/1/2006

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Notes: **None**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo, CIP
Sponsored Programs Administrator
szabo@orsp.rutgers.edu

cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

October 14, 2004

P.I. Name: Breen
Protocol #00-131R

Janice Breen
School of Nursing - Newark
25 Nina Way
Red Bank NJ 07701

Dear Janice Breen:

(Initial / Revised / Continuation)

Protocol # 00-131R
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 10/6/2004 **Expiration Date:** 2/5/2005

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Conditions: **- Continuation Approval for 4 Month Extension. DeNovo due 1/12/2004**
- Approval of Amendment Request Dated 8/26/2004 on 10/6/2004 for Addition of Testing/Recruitment Site (Centra State Medical Center)

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo, CIP
Sponsored Programs Administrator
szabo@orsp.rutgers.edu

cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

December 2, 2003

P.I. Name: Breen
Our Protocol #00-131R

Janice Breen
School of Nursing - Newark
25 Nina Way
Red Bank NJ 07701

Dear Janice Breen:

(Initial / Revised / Continuation)

Protocol # 00-131R
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 11/24/2003 **Expiration Date:** 11/4/2004

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Conditions: **Approval of Amendment Request Dated 10/3/2003 on 11/24/2003 for modification to work site & consent form.**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo
Sponsored Programs Administrator
szabo@orsp.rutgers.edu
cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

September 22, 2003

P.I. Name: Breen
Our Protocol #00-131R

Janice Breen
School of Nursing - Newark
1385 Highway 35, Suite 152
Middletown NJ 07748

Dear Janice Breen:

(Initial / Revised / Continuation)

Our Protocol # 00-131R
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 9/16/2003 **Expiration Date:** 11/5/2003

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- The Principal Investigator must retain all signed documents for at least three years after the conclusion of the research.

Additional Conditions: **Approval of Amendment Request Dated 9/11/2003 on 9/16/2003 (Addition of Advertisement)**

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo
Sponsored Programs Administrator
szabo@orsp.rutgers.edu

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

August 22, 2003

P.I. Name: Breen
Our Protocol #00-131R

Janice Breen
School of Nursing - Newark
1385 Highway 35, Suite 152
Middletown NJ 07748

Dear Janice Breen:

(Initial / Revised / Continuation)

Our Protocol # 00-131R
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 8/18/2003 **Expiration Date:** 11/5/2003

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- All signed documents must be retained by the Principal Investigator for at least three years after the conclusion of the research.

Additional Conditions: Approval of Amendment Request Dated 8/18/2003 on 8/18/2003

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo
Sponsored Programs Administrator
szabo@orsp.rutgers.edu

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, 3 Rutgers Plaza, Cook Campus
New Brunswick, NJ 08901

July 21, 2003

P.I. Name: Breen
Our Protocol #00-131R

Janice Breen
School of Nursing - Newark
1385 Highway 35, Suite 152
Middletown NJ 07748

Dear Janice Breen:

(Initial / Revised / Continuation)

Our Protocol # 00-131R
Protocol Title: "The Effect of Vaginal/Cervical Self-Stimulation in Women With Chronic Pain"

This is to advise you that the above-referenced study has been presented to the Institutional Review Board for the Protection of Human Subjects in Research, and the following action was taken subject to the conditions and explanations provided below:

Approval Date: 7/16/2003 **Expiration Date:** 11/5/2003

This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of the ways in which human subjects are involved in your research. The following conditions apply:

- The research will be conducted according to the most recent version of the protocol that was submitted;
- ORSP will immediately be informed of any injuries to subjects that occur, or problems that arise, in the course of your research;
- Proposed changes will be submitted to the IRB for approval prior to implementation;
- Each person who signs a consent document will be given a copy of that document, if you are using such documents in your research;
- This approval is valid ONLY for the dates listed above, and a Request for Continuing Review form must be submitted to the IRB for review and approval prior to the expiration date to extend the approval period;
- All signed documents must be retained by the Principal Investigator for at least three years after the conclusion of the research.

Additional Conditions: **Approval of Amendment Request Dated 7/7/2003 on 7/16/2003**
Completion of HSCP required for Diane Engel.

Failure to comply with these conditions will result in withdrawal of this approval.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself. The Federal-wide Assurance (FWA) number for the Rutgers University IRB is FWA00003913; this number may be requested on funding applications or by collaborators.

Respectfully yours,

Laszlo Szabo
Sponsored Programs Administrator
szabo@orsp.rutgers.edu
cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB III, Cook Campus - 3 Rutgers Plaza
New Brunswick, NJ 08901

Last Name: Breen
Access No.: 00-131 R

NOTICE OF IRB REVIEW AND APPROVAL (Initial/Revised/Continuation)

The project identified below, for which you requested review and approval by the Rutgers Institutional Review Board for the Protection of Human Subjects in Research, has now been reviewed and approved. This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following conditions:

1. that you will conduct the research according to the plans and protocol you submitted.
2. that you will immediately inform the ORSP of any injuries to subjects that occur in the course of your research.
3. that you immediately inform the ORSP of any problems that arise in the course of your research.
4. that you will immediately request approval from the IRB of any changes that you make in the protocol of the research.
5. that you will give each person who signs the consent document a copy of that document, if you are using such documents in your research.
6. that this approval is valid for only the dates listed below.
7. that you will retain all signed consent documents for at least three years after the termination of the research.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself.

Failure to comply with these conditions will result in the withdrawal of this approval.

Name of Chief Investigator:	Janice Breen
Address:	25 Nina Way Red Bank, NJ 07701
Period of Approval:	11/07/01 to 11/07/02
Title of Project:	THE EFFECT OF VAGINAL/CERVICAL SELF-STIMULATION IN WOMEN WITH CHRONIC PAIN
Additional Conditions:	None.

One month before the end of the period of approval, you will be sent a "Request for Continuing Review" form to complete and return to the Office of Research and Sponsored Programs.

Date: 11/7/01

Signed: Brenda L. Ruotolo

Brenda L. Ruotolo
Sponsored Programs Administrator
ruotolo@orsp.rutgers.edu
p: 732/932-0150 Ext. 2104 f: 732/932-0163

cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB-Annex II, Busch Campus - 58 Bevier Road
Piscataway, NJ 08854-8010

Last Name: Breen
Access No.: 00-131 R

NOTICE OF IRB REVIEW AND APPROVAL (Initial/Revised/Continuation)

The project identified below, for which you requested review and approval by the Rutgers Institutional Review Board for the Protection of Human Subjects in Research, has now been reviewed and approved. This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following conditions:

1. that you will conduct the research according to the plans and protocol you submitted.
2. that you will immediately inform the ORSP of any injuries to subjects that occur in the course of your research.
3. that you immediately inform the ORSP of any problems that arise in the course of your research.
4. that you will immediately request approval from the IRB of any changes that you make in the protocol of the research.
5. that you will give each person who signs the consent document a copy of that document, if you are using such documents in your research.
6. that this approval is valid for only the dates listed below.
7. that you will retain all signed consent documents for at least three years after the termination of the research.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself.

Failure to comply with these conditions will result in the withdrawal of this approval.

Name of Chief Investigator:	Janice Breen
Address:	25 Nina Way Red Bank, NJ 07701
Period of Approval:	11/08/00 to 11/08/01
Title of Project:	THE EFFECT OF VAGINAL/CERVICAL SELF-STIMULATION IN WOMEN WITH CHRONIC PAIN
Additional Conditions:	None

One month before the end of the period of approval, you will be sent a "Request for Continuing Review" form to complete and return to the Office of Research and Sponsored Programs.

Date: 11/8/00

Signed: Brenda L. Ruotolo

Brenda L. Ruotolo
Sponsored Programs Administrator
ruotolo@orsp.rutgers.edu
p: 732/445-2799 f: 732/445-3257

cc: Barry Komisaruk

RUTGERS UNIVERSITY
Office of Research and Sponsored Programs
ASB-Annex II, Busch Campus - 58 Bevier Road
Piscataway, NJ 08854-8010

Last Name: Breen
Access No.: 00-131 R

NOTICE OF IRB REVIEW AND APPROVAL (Initial/Revised/Continuation)

The project identified below, for which you requested review and approval by the Rutgers Institutional Review Board for the Protection of Human Subjects in Research, has now been reviewed and approved. This approval is based on the assumption that the materials you submitted to the Office of Research and Sponsored Programs (ORSP) contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following conditions:

1. that you will conduct the research according to the plans and protocol you submitted.
2. that you will immediately inform the ORSP of any injuries to subjects that occur in the course of your research.
3. that you immediately inform the ORSP of any problems that arise in the course of your research.
4. that you will immediately request approval from the IRB of any changes that you make in the protocol of the research.
5. that you will give each person who signs the consent document a copy of that document, if you are using such documents in your research.
6. that this approval is valid for only the dates listed below.
7. that you will retain all signed consent documents for at least three years after the termination of the research.

Please note that the IRB has the authority to observe, or have a third party observe, the consent process or the research itself.

Failure to comply with these conditions will result in the withdrawal of this approval.

Name of Chief Investigator:	Janice Breen
Address:	25 Nina Way Red Bank, NJ 07701
Period of Approval:	11/22/99 to 11/22/00
Title of Project:	THE EFFECT OF VAGINAL/CERVICAL SELF-STIMULATION IN WOMEN WITH CHRONIC PAIN
Additional Conditions:	None

One month before the end of the period of approval, you will be sent a "Request for Continuing Review" form to complete and return to the Office of Research and Sponsored Programs.

Date: 11/29/99

Signed: Karen M. Janes
Karen M. Janes
Acting Assistant Director
Research Subjects Administration
p: 732/445-2883 f: 732/445-3257

cc:

APPENDIX F

Background Data

Subject code	Age	Sex M ☐ F ☐	Yrs of ed _____
Pain clinic PMC ☐ PP ☐	Race A ☐ B ☐ H ☐ O ☐ W ☐	Marital status: S ☐ M ☐ D/S ☐ W ☐	Rep stage:CB ☐ PM ☐ M ☐ PostMen ☐
Diagnosis (IASP code)	Date of pain onset ___/____/___	Date of LMP ___/____/___	Forms: Psych ☐ Health ☐
Other health problems			Consent ☐ MPI ☐

Medication Dose: Frequency: Time of last dose:			
Medication Dose: Frequency: Time of last dose:			
Medication Dose: Frequency: Time of last dose:			
Non-drug treatments Frequency: Time of last treatment:			

The 4 Dimensions of Pain

Intensity
Intensity is measured, from 0-10, with the globally accepted Visual Analog Scale.

Quality
The quality of pain is characterized by the words used to describe the sensory and emotional components of pain. The words and their intensities may assist caregivers in diagnosing and treating pain.

Location
The location of pain is important in determining diagnosis and suitable interventions.

Duration
The duration of pain indicates whether the pain is continuous or comes & goes.

Why the Painometer®?

The Painometer® is quick and easy to use, has proven validity & reliability, and allows health-care professionals to meet professional standards/guidelines for pain assessments.

World renowned hospitals in the US and Sweden are using the Painometer® as their pain assessment tool.

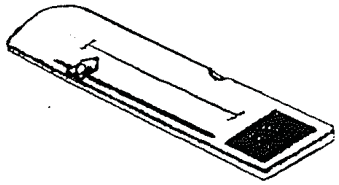
For ordering Painometers, pain sheets and information, contact :

Dola Health Systems
5884 Pimlico Rd.
Baltimore, MD 21209

tel. (410)-664-3590
fax.(410)-664-4235

Email: Dolafgj@aol.com

Introducing The Painometer®



The Painometer® is a hand-held pain assessment tool that takes less than 2 minutes for a patient to complete. It has been developed through more than 10 years of research. The Painometer® is the ***first comprehensive and clinically useful pain assessment tool in the world!***

The Painometer® will help *patients*:
- Communicate pain intensity
- Identify words that describe pain
- Adequately locate pain
- Describe the duration of the pain

The Painometer® will help *health-care professionals:*
- Meet standards & guidelines
- Adequately assess pain
- Determine diagnosis
- Evaluate treatment

Follow these instructions to measure pain correctly.

Instructions For Use

Figure 1

Step 1. Measure pain intensity
On the Painometer® is a 10 cm. straight line with the words *"Worst Possible Pain"* at the top and *"No Pain"* at the bottom. Move the marker from the *"No Pain"* position to the point on the line that best describes how much pain you are experiencing right now.

Step 2. Describe pain duration
At the bottom of the Painometer® the pain is described as:

AA Comes and goes
BB Is Continuous

Use a pencil and circle AA and/or BB to describe the duration of your pain.

Step 3. Turn over the Painometer®

Figure 2

Step 4. Describe physical pain
Look at the words in group 1 and circle the letters in front of the words that describe the pain you are experiencing right now.

Step 5. Describe emotional pain
Look at the words in group 2 and circle the letters in front of the words that describe the pain you are experiencing right now.

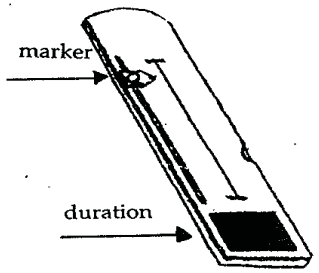
Figure 3

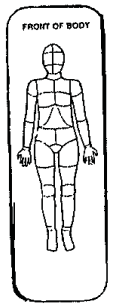
Step 6. Locate pain
Pull out the body chart that is located inside the Painometer®. Using a pencil, mark the location of pain on the diagram. Make sure to include all locations of pain. Turn over the body chart and, once again, mark all locations of pain.

Documenting Pain
The pain assessment is now complete and recorded on the Painometer®. Use those recordings to document the pain on the pain sheet (table 2).

Fig. 3

Fig. 1





body chart

Fig. 2

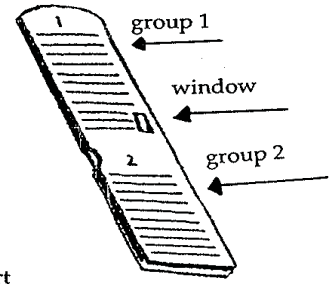


Table 1. Key to word intensity scores

Physical Pain		Emotional Pain	
A	3	O	1
B	1	P	5
C	4	Q	1
D	3	R	5
E	1	S	2
F	4	T	4
G	4	U	5
H	3	V	3
I	5	W	5
J	2	X	4
K	5	Y	2
L	4		
M	5		
N	3		

Table 2. Pain Sheet

1	Date						
	Time						
2. Pain Intensity	10	•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
	5	•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
		•	•	•	•	•	•
	0	•	•	•	•	•	•
3. Relief Acceptable (y/n)							
4. Physical words							
5. Emotional words							
6. Physical score							
7. Emotional score							
8. Location							
9. Duration							

Instructions For Documentation

Table 1 is a key to word intensities. For instance letter A, which represents the word cramping, has an intensity score of 4. These intensity scores enable you to compare your physical and emotional components of pain. **Table 2** is the pain sheet where you document the results from your pain assessment. A complete documentation includes the following 10 steps:

1 Enter the date & time of the assessment.
2 The window on the back of the Painometer® displays your pain intensity, mark it on the intensity scale with a cross.
3 Mark **y** for yes or **n** for no if the pain relief provided was acceptable or not.
4 Enter the letters of the physical pain words chosen.
5 Enter the letters of the emotional pain words chosen.
6 Find and enter the highest score of the physical pain words chosen. Use the key (table 1) to get the pain score. You may also find the table along the side of the tool.
7 Find and enter the highest score of the emotional pain word chosen. Use the key (table 1) to get the pain score. You may also find the table along the side of the tool.
8 Enter each number of location of pain.
9 Enter the duration of the pain (AA and/or BB).
10 Return the marker to the *"No pain"* position and wipe the

Code number:								Date	
Pain Assessment	Date / Time								
	Intensity	10							
		9							
		8							
		7							
		6							
		5							
P A=3 B=1 C=4 D=3 E=1 F=4 G=4 H=3 I=5 J=2 K=5 L=4 M=5 N=3	Chronic pain	4							
	intensity score	3	----------						
	before testing	2							
	_____	1							
		0							
	Physical words								
	Physical score								
E O=1 P=5 R=5 S=2 T=4 U=5 V=3 W=5 X=4 Y=2	Emotional words								
	Emotional score								
	Pain location								
	Pain duration								
	Drug/dose/Route		**Dosage**						
Analgesia	1								
	2								
	3								
	4								
	Non-drug therapies								

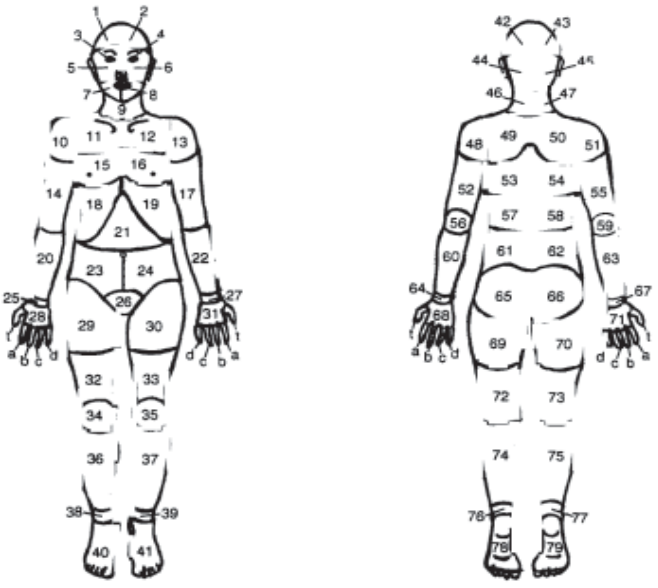
Pain Words

	Physical		Emotional
A	Cramping	O	Nagging
B	Dull	P	Agonizing
C	Splitting	Q	Annoying
D	Burning	R	Killing
E	Sore	S	Tiring
F	Shooting	T	Sickening
G	Radiating	U	Terrifying
H	Hurting	V	Miserable
I	Crushing	W	Torturing
J	Aching	X	Unbearable
K	Stabbing	Y	Troublesome
L	Sharp		
M	Tearing		
N	Pressing		

Non-Drug Therapies

0	None	6	Guided Imagery
1	TENS	7	Distraction
2	Heat	8	Music
3	Cold	9	Hypnosis
4	Relaxation	10	Other (explain)
5	Massage		

Body Chart



APPENDIX H
Experimental data collection sheet

		PDT					PTT			
Minute	Force	1	2	3	4		1	2	3	4
Pre-stim										
Pre-stim										
Pre-stim										
1										
1.5										
2										
2.5										
3										
3.5										
4										
4.5										
5										
5.5										
6										
6.5										
7										
7.5										
8										
8.5										
9										
9.5										
10										
10.5										
11										
11.5										
12										
16										
20										
24										
28										
32										

APPENDIX I

Calculations of POM-VAS

POM-VAS average variability of VS-S = [(POM-VAS post (12 minutes)-VS-S – POM-VAS pre-VS-S Baseline) / POM-VAS pre-VS-S Baseline] X 100

POM-VAS % Δ during (4 minutes) VS-S = [(POM-VAS during (4 minutes) VS-S – POM-VAS pre-VS-S Baseline) / POM-VAS pre-VS-S Baseline] X 100

POM-VAS % Δ during (8 minutes) VS-S = [(POM-VAS during (8 minutes) VS-S – POM-VAS pre-VS-S Baseline) / POM-VAS pre-VS-S Baseline] X 100

Chronic pain intensity will be significantly less during VS-S at four and eight minutes than the average variability of chronic pain intensity.

$H_0: \mu_{D1} = 0$ $H_A: \mu_{D1} < 0$ where μ_{D1} = the mean difference at 4 minutes

$H_0: \mu_{D2} = 0$ $H_A: \mu_{D2} < 0$ where μ_{D2} = the mean difference at 8 minutes

POM-VAS average variability of CS-S = [(POM-VAS post (12 minutes)-CS-S – POM-VAS pre-CS-S Baseline) / POM-VAS pre-CS-S Baseline] X 100

POM-VAS % Δ during (4 minutes) CS-S = [(POM-VAS during (4 minutes) CS-S – POM-VAS pre-CS-S Baseline) / POM-VAS pre-CS-S Baseline] X 100

POM-VAS % Δ during (8 minutes) CS-S = [(POM-VAS during (8 minutes) CS-S – POM-VAS pre-CS-S Baseline) / POM-VAS pre-CS-S Baseline] X 100

Chronic pain intensity will be significantly less during CS-S at four and eight minutes than the average variability of chronic pain intensity.

$H_0: \mu_{1D1} = 0$ $H_A: \mu_{1D1} < 0$ where μ_{1D1} = the mean difference at 4 minutes

$H_0: \mu_{2D2} = 0$ $H_A: \mu_{2D2} < 0$ where μ_{2D2} = the mean difference at 8 minutes

Chronic pain intensity will be significantly less during CS-S at four and eight minutes than during VS-S at four and eight minutes.

$H_0: \mu_{D1} = \mu_{1D1}$ $H_A: \mu_{1D1} < \mu_{D1}$

μ_{D1} = mean difference at 4 minutes (VS-S) and μ_{1D1} = mean difference at 4 minutes (CS-S)

$H_0: \mu_{D2} = \mu_{2D2}$ $H_A: \mu_{D2} > \mu_{2D2}$

μ_{D2} = mean difference at 8 minutes (VS-S), and μ_{1D2} = mean difference at 8 minutes (CS-S)

Calculations of PDT

PDT average variability of VS-S = [(PDT post (12 minutes)-VS-S – PDT pre-VS-S Baseline) / PDT pre-VS-S Baseline] X 100

PDT % Δ during (4 minutes) VS-S = [(PDT during (4 minutes) VS-S – PDT pre-VS-S Baseline) / PDT pre-VS-S Baseline] X 100

PDT % Δ during (8 minutes) VS-S = [(PDT during (8 minutes) VS-S – PDT pre-VS-S Baseline) / PDT pre-VS-S Baseline] X 100

PDT during-VS-S at four and eight minutes will be significantly greater than the average variability of PDT.

H_0: $\mu_{D1} = 0$ H_A: $\mu_{D1} > 0$ where μ_{D1} = the mean difference at 4 minutes

H_0: $\mu_{D2} = 0$ H_A: $\mu_{D2} > 0$ where μ_{D2} = the mean difference at 8 minutes

PDT average variability of CS-S = [(PDT post (12 minutes)-CS-S – PDT pre-CS-S Baseline) / PDT pre-CS-S Baseline] X 100

PDT % Δ during (4 minutes) CS-S = [(PDT during (4 minutes) CS-S – PDT pre-CS-S Baseline) / PDT pre-CS-S Baseline] X100

PDT % Δ during (8 minutes) CS-S = [(PDT during (8 minutes) CS-S – PDT pre-CS-S Baseline) / PDT pre-CS-S Baseline] X 100

PDT during-CS-S at four and eight minutes will be significantly greater than the average variability of PDT.

H_0: $\mu_{1D1} = 0$ H_A: $\mu_{1D1} > 0$ where μ_{1D1} = the mean difference at 4 minutes

H_0: $\mu_{1D2} = 0$ H_A: $\mu_{1D2} > 0$ where μ_{1D2} = the mean difference at 8 minutes

PDT will be significantly greater during CS-S at four and eight minutes than during VS-S at four and eight minutes.

H_0: $\mu_{D1} = \mu_{1D1}$ H_A: $\mu_{1D1} > \mu_{D1}$

μ_{D1} = mean VS-S difference at 4 minutes and μ_{1D1} = mean CS-S difference at 4 minutes

H_0: $\mu_{D2} = \mu_{1D2}$ H_A: $\mu_{1D2} > \mu_{D2}$

μ_{D2} = mean VS-S difference at 8 minutes and μ_{1D2} = mean CS-S difference at 8 minutes

Calculations of PTT

PTT average variability of VS-S = [(PTT post (12 minutes)-VS-S – PTT pre-VS-S Baseline) / PTT pre-VS-S Baseline] X 100

PTT % Δ during (4 minutes) VS-S = [(PTT during (4 minutes) VS-S – PTT pre-VS-S Baseline) / PTT pre-VS-S Baseline] X 100

PTT % Δ during (8 minutes) VS-S = [(PTT during (8 minutes) VS-S – PTT pre-VS-S Baseline) / PTT pre-VS-S Baseline] X 100

PTT during-VS-S at four and eight minutes will be significantly greater than the average variability of PTT.

H_0: $\mu_{D1} = 0$ H_A: $\mu_{D1} > 0$ where μ_{D1} = the mean difference at 4 minutes

H_0: $\mu_{D2} = 0$ H_A: $\mu_{D2} > 0$ where μ_{D2} = the mean difference at 8 minutes

PTT average variability of CS-S = [(PTT post (12 minutes)-CS-S – PTT pre-CS-S Baseline) / PTT pre-CS-S Baseline] X 100

PTT % Δ during (4 minutes) CS-S = [(PTT during (4 minutes) CS-S – PTT pre-CS-S Baseline) / PTT pre-CS-S Baseline] X100

PTT % Δ during (8 minutes) CS-S = [(PTT during (8 minutes) CS-S – PTT pre-CS-S Baseline) / PTT pre-CS-S Baseline] X 100

PTT during-CS-S at four and eight minutes will be significantly greater than the average variability of PTT.

H_0: $\mu_{1D1} = 0$ H_A: $\mu_{1D1} > 0$ where μ_{1D1} = the mean difference at 4 minutes

H_0: $\mu_{1D2} = 0$ H_A: $\mu_{1D2} > 0$ where μ_{1D2} = the mean difference at 8 minutes

PTT will be significantly greater during-CS-S at four and eight minutes than during-VS-S at four and eight minutes.

H_0: $\mu_{D1} = \mu_{1D1}$ H_A: $\mu_{1D1} > \mu_{D1}$

μ_{D1} = mean VS-S difference at 4 minutes and μ_{1D1} = mean CS-S difference at 4 minutes

H_0: $\mu_{D2} = \mu_{1D2}$ H_A: $\mu_{1D2} > \mu_{D2}$

μ_{D2} = mean VS-S difference at 8 minutes and μ_{1D2} = mean CS-S difference at 8 minutes

Duration of effect

What is the duration of the effect of VS-S on chronic pain intensity, pain detection threshold and pain tolerance threshold?

The effect of VS-S on chronic pain intensity, pain detection threshold and pain tolerance threshold will outlast stimulation.

The effect of VS-S on chronic pain intensity will last beyond the termination of VS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

The effect of VS-S on PDT will last beyond the termination of VS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

The effect of VS-S on PTT will last beyond the termination of VS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

What is the duration of the effect of CS-S on chronic pain intensity, pain detection threshold and pain tolerance threshold?

The effect of CS-S on chronic pain intensity, pain detection threshold and pain tolerance threshold will outlast stimulation.

The effect of CS-S on chronic pain intensity will last beyond the termination of CS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

The effect of CS-S on PDT will last beyond the termination of CS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

The effect of CS-S on PTT will last beyond the termination of CS-S at 12 minutes.

H_0: $\lambda(t) = 12$

H_A: $\lambda(t) > 12$

VITA

1947	Born 1947 in Paterson, New Jersey
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