The Effect of Deep Slow Breathing on Pain-Related Variables

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Chapter I
The Problem and Its Scope

Introduction

Arthritis is the leading cause of disability among adults in the United States, affecting an estimated 50 percent of people age 65 and older. The disease costs the United States approximately 128 billion dollars in medical care and lost wages annually and is associated with other health disorders such as diabetes, hypertension, obesity, and cancer. Furthermore, half of those with arthritis also suffer from cardiovascular disease (Centers for Disease Control and Prevention (CDC), 2013), the leading cause of death among both men and women in the United States (Centers for Disease Control and Prevention, 2011).

Osteoarthritis (OA) is the most common form of arthritis, mainly affecting the hands, hips, and knees. Those suffering from OA experience a great deal of pain, limiting physical activity and decreasing quality of life. Fear of pain or worsening symptoms may discourage those with OA from beneficial exercise, leading to other health problems associated with OA (CDC, 2013). Treatment goals for OA include reducing pain, improving quality of life, losing excess weight, and making lifestyle changes that improve health such as diet and physical activity. Because pain is the major limiting factor for those with OA, most treatments are aimed at reducing pain. However, surgical treatment is expensive and non-surgical treatments, such as analgesics, physical therapy, and braces, have low efficacy (Losina et al., 2014). Some treatment, such as pain relievers, may produce other health complications, such as damage to the liver, kidneys, and gastrointestinal (GI) tract (Max & Stewart, 2008; Michael, Schlüter-Brust, & Eysel, 2010).
Clearly, there is a need for effective non-surgical treatments. Exercise has been proposed as an effective and beneficial treatment for those with arthritis. Exercise reduces pain and improves function, quality of life, mood, and confidence to manage health (Centers for Disease Control and Prevention (CDC), 2013). Despite the benefits of exercise, 60 percent of people suffering with the disease do not adhere to physical activity guidelines and 23 percent are categorized as physically inactive (Austin, Qu, & Shewchuk, 2012). This decrease in physical activity (hypokinesis) in those with OA may be a result of pain or fear of worsening symptoms with exercise (Austin et al., 2012). Hypokinesis progresses OA by increasing stiffness and weakness in the joints and causing metabolic acidosis and chronic inflammation making exercise even more challenging (Michael et al., 2010).

Since aerobic and resistance training are effective non-surgical treatments but many with OA will not participate, alternative exercises must be evaluated. Breathing exercises have been used for years in a clinical setting to reduce pain and improve health, especially in labor and delivery (Lothian, 2011). However, they have not been applied as a treatment for OA. Respiration plays an important role in pain signaling and autonomic system activation, emotion regulation, acid/base balance, and anti-inflammatory processes. Recent studies suggest that deep slow breathing (DSB) relieves pain (Chalaye, Goffaux, Lafrenaye, & Marchand, 2009) and improves mood (Busch et al., 2012). Studies in healthy subjects reveal that DSB reduces pain by increasing pain threshold, increasing parasympathetic activity (Chalaye et al., 2009), decreasing sympathetic activity (Busch et al., 2012), and altering pCO₂ and pH (Chaitow, Bradley, & Gilbert, 2014). Breathing also improves mood, which would largely impact those with OA since many suffer from depression as well (Busch et al., 2012).
Deep slow breathing has not been studied as a treatment for OA, but may be an effective method for improving pain, function, and mood. This exercise model may be appealing to patients with OA because the time commitment and cost are less than traditional therapeutic measures. In addition, DSB puts no mechanical stress on the joints and may be relaxing for those with OA. As symptoms improve with the use of DSB, those with OA may be more likely to participate in other physical activities, resulting in further health benefits.

**Purpose of the Study**

The purpose of this study was to determine if a significant difference existed in joint pain perception and heart rate variability (HRV) following a six week breathing exercise program. The Western Ontario and McMaster Osteoarthritis Index (WOMAC) Visual Analog Scale (VAS) is a valid measurement of pain, stiffness, and physical function for those with lower extremity joint pain (Averbuch & Katzper, 2004; Ebrahimzadeh et al., 2014).

The goal of the breathing exercise program was to slow the breathing rate and increase the pause following exhalation. These exercises may improve pain perception by increasing parasympathetic (P-ANS) activity and decreasing sympathetic (S-ANS) activity (Chalaye et al., 2009). The breathing exercises may also temporarily increase pCO$_2$, resulting in enhanced buffering capacity and altered metabolic acid/base homeokinesis. Respiratory and metabolic acid/base homeokinesis affect most physiological processes, including pain and inflammation (Chaitow et al., 2014).
Null Hypothesis

There is no significant difference in WOMAC VAS pain and physical function scores, heart rate variability (LF, HF, and sympathetic/vagal ratio), and expiratory pause following a six week deep slow breathing exercise program.

Significance

As the prevalence of OA rises, cost-effective treatment approaches that target pain are highly valuable in a clinical setting. The role of deep slow breathing (DSB) in improving chronic pain is not well researched. Specifically, the effect of DSB has not been studied in patients with joint pain. Results from this study will provide information about the role of DSB as a treatment for joint pain. A better understanding of the effects and mechanisms of DSB may provide novel and practical approaches to treating joint pain.

Limitations of the Study

1. Subjects with hip and/or knee joint pain were selected for this study. The results may not be generalizable to those with pain in other joints.

2. All subjects kept a journal of breathing exercises at home, diet, daily physical activity, and medications. Directly measuring these variables was not plausible for this study.

3. This study did not compare deep slow breathing to other modes of breathing or exercise programs.
4. The breathing rate was not specified. The goal of the breathing exercises was to decrease frequency and increase depth of breathing by increasing the expiratory pause from pre to post intervention.

5. The trainer and subjects were not blinded in this study.

6. Control subjects did not attend weekly meetings. Treatment subjects may have benefited from checking in with the researcher as well as group support.

**Definition of Terms**

Afferent fibers: A sensory fiber that carries impulses toward the central nervous system (Woolf & Ma, 2007).

Arthritis: Painful inflammation and stiffness of the joints (Michael et al., 2010).

Central sensitization: Augmentation of responsiveness of central pain-signaling neurons to input from low-threshold mechanoreceptors (Woolf & Ma, 2007).

Chronic pain: A long lasting pain (Schaible, 2012).

Deep slow breathing (DSB): 6-7 breaths per minute (Busch et al., 2012; Chalaye et al., 2009).

End tidal carbon dioxide (ETCO₂): The level of carbon dioxide in the air exhaled from the body. Normal values are 4-6% or 35-45 mm Hg (Jonas, 2005). ETCO₂ may be used as a predictor of arterial partial pressure of carbon dioxide (PCO₂) (Yosefy, Hay, Nasri, Magen, & Reisin, 2004).

Expiratory pause: Holding the breath until the first urge to breathe following expiration (Chaitow et al., 2014).
Forced expiratory volume (FEV$_{1.0}$): The volume of air that can be forced out in one second, an important measure of pulmonary function (Menezes et al., 2014).

Heart rate variability: The physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat interval (Malik et al., 1996).

Hyperalgesia: Increased sensitivity to pain which may be caused by damage to nociceptors or peripheral nerves (Woolf & Ma, 2007).

Hypothalamus: A region of the forebrain below the thalamus that coordinates both the autonomic nervous system and the activity of the pituitary, controlling body temperature, thirst, hunger, and other homeostatic systems, and involved in sleep and emotional activity (Eckberg, Nerhed, & Wallin, 1985).

Inflammation: A protective tissue response to injury or destruction of tissues, which serves to destroy, dilute, or wall off both the injurious agents and the injured tissue. The classical signs of inflammation are pain, heat, redness, swelling, and loss of function (Li et al., 2006).

Metabolic acidosis: A pH imbalance in which the body has accumulated too much acid and does not have enough bicarbonate to effectively neutralize the effects of the acid (Robergs, Ghiasvand, & Parker, 2004).

Minute ventilation ($V_E$): The volume of gas inhaled or exhaled from a person’s lungs per minute (Cooper et al., 2003).

Neuropathic pain: Pain arising from disease or injury to the thermo-nociceptive component of the nervous system at any level (Schaible, 2012).
Nociceptors: Sensory receptors that are preferentially sensitive to tissue trauma or a stimulus that would damage tissue if prolonged (Woolf & Ma, 2007).

Osteoarthritis: A disease of the entire joint involving the cartilage, joint lining, ligaments, and underlying bone (Michael et al., 2010).

Pain threshold: The point at which a stimulus, usually one associated with pressure or temperature, activates pain receptors and produces a sensation of pain (Chalaye et al., 2009).

Pain tolerance: The greatest level of pain which a patient is able to withstand (Chalaye et al., 2009).

Parasympathetic autonomic nervous system (P-ANS): A branch of the autonomic nervous system that slows heart rate, increases intestinal and glandular activity, and relaxes the sphincter muscles (Eckberg et al., 1985).

Peripheral sensitization: A lowering of the stimulus (pain) threshold for nociceptor activation and an increase in the frequency of nerve impulse firing (hyperexcitability). Peripheral sensitization can contribute to pain hypersensitivity found at the site of tissue damage/inflammation (Woolf & Ma, 2007).

Sympathetic autonomic nervous system (S-ANS): A branch of the autonomic nervous system that accelerates heart rate, constricts blood vessels, and raises blood pressure (Eckberg et al., 1985).
Vagus nerve: The tenth pair of cranial nerves, supplying the heart, lungs, upper digestive tract, and other organs of the chest and abdomen (Eckberg et al., 1985; Marek, Muckenhoff, & Prabhakar, 2008).

Western Ontario and McMaster Universities Arthritis Index (WOMAC): The WOMAC is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints (Ebrahimzadeh et al., 2014).
Chapter II

Review of Literature

Introduction

Osteoarthritis (OA) is a form of arthritis in which the proteins that make up the articular cartilage begin to degrade. Repetitive stress on the joint leads to degeneration of the cartilage causing pain, swelling, and stiffness. As OA progresses, the articular cartilage begins to flake or form cracks. In advanced stages, the articular cartilage may be absent causing friction, degradation of the bones, and stimulation of bone spurs resulting in more joint pain and swelling (Michael et al., 2010). Since current pain management approaches have low efficacy (Losina et al., 2014), novel approaches are needed. It is difficult to treat OA pain because the exact cause of OA pain is unknown. Deep slow breathing (DSB) has been used for years to reduce pain and improve health. DSB has not been studied as a method for relieving OA pain, but may be a suitable intervention to improve pain, physical function, and mood.

Etiology of Osteoarthritis

The exact cause of OA remains unknown, but it is likely due to an interplay between systemic and local factors. The etiology involves both genetic and non-genetic factors (Felson, 2004). Risk factors for developing OA include age, female gender, weight, ethnicity, joint injury, repetitive overuse of the joint, low physical activity, low bone density, muscle weakness, joint laxity, malformation, malposition, metabolic and endocrine disorders, alcohol and tobacco use,
and nerve injury (Michael et al., 2010). OA is also associated with other chronic diseases, such as diabetes and heart disease. The relationship between OA and other diseases remains unclear, but obesity and lack of physical activity are the main risk factors for developing these chronic diseases (Michael et al., 2010).

Management of Osteoarthritis

Management of OA is important because pain related to this disease results in limited physical function, decreased ability and willingness to exercise, and increased body fat. The resulting factors severely and negatively impact health and life expectancy. Because pain plays such an integral role in the etiology of OA, the goal of most treatments is to reduce pain. Even though treatments are aimed at decreasing pain, relatively few are successful and few prevent progression of the disease. Some treatment approaches are even harmful. Despite the variety of treatments available to those with OA, Losina et al. (2014) report that over half of people with knee OA will require a joint replacement during their lifetime. This demonstrates the low efficacy of non-surgical treatments and the need for conservative and effective treatment approaches.

Physical activity is recommended to reduce pain and improve function, mood, and body composition (Centers for Disease Control and Prevention (CDC), 2013). Exercise recommendations for patients with OA consist of 150 minutes of low impact, moderate intensity aerobic exercise per week combined with two days of resistance training. Even 60 minutes of moderate intensity exercise per week improves pain, function, and health in those with OA (Lubar et al., 2010). Despite the benefits of exercise, most people with OA do not meet these
recommendations and many are physically inactive (Austin et al., 2012). Pain and fear of worsening symptoms with exercise are reported as major barriers to physical fitness (Lubar et al., 2010).

As a result of these barriers to exercise, more research is needed to identify novel and non-invasive approaches to managing OA. Effective treatments must aim to reduce pain and enable those with OA to make healthy lifestyle changes. Breathing has been used for years in a clinical setting to reduce pain and improve health, especially in labor and delivery (Lothian, 2011). Respiration plays an important role in pain signaling, autonomic nervous system activation, emotional regulation, acid/base balance, and anti-inflammatory processes. Respiration’s involvement in many physiological processes and the brain’s ability to consciously control breathing qualify it as a possible intervention for OA. Studies in healthy subjects reveal that deep slow breathing (DSB) reduces pain by increasing pain threshold, increasing parasympathetic activity (Chalaye et al., 2009), decreasing sympathetic activity (Busch et al., 2012), and altering pCO₂ and pH (Chaitow et al., 2014). DSB also improves mood, which would help with depressive symptoms associated with OA (Busch et al., 2012).

DSB has not been studied as an intervention for OA, but may be an effective method for improving pain, function, and mood. This exercise model may be appealing to patients with OA because the time commitment and cost are less than traditional therapeutic measures. In addition, DSB puts no mechanical stress on the joints and may be relaxing for those with OA. As symptoms improve with the use of DSB, those with OA may be more likely to participate in lifestyle changes, such as exercise, that provide further health benefits.
Measurement of Osteoarthritic Pain and Functional Limitation

To evaluate the effect of OA interventions, a valid and reliable measurement must be used. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is one of the most commonly used self-reported measures of lower extremity symptoms and function. It was specifically designed to evaluate pain, function, and stiffness in subjects with OA of the hip and knee. The WOMAC has been studied for over 30 years in various contexts and in subjects of different ethnic backgrounds. The WOMAC is supported as a valid and reliable measurement of pain and function in subjects with hip or knee OA (Bellamy, Buchanan, Goldsmith, Campbell, & Stitt, 1988; Dunbar, Robertsson, Ryd, & Lidgren, 2001; McConnell, Kolopack, & Davis, 2001; Pua, Cowan, Wrigley, & Bennell, 2009; Wolfe & Kong, 1999).

The WOMAC is easy to use and minimal training is needed. The test takes about 12 minutes to administer. A copy of the WOMAC and a ruler for the visual analog scale (VAS) version are the only equipment needed. Subjects use the VAS to answer 24 questions about pain, function, and stiffness. The VAS is 100 mm long and uses anchors of no pain/stiffness/difficulty to extreme pain/stiffness/difficulty. Subjects mark along the 100 mm continuum. A ruler is then used to score the items. Items for each subscale are summed. Possible ranges for pain, stiffness, and function are 0-500, 0-200, and 0-1700, respectively. Usually, total WOMAC score is calculated by summing totals from each subscale. A higher score indicates worse pain, functional limits, and stiffness (Bellamy, 2002).

The validity, reliability, and convenience of the WOMAC make it a good measurement tool for studies regarding pain and function in those with hip and knee OA. For examination of individual patients, determining the minimal meaningful change in WOMAC scores can be challenging. The minimal clinically important improvement (MCII) value, defined as the
smallest change in measurement that indicates substantial improvement in symptoms, may be used to determine the importance of WOMAC change scores. MCII values for hip and knee OA are identified as -15.3 mm and 19.9 mm respectively, for pain, and -7.9 and -9.1 respectively, for physical function (Tubach, 2005). This measurement tool may be applied to studies examining the efficacy of pain treatments for hip and knee OA.

Neurophysiology of Osteoarthritic Pain

In order to understand the role of treatments in mitigating pain, it is imperative to understand what causes pain and how it is processed. Despite the clinical importance of understanding pain, there is surprisingly little research on pain compared with other health conditions. This may partly explain the lack of effective treatments for the chronic pain associated with OA.

Function of pain. Pain plays an integral role in protecting the body from damaging or potentially damaging stimuli. Much of pain is detected by nociceptors: highly specialized sensory receptors of the peripheral somatosensory nervous system. These receptors detect noxious stimuli and send electrical signals to the central nervous system. Nociceptors are located in the viscera, muscles, joints, meninges, and skin and are stimulated by mechanical, chemical, or thermal stimuli. Nociceptors are the free nerve endings of primary afferent Aγ and C fibers. Aγ fibers are small in diameter and lightly myelinated. They carry fast, sharp pain and respond to mechanical and thermal stimuli. They are responsible for the reflex response to acute pain. C fibers are the smallest of primary afferents and are unmyelinated. They have the slowest
conduction and respond to chemical, mechanical, and thermal stimuli. Activation of C fibers results in chronic, slow, burning pain (Woolf & Ma, 2007).

Upon activation, primary afferent fibers synapse with secondary afferent neurons in the dorsal horn of the spinal cord and information is sent to the higher centers in the brain. There are two main pathways by which these signals are sent: the spinothalamic tract and the spinoreticular tract. In the spinothalamic tract, secondary afferents ascend in the contralateral spinothalamic tract to nuclei within the thalamus. Third order neurons then ascend to the somatosensory cortex or the periaqueductal grey matter (PAG). In the spinoreticular tract, fibers ascend the contralateral cord to reach the brainstem reticular formation. Then, they are projected to the thalamus and hypothalamus. There are many further projections to the cortex. The spinothalamic tract transmits signals that are important for pain localization and the spinoreticular tract is involved in emotional aspects of pain (Schaible, 2012; Sofat, Ejindu, & Kiely, 2011; Woolf & Ma, 2007).

Once the pain signal reaches the brain, it is processed by the higher brain centers. Pain is highly individualized and subjective, making it difficult to study. It is affected by mood, beliefs, genetics, and cognition (Max & Stewart, 2008; Rainville, 2002; Tracey & Mantyh, 2007; Wiech, Ploner, & Tracey, 2008; Wiech & Tracey, 2009). Studies using functional magnetic resonance imaging (fMRI) show that a large brain network is stimulated during pain. The most commonly activated brain regions include the primary and secondary somatosensory (S1 and S2) cortices, insular cortex, anterior midcingulate cortex, posterior cingulate cortex, orbitofrontal cortex, prefrontal cortex, and the thalamus. Studies evaluating the validity of pain scales suggest that rated pain directly corresponds to brain activity, supporting the argument that pain is highly
individualized. Some experience painful stimuli more intensely than others. These brain regions must play an important role in pain processing (Kulkarni et al., 2007).

It is clear that the pain pathway is activated during painful OA, but what causes this pain to begin and why does it persist? Since the exact cause of OA is unknown, it is difficult to answer this question. In many cases, OA is probably due to a combination of mechanical stress and humoral factors released by adipose tissues. These factors result in damage to the articular cartilage and surrounding joint tissues. The damaged tissues release protons and other inflammatory mediators, causing inflammation, lowering local pH, and resulting in sensitization of the nociceptor (Sofat et al., 2011).

**Peripheral sensitization.** Normally, the pain threshold is high and only stimuli that are actually or potentially damaging are detected. In OA, acidosis and inflammation cause depolarization and sensitization of the nociceptors. Sensitization decreases the threshold and increases responsiveness of the nociceptors to non-noxious stimuli. Some of the sensitizers present with OA are kinins, amines, prostanoids, growth factors, chemokines, cytokines, protons, and adenosine triphosphate (ATP) (Woolf & Ma, 2007). These sensitizers work by binding to their specific receptor on the nociceptor membrane. This binding occurs as a result of activation of intracellular signal transduction pathways (Doya et al., 2005; Hucho, 2005; Jin & Gereau, 2006; Malik-Hall, Dina, & Levine, 2005; Mizushima et al., 2007; Varga et al., 2006). Other effectors include phosphorylation of transient receptor potential (TRP) and voltage-gated sodium channels which alter thresholds and kinetics (Woolf & Ma, 2007).

Sensitization results in a heightened state of sensitivity. Stimuli that are normally innocuous may be detected as noxious stimuli. Heightened pain sensitivity can be beneficial by reducing use of or contact with the injured joint. However, persistent changes in nociceptor
function are pathological and contribute to OA pain. Typically, restoration of the nociceptor to normal function would suffice. With OA, this does not work because the inflammation will still be present and drive the depolarization of these sensory neurons. In advanced stages of OA, chronic pain when no stimulus seems to be present may be explained by sensitization. With a reduced threshold, normal body temperature or blood vessel pulsation may stimulate low threshold nociceptors and result in pain (Woolf & Ma, 2007).

**Central sensitization.** In addition to peripheral sensitization by localized noxious stimuli, structural and biochemical changes may also occur in the systems that perceive pain (Sofat et al., 2011). Pathological input from the joint may cause complex changes in the central nervous system, known as central sensitization. With central sensitization, nociceptive neurons become hyperexcitable and the processing of noxious stimuli is amplified. Central sensitization has both spinal and supraspinal components (Schaible et al., 2009). Central sensitization is seen in advanced stages of OA. Methods of this sensitization remain unknown and are difficult to study (Schaible, 2012).

**Acid-sensing ion channels.** Protons which are involved in sensitization may also be detected by acid-sensing ion channels (ASICs). These protons are released by damaged tissue and decrease the pH in the joint. This change in pH is detected by ASICs, which may function as a specific type of nociceptor. It is unknown whether ASICs transduce or mediate noxious stimuli. However, since ASICs are highly sensitive to pH, they are considered to be closely linked with pain processing (Voilley, 2004).

Local pH often drops below 7 with inflammation, infection, ischemia, and exercise (Goldie & Nachemson, 1969; Rehncrona, 1985). This dramatic change is detected by ASICs and a signal is sent to the brain. ASIC expression and currents are increased with experimentally
induced inflammation in the rodent paw (Voilley, de Weille, Mamet, & Lazdunski, 2001) and the mouse knee (Masahiko Ikeuchi, Kolker, & Sluka, 2009; M. Ikeuchi, Kolker, Burnes, Walder, & Sluka, 2008). This supports the hypothesis that ASICs have a nociceptive function. ASICs may be related to neuropathic pain. Compression of the spinal nerve root causes both hyperalgesia and increased expression of ASIC3 (Ohtori et al., 2006). This suggests a potential mechanism for neuropathic pain. Ivanavicius et al. (2007) suggest that OA pain has a neuropathic component.

**Neuropathic pain.** Neuropathic pain is non-nociceptive and initiated by a lesion or dysfunction of the nervous system. Pain caused by the nerve injury could be a result of both peripheral and central sensitization in combination with local inflammation. Studies using the monoiodoacetate (MIA) pain model support the theory that OA pain may be partially due to neuropathy. In this model, MIA is injected into the joint and arthritis symptoms develop rapidly, unlike actual OA. MIA blocks glycolysis and is toxic for chondrocytes. Twenty four hours post-injection, chondrocytes shrink, fragmented pyknotic nuclei appear, synovial membrane is expanded by fibrin proteinaceous edema fluid, and the joint is invaded by lymphocytes, macrophages, and plasma cells. Days later, the inflammatory response in the synovium subsides, necrotic cartilage collapses, and chondrocytes are lost. Osteoclastic activity is increased, subchondral bone collapses, and fragmentation of bone trabeculae are surrounded by osteoclasts and some replacement by fibrous tissue and newly laid trabecular bone appear (Schaible, 2012). With MIA injection, a high number of neurons in the dorsal root ganglia (DRG) express ATF-3 immunoreactivity, suggesting neuropathic pain (Ivanavicius et al., 2007; Orita et al., 2011). Furthermore, upregulation of galanin and neuropeptide Y, downregulation of substance P and CGRP in DRG neurons (Im et al., 2010), and activation of spinal microglia (Orita et al., 2011) were found. Similar differences were seen with a surgical model (Orita et al., 2011). In a study
by Ivanavicius et al. (2007), rats with OA showed increased sensitivity to gabapentin, a molecule used to treat neuropathy in humans. These studies provide further evidence for a neuropathic component in OA pain.

**Central pain processing.** In addition to these mechanisms, neuroimaging studies, including functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans, have revealed that structure and activity of pain processing brain regions are altered with OA. Baliki et al. (2008) measured brain activity in response to painful mechanical knee stimulation in subjects with knee OA. Results showed that painful knee stimulation was associated with bilateral activity in the thalamus, secondary somatosensory, insular, and cingulate cortices, and unilateral activity in the putamen and amygdala. Local lidocaine treatment of the knee reduced brain activity seen on fMRI for these regions.

Kulkarni et al. (2007) used PET and compared brain activity between patients with arthritic knee pain, experimental knee pain, and no pain. With arthritic pain, regional cerebral metabolic rate for glucose (rCMR$_{Glu}$) was bilaterally enhanced in all areas of the brain involved in pain processing: posterior cingulate cortex, anterior midcingulate cortex, prefrontal cortex, orbitofrontal cortex, and primary somatosensory cortex. Unilateral activations were seen in the thalamus, anterior perigenual cingulate cortex, amygdala, and supplementary motor area. The most statistically significant activity observed with arthritic pain was in the anterior cingulate cortex, although activation spanned from anterior to posterior midcingulate region.

Interestingly, when arthritic and experimental pain were compared, arthritic pain was the only pain associated with increased activation of the limbic system, involved in affect, aversive conditioning, and motivation. This may explain why many people with OA also suffer from anxiety, depression, and other psychological disturbances. In addition to over-activation of pain
processing centers, those with OA exhibit atrophy of the thalamus (Kulkarni et al., 2007) and the gray matter of pain-related cortical areas (Hess et al., 2011). These atrophies were reversible after arthroplasty suggesting that atrophy is more likely a side effect than a cause (Rodriguez-Raecke, Niemeier, Ihle, Ruether, & May, 2009).

**Descending pathways.** Descending neural pathways may also contribute to OA pain. Neural pathways descending from the brainstem play an important role in balancing inhibition and facilitation of nociception. The diffuse noxious inhibitory control (DNIC) is a form of inhibition that is dysfunctional in those with severe OA. Function is restored following joint replacement. Other studies reveal that with OA, serotonergic descending facilitation (Rahman et al., 2009), as well as increased activation of the periaqueductal gray (PAG) in the brain stem (Gwilym et al., 2009) play a role in OA pain. These studies suggest that an imbalance between inhibitory and excitatory descending systems could play a role in OA pain generation (Schaible, 2012).

**Targeting osteoarthritis pain.** Treating OA pain is difficult since the origin and cause of pain are not yet elucidated. Further research on pain mechanisms and pathways will help provide more effective treatment options for those suffering with OA. Currently, most pain therapies aim to block nociception or neutralize cytokines and inflammatory factors involved in nociception. This is problematic for a number of reasons. It is important that normal nociception is maintained with these treatments to protect the body from undetected tissue damage (Schaible, 2012). Additionally, there will always be more inflammatory mediators readily available to sensitize the nociceptor, causing pain and further damage in those with OA. To date, one medication cannot target all sensitizers (Woolf & Ma, 2007). A treatment that targets the source of pain and the pathways involved rather than the signal produced may be more effective for those suffering
with OA. Breathing may be a suitable alternative approach that targets local and systemic factors involved in pain processing.

**Deep Slow Breathing to Improve Osteoarthritis Pain**

Deep slow breathing (DSB) is often used in a clinical setting to relieve pain or improve health. Practices that utilize DSB include Lamaze (Lothian, 2011), yoga (Sovik, 2000), qi-gong (Li & Yeh, 2005), pranayama (Singh, Malhotra, Singh, Madhu, & Tandon, 2004), tai chi (J. X. Li, Hong, & Chan, 2001), relaxation (Chalaye et al., 2009) and Buteyko breathing (Chaitow et al., 2014). Despite the widespread use of DSB, there are relatively few studies examining the effect of deep breathing as an analgesic (Chalaye et al., 2009). Specifically, there is currently no research examining the use of DSB as an analgesic for osteoarthritis. Most research on DSB and pain is completed using healthy subjects or those with cardiovascular disease. This research suggests that there is a strong relationship between autonomic activity and pain perception. It is proposed that DSB functionally resets the autonomic nervous system and synchronizes neural function in the heart, lungs, limbic system, and cortex (Jerath, Edry, Barnes, & Jerath, 2006). In a study by Chambers, Taddio, Uman, McMurtry, and the Help Eliminate Pain in Kids Team (2009), breathing exercises significantly reduced pain reported by children during immunizations and distress observed by parents or nurses. A few studies have examined possible mechanisms of DSB in providing pain relief (Busch et al., 2012; Chalaye et al., 2009; Jerath et al., 2006).

**Altered pain threshold.** DSB may decrease pain by increasing the pain threshold of nociceptors. Chalaye et al. (2009) examined the effect of deep slow breathing on experimental heat pain and autonomic cardiac activity. They compared natural breathing to DSB (six breaths
per minute), rapid breathing (16 breaths per minute), breathing with a distraction (playing a video game), and a biofeedback control where subjects synchronized their breathing and heart rate. Respiratory rate and depth were measured with a piezo-electric respiratory belt transducer.

Chalaye et al. (2009) hypothesized that DSB and heart rate (HR) biofeedback would produce the strongest analgesic effects and greatest cardiac changes. Results revealed significant differences between the groups for thermal pain threshold and tolerance. Mean pain threshold values significantly increased from baseline following HR biofeedback (+1.6° C, p<0.005), DSB (+1.0° C, p<0.05), and breathing with a distraction (+1.1° C, p<0.05). Mean pain tolerance values significantly increased following HR biofeedback (+0.7° C, p<0.005) and DSB (+0.5° C, p<0.005). Contrariwise, rapid breathing was followed by a decrease in pain threshold (-0.2° C) and no change in pain tolerance although these results were not statistically significant.

DSB and HR biofeedback had the largest impact on pain thresholds and tolerances. DSB had an analgesic effect whether it was done before or after rapid breathing. Rapid breathing had no analgesic effect regardless of the order in which the subject completed the different breathing conditions. In this study, the intensity range from pain threshold to pain tolerance was only 3.3 degrees Celsius. Average changes in thermal pain thresholds were about 1 degree Celsius higher. This may seem unimportant, but when considering the exponential function linking temperature and pain, a one degree increase will produce great changes in perceived pain (Chalaye et al., 2009).

Similarly, Busch et al. (2012) examined the effects of DSB on pain perception and sympathetic arousal in 15 healthy subjects. They specifically examined the difference between attentive versus relaxed DSB. The methods of breathing were similar for both groups. The attentive DSB (aDSB) subjects breathed according to a respiratory feedback task. They were
presented with an ideal breathing curve including frequency and depth. Their own breathing
curve was simultaneously shown to them on a screen with the ideal curve. They were asked to
match their breathing with the ideal curve, requiring their attention and concentration.

The relaxed DSB (rDSB) subjects were told to concentrate on the experience of
breathing. They received verbal instruction during the experiment in order to keep respiration
rates similar to the aDSB condition. The rDSB condition was more similar to a meditative state
and required little cognitive processing. A respiration rate of 7 cycles per minute (cpm) was used
for both groups. The ratio of expiration/inspiration/pause was 60/30/10 (Busch et al., 2012), as
suggested by previous literature (Cappo & Holmes, 1984; Strauss-Blasche et al., 2000).

Busch et al. found a significant increase in pain thresholds of subjects after only three
microcycles of rDSB. aDSB did not alter pain thresholds suggesting that relaxation is an
important part of DSB. This is supported by other research that suggests DSB may reduce pain
intensity rating compared with rapid breathing (Grant & Rainville, 2009). This study was not
able to demonstrate a difference between relaxation and deep breathing, but they lacked a control
group. This actually supports the claim that relaxation is an essential component of pain
perception attenuation. The argument could be made that aDSB is more distracting than rDSB,
but Busch et al. counter this by arguing that some individuals may be just as distracted by
concentrating on certain distracting thoughts during rDSB, just as some may be distracted by
matching their curve to the ideal respiratory curve.

**Sympathetic nervous system activity.** DSB may decrease pain by altering autonomic
nervous system activity. Busch et al. (2012) measured sympathetic activity by measuring skin
conductance levels (SCLs). Results showed significant decreases in SCL in all cycles during the
rDSB condition, signifying slowing of sympathetic activity. Pain thresholds and SCLs were
inversely correlated for rDSB. The inverse correlation suggests that sympathetic activity plays an important role in pain perception. Slowing of the sympathetic system may mediate pain. Other studies report that basal electrodermal activity is significantly reduced during meditation (Travis, 2001), mindfulness-based stress reduction (Lush et al., 2009), or integrative body-mind training (Tang et al., 2009).

Alternatively, aDSB increased sympathetic arousal. Other studies corroborate this finding. Cappo & Holmes (1984) found that challenging breathing exercises increased sympathetic arousal. Furthermore, a study of subjects with high trait anxiety characteristics revealed that rDSB without concentration on a pacing tone had a greater reduction of SCL compared with aDSB. The increase in SCL seen with aDSB in this study was associated with increased anxiety and muscle pain (Ozgocmen, Ozyurt, Sogut, & Akyol, 2006). Decreased sympathetic arousal and pain perception in response to DSB may be a result of downregulation in stress activity (Craig, 2003). This may be due to increased vagal tone and parasympathetic nervous system activity (Chalaye et al., 2009; Chandla et al., 2013).

**Vagal tone and parasympathetic nervous system activity.** Increased vagal activity is hypothesized to decrease pain perception. The vagus nerve is the tenth cranial nerve, nuclei located in the medulla oblongata. The vagus nerve constitutes an important part of the parasympathetic autonomic nervous system. The vagus nerve is connected to regions of the brain controlling the autonomic nervous system, emotions, memory, and social behaviors (Snell, 2001). Homeostasis of most of the body's systems that operate on a subconscious level is regulated by the vagus nerve. Vagal activity is usually continuous and passive and is used an indicator of parasympathetic nervous system activity. Vagal tone cannot be directly measured so other measures are used to represent vagal activity. Increased vagal tone slows the heart rate and
increases heart rate variability. Respiratory sinus arrhythmia (RSA) is a variation in heart rate during the breathing cycle. During RSA, inhalation restrains vagal activity which increases heart rate. Exhalation causes heart rate to decrease and vagal activity to resume. Since vagal tone cannot be directly measured, heart rate variability (HRV) is used to denote vagal activity (Chalaye et al., 2009).

Vagal activity is directly related to breathing. During inspiration, stretch receptors in the lungs are stimulated. This produces a signal which is carried by vagal type C fibers through the nucleus tractus solitarius (NTS) to the hypothalamus. It is hypothesized that different impulse patterns produced by the vagus nerve during breathing affect the hypothalamus which controls autonomic balance. Increased vagal activity also inhibits the sympathetic vasomotor area in the medulla and may affect other brainstem and medullary nuclei that influence autonomic activity (Ganong, 2005). Corticospinal tracts controlling respiration also affect autonomic activity (Snell, 2001). These circuits may work together to decrease sympathetic activity and increase parasympathetic activity (Chandla et al., 2013).

The hypothesis that DSB increases vagal activity is supported by the findings of Chalaye et al. (2009). Mean standard deviation of the N-N interval (SDNN) was used as a general measure of HRV and the peak-to-valley index was used to measure breathing-induced oscillations in heart rate (HR) which is dependent on efferent vagal activity. Mean SDNN values rose significantly from baseline (52.1 ms) to 99.8 ms (p<0.05) following DSB and to 96.4 ms (p<0.05) following HR biofeedback. SDNN values decreased following rapid breathing and distraction conditions although results for these conditions were not statistically significant. Mean peak-to-valley amplitudes increased from baseline (0.099, p<0.05) following DSB (0.296, p<0.05) and HR biofeedback (0.288, p<0.05). Rapid breathing and distraction conditions
resulted in decreased peak-to-valley amplitudes. The rise in SDNN and peak-to-valley amplitude following DSB and HR biofeedback conditions indicate increased vagal activity.

HF power is another measure of vagal activity. HF power was not significantly altered with any of the breathing conditions. Counterintuitively, LF power increased significantly from baseline (1,524 ms\(^2\)) to 9,194 ms\(^2\) (p<0.05) following DSB and 8,463 ms\(^2\) (p<0.05) following HR biofeedback (Chalaye et al., 2009). The interpretation of LF is often disputed. While some consider LF power a measure of sympathetic activity, others consider LF power a measure of both sympathetic and vagal activity. Some suggest that as total power spectral density (PSD) increases, both LF and HF may increase (Malik et al., 1996). Chalaye et al. (2009) suggest that LF power increased with DSB and HR biofeedback as a result of overlap of RSA-associated oscillations and slow HR oscillations. Research is somewhat unclear on the interpretation of LF power relating to autonomic activity.

Chandla et al. (2012) also evaluated the effects of DSB by examining the use of pranayama, a word meaning "extension of the prana or breath." Previous studies revealed that practicing slow breathing pranayama for three months resulted in increased parasympathetic activity and decreased sympathetic activity (Pal, Velkumary, & Madanmohan, 2004). Chandla et al. found that six weeks of slow breathing increased vagal parasympathetic tone. This was seen in the decrease in LF from baseline (76.93 nu) to 50.88 nu (p<0.001) and the increase is HF from baseline (49.26 nu) to 64.60 nu (p<0.001) following six weeks of pranayama. The LF/HF (power %) ratio also decreased from 4.67 (baseline) to 1.58 (p<0.001). These findings are much clearer, suggesting decreased sympathetic activity and increased vagal activity. Pal et al. reported similar findings in increased vagal tone after DSB exercises. Snell (2001) reported that DSB also increased thoracic pressure, venous return, and systolic blood pressure. Changes in blood
pressure are sensed by baroreceptors that send signals to the NTS. The NTS then sends excitatory signals to the nucleus ambiguous which control parasympathetic activity. The NTS is connected with the lateral parabrachial nucleus, ventrolateral medulla, and PAG, and involved in nociception (Telles & Desiraju, 1991). Activation of the baroreceptors also produces excitatory effects on NTS pain inhibitory relays (Ganong, 2005).

**Autonomic alterations due to tissue oxygenation.** Although autonomic nervous system alterations in response to DSB are seemingly due to increased vagal tone, some studies suggest that changes are due to increased tissue oxygenation. Although seemingly logical, there is currently little research to support this claim. Increased tissue oxygenation was seen with DSB, but not with rapid breathing. Researchers suggest that this increase in oxygenation with DSB could explain alterations in autonomic function (Pal et al., 2004; Telles & Desiraju, 1991). In addition, pranayama reduced oxygen consumption per unit work with time (Raju et al., 1994) and reduced oxidative stress levels. Increased superoxide dismutase levels and a decrease in the number of free radicals were also observed with pranayama practice. These results have long-term benefits and may explain the cardiopulmonary benefits associated with pranayama (Bhattacharya, Pandey, & Verma, 2002). In a study of Himalayan high altitude subjects, deep breathing exercises increased arterial oxygen saturation irrespective of age, gender, or altitude. However, the results of this research are questionable since raw data is only given for hematocrit levels (Nepal et al., 2013). Although the research on this aspect of DSB is limited, this may be an important part of how DSB influences the autonomic nervous system and reduces pain.

**Pulmonary function, carbon dioxide and pH.** DSB may alter acid/base balance in the body by improving buffering capacity and pulmonary function. Buteyko breathing is a special form of DSB, based on the theories of Dr. Konstantin Buteyko. Buteyko hypothesizes that many
chronic diseases result from hyperventilation, resulting in carbon dioxide deficiency and metabolic disequilibria. Carbon dioxide is important for many physiological functions such as maintaining acid/base balance, dissociation of oxygen, and many chemical reactions. Buteyko breathing techniques include reduced-volume breathing, slow breathing, breath-holding techniques, and nasal breathing. Emphasis is put on the expiration phase of respiration and breath-holding pauses following expiration (Chaitow et al., 2014).

Buteyko theorizes that deep slow breathing followed by a pause increases carbon dioxide in the blood and enhances the body’s buffering capacity. This, in turn, affects pH which is related to chronic diseases such as OA (Chaitow et al., 2014). This theory is supported by research demonstrating that the expiratory pause decreases minute ventilation which corresponds with carbon dioxide concentration in the alveolar air (Cooper et al., 2003). In addition, Buteyko breathing may increase forced expiratory volume (FEV\textsubscript{1.0}), a predictor of mortality (Menezes et al., 2014) and morbidity (Varela et al., 2007).

Buteyko breathing has mainly been studied in those with pulmonary diseases and has not been studied in OA. Despite the lack of research on Buteyko breathing as a treatment for chronic diseases such as OA, parts of this model may be incorporated into a breathing program for those with OA. The emphasis on expiration and the pause following expiration may be beneficial for improving buffering capacity which alters pain perception (Chaitow et al., 2014).

Summary

Although there is no research examining the effects of DSB as a treatment for OA, evidence suggests that DSB would be beneficial and effective. It is likely that DSB would
alleviate OA pain by increasing the pain threshold, altering autonomic activity, increasing oxygen saturation, decreasing reactive oxygen species involved in pain signaling, and altering acid/base metabolism (Busch et al., 2012; Chaitow et al., 2014; Nepal et al., 2013).

Further research is needed in order to examine the effects of DSB on pain and functionality in those with OA. The WOMAC may be used to evaluate changes in pain and functional limits in subjects with hip or knee OA following DSB training (Bellamy et al., 1988). Results from this research may provide novel OA management approaches that are cost effective and easy to complete.
Chapter III

Methods and Procedures

Introduction

This study was designed to examine the effect of a six week deep slow breathing (DSB) program on pain perception and heart rate variability (HRV) in subjects with lower extremity joint pain. This study provided information about the role of breathing in the management of joint pain. Novel and non-invasive management for joint pain is needed to decrease pain and improve function in those suffering from the disease.

Description of Study Population

Twenty subjects participated in the study. Subjects had been diagnosed with osteoarthritis (OA), defined by the Centers for Disease Control and Prevention (2013) or had received a normative score of less than 50 on the American Academy of Orthopaedic Surgeons (AAOS) Hip and Knee Questionnaire. Subjects were recruited from the Bellingham Senior Activity Center in Bellingham, WA and the Blaine Senior Center in Blaine, WA, following approval of the study from the University Human Subjects’ Committee. Subjects with unilateral joint pain had no history of joint replacement surgery. Subjects with bilateral joint pain that had undergone joint replacement surgery on only one joint were allowed to participate in the study. The joint that had not been operated on was used for assessment with the WOMAC. For subjects with bilateral joint pain that had not undergone joint replacement surgery, the extremity with more severe pain, determined by the WOMAC pain score, was used for WOMAC assessment. No
subjects had undergone joint surgery within the last six months. All subjects obtained medical clearance from a physician to participate in the study.

**Design of the Study**

This study utilized a pretest-posttest experimental design in which subjects were assigned to either the control or treatment group. Subjects were assigned to either the control or treatment group based on their availability for training. Those who could meet the time commitment for the training group were assigned to the training group on a first come first serve basis.

**Instrumentation**

Heart rate variability (HRV) was measured using Biopac Systems MP1500 (Goleta, CA). Disposable adhesive electrodes were used for the subject-EKG interface and HRV measurements were taken with a standard 3-electrode, 1-lead EKG setup which examined lead II. A MP1500 (BIOPAC Systems Inc., Goleta, CA) interfaced with a Pentium III computer was used. AcqKnowledge software (BIOPAC Systems Inc., Goleta, CA) was used for data recording, collection, and data reduction.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Visual Analog Scale (VAS) was used to measure pain and physical function before and after the study. Nutritionist Pro software (Redmond, WA) was used to measure caloric intake and the Bouchard method was used to determine energy expenditure (Bouchard et al., 1983) before and after the study.
Experimental Protocol

Training protocol for all subjects. The study was conducted over a six week period. All subjects were instructed not to alter their diet or physical activity level during the study. Three day diet and three day physical activity logs were completed pre and post breathing intervention. These logs were used to verify that no substantial changes were made in diet or physical activity. A medication log was submitted before and after the study. Subjects were instructed to notify the instructor if they began a new pain medication during the course of the six week DSB training. If a subject began a new pain medication during the study, they were excluded from the study. The control group did not attend weekly breathing training sessions.

Weekly breathing training. Breathing training took place at the Bellingham Senior Activity Center in Bellingham, WA. Subjects were instructed to wear comfortable and loose fitting clothes. Weekly sessions lasted for 30 minutes. Subjects were divided into groups of 2-4 subjects. During DSB training, all subjects sat upright on a chair with back support. Subjects were informed of the discomfort or “air hunger” they may experience during DSB training. Subjects were assured that they could take a break from the breathing exercises if they felt dizzy or out of breath.

During the first twenty minutes of breathing training, a script was used to guide subjects through the breathing exercises. The script was timed and all subjects received the same training. The main focus of the breathing exercises was on inhaling deeply, prolonging the exhalation, and performing the expiratory pause. Additionally, each week subjects were given a focus topic in order to keep their interest in the program. Weeks one and two focused on awareness of breathing, weeks three and four focused on relaxation and tension release, and weeks five and six focused on breathing control.
Specific parameters for controlling depth and frequency of breathing were not used in this study. The goal of the breathing exercises was to increase the depth and decrease the frequency of respiration from initial values for each individual. The expiratory pause aided subjects in reducing breath frequency. The remaining ten minutes of training was used to record respiratory rate and expiratory pause for each subject.

Respiratory rate was measured by counting the number of times the chest or abdomen inflated and deflated in one minute. Subjects performed the expiratory pause following normal inhalation and exhalation. Following exhalation, subjects plugged their nose with their fingers and closed their mouth. This was held until the subject felt the very first urge to inhale. The amount of time that a subject could hold this pause was recorded as the expiratory pause (Chaitow et al., 2014). The data obtained were used for developing the training program and were not used for biofeedback.

At-home breathing protocol. DSB subjects were instructed to complete the DSB exercises with the expiratory pause at home five days a week, 20-30 minutes a day (Chaitow et al., 2014). DSB subjects were given written instructions and a link to an instructional YouTube video on the expiratory pause (see appendix) to help them practice during the week. DSB subjects were educated on the importance of relaxation during DSB and instructed not to complete the breathing exercises while doing an attentive task such as reading, watching TV, conversing with family, or other tasks. Subjects were instructed to do the breathing exercises in a quiet room in an upright, seated position on a chair with back support. Both feet were to be placed on the floor. On the day of the weekly group training session, subjects were not required to complete additional DSB at home.
If subjects missed a weekly training session at the Bellingham Senior Center, they were required to make up the session on another day with the trainer. Subjects kept a breathing log and returned the log to the trainer each week to ensure compliance with the study.

**Measurement Techniques and Procedures**

The WOMAC was used to measure pain (five items) and physical function (17 items). Responses were based on the 1-100 mm visual analog scale. Responses were scored using a ruler to measure the distance in millimeters from the left end to the subjects pencil mark. Scores for each item were summed to obtain scores for each category: pain and physical function. Higher scores indicated worse pain and physical function.

For HRV assessment, subjects were instructed to lie still on an examination table in the laboratory for five minutes. The laboratory was kept quiet and at a comfortable temperature. Alcohol swabs were used to prep the skin for optimal EKG signal acquisition. Three electrodes were configured to examine one lead. Wires were color coded white (right arm [RA]), black (right leg [RL]), and red (left leg [LL]) and were attached at the terminal ends to adhesive electrodes. Proximal ends of the wires were inserted into the EKG port of the MP1500 system. The electrodes attached to the RA, RL, and LL wires were placed on the anterior aspect of the right wrist, and medial aspects of the right and left ankles, respectively. The RA wire represented the negative aspect, the LL wire represented the positive aspect, and the RL wire was used as the ground for lead II.

The experimenter observed the EKG for line noise or unusual rhythms during data collection. The AcqKnowledge software recorded HRV data through EKG for five minutes. The
subject was instructed to close their eyes and remain still and relaxed during the measurement. The data collection was terminated and started over if the subject talked or moved during collection. Once HRV data was collected, data was saved on the computer hard drive and the electrodes were removed from the subject.

HRV variables were obtained from the raw EKG data using AcqKnowledge software which used algorithms following the frequency domain guidelines established by the Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology (Task Force) (BIOPAC 2007; Malik et al., 1996). Power frequency for HRV variables were defined by Task Force guidelines as very low frequency (VLF), \( \leq 0.04 \) Hz, low frequency (LF), 0.04-0.15 Hz, high frequency (HF), 0.15-0.4 Hz, and very high frequency (VHF), \( \geq 0.4 \) Hz (Malik et al., 1996). LF to HF ratio (LF/HF ratio) was calculated from the data using AcqKnowledge software.

The expiratory pause was measured using a SportLine 220 stopwatch. Subjects were taught to perform the expiratory pause by closing their eyes and inhaling and exhaling as usual. Following exhalation, subjects were instructed to close their mouth, plug their nose, and hold this until they felt the very first urge to breathe. At the very first urge to breathe, subjects were instructed to release from plugging their nose and resume breathing. The expiratory pause was recorded with the stopwatch from the time the subject plugged their nose to the time at which they released or inhaled, whichever occurred first. Subjects were allowed to practice the expiratory pause 1-2 times before the pause was recorded. The expiratory pause was then recorded three times and the best of these recordings was used for data analysis.
Data Collection

Data was collected prior to and following the six week DSB program. Data was collected at the same time for both the control and experimental groups. DSB subjects were instructed not to complete breathing exercises on the day of data collection. WOMAC scores, HRV, and expiratory pauses were obtained and recorded.

Data Analysis

Analysis was separated into three facets: subject measurement using WOMAC scores (pain and physical), objective measurement using HRV variables (LF, HF, and LF to HF ratio), and evaluation of the training program using the expiratory pause. Means and standard deviations pre and post intervention were calculated for variables within each facet and compared pre and post. Pain and physical function were each analyzed using a mixed ANOVA. LF, HF, and LF/HF ratio were each analyzed using a mixed ANOVA. The expiratory pause was analyzed using a mixed ANOVA. Caloric intake and energy expenditure were analyzed using two tailed t tests. The alpha level for analysis was set at less than 0.05. A Bonferroni correction was applied for WOMAC and HRV facets ($p=0.025$, $p=0.025$ respectively). Statistical analysis was used to evaluate if there was an interaction between group and time or a main effect for group or time. F values, $p$ values, and effect size were used to analyze each variable. Data analysis was completed with Excel (Microsoft Inc., Redmond, WA) and IBM SPSS (Armonk, NY).
References


